

WELCOME AND INTRODUCTION

Lauren Berger, MPH

Thank you and hello everyone. On behalf of The Leukemia & Lymphoma Society (LLS), thank you for joining us. LLS is committed to improving patients' quality of life. To date, more than \$1.3 billion has been invested in research to advance therapies and save lives, and we are now setting out to fundamentally change how children with pediatric acute leukemia are treated through the *LLS Children's Initiative – Cures and Care for Children*. This is a bold multiyear endeavor to help children with blood cancer and their families through every facet of our mission, including a life-saving research investment, education and support services and advocacy efforts.

LEARNING OBJECTIVES

- Describe an overview of long-term and late effects of treatment for childhood blood cancers
- Explain the importance of following a care plan, consultation in a survivorship program and communication between the treating pediatrician/family physician and family
- Address survivorship guidelines, including screening and management strategies
- Identify strategies and resources to support survivors, including as they continue their education

BEATING CANCER IS IN OUR BLOOD.



Today our presenters will:

- provide an overview of long-term and late effects of treatment for childhood blood cancers,
- explain the importance of following a care plan, consultation in a survivorship program and communication between the pediatrician or family physician and the family,
- address survivorship guidelines,
- and identify strategies and resources to support survivors.

We are pleased to offer continuing education credit. To receive credit, you must participate in the entire webinar and complete the posttest and evaluation and at the end. A Certificate of Completion will then be issued to you as a downloadable PDF (portable document format). Your feedback is really important to help us plan future programs, so please complete the evaluation.

We'd like to thank our collaborator, Clinical Directors Network, for working with us on this program.

FACULTY

Tara O. Henderson, MD, MPH, FASCO

Professor of Pediatrics
Director, Childhood, Adolescent and Young Adult Survivorship Center
Director, Cancer Survivorship and Co-Leader, Cancer Prevention and Control Program
Comprehensive Cancer Center
The University of Chicago
Chicago, IL

Danielle Novetsky Friedman, MD, MS

Assistant Member
Pediatric Long-Term Follow-Up Program
Memorial Sloan Kettering Cancer Center
New York, NY

BEATING CANCER IS IN OUR BLOOD.



I am now honored to introduce our speakers. Dr. Tara Henderson is Professor of Pediatrics; Director, Childhood Adolescent and Young Adult Survivorship Center; Director, Cancer Survivorship and Coleader Cancer Prevention and Control Program at the University of Chicago Comprehensive Cancer Center in Chicago. Dr. Henderson's research is focused on understanding subsequent cancer and late effects in survivors and then developing interventions to increase screening and early detection of these subsequent cancers.

Dr. Danielle Novetsky Friedman is Assistant Member in the Pediatric Long-term Follow-up Program at Memorial Sloan-Kettering Cancer Center in New York. She is a pediatrician specializing in survivorship and late effects and after childhood cancer therapy.

Thank you both for volunteering your time and expertise with us today. It is now my pleasure to turn the program over to you.

DISCLOSURES

Survivorship Care for Childhood and Adolescent Blood Cancer

Dr. Henderson has received research grants from Seattle Genetics

Dr. Friedman has no affiliations to disclose

BEATING CANCER IS IN OUR BLOOD.



PRESENTATION


Danielle Novetsky Friedman, MD MS

Thanks Lauren. This is Danielle Friedman. Thank you again for giving us the opportunity to be here today and participate in this important talk.

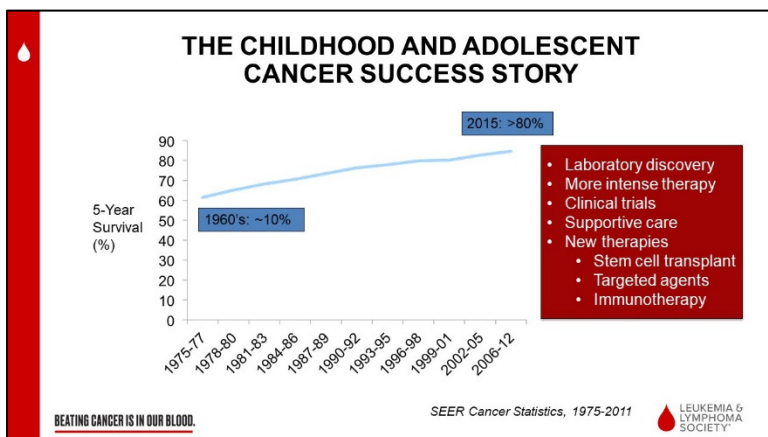
OUTLINE

1. Epidemiology of childhood cancer survivorship
2. Three patient stories from leukemia and lymphoma survivors
3. Models of risk-based survivorship care
 - * Resources for the future

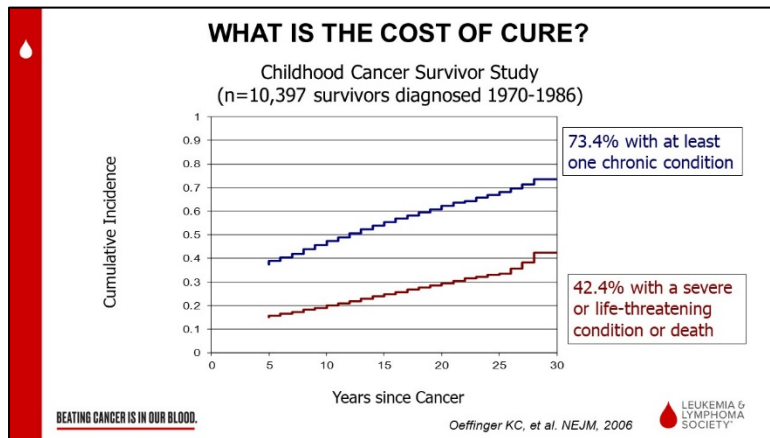
BEATING CANCER IS IN OUR BLOOD.



So briefly, the outline of what we'll review in the next hour. So, I'll start with a discussion of the epidemiology of childhood cancer survivorship. We'll then move on to three patient stories to highlight some of the late effects that we see in leukemia and lymphoma survivors. And then Dr. Henderson will finish, so she'll do the third patient story and then she'll finish with a discussion of model of diversity survivorship care, and then we'll end the talk with a discussion of resources for a future that, hopefully, you can use and integrate into your own clinical practices.

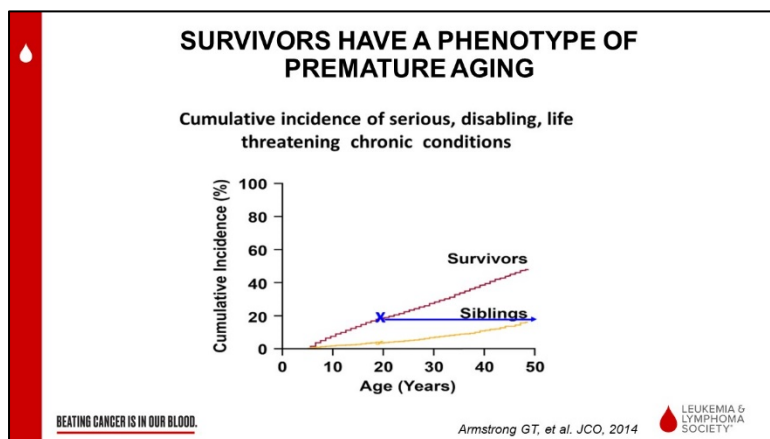


When you think about childhood and adolescent cancer, this has really been one of the major medical successes of the last 60 or 70 years. Such that in the 1960s about 10% of kids diagnosed with cancer survived at least five years whereas today more than 80% of patients diagnosed with a pediatric malignancy will live at least five years. And this is largely attributed to advances in laboratory discovery, clinical trials and supportive care.

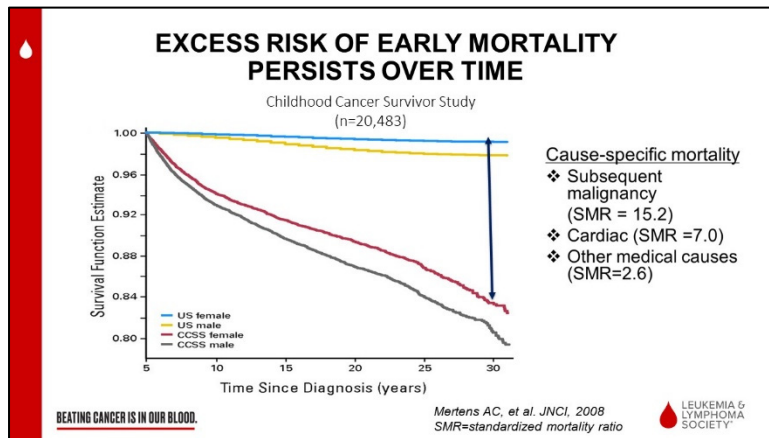


And yet these wonderful improvements have led to an increased recognition of the cost of cure so that we've learned from large cohort studies, such as the Childhood Cancer Survivor Study, that by 30 years after a diagnosis of childhood cancer the cumulative incidence of at least one chronic health condition in our survivors is 73.4% and 42.4% for severe or life-threatening condition or death.

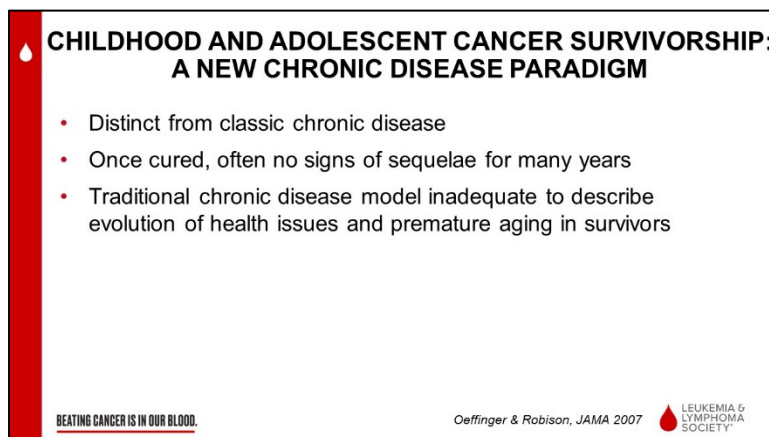
And importantly, when I review this paper and papers like this with fellows and students, I always emphasize that in our world 30 years after a cancer diagnosis means we're talking about 35-year-olds or 40-year-olds. We're not talking about 65-year-olds or 70-year-olds. So, these are people who should not have these types of chronic health conditions.



And so, this recognition of this increased burden of morbidity has led to the description of a phenotype of premature aging in our survivors. Now when we compare a 20-year-old childhood cancer survivor, his or her burden of morbidity or risk of having severe disabling or life-threatening chronic health conditions is similar to a 50-year-old sibling of our patient who has not been treated with cytotoxic therapy for cancers.



And while one might say, “Okay, this is the cost of cure. We have this burden of increased chronic health conditions.” How does this translate into mortality and other heart outcomes? We have also learned that this risk of late effects actually does translate into an excess risk of early mortality that does not go away over time. So that as we get farther away from a primary cancer diagnosis and here we see survival function estimates that increase in time since diagnosis, we would actually expect the childhood cancer survivor shown here in red and gray, their curves would approach those of age-matched U.S. females and males with increasing time since therapy as the risk for recurrence of progression decreasing. But instead we find that it’s not the case and these curves continue to diverge over time so that survivors are less likely to live as they get farther away from their primary cancer diagnosis, but we have learned that this is largely due to their burden of late effects. And so, when we think about what causes this premature mortality, we have found that the biggest risk is due to subsequent cancers, not recurrence or progression of their primary disease, but cardiac causes and other medical causes.



**CHILDHOOD AND ADOLESCENT CANCER SURVIVORSHIP:
A NEW CHRONIC DISEASE PARADIGM**

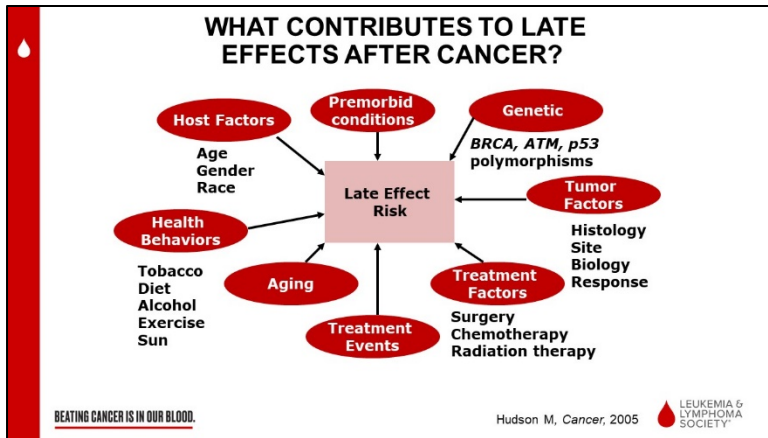
- Distinct from classic chronic disease
- Once cured, often no signs of sequelae for many years
- Traditional chronic disease model inadequate to describe evolution of health issues and premature aging in survivors

BEATING CANCER IS IN OUR BLOOD. Oeffinger & Robison, JAMA 2007 LEUKEMIA & LYMPHOMA SOCIETY

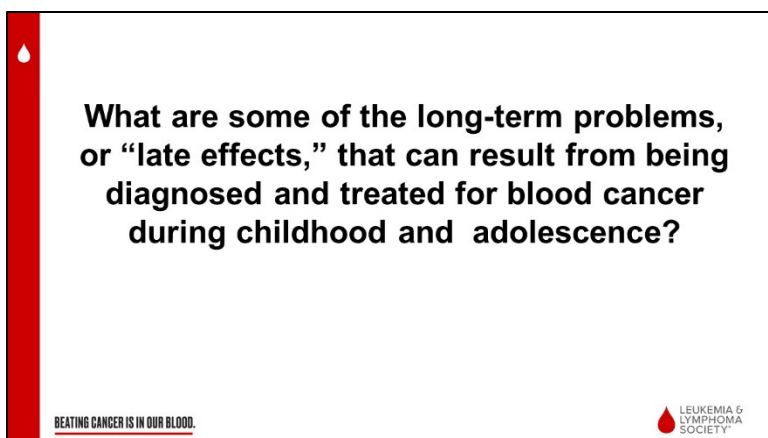
And so these data have led us to describe a new chronic disease paradigm where we recognize that even though our patients are cured and even though they may have no signs or sequelae of late effects for many years, we need a new framework to think about how to describe the evolution of health issues in this population and how to understand the premature aging that we see in childhood cancer survivors. And so, this is a hot area of research right now. A lot of us are thinking about

TRANSCRIPT

mechanisms leading to premature aging so we can understand how to intervene and decrease morbidity in this cohort.



And so for any patient who is a survivor of any childhood cancer, but certainly for today's talk specifically childhood and adolescent blood cancers, we really feel strongly that each person should have someone think through his or her personalized risk of developing late effects that takes into account all of the factors shown on this slide. So, certainly, for those who are diagnosed as teenagers or young adults, we have to think about premorbid conditions, genetic factors, tumor factors, treatment factors which we'll really focus on today. So, what kind of surgery did the patient have? What chemotherapeutic agents were they exposed to? Did they receive radiation therapy? Were they transplanted? Did they receive novel agents? And we'll really sort of delve into that in the course of the next hour. And then also think through potential treatment events that can modify late effects, how the aging process impacts those risks, and what kinds of health behaviors our patients are engaging in now, like do they smoke? What kind of diet do they eat? Are they drinking too much alcohol? What about physical activity and sun exposure without protection? And finally, all of these factors are modified by specific host factors such as age, gender and race.




What are some of the long-term problems, or "late effects," that can result from being diagnosed and treated for blood cancer during childhood and adolescence?

BEATING CANCER IS IN OUR BLOOD. LEUKEMIA & LYMPHOMA SOCIETY


And so, what are some of the long-term problems or what we call late effects that can result from being diagnosed and treated for blood cancer during childhood and adolescence?

LATE EFFECTS: PHYSICAL	
Growth and Development Linear growth Skeletal maturation Intellectual function Emotional/social maturation Sexual development	Organ Function Cardiac Pulmonary Endocrine GI/Hepatic Genitourinary Musculoskeletal Neurocognitive Neurologic Neurosensory
Fertility and Reproduction Sexual function Fertility Health of offspring	Cancer Recurrent (primary) Second cancers

BEATING CANCER IS IN OUR BLOOD. 

Well we know that broadly we can divide the risk of late effects into two categories, and those are physical and psychosocial. It's not so neat. A lot of these things actually overlap into both spheres. So, when we think specifically about physical late effects, we think a lot about growth and development, and so this refers not only to things like linear growth and skeletal maturation but certainly to emotional maturation, sexual development, intellectual function. And then, as our survivors get older, we do think very carefully about fertility and reproduction, including sexual function and health of offspring. Finally, we know that patients are at risk for different late effects related to almost every organ system, and also at risk for the development of not only recurrent progression, but second cancers related to the treatment received for the primary cancer.

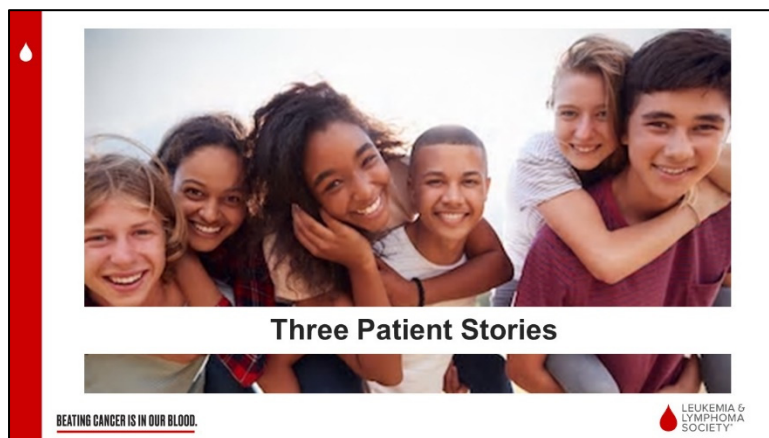
LATE EFFECTS: PSYCHOLOGICAL	
Mental Health - Depression/mood disorders - Cancer-related anxiety - Post-traumatic stress Physical/Body image - Weight loss/gain - Loss of organs/tissues	Education/Vocation - Academic underachievement - Vocational limitations - Under/unemployment - Loss of job/benefits Insurance Discrimination - Access to health care Financial Toxicity - Debt (medical/other)
Chronic Symptoms - Fatigue/ Low energy - Disrupted sleep - Poor memory/concentration - Chronic pain Self-care - Independent living	Social Interaction - Family/peer relationships - Social withdrawal/isolation - Intimacy/marriage/family - Cancer-related stigma

BEATING CANCER IS IN OUR BLOOD. 

And so, moving on to the psychosocial issues that can develop after cancer, these, unfortunately, are probably a whole separate talk but I think it's really important to at least touch on them. So, we know that we have to think about the mental health of our survivors – issues like body image, disrupted sleep, chronic pain. We think a lot about educational achievement, vocational achievement. There's a burgeoning amount of literature that's now on financial toxicity and insurance coverage for young adult childhood cancer survivors. And then social interaction which is really huge for the patients I've seen recently in the context of the COVID pandemic. There is isolation after treatment of childhood cancer and now I think this is especially acute in the context of COVID-19 and, again, probably deserves its own talk as well.

System	Exposure	Potential Late Effects
Cardiac	Chest radiation Anthracyclines	Valvular disease Pericarditis Myocardial infarction Congestive heart failure
Pulmonary	Radiation therapy CCNU/BCNU Bleomycin	Restrictive lung disease
Endocrine	Cranial radiation Total body irradiation High-dose alkylating agents	Hypothalamic-pituitary dysfunction: GH deficiency, ACTH deficiency, FSH/LH deficiency, TSH deficiency Thyroid dysfunction Ovarian or testicular dysfunction
Metabolic	Abdominal radiation Total body irradiation Cranial radiation	Diabetes mellitus Metabolic syndrome Obesity
Hearing	Platinum agents, cranial radiation	Hearing loss
Renal	Surgery (nephrectomy) Radiation therapy Platinum agents Cyclophosphamide/ifosfamide	Renal insufficiency or failure
Neurocognitive	Cranial radiation Young age at treatment High-dose methotrexate	Learning disabilities Cognitive dysfunction
Subsequent malignancies	Alkylating agents Epipodophyllotoxins Radiation therapy	Leukemias Solid tumors

And so, in our late effects clinic, we think about things in a systems-based fashion where we think about specific therapeutic exposures that patients receive and then what potential late effects we have to be thinking about. And rather than going through this whole chart and reading it to you, Dr. Henderson and I actually thought that we could illustrate how to approach the childhood cancer survivor using patient stories that we've encountered in our clinic.



So, we'll review briefly three stories of patients who we've met and cared for who've been treated for a blood cancer and then review with you how we approach their care and what sort of things we think about during a typical clinical encounter.

STORY 1...

14-year old male has been referred to long-term follow up 3 years after completing treatment for standard risk ALL which was diagnosed at age 9.

He received 3 years of multiagent chemotherapy which included low doses of anthracycline, vincristine, cyclophosphamide, asparaginase, 6-MP, methotrexate and steroids.

In taking his history, he notes that he has developed hip pain in the last month and his grades in school have been B's and C's.

BEATING CANCER IS IN OUR BLOOD.



So, in our first story, we have a 14-year-old male who's been referred to our long-term follow-up program three years after completion of therapy for treatment of standard risk ALL (acute lymphoblastic leukemia) with multiagent chemotherapy. He was diagnosed at age nine and he received low doses of anthracycline, vincristine, cyclophosphamide, asparaginase, 6MP (6-mercaptopurine), methotrexate and steroids. And during your history he tells you that he has this hip pain that's been bothering him for the last month and he also notes when you ask him about school that he's been getting a couple of Bs and a lot of Cs in school.

WHAT TESTS SHOULD HIS PROVIDER ORDER TO INVESTIGATE HIS HIP PAIN/BONY PROBLEMS?

- A. Serum calcium
- B. DEXA scan
- C. Hip x-ray
- D. Parathyroid hormone

BEATING CANCER IS IN OUR BLOOD.



So now I'm going to turn it over to you and ask what tests you should be ordering to investigate his hip pain or bony problem. And the choices are A) serum calcium, a B) DEXA (dual energy x-ray absorptiometric) scan, C) a hip x-ray or D) parathyroid hormone.

WHAT TESTS SHOULD HIS PROVIDER ORDER TO INVESTIGATE HIS HIP PAIN/BONY PROBLEMS?

- A. Serum calcium
- B. DEXA scan
- C. Hip x-ray
- D. Parathyroid hormone

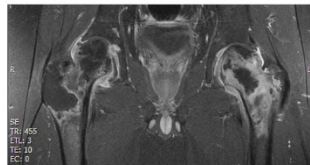
BEATING CANCER IS IN OUR BLOOD.



Okay, And so the results for this question should be a hip x-ray. So, the majority of people got the answer right.

SKELETAL COMPLICATIONS

- Osteonecrosis
 - Associated with:
 - Older age
 - Exposure to steroids
 - Exposure to methotrexate
 - Genetics
 - Low bone mineral density
 - DEXA scans generally not recommended before age 18 years (results not standardized for pediatric patients)
 - Associated with:
 - Older age
 - Exposure to steroids
 - Exposure to methotrexate



BEATING CANCER IS IN OUR BLOOD.



And so, what we do know is that individuals treated with methotrexate or steroids are at risk for two categories of bone problems. So typically more acutely, but this can be progressive and, therefore, present in survivorship settings, we do see osteonecrosis, or sometimes referred to as avascular necrosis, which is associated with the factors shown here, and that should certainly be on your differential.

We also see something called low-bone mineral density, and this would normally be screened in the adult population with DEXA scans. In both my practice and in Dr. Henderson's practice, we do not get DEXA scans in patients before the age of 18 because the results have to be adjusted not only for gender and for age but also for height, and I think this can be tricky and lead to misleading results. So, this too is associated with older age of therapy. We typically see it in individuals who are adolescents at the time of treatment who've been exposed to high doses of steroids or methotrexate, and both of these things are issues to think about. But in an individual who presents with an acute complaint such as hip pain, we would certainly start with an x-ray and work it up probably in a similar fashion to a general pediatrician, but certainly having a lower threshold for referral and additional imaging because we know that our survivors are at risk for these types of skeletal complications.

HOW SHOULD THE PROVIDER ADDRESS SCHOOL ISSUES?

- A. Don't worry about it, he's a normal kid
- B. Refer to neuropsychology
- C. Screen for depression and anxiety
- D. Both B and C

BEATING CANCER IS IN OUR BLOOD.

LEUKEMIA & LYMPHOMA SOCIETY®

Moving on to the other factor that this young man brought up during the visit is the fact that he's mostly getting Cs in school. So how should you address this? Should you A) not worry about? He's a normal kid. Middle school is tough. That's okay. Think about it in the future. Should you B) refer to neuropsychology? Should you C) screen for depression and anxiety? Or should you D) do both B and C?

HOW SHOULD THE PROVIDER ADDRESS SCHOOL ISSUES?

- A. Don't worry about it, he's a normal kid
- B. Refer to neuropsychology
- C. Screen for depression and anxiety
- D. Both B and C

BEATING CANCER IS IN OUR BLOOD.

LEUKEMIA & LYMPHOMA SOCIETY®

Okay, so let's show the audience results for this question. Right, amazing. So, 90% said both B and C, which I agree with. I would do the same.

LEARNING PROBLEMS

- Seen most commonly in those treated with radiation to the brain
- Risk is greatest in individuals under age 3-5 years at treatment
- Special neuropsychological testing required with serial educational/vocational assessments over time

BEATING CANCER IS IN OUR BLOOD.



So, in our childhood cancer survivors, we know that there is an increased risk of learning problems or neurocognitive dysfunction. This is most commonly seen in those who receive radiation therapy to the brain but certainly is a risk for anyone treated; some literature said under the age of three, some said under the age of five.

NEUROPSYCHOLOGICAL OUTCOMES

- Executive functioning (planning, organization, problem solving - not IQ!)
 - Exposure to steroids
 - Exposure to methotrexate
 - Genetics
 - Early screening and social work intervention with schools
- Higher prevalence of adverse psychosocial outcomes in childhood cancer survivors
 - Depression and anxiety
 - Anger
 - Socially withdrawn
 - Early screening and referral to counseling and mental health providers

BEATING CANCER IS IN OUR BLOOD.



And because of these risks, we really recommend specialized neuropsychological testing for all of our survivors who are exposed at a young age to any type of cancer therapy but, certainly, to brain radiation or to methotrexate. And parents always ask us, “Well what kind of neuropsychological outcomes do you see? What kinds of problems should we be aware of?” And this is not an IQ problem; I always, always emphasize this. Most commonly we find that our survivors have issues with executive functioning, so planning, organization, problem-solving. And these can really be pinpointed by neuropsychologists with expertise in this area who can make appropriate recommendations for the school to optimize the educational outcomes of our patients.

In addition to the school related issues, we do find a higher prevalence of adverse psychosocial outcomes in childhood cancer survivors, and so we do think that all providers should be very vigilant in screening for depression, anxiety, anger, being socially withdrawn and thus recommend referral to counselors and mental health providers at the first indication of an issue so that these can be dealt with in a timely manner.

TRANSCRIPT

And so, in summary, for the patient with standard-risk leukemia, this is the patient who is typically not at very high risk for the development of adverse outcomes like late effects. These are patients who often do quite well, but it's still critical that these patients are followed by providers who are familiar with their potential late effects, so that they can be screened and managed appropriately, and so that management and referrals can be made in a timely manner for anyone who is exhibiting any type of problem.


STORY 2...

11-year old female treated for high-risk Acute Lymphoblastic Leukemia when she was 4 years old presenting for LTFU


She received combination chemotherapy followed by allogeneic stem cell transplantation

- Cytoreduction included **cyclophosphamide, thiotepa, and total body irradiation [TBI]** (1375 cGy)

Missed last year's visit because she felt so well...

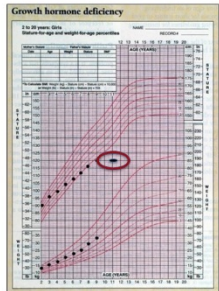


BEATING CANCER IS IN OUR BLOOD.




And so, moving on from the low-risk survivor to the high-risk survivor, we'll now go to story two. This is an 11-year-old girl who was treated for high-risk ALL when she was four years of age. She's presenting for long-term follow-up and received a combination of chemotherapy followed by an allogeneic stem cell transplant. The cytoreduction she received prior to transplant includes cyclophosphamide and thiotepa, as well as total body irradiation. And she comes in today and says she actually missed her visit last year because she felt so well and didn't think it was necessary.

GROWTH CURVE AT TODAY'S VISIT



BEATING CANCER IS IN OUR BLOOD.




So you examine her and she actually looks great but then you plot her on her growth curve, which is quite small and may be difficult to see, but if you look at the top curve which is her height, you can see that she has been drifting downward over time. There is no point from last year, but you can see she's now fallen off the growth curve entirely.

WHAT ARE YOUR CONCERNS FOR THIS PATIENT?

- A. Growth hormone deficiency
- B. Primary hypothyroidism
- C. CBC is normal. No concerns.
- D. Both A and B

BEATING CANCER IS IN OUR BLOOD.




And so, what should you be thinking about for this patient? What are you concerned about? Are you thinking this is A) growth hormone deficiency, B) an underactive thyroid? Are you not concerned because her exam is otherwise normal, her C) CBC is normal so she's good to go or is it D) both A and B?

WHAT ARE YOUR CONCERNS FOR THIS PATIENT?


- A. Growth hormone deficiency
- B. Primary hypothyroidism
- C. CBC is normal. No concerns.
- D. Both A and B

BEATING CANCER IS IN OUR BLOOD.




Okay, so let's look at the audience results and close the poll. Amazing, great. So, I agree with the 90% of people who responded both A and B. We would be thinking about growth hormone deficiency and primary hypothyroidism or an underactive thyroid gland.

<u>Transplant Population</u>	<u>Potential Late Effects</u>
Prior therapy	<ul style="list-style-type: none"> • Endocrinopathies • Osteoporosis
Preconditioning chemotherapy	<ul style="list-style-type: none"> • Osteonecrosis • Gonadal dysfunction
TBI	<ul style="list-style-type: none"> • Insulin resistance/dyslipidemia • Renal insufficiency
Post SCT chemo	<ul style="list-style-type: none"> • Pulmonary complications • Cataracts
GVHD	<ul style="list-style-type: none"> • Oral/dental problems • Gait and balance disturbances

BEATING CANCER IS IN OUR BLOOD. 

And so, you know, moving from our case one to case two, which is a transplant survivor, this is actually a very high-risk population, especially those people who are exposed to total body irradiation or TBI.

<u>Transplant Population</u>	<u>Potential Late Effects</u>
Prior therapy	<ul style="list-style-type: none"> • Endocrinopathies • Osteoporosis
Preconditioning chemotherapy	<ul style="list-style-type: none"> • Osteonecrosis • Gonadal dysfunction
TBI	<ul style="list-style-type: none"> • Insulin resistance/dyslipidemia • Renal insufficiency
Post SCT chemo	<ul style="list-style-type: none"> • Pulmonary complications • Cataracts
GVHD	<ul style="list-style-type: none"> • Oral/dental problems • Gait and balance disturbances

BEATING CANCER IS IN OUR BLOOD. 

Patients in this category are at risk for all of the potential late effects listed here including the osteonecrosis that we discussed in case one, but certainly for a range of endocrinopathies, which is what we see in the patient described in story two. And so, we know, for those of us who work on the pediatric side, that endocrine complications are the most prevalent late effects that we see in survivors.

LATE EFFECTS: ENDOCRINE COMPLICATIONS

- Most prevalent late effects in survivors of childhood cancer
- Observed in 40-60% of survivors followed into adulthood
- Most often seen in survivors treated with:
 - Radiation impacting the brain (including TBI)
 - High-dose alkylating agents

BEATING CANCER IS IN OUR BLOOD.



And so, for this patient when we think about why she isn't growing well, we really have to think about a variety of potential issues.

POOR LINEAR GROWTH (1)

Growth hormone deficiency (endocrine):

- Common after radiation doses ≥ 18 Gy impacting the brain
- Children treated with total body irradiation (TBI) doses ≥ 12 Gy are also at risk
- Screening: Height should be plotted every 6 months on standardized growth curves and pubertal development should be monitored
- Those with the above risk factors and poor growth rate should undergo formal growth hormone stimulation testing

BEATING CANCER IS IN OUR BLOOD.



So, certainly, as everyone who responded noted, we have to think about growth hormone deficiency. This is something that we see after radiation doses greater than or equal to 18 Gy to the hypothalamus, but we also know that children treated with TBI doses greater than or equal to 12 Gy, are also at risk. And so, for these patients, their height should be plotted every six months on standardized growth curves, and at the same time providers should be monitoring the puberty and the development of these patients. And so why is that?

So, we know that those who are treated with these doses of radiation for hypothalamus are also at risk for precocious puberty and an altered tempo of puberty. So even if they go into puberty when they are a little bit older and within the normal range, it can happen quite quickly. And so, if someone starts going into puberty and starts making sex hormones, then their growth can look normal on the growth curve but then they'll stop growing prematurely and you'll have missed their growth hormone deficiency entirely. So precocious puberty or rapid tempo puberty can mask growth hormone deficiency, so it's really critical that these patients are not only plotted on a growth curve, but Tanner staged at every single visit. And then those who are at risk who have a poor growth rate should be referred to an endocrinologist and should have formal growth hormone stimulation testing.

POOR LINEAR GROWTH (1)

Impaired spinal growth (non-endocrine):

- Patients treated with spinal and/or total body irradiation may demonstrate stunted spinal growth
 - Becomes most apparent during puberty
- Due to radiation-induced direct damage to the growth plate, usually the vertebrae
- Monitor serial sitting heights
 - No clear data on utility of treatment

BEATING CANCER IS IN OUR BLOOD.



Now the thing that's tricky about individuals who get total body irradiation or any radiation to the spine is that they are also at risk for impaired spinal growth. So for individuals who even get lung radiation, abdominal radiation, certainly TBI, we know that their spines will not grow as well as they would have if they had not been exposed to radiation, and this is due to radiation-induced damage to the growth plates of the vertebrae and cannot be overcome by growth hormone treatment for those who are growth hormone deficient.

So in our clinic, we have a special sitting height machine that we make ourself that we can keep track of individual spinal growth, and that helps us think through whether they are not growing well because their spines aren't growing well or because we have to be thinking about something else like growth hormone deficiency or both. But certainly, that has to be considered as well for any individual who's been exposed to radiation impacting the spine who isn't growing as well as they should have.

THYROID DYSFUNCTION

- Common after radiation to the neck
- Associated with tyrosine kinase inhibitor exposure (sunitinib, imatinib, etc)
- Risk increases with higher radiation doses
- Risk increases over time
- Screening: Annual TSH
- Easily treated with a single daily pill (levothyroxine)

BEATING CANCER IS IN OUR BLOOD.



Finally, other things to think about are thyroid dysfunction. We know that those who get radiation to the neck, those who get tyrosine kinase inhibitors can develop thyroid problems. We see that this risk actually increases over time. It doesn't get lower as you get farther from treatment. And so, these patients should also be screened with thyroid stimulating hormone levels once a year in their blood work. And for those who are hypothyroid, we can treat this very easily with a single daily pill of levothyroxine.

GONADAL DYSFUNCTION

- Risk greatest after:
 - Radiation to the ovaries (or testes for boys)
 - Treatment with high doses of alkylating agents (cyclophosphamide, procarbazine, busulfan, thiotepa)
- In girls, younger age at treatment is protective
- Screening: Monitor serial blood tests of ovarian function as well as pubertal development, menstrual regularity
- Post-treatment egg freezing may be an option for menstruating females

BEATING CANCER IS IN OUR BLOOD.



Finally, in addition to precocious puberty, we also have to think of potential damage to the ovaries in terms of growth. So, for girls who get TBI, total body irradiation, or a high-dose alkylating agent, we know that they may not go into puberty on their own at all. And if they're not producing sex hormones when they're supposed to be, that can also impact linear growth. And so, these patients should have serial blood tests looking at their ovarian function as well as their development as well. And then if there's time at the end of the talk, we can talk about the option of egg freezing for those who do go through puberty on their own with normal gonadotropins as a means of post treatment fertility preservation.

And so, this is sort of the spectrum of potential late effects that we think about both in low-risk leukemia survivors and high-risk leukemia survivors. And with that, I'm going to turn it over to Dr. Henderson who's going to present a lymphoma patient for a different view of late effects in that population. Dr. Henderson.


Tara O. Henderson, MD, MPH, FASCO

Thanks so much, Danielle. That was a beautiful job.

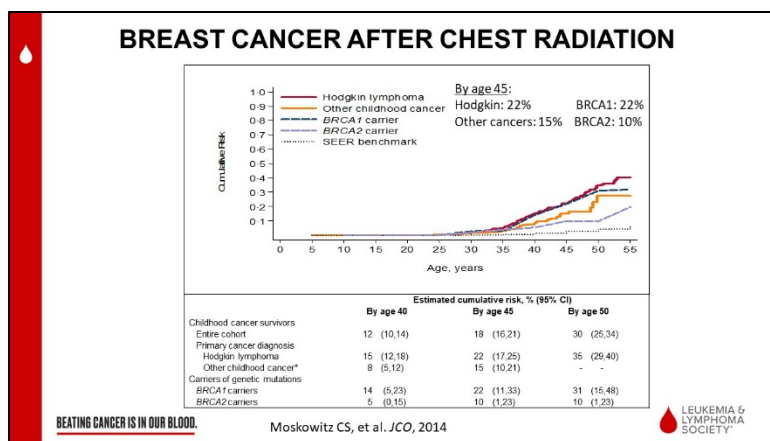
STORY 3...

26-year old female seeking to establish care in your practice
 Recently moved to NYC from California
 History notable for diagnosis of *Hodgkin lymphoma, Stage IIB, Nodular Sclerosing* at age 11
 Treatment included multiagent chemotherapy and mantle radiation (25 Gy)

On exam, you palpate a breast mass...

BEATING CANCER IS IN OUR BLOOD. 

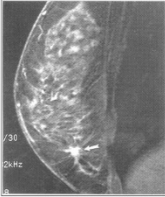
So, our story three is a patient who's a little bit older than the pediatric age. Is a 26-year-old woman who's coming to establish care in your practice. She moved from New York City to California, most likely from the COVID crisis, and history was notable for a diagnosis of Hodgkin lymphoma Stage IIb nodular sclerosing at age 11. She was treated with a combination of chemotherapy, which included anthracycline, as well as mantle radiation up to a dose of 25 Gy. And when you do her physical exam, you palpate a breast map.



And this brings us to a topic that I spend a lot of time thinking about, which is breast cancer after having received chest radiation as a child. Breast cancer after chest radiation is the most common secondary malignancy that we see in childhood and adolescent cancer survivors. So, I think that this graphic is pretty remarkable. What we did was an analysis with Danielle and my colleague, Chaya Moskowitz in New York, where she looked at a cohort of Hodgkin lymphoma survivors, looked at the risk of getting breast cancer across a whole host of ages in the general population and then actually looked at a cohort of women who carry the BRCA1 or 2 breast cancer gene mutation. And you can see that having had chest radiation as a child in the red line in this graph, you incur a higher risk of developing breast cancer than if you do with the BRCA1 or 2 gene mutation. So, we're seeing about 20% of these women developing breast cancer by the age of 40.

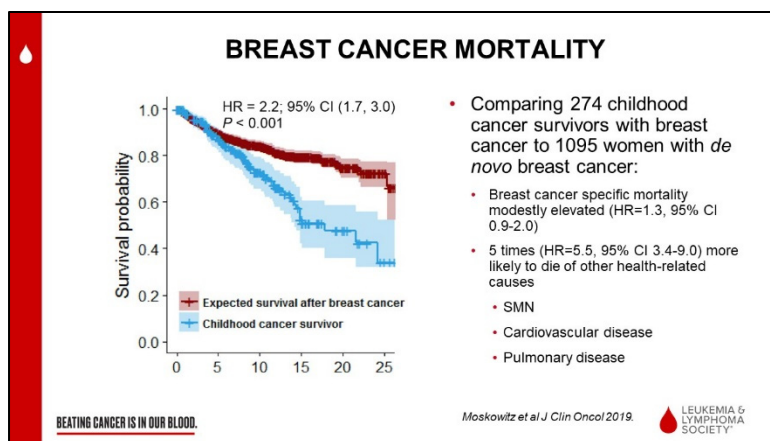
BREAST CANCER SCREENING GUIDELINES AFTER CHEST RADIATION

- For all females exposed to chest-directed radiation (including TBI):
 - **Clinical breast exam** by a health care provider annually from puberty to age 25; then every 6 months after age 25
 - **Annual breast MRI and mammogram** beginning at age 25 or 8 years after completion of therapy, whichever occurs later



BEATING CANCER IS IN OUR BLOOD. www.survivorshipguidelines.org LEUKEMIA & LYMPHOMA SOCIETY

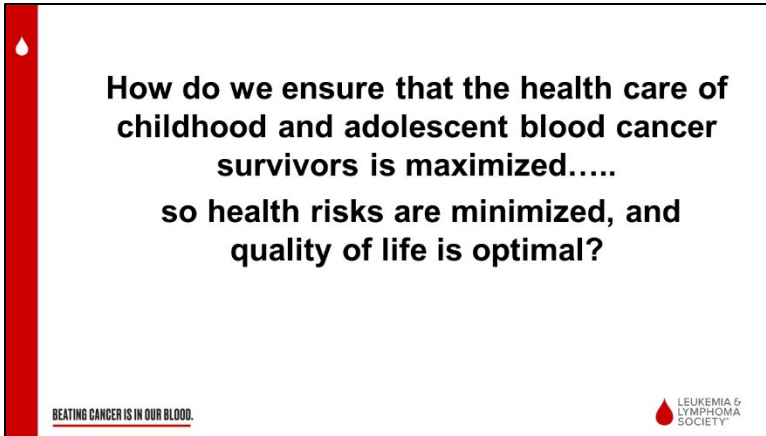
So, as a result of what we've observed in women who have gotten chest radiation for their childhood cancer and in many cases that's Hodgkin lymphoma, we've developed breast cancer screening guidelines for any woman who's received any chest directed radiotherapy. And these guidelines include a clinical breast exam by a healthcare provider from puberty to age 25 and then every six months after age 25 and then an annual breast MRI and mammogram starting at the age 25 or eight years after completion of therapy, whichever occurs later.



What's important to know about breast cancer mortality, and I wanted to bring up this slide because I wanted everyone to understand when you're thinking about a Hodgkin lymphoma survivor who received chest radiation, we don't want to just think about breast cancer. So, Dr. Moskowitz and I went back to these women who developed breast cancer, so we identified almost 275 of these women, and we compared them to over 1,000 women who developed breast cancer in the general population. And we looked at your risk of death from breast cancer, whether you had breast cancer in the general population, or you had chest radiation, and we found that your risk of breast cancer associated death was just slightly elevated. But what was more remarkable is these women were five times more likely to die of other health-related causes, so other second cancers, cardiovascular disease and pulmonary disease. And this really drives home the point that these patients who had had chest radiation or Hodgkin lymphoma as a child need specialized healthcare, even specialized


TRANSCRIPT

healthcare if you're diagnosed with a secondary cancer, to take into account all these other health effects that Danielle discussed earlier in our talk.

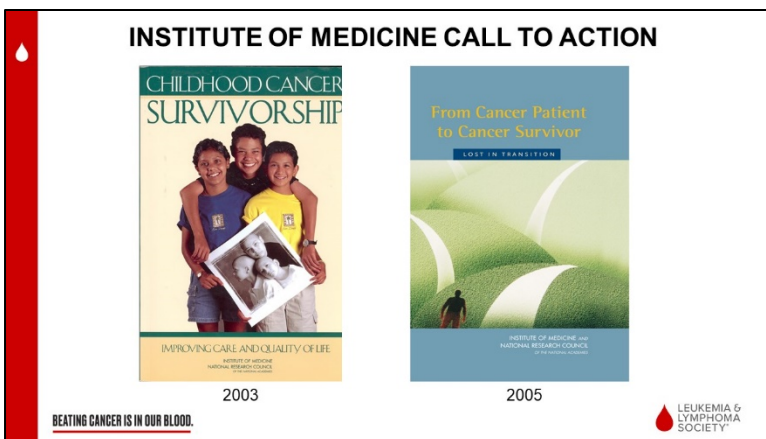


How do we ensure that the health care of childhood and adolescent blood cancer survivors is maximized..... so health risks are minimized, and quality of life is optimal?

BEATING CANCER IS IN OUR BLOOD.



So, taking all of these stories together and what we've learned about these hosts of health risks, how do we ensure that the healthcare of childhood and adolescent blood cancer survivors is maximized so that health risks are minimized and the quality of life is optimal?




INSTITUTE OF MEDICINE CALL TO ACTION

CHILDHOOD CANCER SURVIVORSHIP
IMPROVING CARE AND QUALITY OF LIFE
2003

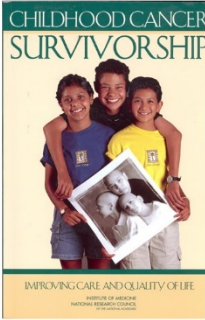
From Cancer Patient to Cancer Survivor
LOST IN TRANSITION
2005

BEATING CANCER IS IN OUR BLOOD.



So, the Institute of Medicine has been thinking about this for a while and they had two calls to action.

INSTITUTE OF MEDICINE CALL TO ACTION




CHILDHOOD CANCER SURVIVORSHIP
IMPROVING CARE AND QUALITY OF LIFE
INSTITUTE OF MEDICINE
NATIONAL RESEARCH COUNCIL ON HUMAN RESOURCES

2003

2003 Recommendations:

- Risk-based health care
 - Monitor for cancer recurrence
 - Surveillance and intervention for late effects and second cancers
- Prevention/education
 - Lifestyles, health behaviors
 - Education
 - Assistance with financial challenges

BEATING CANCER IS IN OUR BLOOD.



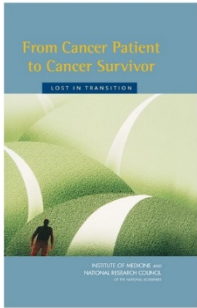
In 2003, they wrote a mandate for all survivors of childhood and adolescent cancer and recommended risk-based healthcare for these patients.

So, what's risk-based healthcare? This is for monitoring for cancer reoccurrence, lifelong surveillance and intervention for late effects in secondary cancers and education and prevention around teaching patients about healthy lifestyles and health behaviors, educating them about their past treatment and their risks and helping them with financial and other psychosocial challenges.

INSTITUTE OF MEDICINE CALL TO ACTION

2005 Recommendations:


- Survivorship Care Plan for all cancer survivors
 - Roadmap for post-treatment care
 - Created by oncology provider
 - For survivor, primary care providers



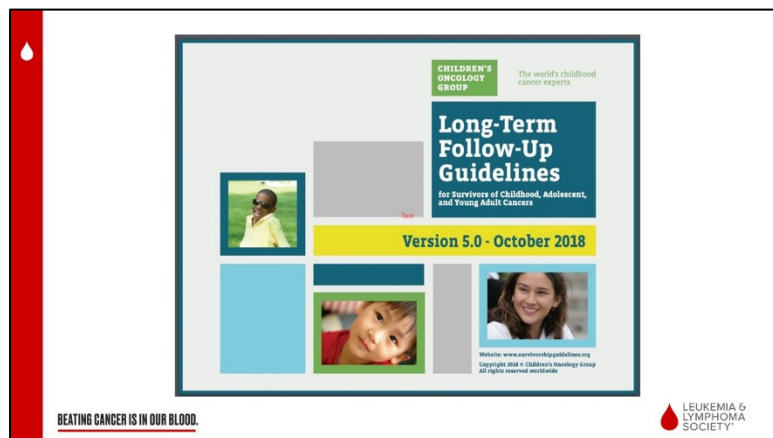
From Cancer Patient to Cancer Survivor
LOST IN TRANSITION
INSTITUTE OF MEDICINE
NATIONAL RESEARCH COUNCIL ON HUMAN RESOURCES

2005

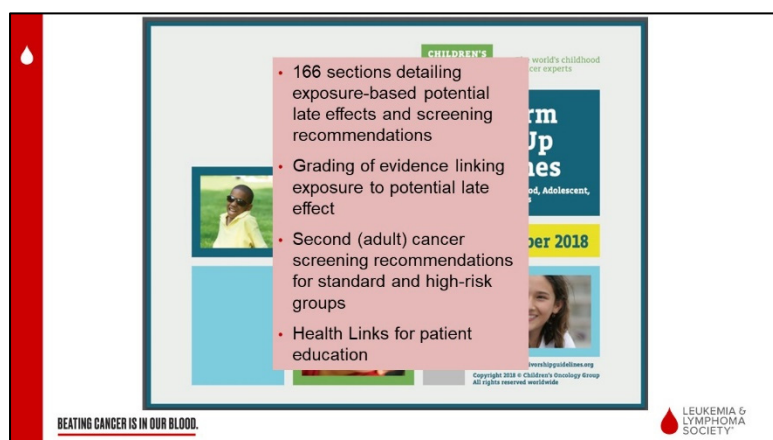
BEATING CANCER IS IN OUR BLOOD.



They had a follow-up recommendation in 2005 when they recommended for all cancer survivors, and this wasn't just for childhood and adolescent cancer survivors but for adult cancer survivors as well that everyone receive a survivorship care plan when they completed therapy. And what is a survivorship care plan? Basically, it's your roadmap for post-treatment care that's created by your oncology provider that's for both the survivor as well as their primary care doctor that gives a brief summary of the treatment they received and their risk of late effects and how they should be followed.



In response to the 2003 Institute of Medicine call that I mentioned that called for risk-based healthcare, the Children's Oncology Group, which is our consortium of clinical trials in the United States and Canada, we developed long-term follow-up guidelines for childhood cancer survivors. These guidelines are pretty comprehensive.



They include 166 sections that detail exposure-based potential late effects and screening recommendations. So, it's not the primary cancer that you had but you look through, based on whether they had anthracyclines or alkylators or brain radiation or TBI, all of the therapies we've been mentioning throughout the talk. We grade the evidence linking the exposure to the late effects. We have secondary cancer screening recommendations for both standard and high-risk groups. So basically, you know, for a standard risk group would be Pap (Papanicolaou) smears if you didn't have any radiation; if you didn't have chest radiation to the chest, your breast cancer screening recommendations that are consistent with the general population, as well as high-risk recommendations for high-risk groups. So those would be the ones I showed you earlier with breast cancer screening if you received chest radiation, starting at an earlier age and adding an MRI.

Another example is screening for colorectal cancer. We know that patients that received abdominal or pelvic radiation as part of their treatment for a childhood cancer are at an increased risk of getting colorectal cancer, and we recommend that they start screening at the age of 30.

CHEMOTHERAPY			ANTHRACYCLINE ANTI-BIOTICS (CONT)																						
Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling/ Further Considerations																					
33	Anthracycline Antibiotics Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone	Cardiac Toxicity Cardiomyopathy Subclinical left ventricular dysfunction Congestive heart failure Arrhythmias	HISTORY Shortness of breath Dyspnea on exertion Orthopnea Chest pain Puffiness If under 25 yrs: abdominal symptoms (nausea, vomiting) Yearly	HEALTH LINKS Heart Health Cardiovascular Risk Factors Diet and Physical Activity																					
	To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotopic equivalents prior to calculating total cumulative anthracycline dose. Clinical judgment should ultimately be used to determine indicated screening for individual patients. Daunorubicin: Multiply total dose x 1 Doxorubicin: 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		PHYSICAL Blood pressure Cardiac exam Yearly	COUNSELING Encourage appropriate weight, blood pressure and heart healthy diet. Regarding exercise: • Regular exercise is generally safe and should be encouraged for patients who have normal LVEF/systolic function. • Survivors with myocardial cardiomyopathy should consult cardiologists 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 ECG every 2 years) who plan to participate in intense exercise. • If QTc interval is prolonged: Caution regarding use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antiarrhythmics, macrolide antibiotics, metronidazole).																					
			SCREENING ECG (or comparable imaging to evaluate cardiac function)	POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION Section 103 is an expert emerging finding about echocardiogram images are acceptable. Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmias, or prolonged QTc interval. Female patients only. For patients who are pregnant or planning to become pregnant, additional cardiac evaluation is indicated in patients who received: • >250 mg/m ² anthracyclines • >35 Gy chest radiation, or • Anthracycline (any dose) combined with chest radiation (>15 Gy) Evaluation should include a baseline echocardiogram (pre- or early pregnancy). For those without prior abnormalities and with normal pre- or early pregnancy baseline echocardiograms, follow-up echocardiograms may be obtained at the provider's discretion. Those with a history of systolic dysfunction or with pre- or early pregnancy systolic dysfunction are at highest risk for pregnancy-associated cardiomyopathy. Such individuals should be monitored carefully during pregnancy and during labor and delivery due to increased risk for cardiac failure.																					
			ECG (or comparable imaging to evaluate cardiac function) <table border="1"> <thead> <tr> <th>Recommended Frequency of ECG or Imaging</th> <th>Recommended Frequency</th> <th>Recommended Frequency</th> </tr> </thead> <tbody> <tr> <td>Anthracycline Dose*</td> <td>Frequency</td> <td>Recommended Frequency</td> </tr> <tr> <td>None</td> <td>< 15 Gy chest</td> <td>No screening</td> </tr> <tr> <td>< 150 mg/m²</td> <td>> 15 - < 35 Gy</td> <td>Every 2 years</td> </tr> <tr> <td>> 150 mg/m²</td> <td>< 15 Gy chest</td> <td>Every 2 years</td> </tr> <tr> <td>> 150 mg/m²</td> <td>> 15 - < 35 Gy</td> <td>Every 2 years</td> </tr> <tr> <td>> 150 mg/m²</td> <td>> 35 Gy chest</td> <td>Every 2 years</td> </tr> </tbody> </table> *Based on doxorubicin isotopic equivalent dose. See also cumulative equivalent dose table. *Equivalent cumulative dose with anthracycline used to treat patients in this section. See Section 103, for details.	Recommended Frequency of ECG or Imaging	Recommended Frequency	Recommended Frequency	Anthracycline Dose*	Frequency	Recommended Frequency	None	< 15 Gy chest	No screening	< 150 mg/m ²	> 15 - < 35 Gy	Every 2 years	> 150 mg/m ²	< 15 Gy chest	Every 2 years	> 150 mg/m ²	> 15 - < 35 Gy	Every 2 years	> 150 mg/m ²	> 35 Gy chest	Every 2 years	SYSTEM = Cardiovascular SCORE = 1
Recommended Frequency of ECG or Imaging	Recommended Frequency	Recommended Frequency																							
Anthracycline Dose*	Frequency	Recommended Frequency																							
None	< 15 Gy chest	No screening																							
< 150 mg/m ²	> 15 - < 35 Gy	Every 2 years																							
> 150 mg/m ²	< 15 Gy chest	Every 2 years																							
> 150 mg/m ²	> 15 - < 35 Gy	Every 2 years																							
> 150 mg/m ²	> 35 Gy chest	Every 2 years																							
			EKG (include evaluation of QTc interval) Baseline at entry into long-term follow-up, repeat as clinically indicated.																						
Additional Information Although Mitoxantrone technically belongs to the anthraquinone class of anti-tumor antibiotics, it is related to the anthracycline family and is included in this section because of its cardiac toxic potential.																									

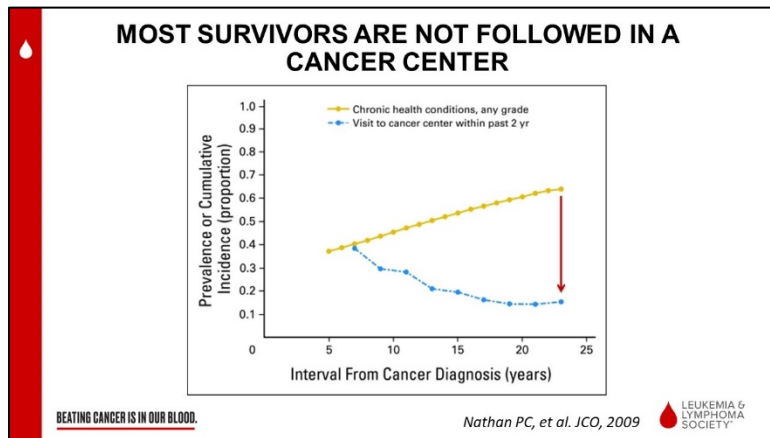
This is one of the pages from the guidelines and I apologize if you can't see specifically the words here, but I'll just highlight the boxes. The first box shows patients exposed to anthracycline chemotherapy, so that's daunorubicin, doxorubicin, epirubicin, for example. These patients are at risk for the late effects of cardiac toxicity. They recommend what you should be looking for on history, on physical exam and then detail how we should be screening with echocardiograms for these patients based on their exposure to chest radiation and their cumulative dose of anthracycline chemotherapy.

Are survivors receiving risk-based health care, such as early breast cancer screening for women exposed to chest radiation, after treatment for childhood blood cancer?

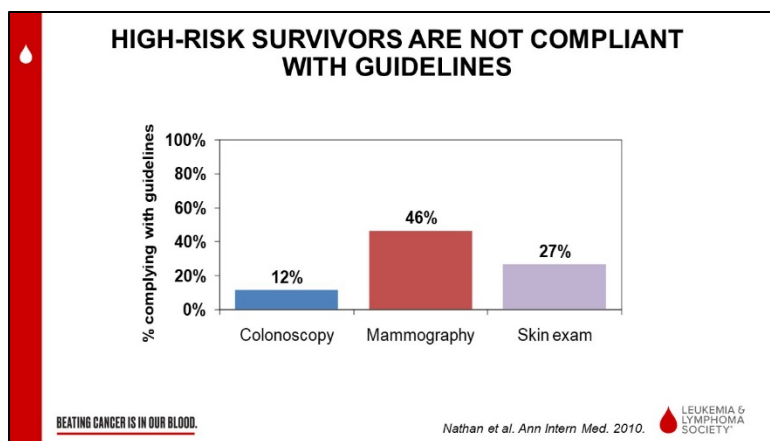
LEUKEMIA & LYMPHOMA SOCIETY®

BEATING CANCER IS IN OUR BLOOD.


So the question we ask, and, again, Danielle and I have been thinking a lot about this, are survivors receiving this recommended risk-based healthcare that have been recommended since 2003 such as early breast cancer screening for women exposed to chest radiation after treatment for a childhood blood cancer?



So, I want to highlight where these patients are getting their care. So, this is a slide where we looked in the Childhood Cancer Survivor study, which is a large cohort of over 14,000 childhood cancer survivors, and we looked at their healthcare practices. So, you can see this yellow line shows their chronic health conditions as they increase with time after their primary diagnosis. The blue line shows their visits to the cancer center since their diagnosis. And you can see that the visits to the cancer center really fall off with time while these chronic health events increase with time.




We've also learned that these high-risk survivors are not compliant with their guidelines. So basically, we looked at people exposed to abdominal radiation, people exposed to chest radiation, as well as any radiation, and looked if they were compliant with our Children's Oncology Group guideline that I showed you earlier. And we saw that only 12% of survivors exposed to abdominal or pelvic radiation are receiving their early colonoscopy screening, less than half the women who were exposed to chest radiation are getting appropriate early breast cancer screening and only a quarter of survivors who received radiation are getting yearly dermatologic exams.




Are physicians aware of available long-term follow-up guidelines for childhood and adolescent blood cancer survivors?

BEATING CANCER IS IN OUR BLOOD.



And that makes us think, okay, are the physicians aware of these long-term follow-up guidelines for childhood and adolescent blood cancers?




PERSPECTIVES ON SURVIVORSHIP CARE

- In a recent survey of 1110 internists, on average, primary care providers reported being:
 - **“Somewhat uncomfortable”** caring for childhood cancer survivors
 - **“Somewhat unfamiliar”** with available surveillance guidelines

BEATING CANCER IS IN OUR BLOOD.

Suh E, et al. Ann Intern Med, 2014



So, I wanted to give a little perspective on survivorship care. So earlier in my career, I spent a lot of time doing nationally representative survey studies of both primary care doctors as well as pediatric oncologists. And our most recent survey, we surveyed over 1,100 general internists that were a nationally representative sample, and we found that these primary care providers were somewhat comfortable with caring for our survivors but they noted they were somewhat unfamiliar with available surveillance guidelines.

PERSPECTIVES ON SURVIVORSHIP CARE: PCPS

- However, in response to a clinical vignette:
 - **90.6%** of respondents did not appropriately recommend yearly breast cancer surveillance
 - **85.1%** did not appropriately recommend cardiac surveillance
 - **23.6%** did not appropriately recommend yearly thyroid surveillance

Question and Answer Choices	Responses, n (%) ^a
Breast cancer surveillance	
In thinking about CL's medical care, how would you approach breast cancer screening?	
I would follow current accepted guidelines for average risk individuals and ask her to begin yearly mammograms when she turns 50	220 (20.0)
I would recommend yearly mammograms starting this year	196 (17.8)
I would recommend every-other-year mammograms starting this year	123 (11.2)
I would recommend yearly breast magnetic resonance imaging and mammograms starting this year	103 (9.4)
Don't know or unsure	458 (41.6)
Missing	10
Cardiac surveillance	
You see that CL had an echocardiogram 6 years after chemotherapy. The echocardiogram was normal. How would you approach cardiac care for this patient?	
I would not proceed with further testing	507 (45.5)
I would refer her at this time to a cardiologist for evaluation and stress testing	81 (7.4)
I would recommend every-other-year echocardiogram ^b	166 (14.9)
I would recommend yearly echocardiogram	85 (7.7)
Don't know or unsure	200 (18.0)
Missing	8
Thyroid surveillance	
You review CL's past laboratory results and see that she has undergone yearly thyroid function tests. They have all been normal. What would be your approach to thyroid screening?	
I would repeat thyroid-stimulating hormone and free thyroxine test and plan to check both yearly ^c	843 (76.4)
I would check thyroid-stimulating hormone this year and then discontinue if test is normal	56 (5.1)
I would discontinue thyroid function tests since they have been normal	70 (6.3)
Don't know or unsure	119 (10.9)
Missing	6

^a Correct answers.
^b Percentage were not calculated for answer choice "missing."

And we took the time during this survey to give them a little clinical vignette. And you can't see the vignette there, but it actually was similar to the vignette of story number three. We presented them a Hodgkin lymphoma survivor who received anthracycline chemotherapy as well as mantle radiation, which is the radiation that impacts the neck, the chest, the armpit and below the diaphragm. We asked them about breast cancer surveillance, cardiac surveillance and thyroid surveillance. And it was remarkable what we found among these general internists. Over 90% of internists did not appropriately recommend yearly breast cancer surveillance, 85% didn't appropriately recommend cardiac surveillance and only a quarter didn't appropriately recommend yearly thyroid surveillance but only 5% answered in full accordance with the COG (Children's Oncology Group) guidelines.

PERSPECTIVES ON SURVIVORSHIP CARE: PCPS

- However, in response to a clinical vignette:
 - **90.6%** of respondents did not appropriately recommend yearly breast cancer surveillance
 - **85.1%** did not appropriately recommend cardiac surveillance
 - **23.6%** did not appropriately recommend yearly thyroid surveillance

5.4%
answered in full accordance with
COG guidelines

Question and Answer Choices	Responses, n (%) ^a
Breast cancer surveillance	
In thinking about CL's medical care, how would you approach breast cancer screening?	
I would follow current accepted guidelines for average risk individuals and ask her to begin yearly mammograms when she turns 50	220 (20.0)
I would recommend yearly mammograms starting this year	196 (17.8)
I would recommend every-other-year mammograms starting this year	123 (11.2)
I would recommend yearly breast magnetic resonance imaging and mammograms starting this year	103 (9.4)
Don't know or unsure	458 (41.6)
Missing	10
Cardiac surveillance	
You see that CL had an echocardiogram 6 years after chemotherapy. The echocardiogram was normal. How would you approach cardiac care for this patient?	
I would not proceed with further testing	507 (45.5)
I would refer her at this time to a cardiologist for evaluation and stress testing	81 (7.4)
I would recommend every-other-year echocardiogram ^b	166 (14.9)
I would recommend yearly echocardiogram	85 (7.7)
Don't know or unsure	200 (18.0)
Missing	8
Thyroid surveillance	
You review CL's past laboratory results and see that she has undergone yearly thyroid function tests. They have all been normal. What would be your approach to thyroid screening?	
I would repeat thyroid-stimulating hormone and free thyroxine test and plan to check both yearly ^c	843 (76.4)
I would check thyroid-stimulating hormone this year and then discontinue if test is normal	56 (5.1)
I would discontinue thyroid function tests since they have been normal	70 (6.3)
Don't know or unsure	119 (10.9)
Missing	6

^a Correct answers.
^b Percentage were not calculated for answer choice "missing."


So, this shows that while these primary care doctors are comfortable with taking care of these patients, we have a knowledge gap from the time that we take care of them in the cancer center and send them out to primary care.

SIGNIFICANT GAPS IN PROVIDER KNOWLEDGE

AYA Hodgkin Lymphoma Survivor Vignette

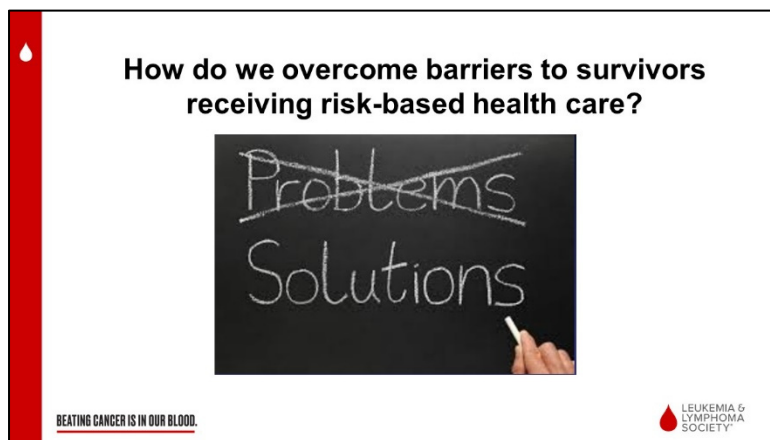
Responses Concordant with COG Guidelines	General Internists (N=1110)	Family Physicians (N=1124)	Pediatric Oncologists (N=665)
Breast cancer screening	27%	16%	66%
Thyroid screening	76%	74%	76%
Cardiac screening	15%	10%	57%
Total	5%	2%	33%

Henderson, et al. *J Clin Oncol* 2010; Nathan P, et al. *J Cancer Surv* 2013; Suh E et al, *Ann Intern Med* 2014

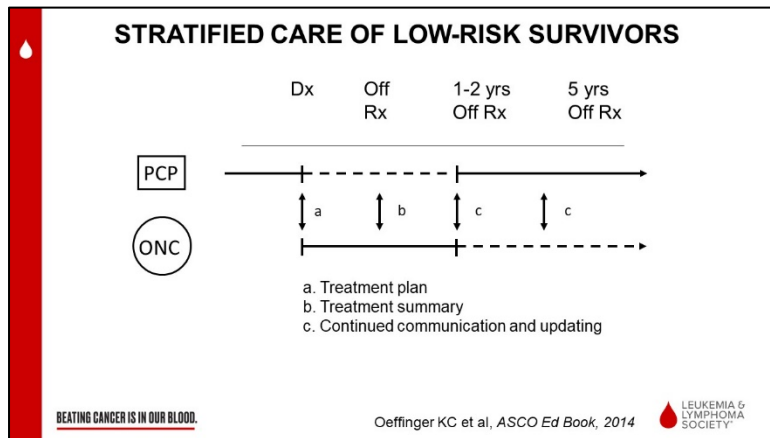


BEATING CANCER IS IN OUR BLOOD.

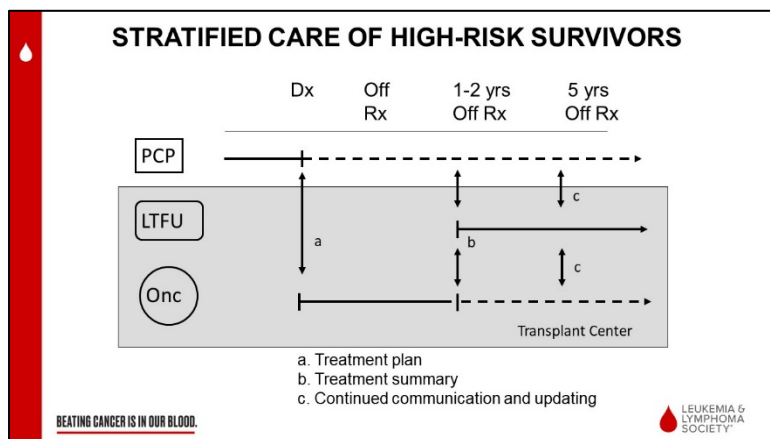
This is another slide showing the significant gaps in screening, and you can see the general internist that I just described to you here as compared to our survey where we went to 1,100 family physicians in North America. This is a study with the American Academy of Family Physicians both in the U.S. and Canada, and we surveyed all pediatric oncologists in the Children’s Oncology Group. And, again, only 2% of the family physicians were in concordance with all three of our questions and only a third of the pediatric oncologists. And while the pediatric oncologists did better, as I noted, these guidelines were developed in the Children’s Oncology Group, so I would hope that these numbers would be higher.



So, I’ve shown you some data that shows our gaps in knowledge. And the question then becomes how do we overcome these barriers to make sure survivors receive their recommend risk-based healthcare?



So, this is a stratified care model that our colleague, Kevin Oeffinger, developed with Dr. McCabe also at Sloan-Kettering (Memorial Sloan-Kettering Cancer Center) where we talked about how we think about our interaction with the primary care doctors both before and after our therapy for cancer. So, you can see, I mean this is basically how we do it now. The primary care doctor or pediatrician is following the patient. You have the cancer diagnosis. These patients then follow with the oncologist, and it almost feels like there's a black box where we aren't doing the best job we can with communicating with the pediatrician. And then two years off therapy this gets transitioned back.



Our new models where we're trying to make a more consistent and collaborative approach to this is the long-term follow-up model where we start to follow these patients two years off therapy and we communicate back and forth to both the primary care doctor and the cancer center.

STRATEGIES FOR OPTIMIZING CARE

- Provide longitudinal, stratified risk-based health care for survivors of childhood blood cancer
 - Dedicated LTFU Programs
 - Partnerships with local providers
- Investigate the health outcomes and health care needs of this population
 - Research is key!
- Educate health care professionals regarding health care of survivors
 - More sessions like this one!

BEATING CANCER IS IN OUR BLOOD.



I think strategies for optimizing care to give this longitudinal risk-based healthcare that I talk about, there's different types of ways. So, we have dedicated long-term follow-up programs. Danielle and I both have the advantage of being one, which, you know, you could say are the gold standard that I follow patients from two years off therapy throughout the lifespan. But even some of the dedicated long-term follow-up programs don't see patients past a certain age. So, when they age out of pediatrics, they have to go find a primary care doctor. So, it's really important in these long-term follow-up programs that we partner with local providers so that there isn't this loss to follow-up that we've demonstrated to you.

I think it's really important that we continue to investigate the health outcomes of this population and the healthcare needs of this population. So, we're giving new therapies all the time for this population, both leukemia and lymphoma survivors. We have CAR (chimeric antigen receptor) T-cells. We have PD (programmed death)-1 inhibitors, brentuximab-vedotin. There are all sorts of immunologic therapies that we're now giving patients that we really don't know how they impact their long-term health, and we need to monitor that so we know how to care for them in the future. And research and continued research is the key to this.

We also really need to think about educating healthcare professionals both within the cancer center and outside the cancer center, and we need a diverse population of healthcare professionals – educated nurses, social workers, psychologists as well as our physician colleagues. This kind of session is key. Danielle and I were so excited to be able to talk to all of you to make this connection and know that this education is happening.


CANCER TREATMENT SUMMARY

SUMMARY OF CANCER TREATMENT			
Date of preparation: 01/20/20			
Name: Jane Doe		Date of Birth: 01/01/1981	
Cancer Diagnosis: Hodgkin's lymphoma			
Treatment center: Children's Hospital of Philadelphia			
Date of diagnosis: 01/01/2019		Age at diagnosis: 14 years	
Date of completion of therapy: 08/01/2019			
Surgery			
Date	Procedure		
01/01/2019	Surgery of node		
02/01/2019	Surgery of node		
Radiation Therapy			
Date start	Date Stop	Field	Dose (cGy)
01/01/2019	01/01/2019	neck/chest	2000
Chemotherapy			
Drug Name	Dose (units or mg/m ²)		
Cyclophosphamide (Cytoxan)	Yes - 8500 mg/m ²		
Procarbazine	Yes		
Vinorelbine	Yes - 7241 mg/m ²		
Follow-up			
Any cancer history	Complete physical exam every year		
Second cancers, especially breast cancer	Inspection and palpation of irradiated skin and soft tissue every year Breast self-exam every month Clinical breast exam every 6 months Mammogram every year starting at age 29		
Heart problems	Echocardiogram every 2 or more years after completion of therapy		
Lung problems	Baseline pulmonary function tests at 2 or more years after completion of therapy		
Thyroid problems	Thyroid profile (free T ₄ and TSH) every year		
Life-threatening infection	Seek medical attention with fever 101°F for blood culture and antibiotic		

**Screening recommendations from the Cancer Research Children's Oncology Group Long Term Follow-Up Guidelines at www.cancertherapy.com

See Project Vision website www.leukemia-lymphoma.com for further information about health care following treatment for lymphoma disease.


BEATING CANCER IS IN OUR BLOOD.



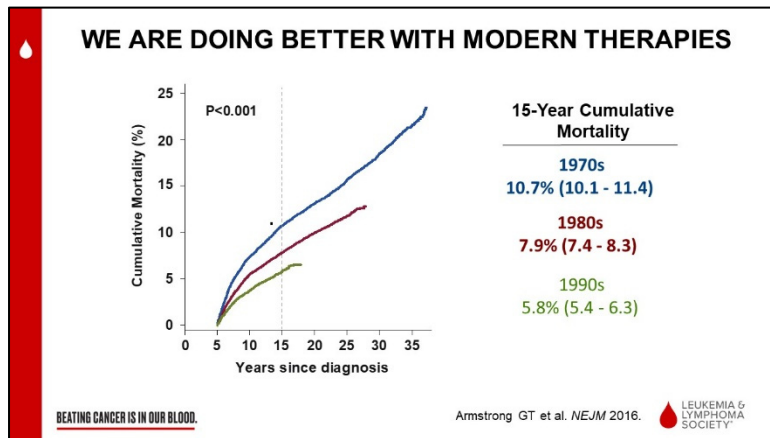
The other thing that is important is that survivorship care plan that we talked about. The Institute of Medicine recommended that all survivors get a survivorship care plan. This is an example from Sloan-Kettering. We use a similar one at the University of Chicago that is a cancer treatment summary. So up here at the top you have the patient's name, her birthday, the name of the diagnosis, where she was diagnosed, the date of diagnosis, when she came off therapy, and then a brief summary of her surgeries, her radiation therapy, her chemotherapy drugs and exposures. And then forward down at the bottom it's the key follow-up that needs to happen for these patients. What do you need to be thinking about and what are the tests that need to be followed and at what age group?

How does the understanding of long-term outcomes of cancer survivors impact cancer treatments?

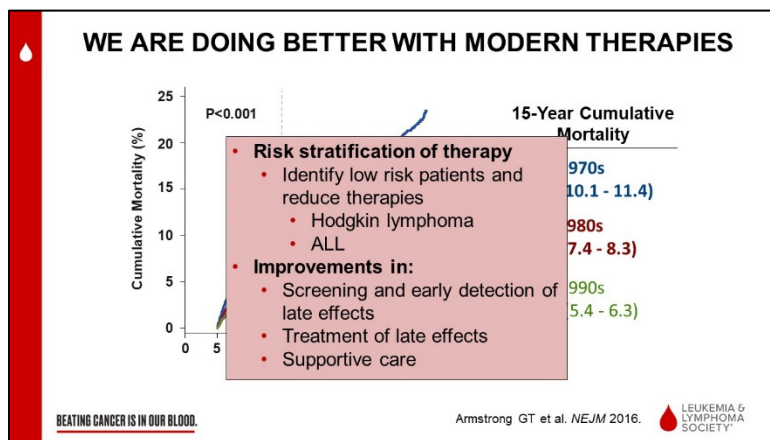
BEATING CANCER IS IN OUR BLOOD.



So, I just wanted to end here with how this understanding of long-term outcomes of cancer survivors is so important not just for the care of those survivors but how it impacts cancer treatment.



So first I want to end on a really good note. We have learned in the past few years that we really are doing better in the long term with moderate therapies. So, Greg Armstrong is the principal investigator of the Childhood Cancer Survivor Study. And in the past few years, we went from the cohort being 14,000 survivors to actually including another 10,000 survivors treated in more modern eras to now we're following almost 24,000 of these survivors. And so, we were able to look at the mortality rates or death rates based on the decade of treatment. And you can see in the 1970s at 15 years after therapy 10% of our survivors have died but in the 1980s this went below 8% and now, we're below 6%.



And we think this is due to risk stratification of therapy, so we've been able to understand who are low-risk patients and how we can reduce those therapies. And we've done this both with Hodgkin lymphoma and ALL, and we're continuing to do it both where we have open trials in high-risk Hodgkin lymphoma trying to tweak who gets radiation, bringing in an immunotherapy and, similarly, for ALL we are learning more and more about the biology of this disease such that we can minimize the therapy in those that we can. We also have improved screening and early detection of late effects, and as I described to you throughout this talk today, we're getting better at treatment of late effects and we're also much better at supportive care.

SUMMARY

- Survivors of childhood and adolescent blood cancer face lifelong, long-term risks
- Many late effects are modifiable
- Goal of risk-based survivor care:
 - Reduce morbidity and mortality
 - Enhance quality of life
- Importance of shared-care model involving oncologist/survivorship team, primary care provider, and the patient/family

BEATING CANCER IS IN OUR BLOOD.



So, in summary, I think that Danielle and I have shown that survivors of childhood and adolescent blood cancer face lifelong, long-term health risks. And some of these health risks are really modifiable, and so it's important that patients receive lifelong, risk-based survivor care to make sure that the morbidity and mortality of these health risks are minimized. And that, in turn, will help with quality of life. We think it's important to have a shared care model where we involve both the oncologist, the long-term follow-up survivorship team as well as the primary care provider and bringing in the primary care provider throughout treatment and the patient and the family.

I want to turn this over now to LLS to talk a little bit about resources for our survivors. And it was my pleasure to speak with all of you today, and I look forward with Danielle to answer some questions.

Lauren Berger, MPH

Thank you, Dr. Henderson and Dr. Friedman, for an informative and important presentation. I am now pleased to share resources for you and for your patients, and following this, as Dr. Henderson said, we'll have a question and answer session, taking questions from the live audience.

RESOURCES FOR HCPS

- Free CME & CE courses – www.LLS.org/CE
- Podcasts – www.LLS.org/HCPpodcast
- Staying Connected: Facilitating the Learning Experience During and After Cancer Treatment – www.LLS.org/StayingConnected



BEATING CANCER IS IN OUR BLOOD.




The Leukemia & Lymphoma Society offers continuing education activities, including CME/CE webinars, such as this one. For information, please visit the CE web page listed on this slide – LLS.org/CE.

Our Podcast Series for Healthcare Professionals, Treating Blood Cancers, features episodes on topics such as Long-term and Late Effects of Childhood Cancer, Challenges for Young Adult Cancer Survivors, and Treating Children with Cancer During the COVID-19 Pandemic.


Staying Connected: Facilitating the Learning Experience During & After Cancer Treatment, is an online program focused on educating professionals on the effects of childhood and AYA cancer to enable them to support survivors, as they continue their education journey. The interactive modules on treatment and long-term and late effects, education challenges, psychosocial issues, and grief, include video clips of children, family members, and healthcare and education professionals. It offers six and a half hours of continuing education credit. You can learn more at LLS.org/StayingConnected.

RESOURCES FOR HCPS AND PATIENTS

- LLS Online Community
HCP, Patient/Survivor & Caregiver account types:
www.LLS.org/community
- LLS Children's Initiative: Cures & Care for Children
\$100 million multi-year endeavor to attack pediatric blood cancer
- Global precision medicine clinical trial/pediatric acute leukemia in collaboration w/NCI & COG:
www.LLS.org/PedAI



BEATING CANCER IS IN OUR BLOOD.

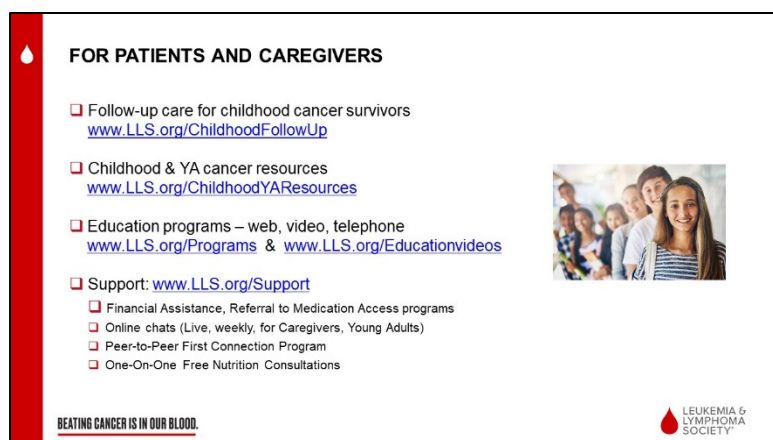


LLS' online community enables you to connect with other healthcare professionals and to access summaries of journal articles. You can also refer patients and caregivers to sections specifically for them. Use the URL on this slide to learn more and to participate.

TRANSCRIPT

Our new Children's Initiative will address the urgent need for new, more precise, and more effective treatments for children with cancer. LLS is funding research grants focused on deepening our understanding of the unique genetic causes and molecular biomarkers of pediatric blood cancer and how best to target them. The goal is to accelerate more curative therapies, with fewer side effects for children and young adults. Among the most promising treatment approaches is harnessing the power of the immune system to fight cancer. We're also supporting research to address the long-term effects of treatment, such as heart damage, infertility, and cognitive impairments.


We are excited to collaborate with the National Cancer Institute and the Children's Oncology Group to launch a global precision medicine clinical trial for children with acute leukemia. This PedAL trial will take place at more than 200 sites worldwide and will test multiple targeted therapies for children who experience a relapse of acute leukemia.



FOR PATIENTS AND CAREGIVERS

- ❑ Follow-up care for childhood cancer survivors
www.LLS.org/ChildhoodFollowUp
- ❑ Childhood & YA cancer resources
www.LLS.org/ChildhoodYAResources
- ❑ Education programs – web, video, telephone
www.LLS.org/Programs & www.LLS.org/Educationvideos
- ❑ Support: www.LLS.org/Support
 - ❑ Financial Assistance, Referral to Medication Access programs
 - ❑ Online chats (Live, weekly, for Caregivers, Young Adults)
 - ❑ Peer-to-Peer First Connection Program
 - ❑ One-On-One Free Nutrition Consultations


BEATING CANCER IS IN OUR BLOOD.



LLS offers resources on disease and survivorship, including follow-up care for childhood and YA cancer survivors. I encourage you to access these resources via the user-friendly URLs on this slide and to share them with the patients and families you treat. We have various patient - telephone and web education programs, videos and podcasts and also offer important financial and other support services.

Our newest patient resources include Free Mobile Apps, such as *Coloring for Kids*, which allows children to express their creativity and offers activities to help them learn about blood cancer and its treatment, and *LLS Health Manager*, which helps patients and caregivers track side effects, medication, food and hydration, as well as questions for their healthcare team.

FREE GUIDES, BOOKLETS, AND FACT SHEETS
For Patients, Caregivers and Professionals
www.LLS.org/Booklets



BEATING CANCER IS IN OUR BLOOD. LEUKEMIA & LYMPHOMA SOCIETY®


You can download or suggest that your patients download or order free copies of booklets and fact sheets displayed on this slide or any of our other booklets on disease and treatment, finances, and psychosocial support, at LLS.org/booklets. These materials are available in several languages.

We know that you want to know that the materials you provide for your patients are accurate. LLS educational materials are reviewed or written by a medical or professional content expert whose name, place of practice, and credentials are cited on the document.

ADDITIONAL RESOURCES

Information Resource Specialists: one on-one information & support on treatment, financial & psychosocial resources www.LLS.org/IRC

Clinical Trial Nurse Navigators: RNs with expertise in blood cancers work one-on-one with patients, caregivers or HCPs, or You can Refer a patient www.LLS.org/CTSCreferral



An extension of your team, providing support to you & your patients

- ☐ Phone: (800) 955-4572, M-F, 9 am to 9 pm ET
- ☐ Email: infocenter@LLS.org
- ☐ Live chat: www.LLS.org/InformationSpecialists

BEATING CANCER IS IN OUR BLOOD. LEUKEMIA & LYMPHOMA SOCIETY®

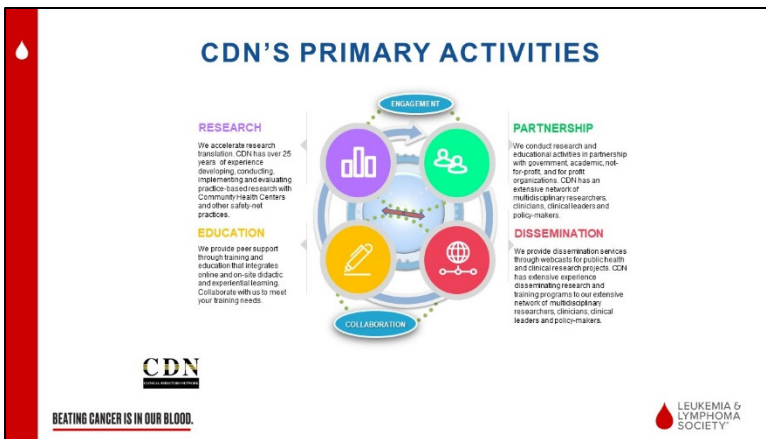
The Leukemia & Lymphoma Society's Information Specialists are master's level oncology social workers, nurses, and health educators who provide personalized assistance through treatment, financial and psychosocial challenges and give accurate, up-to-date, disease, treatment and support information. They help patients develop questions to ask you, their healthcare team, and will send copies of booklets and other materials free of charge. Information Specialists also talk to healthcare providers about situations you may be encountering with your patients. They can provide resources or do some research if needed and get back to you. They can also refer you or your patients to our regional staff for additional resources. Information Specialists assist callers in several languages and through translations in many more languages.

We are pleased to also offer free one-on-one nutrition consultation with our registered dietician.

TRANSCRIPT

Our clinical trial nurse navigators, who are registered nurses with expertise in blood cancers, work one-on-one with patients and caregivers via telephone to find an appropriate clinical trial and to assist through the clinical trial process.

All of these specialists can serve as additional resources to your healthcare team. To refer your patient, or for you to contact us directly, please use the information listed here to call (800) 955-4572 or connect via email or chat.



And our collaborator on this program, Clinical Directors Network, is an A H R Q (Agency for Health Research and Quality) designated Center of Excellence for practice-based research and learning. And CDN develops, conducts, implements and evaluates practice-based research with community health centers and other safety-net practices in partnership with governments, academics, not-for-profit and for-profit organizations.

CDN WEBCASTS, DISSEMINATION, TRAINING, SUPPORT TOOLS & CONTINUING MEDICAL EDUCATION (CME) & CONTINUING MEDICAL EDUCATION (CME) SUMMER 2020

UPCOMING WEBINAR SCHEDULE

Thursday, July 16, 2020, 1:00 PM - 2:00 PM ET
Survivorship Care for Childhood and Adolescent Blood Cancer
Presented by: Eric S. Sullivan, MD, MPH, FAACP, Professor of Pediatrics, Director, Childhood, Adolescent and Young Adult Survivorship Center, Director, Cancer Survivorship and Co-Leader, Cancer Prevention and Control Program, Comprehensive Cancer Center, The University of Chicago, Chicago, IL
Danielle Novinsky Friedman, MD, MS, Assistant Member, Pediatric Long-Term Follow-up Program, Memorial Sloan-Kettering Cancer Center, New York, NY
Sponsored by: The Leukemia & Lymphoma Society (LLS) and Clinical Directors Network, Inc. (CDN)

Friday, July 17, 2020, 12:00 PM - 1:00 PM ET
Opioid Prescribing in the Era of COVID-19
Presented by: Juanita L. Daniels, MD, MEd, FAAP, Associate Professor of Medicine, Division of General Internal Medicine, Albert Einstein College of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center
Hector R. Perez, MD, MS, Assistant Professor of Medicine, Division of General Internal Medicine, Albert Einstein College of Medicine and Montefiore Medical Center
Sponsored by: The Opioid Post-Marketing Requirements Consortium (OPRC), Bureau Healthcare, Inc. Virtual Training Series (AHRQ), Grant No. 1P30-HS-021607 and Clinical Directors Network, Inc. (CDN)

Friday, July 24, 2020, 1:00 PM - 2:00 PM ET
See in the Time of COVID-19
Presented by: Kenneth H. Mayer, MD, Medical Research Director, Family Health, Co-Director, The Family Institute, Professor of Medicine, Harvard Medical School, Harvard Physician, Infectious Disease Division, Beth Israel Deaconess Medical Center
Sponsored by: CDN Center of Excellence (COE) for Practice-based Research and Learning, Inc. Virtual Training Series (AHRQ), Grant No. 1P30-HS-021607 and Clinical Directors Network, Inc. (CDN)

PREVIOUS TOWN HALLS/WEBINARS

COVID-19 Virtual Town Hall: Leading in a Time of Rapid Change
Presented by: Eric S. Sullivan, PhD, Research Director, Center for Primary Care of Harvard Medical School, Lecturer, Department of Global Health and Social Medicine, Harvard Medical School
John Lu, PhD, MPH, Assistant Professor of Public Health Policy and Management, School of Global Public Health, Stern School of Business (Jaffar), NYU
Discussion: 1) Cultivating team culture and resilience; 2) Maintaining relationships and meaning in work
COVID-19 Virtual Town Hall with CDN Board of Directors: Addressing Mental Health Issues for Staff and Patients & Reductions in Workforce and Patient Volume
Presented by: CDN Board of Directors
Discussion: 1) Mental health of their staff and patients, 2) implementing stress management techniques, and 3) tracking/rapid reductions in patient volume
Prescription Pain Medication Use in the Community
Presented by: Linda B. Cotler, PhD, MPH, FAPE, Associate Dean for Research, College of Public Health and Health Professions and Dean's Professor of Epidemiology at the University of Florida
Sponsored by: The Opioid Post-Marketing Requirements Consortium (OPRC), Bureau Healthcare, Inc. Virtual Training Series (AHRQ), Grant No. 1P30-HS-021607 and Clinical Directors Network, Inc. (CDN)
The Resilient Researcher in Research Training: Diversity and Inclusion in Clinical Research
Presented by: Sylvia Teet-Adams, PhD, RN, NIA, Near Admiral, US Public Health Service Commissioned Officer, Principle Deputy Assistant Secretary for Health
Sponsored by: The Holborn Family Center for Research Nursing, Rockefeller University Center for Clinical and Translational Science (NIA/AGS), Grant No. R01HL175-000043, Clinical Directors Network, Inc. (CDN) and the NY PRIN Virtual Training Series (AHRQ) 1P30-HS-021607

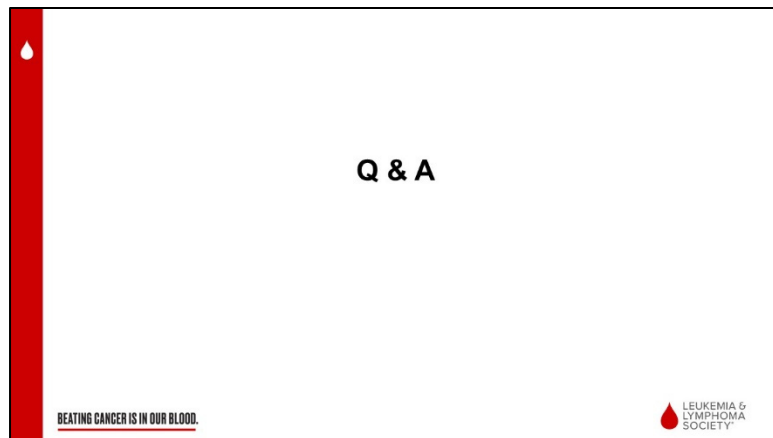
Visit the CDN Webcast Library! View our many archived CME-accredited webcasts at: www.cdnlib.org/online-library

BEATING CANCER IS IN OUR BLOOD. WWW.CDNNETWORK.ORG

LEUKEMIA & LYMPHOMA SOCIETY

CDN also provides continuing educational research and quality improvement support to primary care practices and other healthcare professionals through developing and disseminating CME (continuing medical education) accredited training, both onsite and online through interactive websites. CDN's distance learning activities carry continue education credits and here is a listing of CDN's upcoming webinars.

QUESTION-AND-ANSWER SESSION



Lauren Berger, MPH

It is now time for the Question-and-Answer portion of our program. So, the first question, “As an oncology nurse and pediatric cancer survivor, what recommendations do you have to establish care with a long-term survivor clinic for pediatric cancer survivors? Most survivorship clinics will not accept patients five years past treatment.”

Danielle Novetsky Friedman, MD MS

I think this is a huge issue and it’s something that we struggle with. In our center, we’re really lucky that we have a program that continues lifelong. So, in the program in which I work, we take care of patients basically through college and there’s no limit in terms of are you five years off treatment, ten years off treatment. We are thrilled to participate in care at any timepoint but then we also have a dedicated program for adult survivors of childhood cancer. So we don’t always encounter this on a daily basis, but I know online there are listings of survivorship programs¹ that I can try to send to Lauren after this, and it is an area that we as a survivorship community really have to think about and do better with because, certainly, there is a need. And it’s a great question and it’s something that we do need to address systematically.

Tara O. Henderson, MD, MPH, FASCO

I agree. Similar to Danielle, we see patients who weren’t treated here. One of the requirements for our program is that we do want to get a summary of treatment. And I had seen on the questions on the side that someone asked about this question, like what if you’ve gone so far you don’t know your

¹ Resources for this Program are available at <http://www.cancereducation.com/cancersyspagesnb/a/lls/lls18123arc/lls18123arcresources.html>

TRANSCRIPT

treatment? And I think that that is really the key for even the patients that can't get into a long-term follow-up program.

Calling back to your treating oncologist and asking for a treatment summary, that gives you the knowledgebase and power to even go to your primary care doctor and get that risk-based healthcare. So even if you can't get into a specialized long-term follow-up program, if you can get that treatment summary from your treating oncologist, then you can communicate with the primary care doctor. That will give the primary care doctor a way to get back in touch with the treating oncology program and they can guide the primary care doctor to help give the care that the patient would need.

Lauren Berger, MPH

Thank you for that question and those really important answers. Yes, we did receive several questions on similar topics.

“You talked about serial ovarian labs for females after radiation and/or alkylating agents for Hodgkin lymphoma. Do you also draw serial AMH (anti-Mullerian hormone) levels as a potential measure of ovarian reserve in order to further counsel female survivors about premature ovarian insufficiency?”

Tara O. Henderson, MD, MPH, FASCO

It's a great question. We're not routinely longitudinally following AMH at this point. It's something that's being studied in the survivors of adolescent and childhood cancer, but we work closely with our reproductive endocrinology colleagues in terms of referring these patients early. But in terms of in the long-term follow-up clinic following AMH serially, that's not a standard of care in our practice at this point. I don't know, Danielle, if you have a different thought.

Danielle Novetsky Friedman, MD MS

Yes, it's especially tricky because from the data, which are limited, that have been published in childhood cancers survivors, we know that AMH levels aren't necessarily reliable in women who are younger than age 25 and there are no normative values. So certainly, in our clinic, where we follow a lot of high-risk survivors, we talk about egg freezing as a means of fertility preservation as soon as girls get their periods if their LH (luteinizing hormone) and FSH (follicle stimulating hormone) levels are normal. And we know that when we send them to the reproductive endocrinologist, the first thing they get is this AMH level which they use as a criterion for who should move forward and who shouldn't. So, in many ways we are stuck, and it's an excellent question, but we just don't have the data at this point to support doing serial AMH levels even though, you know, we may get there a couple years from now.

Lauren Berger, MPH

Thank you. The next question, “Do you have medication recommendations and weight loss strategies for survivors with metabolic syndrome, especially suffering from obesity, and is there expertise that we can refer out to?”

Danielle Novetsky Friedman, MD MS

This is sort of what my research focus is on. I'm very interested in mechanisms leading to metabolic syndrome in our childhood cancer survivors and in diabetes and other things. And, again, unfortunately, the short answer is no. We don't have any specific recommendations that are different from what we would think about in the general population. We talk a lot about diet and eating a lot of fruits and vegetables and physical activity recommendations. We have a nutritionist who's a critical part of our program and really encourage our patients to see her. She'll do Skype visits after the in-person visit. So, you know, this is another one where I hope I'll have a better answer a couple of years from now, but today we don't have anything specific that is different from what we would recommend for any other person with metabolic syndrome or diabetes at a young age.

Lauren Berger, MPH

Okay, thank you. We received several questions asking for more explanation and management for long-term cognitive and neurological issues related to children and young adults, such as problems with attention, focus, memory from both chemotherapy and radiation.

Tara O. Henderson, MD, MPH, FASCO

I think that this is something that Danielle highlighted and that, you know, especially leukemia survivors, I mean, in general, patients with lymphoblastic leukemia who come to see us now, in general, these patients do extraordinarily well with moderate therapy if they just get standard upfront treatment. But one of the issues that we do see with giving steroids and methotrexate at a young age is there can be impact on executive function and learning.

Now there's an element of this that we don't necessarily measure what you're at risk for before getting leukemia, so there, of course, is genetics that could contribute to this. But every time we see a new leukemia patient in clinic, we talk about school and refer to neuropsychology pretty much consistently. I have the privilege of having a neuropsychologist sit with me in clinic and we have them refer these patients to these specialists so that they can interact with the schools. But I think that making sure that learning is addressed and that this is communicated appropriately with schools and patients are given the accommodations that they need is extraordinarily helpful for this population. And so just always, you know, having a low threshold to refer I think is the key. If there's any concern about school or any concern about psychosocial issues, I always work with my neuropsychology, psychology and social work colleagues to make sure that the patients and the families are getting the support they need.

Lauren Berger, MPH

I'll add another plug for The Leukemia & Lymphoma Society Staying Connected program because there's a module specifically focusing on this and education issues ([LLS.org/StayingConnected](https://lls.org/StayingConnected)).

And the next question is about premature aging, "Can you please provide more information about what this means in terms of aging and what this really affects?"

Tara O. Henderson, MD, MPH, FASCO

When we talk about premature aging, what we've been able to do is compare. I think our colleague Kirsten Ness; she's an epidemiologist and physical therapist at St. Jude, and she has done this work looking at measures of frailty, so basically, how quickly you walk, what your grip strength is, your muscle mass. And they looked at these standard measures of frailty which sort of tells us if you're aging or not in childhood cancer survivors and then compared them to people in the general population who are around the same age, and then looked at people with cardiovascular disease.

And so basically what we found is that a 35-year-old childhood cancer survivor has similar measures of frailty as someone who's 50 or 60 in the general population. So, it's showing that there's loss of muscle mass and strength, and it looks like that getting chemotherapy and radiation at a young age sort of accelerates the aging process.

The patients that Dr. Ness looked at were survivors treated in earlier generations than now, so I want to say that our treatments today are very different than the treatments that they were giving at that time, so we really have, for example, Hodgkin lymphoma patients, much fewer of them get radiation. If they do get radiation, the dose is lower, and the beam is in a much smaller field. So, my guess is that when we see this generation of survivors get to the 30–35-year-old age range, we may not see the same dramatic increase in aging that we're seeing now. But that's sort of what we're thinking about when we think about aging.

Danielle, I don't know if you wanted to add to that.

Danielle Novetsky Friedman, MD MS

I was going to say the same thing.

And just that the types of chronic conditions we're seeing in 20 and 30-year-olds you typically wouldn't see in this age group. So certainly, we think about frailty, but we also think about the fact that we're seeing chronic health conditions that you would typically see in 60-year-olds in 30-year-olds who were treated for cancer 20 years younger or 20 years earlier.

Lauren Berger, MPH

Thank you. And we'll take one more question, and that is, "Is there a need for males to get breast screening?"

Tara O. Henderson, MD, MPH, FASCO

Actually, there isn't, so we are not seeing men getting breast cancer after chest radiation, so that is one area that we don't need to worry about. I did see a question in there that I'll follow that up with about genetic predisposition. And I do think that what we're learning more about is that more childhood and adolescent cancer survivors have genetic predisposition than we previously realized. So, when I trained in the early 2000s, we thought this number was about 5% and now it's looking

TRANSCRIPT

more like the rate is, you know, 11% to 15%. And so we are recommending that survivors see genetic counselors and get a really detailed family history to see if they potentially should get genetic testing because if there is association with any cancer predisposition, those survivors could get appropriate cancer screening as well based on what that predisposition gene is. So, we are learning every day that thinking about cancer predisposition in this population is really important. And we actually have a lab here at the University of Chicago. My colleague, Lucy Godley, is really focused on the genetic predisposition of hematologic malignancy. And so, we can see that there are, for example, families that have Hodgkin lymphoma in them, but we've not identified a specific gene. And so, she's actually doing large studies where she's doing skin biopsies and testing of families with lymphoma and heme malignancies to try to understand even more what underlies some of the families that get these cancers.

Lauren Berger, MPH

Well thank you for answering not only that additional question but all of your questions. We've seen so much interest and we certainly will have more information on our website as well as plan a future program.

CLOSING REMARKS



Lauren Berger, MPH

We hope the information presented in this webinar will be useful in your work with patients and their families.

Please be sure to complete the webinar posttest and the evaluation using the link on the screen. If you are seeking continuing education credit for your participation, upon completion of these steps, your certificate will be generated as a PDF.

If you have any questions about this or other LLS continuing education courses, please email us at ProfEducation@LLS.org.

Thank you so much to Dr. Henderson and Dr. Friedman for volunteering your time and expertise and for your continued dedication to patients and fellow healthcare professionals. We wish you a wonderful day and look forward to your participation in future professional education activities.