

Facts About Blood Cancer Survivorship Treatment and Ongoing Patient Care

Introduction

An estimated 1.5 million Americans are currently living with, or in remission from, blood cancer.¹ The ongoing medical needs of these individuals are distinctly different from the general population due to the physical, psychological, and financial effects of their disease and treatment. Late physical effects can present years or decades after treatment and, therefore, require therapy-specific surveillance and management.²

With the 5-year relative survival rates of blood cancers improving drastically over the last 60 years, including a decrease in the mortality rate of leukemia by 19.5 percent, lymphoma by 35.5 percent and myeloma by 17.5 percent from 2000 to 2017, the importance of high-quality survivorship care cannot be understated.¹

Survivorship care focuses on a patient's overall health and extends beyond the active treatment of cancer. It is a life-long pursuit that can involve multiple members of the patient's healthcare team, including hematologist-oncologists, community and academic-based oncologists, primary care physicians, physician assistants, nurses, social workers, allied health professionals, and numerous other specialists. However, despite the importance of quality survivorship care, models for delivering this care are not well defined.

Studies on care delivery underscore the importance of a collaborative approach to survivorship care. While many cancer survivors receive post-treatment care in the primary care setting, one study found that only 5.4% of general internists accurately answered three surveillance-related questions regarding an adult survivor of Hodgkin lymphoma.^{3,4} This research reinforces the importance of survivorship education to support providers throughout the entire continuum of care.

This fact sheet will review current topics including long-term and late effects of therapy, follow-up care and monitoring, survivorship care planning, health promotion, and resources for blood cancer survivors and healthcare providers.

Who is a Cancer Survivor?

"In cancer, survivorship focuses on the health and well-being of a person with cancer from the time of diagnosis until the end of life. This includes the physical, mental, emotional, social, and financial effects of cancer that begin at diagnosis and continue through treatment and beyond. The survivorship experience also includes issues related to follow-up care (including regular health and wellness checkups), late effects of treatment, cancer recurrence, second cancers, and quality of life. Family members, friends, and caregivers are also considered part of the survivorship experience."

- National Cancer Institute

In this fact sheet, the term "survivor" refers to any person who has ever been diagnosed with cancer. It is important to note, however, that some individuals do not feel comfortable being described as a survivor, especially during active treatment. Care should be taken when selecting terminology to use with patients.

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Highlights

- » Long-term and late effects of therapy can persist, and sometimes increase, over time. These effects are a major cause of morbidity and mortality among blood cancer survivors.
- » Blood cancer survivors need risk-based follow-up care and monitoring. Their ongoing medical needs are distinctly different from the general population due to their disease and treatment.
- » Survivorship care planning helps to ensure that blood cancer survivors receive high-quality care based on their individual risks and exposures. Guidelines are available to help providers with care planning.
- » Health promotion activities decrease the risk of comorbidities and improve survivors' quality of life.

Long-term and Late Effects of Therapy

Long-term and late effects of therapy persist, and sometimes increase, over time.⁵ Long-term effects refer to side effects that continue for months or years after treatment. With some chronic blood cancers, therapy and its side effects may continue for years or even life. Late effects refer to side effects that do not appear until after treatment. Some late effects, like secondary malignancies and anthracycline-induced heart failure, may present many years or decades after treatment.⁶

Long-term and late effects are a major cause of morbidity and mortality among cancer survivors. One study of siblings found that 24-year-old childhood cancer survivors had the same cumulative incidence of severe, life-threatening, and fatal health conditions as their 50-year-old siblings.⁷ Similarly, another study of childhood cancer survivors found that the 20-year cumulative incidence of at least one grade 3–5 chronic condition for survivors diagnosed in the 1970s, 1980s, and 1990s was 33.2%, 29.3%, and 27.5%, respectively.⁵ This is in contrast to siblings in the study who had a 20-year cumulative incidence of 4.6%.⁵

Because long-term and late effects vary based on the type of treatment a patient received, it is important that survivors receive exposure-specific surveillance and management. Common agents used in the treatment of blood cancers are discussed below.

Chemotherapy / Anticancer Drug Therapy

The powerful chemicals and drugs used to kill cancer cells in the body have different side effect profiles that should be considered when caring for survivors. Below is a high-level review of long-term and late effects of agents commonly used to treat blood cancers. Lifelong

surveillance and follow-up care should be tailored to each survivor's prior therapeutic exposures.

- **Alkylating agents** work by damaging the cancer cell's DNA. Major long-term and late effects associated with alkylating agents include hormonal dysfunction, low sperm counts, ovarian hormone deficiencies, infertility, myelodysplasia, acute myeloid leukemia (AML), pulmonary fibrosis, cataracts, urinary tract toxicity, bladder cancer, and renal toxicity.^{6,8} Examples of alkylating agents used in the treatment of blood cancer include:
 - carmustine (BiCNU[®])
 - chlorambucil (Leukeran[®])
 - cyclophosphamide (Cytoxan[®])
 - melphalan (Alkeran[®])
 - procarbazine (Matulane[®])
- **Antimetabolites** kill cancer cells by mimicking the substances cancer cells need to build DNA and RNA. Neurocognitive deficits, hepatic dysfunction, and reduced bone mineral density are all potential long-term and late effects.⁸ Examples of antimetabolites used in the treatment of blood cancer include:
 - cytarabine (cytosine arabinoside, ara-C, Cytosar-U[®])
 - fludarabine (Fludara[®])
 - methotrexate (Rheumatrex[®], Trexall[®])
- **Antimitotic drugs** block cancer cell mitosis, thus preventing cancer cells from multiplying. Long-term and late effects include peripheral neuropathy and vasospastic attacks.⁸ Antimitotic drugs used to treat blood cancer include:
 - vinblastine (Velban[®])
 - vincristine (Oncovin[®])
- **Antitumor antibiotics**, including anthracyclines, treat cancer by interfering with DNA and RNA synthesis. Long-term and late effects include AML, cardiac toxicity, and pulmonary toxicity.^{6,8} Examples of antitumor antibiotics include:
 - bleomycin (Blenoxane[®])
 - daunorubicin (Cerubidine[®])
 - doxorubicin (Adriamycin[®], Doxil[®])
 - idarubicin (Idamycin[®])
 - mitoxantrone (Novantrone[®])

** mitoxantrone is an anthracycline analog*

- **Corticosteroids** are hormones used in high doses for treatment of leukemia, lymphoma, and myeloma. They also work as immunosuppressants in the treatment of graft-versus-host-disease (GVHD) following allogeneic stem cell transplantation. Reduced bone mineral density, osteonecrosis, and cataracts are potential long-term and late effects.⁸ Examples of corticosteroids used to treat blood cancer include:
 - dexamethasone (Decadron[®])
 - hydrocortisone
 - methylprednisolone (Medrol[®])
 - prednisone

- **DNA-repair enzyme inhibitors** destroy cancer cells by attacking proteins involved in DNA repair. Long-term and late effects include AML and myelodysplastic syndromes.⁸ Examples of DNA-repair enzyme inhibitors include:
 - etoposide (VP16, Etopophos[®], Toposar[®], VePesid[®])
 - teniposide (Vumon[®])
 - topotecan (Hycamtin[®])

- **Heavy metals** work by inhibiting cell division. Long-term and late effects include ototoxicity, peripheral neuropathy, renal toxicity, hormone dysfunction, infertility, myelodysplasia, and AML.⁸ Examples of heavy metals include:
 - carboplatin (Paraplatin[®])
 - cisplatin (Platinol[®])

- **Immunomodulators** modify the immune system's response and are used in the treatment of myeloma and other conditions. Neuropathy is a potential long-term side effect. Examples used in the treatment of myeloma include:
 - lenalidomide (Revlimid[®])
 - thalidomide (Thalomid[®])

- **Proteasome inhibitors** inhibit proteasome function and are used in the treatment of myeloma. Long-term and late effects include peripheral neuropathy. Examples of proteasome inhibitors include:
 - carfilzomib (Kyprolis[®])
 - ixazomib (NINLARO[®])
 - bortezomib (Velcade[®])

The Children's Oncology Group (COG) has developed exposure-based guidelines for individuals who received chemotherapy as a child, adolescent, or young adult. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) also offers guidance related to long-term and late effects.

Visit:

- www.survivorshipguidelines.org/ to view *COG Long-term Follow-up Guidelines*
- www.NCCN.org (search for *Survivorship Guidelines* in upper right search box)

Immunotherapy

Immunotherapy, or biological therapy, works by activating a patient's immune system to fight cancer.

The long-term and late effects of novel immunotherapies are still a subject of active research. The most common immediate side effects of immunotherapy include flu-like symptoms, but more severe symptoms such as hypotension, cytopenia, shortness of breath, and allergic reaction are also possible. Some side effects can occur weeks or months following treatment.^{9,10} Inflammatory and autoimmune responses triggered by immunotherapy can be irreversible or deadly without intervention.^{9,10} Types of immunotherapies used in the treatment of blood cancer include:

- Chimeric antigen receptor (CAR) T-cell therapy
- Cytokine treatment
- Donor lymphocyte infusion
- Monoclonal antibody therapy
- Radioimmunotherapy

CAR T-cell therapy is a unique type of immunotherapy that involves reengineering a patient's own T cells in a laboratory then reinfusing them back into the patient. The side effects of CAR T-cell therapy are typically reversible, but deaths have been reported. Potential side effects include:

- Cytokine-release syndrome (CRS)
- Macrophage activation syndrome (MAS)
- Neurologic toxicities
- Tumor lysis syndrome (TLS)
- Anaphylaxis
- On-target, off-tumor toxicity
- B-cell aplasia

Patients should be carefully monitored and encouraged to report any abnormal signs or symptoms they experience. If a patient received their CAR T-cell therapy in a center different from where they typically receive cancer treatment, communication between both oncology teams is important to ensure proper long-term management and care.

Visit:

- www.LLS.org/HCPbooklets to view **Facts About Chimeric Antigen Receptor (CAR) T-Cell Therapy**
- www.NCCN.org (search for **Management of Immunotherapy-Related Toxicities** in upper right search box)

Radiation Therapy

Radiation therapy is used in the treatment of some blood cancers. If a patient received radiation therapy, it is important to be aware of the location and dose of the treatment. Some long-term effects of radiation, such as subsequent cancers, can be severe and require early diagnosis and intervention. Two important examples of radiation in the treatment of blood cancers are chest radiation for the treatment of Hodgkin lymphoma and total body irradiation (TBI) administered as part of the conditioning regimen prior to stem cell transplantation.

Survivors who received chest radiation for Hodgkin lymphoma should be routinely monitored for their increased risk of breast cancer, cardiovascular disease, and thyroid dysfunction.^{4,11,12} Compared to the general population, female Hodgkin lymphoma survivors who received chest radiation at young ages have a five to twenty times increased risk of developing breast cancer.¹¹ Late effects of chest radiation for Hodgkin lymphoma include:

- Breast cancer
- Cardiovascular disease
- Thyroid dysfunction

Survivors who received TBI are at risk for numerous late effects.^{8,13} COG has developed detailed guidelines on monitoring survivors who received TBI as a child, adolescent, or young adult. Late effects of TBI include:

- Cataracts
- Dental abnormalities
- Endocrine disorders
- Fertility disorders
- Musculoskeletal growth problems

- Nephrotoxicity
- Neurocognitive deficits
- Osteoporosis
- Pulmonary toxicity
- Secondary malignancies

Visit:

- www.survivorshipguidelines.org/ to view **COG Long-term Follow-up Guidelines**
- www.NCCN.org (search for **Survivorship** in upper right search box)

Stem Cell Transplantation

Hematopoietic stem cell transplantation (SCT) works by infusing healthy hematopoietic progenitor cells into a patient following conditioning with chemotherapy and/or radiation therapy.¹⁴ An autologous SCT uses the patient's own cells while an allogeneic SCT uses cells from a matched donor.

Survivors of SCT are at risk for long-term and late effects of exposures they received before, during, and after transplant. When planning care for a SCT survivor, providers should consider the patient's conditioning regimen, which may have included high-dose chemotherapy and TBI. Providers should also consider the type of transplant the patient received and any post-treatment complications, which in the case of allogeneic SCT may include graft-versus-host disease (GVHD) and subsequent treatment.¹⁵

Long-term and late side effects of SCT can include:¹⁵⁻¹⁷

- Bone disease
- Cardiovascular disease
- Disease relapse
- Endocrine dysfunction
- Graft failure
- GVHD (after allogeneic SCT)
- Infertility
- Late infections
- Organ-specific complications (including liver, kidneys, heart, and lungs)
- Post-transplant lymphoproliferative disorders (after allogeneic SCT)
- Psychosocial concerns
- Secondary malignancies

Patients should be encouraged to report any complications, including symptoms of chronic GVHD following allogeneic SCT. A list of symptoms can be found in Table 1. In addition to monitoring for long-term and late effects, these survivors will also need to be revaccinated with childhood immunizations and should be encouraged to live a healthy lifestyle. They also may need supportive resources related to financial and psychosocial concerns.

Visit:

- www.NCCN.org (search for *Hematopoietic Cell Transplantation* in upper right search box)
- www.astct.org for resources regarding transplantation and cellular therapy

Table 1. Symptoms of Chronic GVHD following Allogeneic SCT ^{14,17,18}

More Often	Less Often
<p>Skin</p> <ul style="list-style-type: none"> • Rash • Redness • Dry, tight, itchy skin • Change in texture • Change in color • Intolerance to temperature changes due to damaged sweat glands • Hair loss, thinning, or greying 	<p>Lungs</p> <ul style="list-style-type: none"> • Shortness of breath • Difficulty breathing • Persistent cough • Wheezing • Bronchiolitis obliterans syndrome
<p>Nails</p> <ul style="list-style-type: none"> • Change in texture • Hard, brittle nails • Nail loss 	<p>Gastrointestinal Tract</p> <ul style="list-style-type: none"> • Loss of appetite • Unexplained weight loss • Nausea • Vomiting • Diarrhea • Stomach pain
<p>Eyes</p> <ul style="list-style-type: none"> • Dry eyes • Tearful eyes • Gritty or painful eyes • Blurred vision • Persistent irritation 	<p>Joints</p> <ul style="list-style-type: none"> • Joint stiffness and pain • Contractures
<p>Mouth</p> <ul style="list-style-type: none"> • Very dry mouth • Pain and sensitivity • Sores • Chapped lips • Gum disease and tooth decay • Lichen planus-like changes 	<p>Female Genitalia</p> <ul style="list-style-type: none"> • Vaginal dryness, itching, and pain • Ulcers and scarring on the vagina • Narrowing of the vagina • Difficult and/or painful sex
<p>Liver</p> <ul style="list-style-type: none"> • Swelling in the abdomen • Jaundice • Abnormal liver function test results 	<p>Male Genitalia</p> <ul style="list-style-type: none"> • Narrowing and/or scarring of the urethra • Itching and scarring on the penis and scrotum • Irritation of the penis
	<p>Muscles</p> <ul style="list-style-type: none"> • Muscle pain, weakness, and cramps
	<p>Nervous System</p> <ul style="list-style-type: none"> • Numbness, tingling, and pain • Poor coordination

Follow-up Care and Monitoring

The importance of follow-up care and monitoring cannot be overstated due to the unique needs of blood cancer survivors. Below is a brief review of important areas of concern. A list of comprehensive guidelines can be found in Table 2.

Table 2. Survivorship Guidelines	
Comprehensive recommendations can be found in the survivorship guidelines published by the NCCN Guidelines®, Children’s Oncology Group (COG), and American Society of Clinical Oncology (ASCO).	
NCCN Guidelines	www.NCCN.org (search for <i>Guidelines Survivorship</i> in upper right search box)
COG	www.childrensoncologygroup.org/survivorshipguidelines
ASCO	www.asco.org/practice-patients/guidelines/patient-and-survivor-care
NCCN=National Comprehensive Cancer Network® (NCCN®)	

Adherence to Therapy

Adherence to therapy is important for all blood cancer survivors, including those receiving a “watch and wait” approach. This topic is especially relevant in the treatment of blood cancer due to the increasing role of oral therapy, which shifts responsibility for adherence from providers to patients. Poor adherence to therapy can result in drug resistance, reduced response to therapy, disease progression, and death.

Communication between patients and providers is one of the most important methods for supporting patient adherence to treatment. Providers should encourage open communication and address potential barriers to adherence, which may include:

- Financial concerns
- Medication side effects
- Knowledge deficits regarding the disease and/or treatment
- Overuse, underuse, or misuse of treatment
- Confusion due to the complexity of treatment

Anxiety and Depression

Identifying and treating anxiety and depression can improve quality of life and potentially influence morbidity and mortality.¹⁹ Providers should use validated tools to routinely assess survivors for symptoms of anxiety, depression, and distress. They should also encourage patients to inform a healthcare provider when they are feeling distress.⁶

Referral to a mental health specialist and use of pharmacologic and nonpharmacologic interventions are all valid treatment options.¹⁹ Any patient at risk of harming themselves or others should be referred for emergency evaluation.

Providers can use the NCCN *Guidelines Distress Thermometer* to help patients rate their level of distress. Visit www.NCCN.org (search for *Distress Thermometer* in upper right search box to access this free resource.)

Cardiotoxicity

Cardiovascular disease is a leading cause of morbidity and mortality in blood cancer survivors.²⁰ Increased risk has been identified in survivors of leukemia, lymphoma, multiple myeloma, and recipients of hematopoietic SCT.²⁰⁻²²

Cardiovascular risk is influenced by multiple factors including cardiotoxic drug therapy, high-dose radiation to the chest, and non-cancer related factors including older age, history of cardiac disease, and presence of cardiovascular risk factors.^{20,23} Individual risk should be taken into consideration prior to treatment and careful monitoring should occur based on current guidelines. Survivors should be routinely assessed for signs and symptoms of cardiovascular disease and routine testing may be needed to monitor high-risk survivors.²³

All survivors should be counseled on the importance of minimizing modifiable risk factors such as hypertension, obesity, dyslipidemia, tobacco use, and diabetes mellitus. They should also be educated on the importance of a healthy diet and exercise.²³

Cognition

Survivors may experience cognitive dysfunction as a side effect of some blood cancer therapies. Although this is still an area of active research,

potentially helpful interventions may include: 1) validating the patient's experience; 2) screening for contributing factors, such as depression, fatigue, and poor nutrition; and 3) teaching strategies for the management of symptoms, such as organizational strategies, mindfulness, physical activity, and cognitive training.⁶

In the case of at-risk pediatric cancer survivors, guidelines developed by COG recommend neuropsychological evaluation at the start of long-term follow-up and periodically as needed.⁸ Recommended management includes collaboration with the survivor's school and referral to community services. LLS offers a continuing education program to inform school and college personnel about the effects of cancer treatment and improve the learning experience during and after treatment.

Visit www.LLS.org/StayingConnected to view *Staying Connected: Facilitating the Learning Experience During & After Cancer Treatment*

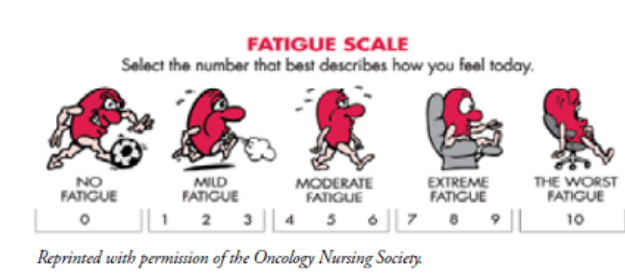
Fatigue

Fatigue is common in blood cancer survivors and can persist for many years after treatment ends. Survivors who report moderate to severe fatigue should receive a comprehensive assessment that includes a thorough physical exam, laboratory evaluation, and other relevant diagnostic testing.^{6,24}

Potential treatment options include:

- Treating anemia
- Nutrition management
- Physical activity
- Psychosocial interventions
- Managing other contributing factors (such as pain, medication side effects, depression, and comorbidities)

To help assess patient fatigue, providers may choose to use a visual tool such as the Oncology Nursing Society Fatigue Scale below.



Fertility

Infertility is a potential risk of some cancer treatments and should be discussed with patients before the start of therapy.^{6,25} Healthcare providers should initiate this discussion because patients and/or their caregivers may not think to ask about fertility preservation during the immediate period following diagnosis.

Providers should refer patients to a reproductive specialist for fertility preservation.^{6,25} Sperm, oocyte, and embryo cryopreservation are all standard practices. Other options, including testicular tissue cryopreservation, ovarian tissue cryopreservation, and ovarian in vitro maturation, may also be considered.

Critically ill blood cancer patients may need to start cancer treatment before initiating fertility preservation. This is especially true in women because oocyte and embryo cryopreservation require 10-14 days of hormonal ovarian stimulation followed by oocyte retrieval.²⁶ Alternative options can be considered for these patients, such as performing oocyte or embryo cryopreservation between induction and consolidation therapy.^{26,27} Fertility preservation is especially important before proceeding to SCT.²⁶

Following therapy, survivors are usually advised to wait at least two years before attempting conception.²⁸ However, survivors should be encouraged to talk with their healthcare provider about their specific situation.

Neuropathy

Some blood cancer treatments cause peripheral neuropathy. Patients should be encouraged to immediately report neuropathy symptoms to their provider because symptoms are likely to worsen without intervention.

If a patient is receiving active treatment with neurotoxic chemotherapy, management may include dose reduction, dose delaying, stopping the neurotoxic agent, or substitutions.²⁹ Other management options include treating underlying medical conditions (such as diabetes or hypothyroidism), physical or occupational therapy, and management with medication.

Unfortunately, neuropathy cannot always be prevented, and interventions often do not fully

remediate the problem. Sometimes neuropathy improves over time but may never fully resolve.

Pain

Pain can significantly impact quality of life and can be caused by the disease itself and/or therapies used to treat the disease. Pain is especially common in patients with myeloma, although it can occur in patients with any form of blood cancer.³⁰

According to current guidelines from NCCN Guidelines and ASCO, some important ways to properly assess and manage pain include:^{6,31}

- Conducting a thorough pain evaluation on first encounter with the patient and screening for pain at each subsequent encounter
- Determining the cause of pain, which may be related to the primary disease, treatment, secondary malignancy, late-onset side effects, recurrent disease, and many other causes
- Considering pharmacologic and/or nonpharmacologic methods for pain management
- Collaborating with a pain specialist and/or other healthcare professionals to manage patients with complex needs

To help patients rate their pain, providers can use a pain assessment tool like the Wong-Baker FACES® Pain Rating Scale below.



Screening for Relapse and Subsequent Primary Cancers

Cancer survivors have a higher rate of cancer than the general population. Reasons for this include genetic susceptibilities, treatment exposures, and lifestyle-related factors such as smoking and environmental exposures.⁶

Blood cancer survivors should receive routine cancer screenings in addition to specific screenings informed by their cancer, treatment, and individual

risk factors. COG and NCCN Guidelines both offer guidelines for screening and early detection of treatment-related secondary cancers. Additionally, NCCN Guidelines disease-specific guidelines include detailed recommendations related to monitoring for disease relapse.

Patients should be educated about their risk and encouraged to report abnormal signs and symptoms, which may include pain, fatigue, lymphedema, weight loss, bleeding, bruising, and other symptoms.

Visit:

- www.survivorshipguidelines.org/ to view *COG Long-term Follow-up Guidelines*
- www.NCCN.org (search for *Survivorship* in upper right search box)
- www.NCCN.org (search for *Treatment by Cancer Type* in upper right search box to view disease-specific guidelines)

Sexual Health

Sexual dysfunction is common among people with cancer and should be routinely assessed.^{32,33} Sexual dysfunction affects a patient's quality of life and can be influenced by physical, psychological, and emotional factors. Patients with sexual dysfunction should be referred to an appropriate specialist for treatment.

Patients should also be counseled on the importance of protection against sexually transmitted infections and use of birth control.

Providers can use the NCCN Guidelines Survivorship Assessment as part of their routine assessment of blood cancer survivors. Please create a free account to log in and access the assessment, which is included in the *NCCN Guidelines for Survivorship*: www.NCCN.org (search for *Guidelines for Survivorship* in upper right search box)

Survivorship Care Planning

Survivorship care planning is important because late effects may occur and/or increase over time, many adults do not receive long-term care from a survivorship specialist, and life-long follow-up care is recommended.^{3,5}

One way to support survivorship care is by developing individualized care plans for blood cancer survivors. A survivorship care plan is typically created by a member of the oncology team and given to the survivor and their primary care provider. Care plans are personalized for each patient and include a summary of treatment, risks, and plan of care, including monitoring and screenings.

In addition to care plans, several other resources are available to support evidence-based survivorship care. COG has developed extensive long-term follow-up guidelines and exposure-based recommendations to guide the care of survivors who were treated for cancer as a child, adolescent, or young adult.⁸ An example from the guidelines is included in Table 3. Additionally, Passport for Care[®] developed a tool that generates treatment-specific guidance related to potential late effects, recommended screenings, and relevant guidelines for childhood cancer survivors. NCCN Guidelines Survivorship Guidelines are another helpful resource to guide care.

Visit:

- www.cancer.net/survivorship/follow-care-after-cancer-treatment/asco-cancer-treatment-and-survivorship-care-plans to access ASCO Cancer Treatment and Survivorship Care Plans
- www.survivorshipguidelines.org/ to view *COG Long-term Follow-up Guidelines*
- www.passportforcare.org/en/ to access Passport for Care[®]
- www.NCCN.org (search for *Guidelines for Survivorship* in upper right search box)

programs, educational seminars, and support groups.

Healthcare providers can also help patients by directing them to the LLS patient resources related to survivorship care.

Visit www.LLS.org/publications to view *Survivorship Workbook for Adults* (also available for young adults and children & adolescents) and *Communicating with Your Healthcare Team: Survivorship*. These patient resources are available in English and Spanish

Empowering Survivors

Healthcare providers can empower blood cancer survivors by educating them about their post-treatment needs and encouraging them to report signs and symptoms of concern. Survivors should also be informed about other survivorship services that are available to them, such as screening

Table 3. Example of the detailed recommendations found in *Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers*

CHEMOTHERAPY			ANTIMETABOLITES	
Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling / Further Considerations
24	Antimetabolites Cytarabine (high dose IV)	Neurocognitive deficits Functional deficits in: -Executive function (planning and organization) - Sustained attention -Memory (particularly visual, sequencing, temporal memory) -Processing speed -Visual-motor integration - Fine motor dexterity Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change	HISTORY	HEALTH LINKS
			Educational and/or vocational progress Yearly	Educational Issues
			SCREENING	POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
			Referral for formal neuropsychological evaluation Baseline at entry into long-term follow-up, then periodically as clinically indicated for patients with evidence of impaired educational or vocational progress	Referral to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources and/or social skills training. Psychotropic medication (e.g., stimulants) or evidence-based rehabilitation training. Caution – lower starting dose and assessment of increased sensitivity when initiating therapy is recommended. Referral to community services for vocational rehabilitation or for services for developmentally disabled.
				SYSTEM = CNS SCORE=2A
Additional Information				
High-dose IV is defined as any single dose ≥ 100 mg/m ² . Formal neuropsychological evaluation includes test of processing speed, computer-based attention, visual motor integration, memory, comprehension of verbal instructions, verbal fluency, executive function and planning. Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., slow processing speed, attention problems). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New and progressive deficits may emerge over time. Acute toxicity predominates if cytarabine is administered systemically as a single agent. Cytarabine may contribute to late neurotoxicity if combined with high dose or intrathecal methotrexate and/or cranial radiation. Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors, as appropriate, that may increase risk. <ul style="list-style-type: none"> - Patient factors: Younger age at treatment, especially age <3 years, female sex, family history of learning or attention problems - Cancer/Treatment factors: CNS leukemia/lymphoma, relapsed leukemia/lymphoma treated with CNS-directed therapy, longer elapsed time since therapy, combination with corticosteroids, methotrexate (IT, IO, high-dose IV), radiation dose ≥ 24 Gy, TBI, especially single fraction TBI (10 Gy), cranial radiation - Pre-morbid/Co-morbid medical conditions: Pre-morbid learning or attention problems 				
References				
Buizer AI, de Sonnevle LM, Veerman AJ: Effects of chemotherapy on neurocognitive function in children with acute lymphoblastic leukemia: a critical review of the literature. <i>Pediatr Blood Cancer</i> 52:447-54, 2009 Kadan-Lottick NS, Zeltzer LK, Liu Q, et al: Neurocognitive functioning in adult survivors of childhood non-central nervous system cancers. <i>J Natl Cancer Inst</i> 102:881-93, 2010				

From the *Children’s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers*, Version 5.0, October 2018, used with permission.

Health Promotion

Healthy habits are associated with faster recovery, decreased risk of comorbidities, and improved quality of life.^{6,34} Below are ways to help blood cancer patients live a healthy lifestyle.

Healthy Lifestyle

Blood cancer survivors should be encouraged to live a healthy lifestyle, including eating a healthy diet, engaging in physical activity, and maintaining a healthy weight. They should also be educated about other health-promotion behaviors such as getting adequate sleep, practicing sun safety, avoiding tobacco products, and protecting their mental health.^{6,34}

Survivors should receive routine health screenings based on their age, sex, and individual risk factors, in addition to screenings related to their cancer and treatment effects.

Numerous resources are available to help survivors maintain a healthy lifestyle. Resources offered by LLS include free one-to-one nutrition consultations, informational fact sheets, and comprehensive workbooks.³⁴ Additionally, Livestrong and the YMCA have partnered to develop a physical activity program specifically for cancer survivors.

Visit:

- www.LLS.org/nutrition to refer your patient for a nutrition consultation
- www.livestrong.org/what-we-do/program/livestrong-at-the-ymca to learn more about the physical activity program offered by Livestrong and YMCA
- www.LLS.org/HCPbooklets to view *Food Insecurity (Fact Sheet for HCPs)*

Immunizations

Vaccines may not trigger an adequate immune response in individuals who are immunocompromised. Patients should be vaccinated with inactivated or recombinant vaccines two or more weeks before the start of therapy or three or more months after the conclusion of cancer therapy.⁶ Additionally, live attenuated vaccines are contraindicated in actively immunocompromised patients, including HCT survivors with active GVHD and/or immunosuppression.

Vaccination should be delayed for 6 months following the conclusion of treatment with anti-B-cell antibody therapy.⁶ Special consideration is also needed for patients who received CAR T-cell therapy. However, data regarding the use of vaccines in this population is limited.⁶

Survivors six months of age and older should receive the inactivated influenza vaccine annually, unless otherwise contraindicated. The nasal spray should not be administered because it is a live vaccine. If directed by their doctor, immunocompromised adult survivors can also receive the Shingrix[®] vaccine to prevent shingles. However, they should not receive Zostavax[®] because it is a live vaccine. Caregivers and close contacts should also not receive the live shingles vaccine.

Some blood cancer survivors will need to be revaccinated with childhood immunizations following the conclusion of treatment and children who had to delay vaccination will need a catch-up schedule. Healthcare providers should be encouraged to talk with their patients about their immunization needs.

- Visit www.NCCN.org (search for Guidelines for Survivorship in upper right search box for detailed information regarding vaccines and cancer survivors.)

COVID-19 Immunizations

Coronavirus disease 2019 (COVID-19) vaccines are safe for most blood cancer survivors. The vaccination schedule for moderately to severely immunocompromised individuals can be found in the LLS fact sheet for HCPs, [COVID-19 Prevention and Treatment for Blood Cancer Patients](#).

When possible, patients should be vaccinated before the start of lymphocyte-depleting therapy. Survivors who have already started therapy before vaccination may defer vaccination until six months following the completion of therapy or evidence of lymphocyte recovery.^{35,36} Examples of lymphocyte-depleting therapies include rituximab, blinatumomab, anti-thymocyte globulin, and alemtuzumab.

Although the effectiveness may be reduced, COVID-19 vaccines could be given as early as three months

following HCT or CAR T-cell therapies.³⁶

Due to the changing nature of the COVID-19 pandemic and response, visit:

- www.LLS.org/HCPbooklets to access *COVID-19 Prevention and Treatment for Blood Cancer Patients*
- www.LLS.org/covid-19-resources (resource for patients) for the most up-to-date information regarding COVID-19 and blood cancer.

Infection Prevention

Immunocompromised survivors are at greater risk for infection. These individuals should be educated about protective precautions, which include:

- **COVID-19 prevention:** Blood cancer survivors should be advised on methods to reduce their COVID-19 risks.

For current provider information guiding the prevention and treatment of COVID-19, visit www.LLS.org/booklet/covid-19-prevention-and-treatment-blood-cancer-patients

- **Personal hygiene and lifestyle:** Immunocompromised survivors should be encouraged to practice careful personal hygiene, including bathing daily and washing their hands frequently. To prevent abrasions, they should be encouraged to use an extra-soft toothbrush and electric shavers. Patients should be encouraged to carefully follow their healthcare team's instructions related to the care of medical devices such as indwelling ports and catheters.

Immunocompromised survivors should also be educated about making lifestyle choices that decrease the risk of infection. For example, they should avoid crowds and individuals with a contagious disease. Immunocompromised survivors should also wear gloves when gardening, designate someone else to handle pet feces, and avoid cuts and burns. Any injuries should be carefully treated and monitored.

- Visit www.NCCN.org (search for *Guidelines for Survivorship* in upper right search box for detailed information on cancer survivorship and reducing infection risk.)

- **Food safety:** Immunocompromised survivors should be encouraged to prevent food-borne illness. Recommendations include thoroughly washing all produce, using a meat thermometer to confirm the safe internal temperature of meats, and avoiding eating raw and unpasteurized foods.

- **Travel:** Healthcare providers should encourage their patients to speak with their healthcare team before traveling. Precautions may include pre-travel vaccination and prophylaxis against specific infections.

Support and Resources

The Information Resource Center (IRC) at LLS is staffed by highly trained oncology social workers, nurses, and health educators who are available to assist everyone touched by blood cancer, including healthcare providers and their patients.

IRC staff can direct healthcare providers to LLS professional resources including continuing education, academic grant opportunities, research funding, and free information. They can also help patients by assisting with the challenges of their diagnosis, including financial and social challenges, providing disease, treatment, and survivorship information, and referring patients to the Clinical Trial Support Center (CTSC) to conduct individualized clinical-trial searches.

The IRC can be contacted by live chat via the link below, by phone at (800) 955-4572, or by email at infocenter@LLS.org. The hours of service by phone are 9 a.m. to 9 p.m. ET, Monday through Friday. IRC staff can communicate in 170 languages via interpreter.

Visit www.LLS.org/IRC to contact the Information Resource Center (IRC) at LLS

Supporting the Whole Patient

Blood cancer survivors face many challenges that extend beyond their physical health. These challenges include psychosocial concerns, financial concerns, and the need for reliable health information.

- **Psychosocial Concerns:** Psychosocial challenges are common among blood cancer survivors and can decrease their quality of life. In one study, 39% of blood cancer patients ages 15–39 had one or more psychological impairment, including anxiety, depression, or posttraumatic stress.³⁷

LLS offers numerous supportive resources for survivors and their caretakers. Examples include support groups, peer-to-peer support, caregiver support, and online chats.

Visit www.LLS.org/support-resources to access these free psychosocial services.

- **Financial Concerns:** A report commissioned by LLS in 2018 underscores the financial burden of blood cancer treatment. According to the report, which analyzed insurance claims from 2,332 commercially insured patients, the average allowed spending for treating blood cancer was \$156,000 in the first year following diagnosis. The ongoing cost was also extremely high. The average allowed spending during the three years following diagnosis was over \$800,000 for treating acute leukemia and \$200,000 for treating chronic leukemia.³⁸

LLS offers several financial assistance programs for patients, including co-pay assistance, travel assistance, and urgent need programs. LLS also has specialists available to talk with patients about programs offered by LLS and other organizations.

Visit www.LLS.org/support-resources/financial-support to learn more about LLS' patient financial assistance programs.

- **Health Information:** Increasing patient knowledge can influence health outcomes and support patient compliance and decision-making. LLS offers numerous resources to help cancer

survivors navigate their diagnosis, treatment, and beyond. These services include nutrition consultations, up-to-date information, and one-to-one support from information specialists.

Visit:

- www.LLS.org/nutrition to refer your patient for a nutrition consultation

or

- www.LLS.org/article/patient-referral-form to refer your patient to be contacted by an LLS Information Specialist (available in English and Spanish)

You can also encourage your patients to contact an information specialist directly at www.LLS.org/information-specialists and welcome them to learn more about survivorship care and follow-up via www.LLS.org/treatment/follow-care-and-survivorship

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We're Here to Help

LLS is the world's largest voluntary health organization
dedicated to funding blood cancer research, education
and patient services. LLS has regions throughout the
United States and Canada. To find the region nearest to
you, visit our website at www.LLS.org/chapterfind or
contact

The Leukemia & Lymphoma Society

3 International Drive, Suite 200, Rye Brook, NY 10573
Phone Number: (800) 955-4572 (M-F, 9 a.m. to 9 p.m. ET)

Website: www.LLS.org

To refer your patient for a nutrition consultation:

- Call: 877-467-1936
- Visit: www.LLS.org/nutrition

LLS offers free information and services for patients and
families touched by blood cancers as well as for healthcare
professionals. The resources listed below are available to
you and your patients.

Consult with an Information Specialist. Information
Specialists are highly trained social workers and nurses
who assist through treatment, financial, and social
challenges. They offer up-to-date disease and treatment
information. Language services are available.

For more information, please

- Call: (800) 955-4572 (M-F, 9 a.m. to 9 p.m. ET)
- Visit: www.LLS.org/IRC
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/information specialists

Clinical Trials Support Center (CTSC). Work one-on-one with an LLS clinical trial nurse navigator who will personally assist throughout the entire clinical trial process. A nurse navigator will help identify potential clinical trials and overcome the barriers to enrollment (navigators help HCPs and patients). For more information about this free service, please

- Call an Information Specialist: (800) 955-4572 to be referred to the CTSC
- Visit: www.LLS.org/CTSC
- Complete a referral form for your patient at: www.LLS.org/CTSCreferral

Nutrition Consultations. PearlPoint Nutrition Services® for patients and caregivers of all cancer types, offering free nutrition education and consultations with registered dietitians who have expertise in oncology nutrition.

Visit: www.LLS.org/nutrition

Free Information Booklets. LLS offers free education and support publications that can either be read online or downloaded. Free print versions can be ordered. For more information, please visit: www.LLS.org/booklets

Información en Español. (LLS information in Spanish.) Para mayor información por favor visite: www.LLS.org/espanol.

LLS Community. LLS Community is an online social network and registry for patients, caregivers, and healthcare professionals. It is a place to ask questions, get informed, share your experience, and connect with others.

To join visit: www.LLS.org/community

LLS Regions. LLS offers community support and services in the United States and Canada including in-person support groups and other great resources.

Call: (800) 955-4572

Visit: www.LLS.org/chapterfind

Patti Robinson Kaufmann First Connection® Program.

A free peer-to-peer support program that connects patients and their loved ones to a trained peer volunteer who has gone through a similar experience.

www.LLS.org/firstconnection

Resources for Healthcare Professionals: webinars, podcasts, in-person education programs and fact sheets

- www.LLS.org/CE
- www.LLS.org/HCPpodcast
- www.LLS.org/HCPbooklets
- www.LLS.org/HCPvideos
- www.LLS.org/stayingconnected (free online course on the effects of childhood and AYA cancer treatment to help improve the learning experience during and after treatment)

Resources for your Patients:

- www.LLS.org/treatment/types-treatment for up-to-date patient information regarding blood cancer treatment
- www.LLS.org/booklets to access free publications, including:
 - *Blood and Marrow Stem Cell Transplantation*
 - *Cancer-Related Fatigue Facts*
 - *Chimeric Antigen Receptor (CAR) T-Cell Therapy*
 - *Communicating with Your Healthcare Team: Survivorship*
 - *Fertility and Cancer*
 - *Immunotherapy*
 - *Managing Stress: How Stress Affects You and Ways to Cope*
 - *Oral Treatment Adherence Facts*
 - *Pain Management Facts*
 - *Post-Transplant Lymphoproliferative Disorders*
 - *Sexuality and Intimacy Facts*
 - *Side-Effect Management: Managing Peripheral Neuropathy (Nerve Damage)*
 - *Side-Effect Management: Memory and Concentration Problems in Adults*
 - *Side-Effect Management: Reducing Your Risk of Infection*
 - *Survivorship Workbook for Adults*
 - *Survivorship Workbook for Children and Adolescents*
 - *Survivorship Workbook for Young Adults*
 - *Watch and Wait Fast Facts*

Other patient resources include:

- www.LLS.org/programs
- www.LLS.org/educationvideos
- www.LLS.org/podcast

Additional Resources

The National Cancer Institute (NCI)

www.cancer.gov

(800) 422-6237

The National Cancer Institute, part of the National Institutes of Health, is a national resource center for information and education about all forms of cancer. The NCI also provides a clinical trial search feature, the PDQ® Cancer Clinical Trials Registry, at www.cancer.gov/clinicaltrials, where healthcare professionals and patients can look for clinical trials.

Children's Oncology Group (COG)

www.survivorshipguidelines.org

www.childrensoncologygroup.org/survivorshipguidelines

The Children's Oncology Group (COG), a National Cancer Institute supported clinical trials group, is the world's largest organization devoted exclusively to childhood and adolescent cancer research. The COG unites more than 10,000 experts in childhood cancer at more than 200 leading children's hospitals, universities, and cancer centers across North America, Australia, New Zealand, and Europe in the fight against childhood cancer. COG provides important information for children and their families from the time of diagnosis, through treatment and following cure.

National Comprehensive Cancer Network® (NCCN®)

www.nccn.org

The NCCN is a not-for-profit alliance of 32 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, equitable, and accessible cancer care so all patients can live better lives.

American Society of Clinical Oncology (ASCO)

www.asco.org/practice-patients/guidelines/patient-and-survivor-care

The world's leading professional organization for physicians and oncology professionals caring for people with cancer.

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