#### REVIEW

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# Living with hematologic cancer: Recommendations, solutions

# ABSTRACT

Patients with hematologic cancers such as leukemia, lymphoma, and multiple myeloma are living longer than ever. The survival rate of patients with most hematologic cancers has doubled since 1974, and these once-terminal diagnoses are now chronic health conditions. This article reviews the care of patients with hematologic cancers, including those previously treated for childhood, adolescent, and young-adult cancers, discusses the role of primary care in a multidisciplinary team approach, and reviews innovative ways to deliver needed care.

# **KEY POINTS**

The definition of survivorship is different in patients with hematologic cancer than in patients with solid tumors, as treatment is often ongoing and lacks a clear stopping point.

Routine health maintenance is especially important for patients with hematologic cancers, who face a heightened risk of secondary cancers and other conditions.

Survivorship plans can improve communication between the primary care provider, patient, and oncology team.

Physicians should emphasize the importance of a healthy lifestyle and routine health maintenance for their patients who are cancer survivors.

A DULTS WITH LEUKEMIA, lymphoma, multiple myeloma, and other hematologic cancers are living longer, and more than 1.2 million patients with these cancers are alive in the United States.<sup>1</sup> Most adults with nonpediatric cancers are diagnosed in the fifth to seventh decade, and many now survive more than 5 years. The survival rate of patients with most hematologic cancers has doubled since 1974, transforming once-terminal diagnoses into chronic conditions. According to one estimate, there will be 18 million cancer survivors (all types of cancer) by 2022, and nearly 2 million of these will be survivors of hematologic cancers.<sup>2</sup>

Although survivors of hematologic cancers are at risk of complications of their cancer treatment, they often do not receive routine health maintenance and see their primary care providers only for acute issues.

Primary care providers can play a major role in monitoring the health of hematologic cancer survivors. This requires staying up-todate on diagnosis, management, and surveillance in this group and being able to address their survivorship issues.<sup>3</sup>

In this article, we focus on survivorship considerations in patients with previously treated hematologic cancers, including childhood, adolescent, and young-adult cancers. We discuss the role of primary care in the multidisciplinary approach to the continuing care of these patients, and we review innovative technologic solutions to the challenges of delivering care to this group.

# SURVIVORSHIP BEGINS AT DIAGNOSIS

The definition of cancer survivorship has changed in the last decade, particularly with hematologic cancers.<sup>4</sup>

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Survivorship was once considered the time after the patient successfully completed cancer treatment. But most patients with hematologic cancers will likely need to continue treatment until they die, with essentially unpredictable and intermittent periods of remission and relapse. Advances in cancer treatment and supportive care have led to longer life. Thus, a commonly recognized definition of survivorship begins at diagnosis rather than later in the disease course and continues through the balance of the patient's life.<sup>5</sup>

#### The survivorship care plan

In 2005, the Institute of Medicine released a report<sup>6</sup> calling attention to cancer survivors and their special needs. At that time, a growing number of patients were not returning to their primary care physicians to receive health maintenance after completing their cancer treatment. A proposed solution was for the oncologist to develop a personalized survivorship care plan, which would help the patient understand the treatments received, the importance of health maintenance, and the need for follow-up surveillance.<sup>5</sup>

The survivorship care plan was originally intended for patients who had completed their cancer treatment. But patients with hematologic cancers tend to need lifelong treatment. Nevertheless, major organizations such as the American Society of Hematology and the American Society of Clinical Oncology consider a survivorship care plan an essential part of cancer care for all patients and not just those with solid tumors.<sup>7</sup>The plan should consist of a written treatment summary and recommendations for follow-up care.

#### EFFECTS OF HEMATOLOGIC CANCER AND ITS TREATMENT

Hematologic cancers and their treatment put patients at risk of many complications, including endocrinopathies, such as hypothyroidism or diabetes secondary to chronic steroid and immunosuppressant use, and cardiovascular events, such as congestive heart failure and stroke due to high-dose chemotherapy. Survivors are also at risk of secondary cancers and recurrence of the primary cancer.<sup>8–15</sup>

Despite the gravity of a cancer diagnosis, cancer patients do not always adhere to a healthy lifestyle. A survey of over 400,000 cancer survivors found that 15% were current cigarette smokers, 27.5% were obese, and 31.5% had not engaged in physical activity during the previous 30 days.<sup>16</sup>

# THE PRIMARY CARE CLINICIAN AND SURVIVORSHIP CARE

Many hematologic oncology practices include not only medical oncologists but also ancillary team members such as nurse practitioners, nurse specialists, physician assistants, registered nurses, and in some cases a social worker or nutritionist. Patients with hematologic cancers often rely on this team for most of their care while undergoing cancer treatment.

Depending on the type of cancer, and especially after a period of stable disease or remission, some patients transition away from the oncology team, particularly if they live far away, and receive care from their local primary care clinician.

Although the Institute for Medicine intended the survivorship care plan<sup>6</sup> to be a patient-focused tool, primary care providers can benefit from it too. In survey of oncologists and primary care providers in the United States,<sup>17</sup> 49% of the 1,130 oncologists said they almost always provided care plans to patients, and 85% perceived a greater benefit for primary care providers to have these plans than for cancer survivors. However, only 13% of the 1,120 primary care providers surveyed said they consistently received a care plan from the oncologist. The study suggests that oncologists should make a better effort to share these plans with primary care providers to enhance the coordination of care.

Empowering patients to take control of their health is an essential component of survivorship care

# COMPONENTS OF A SURVIVORSHIP CARE PLAN AND SELF-MANAGEMENT

Although personalized survivorship care plans are not routinely used in patients with blood cancers,<sup>18</sup> they are as important in hematologic cancer survivors as in patients with solid tumors.

The plan should consist of a treatment summary and information on essential components of a healthy lifestyle and should take into consideration coordination of care among primary and other providers, health maintenance recommendations, information on early detection and screening, and psychosocial welfare. Guidance on preventive screening for physical, financial, and psychosocial well-being should be generated by the oncology team or primary care provider and can be helpful to patients and caregivers as they navigate the healthcare system. (See https://cancercontrol. cancer.gov/pdf/ASCO-Survivorship-Care-Plan.pdf for a sample survivorship care plan.)

Although patients with hematologic cancer often have a highly variable course with multiple periods of remission and relapse, the survivorship care plan and treatment summary are essential components of their ongoing care.

Self-management of chronic illness refers to daily activities to keep the illness under control, minimize its impact on physical health and function, and help the patient cope with the psychosocial sequelae of the illness.<sup>19</sup> Empowering patients and their caregivers to take control of their health is an essential component of survivorship care. Patients and caregivers can be valuable partners to primary care providers and the oncology team in ongoing care to ensure proper testing and monitoring for secondary illnesses.

Video technology allows patients to connect with their healthcare providers without having to leave home or take time off from work

# INFORMATION TECHNOLOGY SOLUTIONS

Implementation of a survivorship care plan can be facilitated by integrating the plan and treatment summaries into the patient's electronic medical record and encouraging the patient to be a part of the process.<sup>20</sup> Many electronic medical record systems such as Epic can automatically fill in treatment summaries and provide patients access to a survivorship care plan tailored to their needs, but these features are not routinely used, and output can be lengthy and hard to follow.<sup>21,22</sup>

There has been a surge in research in information technology and care plan delivery since the Health Information Technology for Economic and Clinical Health (HITECH) Act was passed in 2009,<sup>23</sup> specifically in innovative strategies to proactively screen for, assess, and manage disease- and treatment-related symptoms in cancer survivors. As a result, patients and families can be more engaged in their care, and providers can better guide survivorship concerns. Providers can create their own survivorship care plans or use electronic resources to generate one. The American Society of Clinical Oncology and the National Comprehensive Cancer Network provide printed templates in which the patient, primary care provider, or oncology team can complete a care plan. Newer electronic platforms such as the Carevive system are also available. Brief electronic outcome questionnaires can be completed by the patient at home or in the waiting room to assess symptoms, evaluate health maintenance practices, and generate a plan of care to review with the patient.

### EMERGING TECHNOLOGY: TELEMEDICINE, VIRTUAL VISITS

Technology can help patients and the healthcare team in survivorship monitoring. Telemedicine, the exchange of medical information via electronic communication, includes video conferencing for patient consultations, transmission of still images, patient portals, and remote monitoring of vital signs.<sup>24</sup>

This technology is critical to deliver highquality acute and chronic care to patients in remote or rural areas, locally to patients unable to travel to the clinic, and internationally.<sup>25–28</sup> As patients become more technologically savvy, providers can try novel strategies to provide patients access to care. As of September 2015, there were at least 165,000 health applications (apps) for smartphones to help patients better manage aspects of their care such as diet, exercise, blood pressure, and blood sugar levels.<sup>29</sup>

Video technology such as Express Care Online allows patients to connect with their healthcare providers for video and virtual visits without having to leave home or take time off from work. It also allows oncology providers to have virtual face-to-face contact with patients undergoing treatment phases, and primary care providers to have easier contact with patients during maintenance and remission phases. This technology allows for earlier detection of illness and provides broader access to care. Virtual visits may even prevent needless hospitalization in some cases or, conversely, alert the physician to tell the patient with alarming symptoms of an acute event, that it is time to go to the hospital.

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# TABLE 1

# Follow-up beyond routine screening

# AFTER HODGKIN LYMPHOMA AND ACUTE LYMPHOBLASTIC OR MYELOGENOUS LEUKEMIA<sup>5,30,33,36</sup>

#### Risks

Subsequent neoplasms and recurrence

Cardiac disease (after chest radiation)

Oral cancer, osteonecrosis (after azathioprine or radiation to the jaw)

Osteoporosis

Chronic pain, peripheral neuropathy, Raynaud phenomenon

Pulmonary fibrosis, interstitial pneumonitis (after mediastinal radiation and high doses of bleomycin) Cataracts (after high doses of radiation to head)

Bladder fibrosis, hemorrhagic cystitis, impaired kidney function, bladder cancer (after abdominal radiation) Esophageal strictures, gastroesophageal reflux disease, enterocolitis, bowel obstruction Infections

**Educate** on sun exposure, signs of cancer, healthy high-fiber diet, avoidance of alcohol, smoking cessation, hand-washing, vaccination, avoidance of people with colds, need to report symptoms

#### Screen

For skin cancer every year

Mammography every 2 years for women age 50 to 7437

Colonoscopy every 5 years after age 35, or 10 years after abdominal radiation

Echocardiography at baseline and periodically

Annual liver screening with aspartate aminotransferase, alanine aminotransferase, and bilirubin for patients who received  $\geq$  3,000 cGy to upper abdomen, or received methotrexate, mercaptopurine, or thioguanine Dual-energy x-ray absorptiometry per World Health Organization recommendations

**Vaccinate** against pneumococcus (PCV 13 for immunocompromised individuals),<sup>38</sup> influenza (inactivated); live-attenuated virus vaccines (eg, herpes zoster, influenza) can be used with caution and in close contacts of cancer survivors; consider prompt antibiotics to cover gram-positive organisms in those with hypogamma-globulinemia, compromised immunity

**Monitor for relapse:** computed tomography (CT) to evaluate response, then chest radiography or CT every 6 to 12 months for 2 to 5 years

Specialist evaluation as appropriate

**FOR OLDER PATIENTS** with chronic lymphocytic leukemia, acute myelogenous leukemia, multiple myeloma and non-Hodgkin lymphoma<sup>22,39</sup>

# Risks

Early onset of diabetes (secondary to steroid use), hypertension (secondary to chemotherapy), osteoporosis (especially after multiple myeloma), cataracts (from steroids), and cardiovascular disease (especially with anthracycline and alkylating agent chemotherapy); reinforce healthy lifestyle, proper screening

# AFTER ALL CANCERS 33,34

**Address** educational issues, emotional issues, financial issues, chronic pain, cognitive function, sleep disorders, immunizations, and healthy lifestyle (smoking cessation, weight management, diet, exercise)

# SURVEILLANCE FOR LATE TREATMENT EFFECTS

Guidelines for surveillance for late treatment effects include the following:

 Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancer<sup>30</sup>

 National Comprehensive Cancer Network Guidelines for Age-Related Recommendations: Adolescent and Young Adult Oncology<sup>31</sup>

# TABLE 2

# Screening after hematopoietic cell transplant

#### Cardiovascular risk-factor assessment

#### Immune system

If on chronic graft-vs-host disease prevention: gram-positive encapsulated organism prophylaxis, *Pneumocystis carinii* pneumonia prophylaxis, cytomegalovirus testing

Revaccinate after stem cell transplant, yearly inactivated influenza vaccine

**Ocular** clinical symptom evaluation, ocular fundus examination if previously abnormal

Dental assessment

#### Pulmonary

Clinical pulmonary assessment Smoking avoidance counseling Pulmonary function testing if previously abnormal Chest radiography if previously abnormal

#### Liver

Liver enzyme testing if previously abnormal Serum ferritin testing if previously abnormal

#### Kidney

Blood pressure screening Urine protein screening Blood urea nitrogen and creatinine testing

#### Muscle and connective tissue

Evaluate for muscle weakness if on chronic graft-vs-host disease prevention Physical activity counseling and routine exercise

#### \_\_\_\_\_

Bone and spine Bone density testing (adult women, all allogeneic transplant recipients and patients at high risk for bone loss), reassess if previously abnormal

# **Nervous system**

Clinical neurologic evaluation Evaluate for cognitive development

# **Endocrine system**

Thyroid function testing Growth velocity in children Gonadal function assessment in prepubertal children and in adults if previously abnormal

Skin self-examination and sun exposure counseling

# **Gynecologic examination**

**Secondary cancers** Vigilance counseling and screening

**Psychosocial**, financial, and quality-of-life clinical assessment, sexual function assessment

Based on information in references 30 and 32

- National Comprehensive Cancer Network Guidelines for Treatment of Cancer by Site and Survivorship<sup>31</sup>
- American Society for Blood and Marrow Transplantation, for survivors of hematopoietic cell transplantation.<sup>32</sup>

Survivors of childhood blood cancers are at increased risk of cardiac effects of high-dose or anthracycline chemotherapy (eg, doxorubicin for lymphoma, idarubicin for leukemia), skin cancer, sex-specific cancers (breast cancer, cervical cancer, prostate cancer), and osteoporosis.<sup>5,30,33,34</sup>

For adult survivors of childhood cancers, it is generally recommended to screen for secondary conditions according to the US Preventive Services Task Force. The clinician must also consider the age at cancer diagnosis (child, young adult, or adult), the length of time since chemotherapy (months vs years), and the type of chemotherapy received.

A myriad of recommendations exist according to cancer type, location, stage, and age at diagnosis, but no clear consensus for screening exists. The major survivorship surveillance guidelines of the Children's Oncology Group, National Comprehensive Cancer Network, and American Society for Blood and Marrow Transplantation are very detailed and lengthy and therefore not user-friendly for the busy clinician. While these guidelines contain minor differences as to what to test for and when to test, they differ mainly in considerations of the length of exposure to chemotherapy and radiation (eg, children, young adults, and older adults), length of time from completion of treatment to assessment of late complications, and whether the patient underwent hematopoietic stem cell transplant.<sup>35,36</sup>

**Table 1** reviews hematologic malignancies and conditions that blood cancer survivors are at risk for and general routine screening recommendations.<sup>5,22,30,33,34,36–39</sup> In general, an assessment by a healthcare provider is recommended annually to screen for late effects of cancer and its treatment. Most important are screening for cardiac toxicity, giving immunizations, and preventing second cancers.

Table 1 reflects general recommendations for healthcare screening in childhood, adolescent, or young adult cancer survivors who see adult primary care physicians and for adult cancer survivors (acute leukemias, lymphomas, and multiple myeloma).

**Table 2** focuses on screening and prevention specifically after hematopoietic cell transplantation.<sup>30,32</sup> These tables are not meant to be allinclusive but to provide evidence-based recommendations for health surveillance at a glance.

# SURVIVORS NEED ONGOING CARE

Recent successes in the treatment of hematologic cancers have led to dramatic changes in the overall health of these patients. In many instances, cancer survivors in the United States are considered to have a chronic illness with survival rates surpassing those in the past. A longer life span is counterbalanced by cumulative physical, financial, and psychosocial issues that require a multidisciplinary team to monitor and manage.

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Childhood cancer survivors face the same psychosocial and financial issues as survivors of adult-onset cancers and are at heightened risk of preventable conditions. Ultimately, it is up to the survivor to selfmanage many long-term treatment-related symptoms.

A survivorship care plan and treatment summary to guide the patient, primary provider, and oncology team is an essential component of quality care. Screening guidelines vary according to the age at treatment and length of time from therapy, but general screening and the use of technology and information technology solutions to deliver care can help survivors. These solutions have the potential to transform healthcare delivery in the future and provide the opportunity for ongoing, comprehensive care.

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