REVIEW ARTICLE

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Cancer Survivorship

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Advances in cancer screening and early detection, improvements in therapeutics, and supportive care all contribute to decreasing cancer mortality. Figure 1 shows the changing demographic characteristics of the cancer population from 1975 through 2040. There will be an estimated 26 million survivors in 2040, the majority of whom will be in their 60s, 70s, or 80s.[1] Nearly every health care provider will encounter cancer survivors. This review is primarily intended for primary care physicians, obstetrician–gynecologists, midlevel providers, and subspecialists who have patients who are cancer survivors. The review also serves as a primer for surgeons, radiotherapists, and medical oncologists who may not be familiar with the broad topic of survivorship. At present, the care of cancer survivors is often an afterthought, tends to be fragmentary, and is not well integrated into the mainstream of cancer care. Also, the best models for providing survivor care remain undefined.

According to the Office of Cancer Survivorship at the National Cancer Institute[2] and other organizations (e.g., the Centers for Disease Control and Prevention and the National Coalition for Cancer Survivorship), survivorship starts at the time of diagnosis and lasts throughout the lifespan. This holistic definition encourages clinicians to think about the care of survivors as an integral part of the cancer care continuum. Included in the definition of survivors are family members, friends, and caregivers. The primary reason for including these persons is that in most cases cancer is not experienced alone. Caregivers are the unsung heroes, providing physical and emotional support to the cancer survivor. Recognition of the adverse health effects and emotional toll on caregivers is part of this broad definition of survivorship.

The National Academies of Sciences, Engineering, and Medicine, in a landmark publication, identified the essentials of survivor care,[3] and these were expanded in the American Society of Clinical Oncology (ASCO) Core Curriculum for Cancer Survivorship Education.[4] The topics addressed in these reports are reviewed below.

Surveillance for Recurrence and Screening for Second Primary Cancers

ASCO,[5-7] the National Comprehensive Cancer Center Network (NCCN),[8] the American Cancer Society,[9,10] the Children's Oncology Group,[11] and other organizations[12-16] issue site-specific guidelines for the follow-up care of cancer survivors (Table 1). With few exceptions, these are not evidence-based guidelines but are instead based on expert consensus. The evidence that surveillance for metastases reduces cancer mortality or improves health-related quality of life is limited. The basis of most surveillance recommendations is knowledge of the cancer-specific natural history of recurrence or an analysis showing that the benefits of surveillance testing outweigh its harms. However, the benefits-outweigh-harms analysis does not take

into account the distress that surveillance testing causes and the financial costs of such testing.

Randomized, controlled trials of surveillance testing have had opposite results in two different populations of cancer survivors. Randomized trials do not support surveillance for metastatic disease in asymptomatic female survivors of breast cancer[6] (Table 1). In a minority of cases, imaging or measurement of serum tumor markers reveals metastases before they become symptomatic. However, the overall survival is unchanged between the asymptomatic screened population and women who undergo surveillance testing when they are symptomatic. In contrast, survivors of colorectal cancer undergo periodic surveillance imaging and tumor-marker testing (Table 1). Metastatic disease in the liver occurs in 60% or more of colorectal cancer survivors, and in 20 to 35% of patients with metastatic disease, the metastases are resectable.[17] Surveillance improves the likelihood of finding resectable hepatic metastases. Randomized trials show that liver resection with systemic chemotherapy results in long-term survival in some cases.[18]

All persons with potentially curable cancers should have the recommended sex- and age-specific routine screenings, tests, and care that are recommended for the general population (e.g., colonoscopy, mammography, Papanicolaou smears and human papillomavirus testing, dual-energy x-ray absorptiometry [DXA], vaccinations, and screening for hypertension, lipid abnormalities, and diabetes). Screening recommendations for new primary cancers in cancer survivors may differ from the screening recommendations for healthy persons with no history of cancer. For example, Hodgkin's disease survivors who have been treated with mantle irradiation have an increased risk of breast cancer.[19] Among women who underwent mantle irradiation for the treatment of Hodgkin's disease in adolescence, annual breast screening with magnetic resonance imaging (MRI) beginning at 25 years of age is associated with a reduction in mortality from breast cancer, as compared with breast screening starting at 40 years of age.[20]

LONG-TERM AND LATE EFFECTS OF CANCER TREATMENT

Long-term treatment effects are side effects that begin during and extend beyond treatment,[21-34] whereas late effects occur after treatment ends[32,35-38] (Table 2). Both late and long-term effects vary according to treatment exposures and individual host factors. Also, radiation causes late effects with long latency periods — primarily, radiation-induced second cancers and cardiovascular disease.[35,39,40]

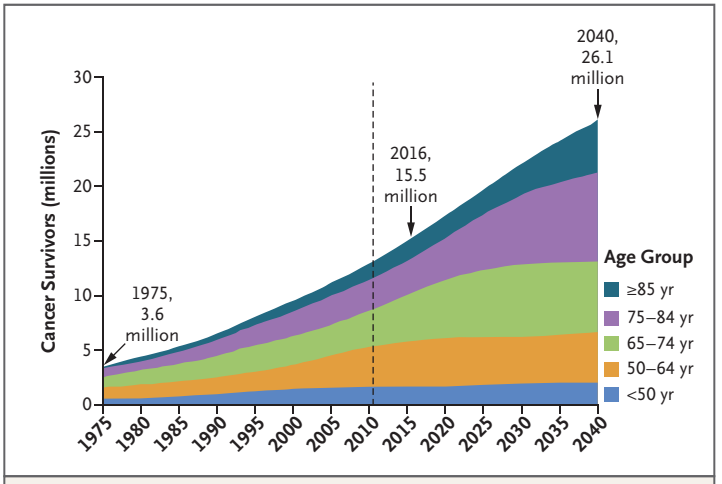

Figure 1. Changing Demographic Characteristics of Cancer Survivors in the United States.

Shown is the number of cancer survivors according to age group, starting in 1975, when there were 3.6 million cancer survivors, and projected to 2040, with an estimated 26.1 million survivors. The vertical broken line at 2011 indicates the year when the first baby boomers (a population born between 1946 and 1964) turned 65 years old. Data are from Bluethmann et al.[1]

An emerging concept is that chemotherapy causes premature or accelerated aging in both survivors of cancer in adulthood and survivors of cancer in childhood.[41,42] In addition to increased coexisting conditions in cancer survivors, healthy aging and chemotherapy-related side effects have several putative biomarkers in common, including telomere shortening, decreases in maximal oxygen consumption, and increased levels of inflammatory cytokines. Hormone deficiencies also contribute to senescence.[43] Chemotherapy causes primary hypogonadism in premenopausal women, and long-term treatment with antiandrogens, gonadotropin hormone–releasing agonists, and antiestrogens suppresses circulating androgen and estrogen levels.

Premature aging is most evident in survivors of childhood cancers, the majority of whom have coexisting medical conditions, which may be life-threatening, by the age of 45 years.[44] Trying to distinguish chemotherapy-related accelerated aging from the natural aging process in adults can be challenging. For example, the rates of cardiac

Table 1. Suggested Site-Specific Surveillance Recommendations for Cancer Survivors.*

Disease Site	Recommendations	Comments
Head and neck cancer[5]†	Physical examination every 1–3 mo for 1 yr, then every 2–6 mo for 2–5 yr and annually after 5 yr Baseline imaging 6 mo after completion of treatment Indirect laryngoscopy performed by an ENT physician periodically Low-dose CT scans for lung-cancer screening, indicated for persons at high risk because of a history of smoking	If new or persistent symptoms develop, imaging is performed as appropriate to the clinical situation
Breast cancer[6]†	Physical examination every 3–4 mo for 3 yr, then every 6 mo for 2 yr, and annually after 5 yr‡ Breast imaging annually	Imaging or measurement of tumor markers is not indicated in women without symptoms; if new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Prostate cancer[7]§	Digital rectal examination annually for 5 yr PSA test every 6–12 mo for 5 yr	Imaging in men without symptoms is not indicated; if new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Colorectal cancer[10]§	Physical examination and CEA test every 3–6 mo for 5 yr CT imaging of chest, abdomen, and pelvis annually for 3 yr Colonoscopy annually for 6 yr after surgery	If new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Non–small-cell lung cancer[12]	History taking and physical examination every 3–6 mo for 1–2 yr, then annually for 3–5+ yr Low-dose axial CT scanning every 6 mo for 1–2 yr, then annually for 3–5+ yr¶	If new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Testicular cancer[13]	Follow-up guidelines, which depend on histologic features (e.g., seminoma or nonseminoma) and stage	If new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Gynecologic cancer[14]	Follow-up guidelines, which depend on histologic features (e.g., endometrial, cervical, or ovarian cancer) and stage	If new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation
Lymphoma[15]	Follow-up guidelines, which depend on histologic features (diffuse large lymphoma, follicular lymphoma, or Hodgkin's disease) and stage	If new or persistent symptoms develop, imaging is indicated as appropriate to the clinical situation

* Regarding cancer treated with bone marrow transplantation,[16] virtually every organ system may be affected by high-dose chemotherapy with allogeneic or autologous bone marrow transplantation. Specific surveillance guidelines for long-term and late effects of childhood cancers depend on organ site and exposure risk; in children who receive high-dose chemotherapy with allogeneic bone marrow transplantation, almost every organ system may be affected[11,15] (https://childrensoncologygroup.org/index.php/survivorshipguidelines). CEA denotes carcinoembryonic antigen, CT computed tomography, DXA dual-energy x-ray absorptiometry, ENT ear, nose, and throat, and PSA prostate-specific antigen.

† The American Society of Clinical Oncology practice guidelines are available at www.asco.org/practice-guidelines/cancer-care-initiatives/prevention-survivorship/survivorship-compendium.

‡ The recommendations are for women receiving antiestrogen therapy.

§ American Cancer Society surveillance guidelines for survivors of prostate and colorectal cancers are available at www.cancer.org/health-care-professionals/american-cancer-society-survivorship-guidelines/prostate-cancer-survivorship-care-guideline.html and www.cancer.org/health-care-professionals/american-cancer-society-survivorship-guidelines/colorectal-cancer-survivorship-care-guidelines.html, respectively.

¶ Surveillance with low-dose CT for more than 5 years is controversial.

events in the general population increase with aging, and such events also occur as a rare late effect of treatment with anthracyclines (e.g., cardiomyopathy) and radiation therapy (e.g., microvessel disease, myocardial infarction, and cardiomyopathy).[45] Another example is sarcopenia. A muscle-wasting syndrome similar to cancer cachexia, sarcopenia occurs as part of normal aging[46] and also occurs in some cancer survivors treated with chemotherapy.[47]

Treatment of late and long-term effects in cancer survivors is often extrapolated from the treatment of the same medical conditions in populations without cancer. Osteoporosis serves as an example. Generally, trials of treatment in cancer survivors rely on a surrogate end point for fracture: the measurement of bone mineral density from DXA. Decreasing bone mineral density results in reduced T scores, which predict fractures. Several guidelines outline approaches to preventing and treating osteoporosis in cancer survivors. (For references, see the Supplementary Appendix, available with the full text of this article at NEJM.org.)

Table 2. Long-Term and Late Effects of Treatment for Cancer.*

Effects	Cause	Risk Factors	Frequency	Interventions
Long-term effects				
Chronic pain[21]	Cancer-related causes: pathologic fractures; CNS, visceral, and bone metastases; nerve entrapment syndromes Chemotherapy-related causes: peripheral neuropathy, Raynaud's syndrome, avascular necrosis Radiation-related causes: plexopathies, myelopathy, mononeuropathy, enteritis and proctitis, cystitis, lymphedema, second cancers, chest-wall syndrome Hormonal therapy–related causes: arthralgia and myalgia, gynecomastia, dyspareunia, osteoporotic compression fractures Postsurgical pain: lymphedema; pain syndromes after mastectomy, pelvic-floor surgery, head-and-neck dissection, and thoracotomy; phantom limb pain	Inadequate pain control, younger age, lower level of education, depression	Common†	Drugs: antidepressants, nonopioid and opioid drugs, cannabis, intrathecal and epidural drug-delivery systems Nondrug interventions: exercise, cognitive behavioral therapy, guided imagery, mindfulness practice, meditation, hypnosis, massage, acupuncture, kyphoplasty, nerve blocks
Infertility[22]	Chemotherapy (e.g., alkylators), pelvic irradiation and surgery, cranial irradiation	Older age, higher dose and longer duration of treatment	Common	Sperm banking, egg harvesting and in vitro fertilization, cryopreservation of eggs before treatment
Gonadal failure[23,24] and menopausal and vasomotor symptoms[25,26]	Alkylators (in premenopausal women); oophorectomy and orchiectomy; GnRH agonists, antiestrogens, and antiandrogens	Older age (in premenopausal women), obesity	Common	Drugs: SSRIs, SNRIs, pregabalin, gabapentin Nondrug interventions: acupuncture and hypnosis; no role for physical activity
Chemotherapy-induced peripheral neuropathy[27]	Taxanes (microtubule inhibitors — e.g., paclitaxel and docetaxel), platins (cisplatin and oxaliplatin), vinca alkaloids, proteasome inhibitors	Higher cumulative dose and longer duration of treatment, higher bolus infusions (vs. lower dose continuous or lower dose IV bolus infusion), overweight or obesity, lack of physical activity, increasing age, diabetes, combinations of taxanes with platins, docetaxel (vs. paclitaxel)	Common	Drugs: duloxetine (moderate effect on painful neuropathy); conflicting data on tricyclic antidepressants, gabapentin, and topical agents (baclofen, amitriptyline, ketamine); so far, no drugs prevent chemotherapy-induced peripheral neuropathy, but careful clinical monitoring for symptoms of peripheral neuropathy, a low threshold for withholding the dose until symptoms resolve, and restarting treatment at a reduced dose may prevent permanent neuropathy or lessen the symptoms after treatment Nondrug interventions: frozen gloves and socks‡

Table 2. (Continued.)

Effects	Cause	Risk Factors	Frequency	Interventions
Fatigue[28]	Chemotherapy, radiation therapy, immunotherapy, high-dose chemotherapy with autologous or allogeneic bone marrow transplantation	Vasomotor symptoms; decreased physical activity; insomnia; cardiopulmonary, renal, and endocrine dysfunction; anemia; pain; depression; anxiety; coexisting conditions; medicines; nutritional issues	Common	Drugs: antidepressants and anxiolytics, psychostimulants (e.g., methylphenidate), ginseng Nondrug interventions: physical activity, cognitive behavioral therapy, psychoeducational therapy, yoga, mindfulness practice, meditation, acupuncture
Insomnia[29]	Chemotherapy, vasomotor symptoms, radiation therapy, high-dose chemotherapy with bone marrow transplantation	Lower educational level, lack of physical activity, vasomotor symptoms, genitourinary and gastrointestinal symptoms, increased BMI, night sweats, inadequate social support, poor sleep hygiene	Common	Drugs: sedatives or hypnotics, melatonin, treatment of vasomotor symptoms Nondrug interventions: sleep hygiene, increased physical activity, cognitive behavioral therapy
Sexual dysfunction[30]	Chemotherapy; tamoxifen (in premenopausal women) and aromatase inhibitors; antiandrogens, prostatectomy, and irradiation for prostate cancer; pelvic surgery and irradiation; negative body image	Problems with sexual satisfaction before cancer, older age, vasomotor symptoms, negative body image, depression and increased distress, fatigue, dissatisfaction with partner (after treatment)	Common	Drugs (women): vaginal moisturizers, intravaginal DHEA, intravaginal estrogens,§ treatment of vasomotor symptoms, antidepressants Drugs (men): 5-phosphodiesterase inhibitors, alprostadil injection or suppository, treatment of vasomotor symptoms, antidepressants Nondrug interventions: couples counseling, counseling regarding body image and sexual responses, increasing physical activity, vaginal dilators and laser therapy in women, penile implants in men
Metabolic syndrome[31]	Cranial irradiation, advanced prostate cancer or prostate cancer with higher Gleason scores	Inflammation, obesity, insulin resistance	Common	Drugs: NA; treatment of diabetes and use of antihypertensives and lipid-lowering drugs as clinically indicated Nondrug interventions: increasing physical activity
Bone loss[32]	Gonadal failure, antiandrogens, antiestrogens	Low BMI, personal or parental history of nontraumatic fracture, current smoking, 3 or more alcoholic drinks per day, long-term glucocorticoid use, rheumatoid arthritis	Common	Drugs: adequate dietary vitamin D_3 and calcium, bisphosphonates, rank-ligand inhibitors Nondrug interventions: physical activity that includes resistance training and weight-bearing exercise
Cognitive dysfunction[33]	Chemotherapy, distress, medications, pain, fatigue, depression, anxiety, cranial irradiation, intrathecal chemotherapy	SNPs in apolipoprotein E4 and catechol-*O*-methyltransferase genes, proinflammatory cytokines generated by chemotherapy, prolonged intensive chemotherapy, older age	Common	Drugs: NA Nondrug interventions: cognitive behavioral therapy, compensatory strategies for executive-function deficits, physical activity
Cardiac damage				

Heart failure[34-36]	Anthracyclines	Preexisting heart disease, high total cumulative dose of anthracycline, route of administration of anthracycline (higher risk with IV bolus than with continuous infusion or lower doses weekly), mediastinal irradiation, older age	Rare¶	Avoid anthracyclines if patient has risk factors for heart disease or baseline LVEF ≤50% Drugs: dexrazoxane is used to prevent cardiac toxicity in children receiving anthracyclines If LVEF drops to <50%, doxorubicin should be discontinued, with referral made to a cardiologist
Valvular damage and coronary artery disease[35]	Radiation therapy‖	Radiation-field arrangements with exposure of normal tissue, lower-energy sources, preexisting heart disease, and older age	Rare	Referral to cardiologist; treatment of cardiomyopathy and myocardial infarction according to standard practices
Cardiac dysfunction[34,36]	Trastuzumab	Older age and low baseline LVEF	Rare	Monitoring of LVEF; if it drops below 50%, trastuzumab should be withheld, with referral made to a cardiologist; in most cases, recovery of LVEF will occur with cardiac medications**
Late effects				
Osteoporotic fractures[32]	Gonadal failure, aromatase inhibitors, antiandrogens	Low BMI, personal or parental history of nontraumatic fracture, current smoking, ≥3 alcoholic drinks per day, long-term glucocorticoid use, rheumatoid arthritis	Common	DXA screening, adequate dietary vitamin D_3 and calcium, bisphosphonates, rank-ligand inhibitors
Uterine cancer[37]	Tamoxifen	Postmenopausal status	Very rare††	Surgery; no role for screening with blind endometrial biopsies because of rarity (0.8% incidence at 8 yr)
Myelodysplastic syndromes and leukemia[38]	Alkylators, anthracyclines, epipodophyllotoxins	Colony-stimulating factors	Very rare	Treatment guided by the cancer that develops; treatment-related myelodysplastic syndromes and leukemia are less responsive to therapy
Sarcomas; leukemia; lung, breast, thyroid, skin, and gastrointestinal cancers[39,40]	Radiation therapy‖	Radiation-field arrangements involving exposure of normal tissue, larger fraction sizes, and lower-energy sources	Very rare	Treatment guided by the cancer that develops; radiation-related cancers are less responsive to therapy

* BMI denotes body-mass index, CNS central nervous system, DHEA dehydroepiandrosterone, DXA dual-energy absorptiometry, GnRH gonadotropin-releasing hormone, IV intravenous, LVEF left ventricular ejection fraction, NA none available, SNP single-nucleotide polymorphism, SNRI serotonin–norepinephrine reuptake inhibitor, and SSRI selective serotonin-reuptake inhibitor.

† Occurs in at least 10% of patients.

‡ Small phase 2 trials suggest that frozen gloves and socks can prevent or lessen neuropathy.

§ The clinician should thoroughly discuss with the patient the nonquantifiable risks (i.e., recurrence) and benefits (i.e., reduced dyspareunia and improved quality of life) of intravaginal estrogens.

¶ Cardiac damage, including arrhythmia, occurs in less than 1% to 5% of patients.

‖ Radiation delivery has changed over the past 40 years, with radiation-field arrangements that minimize exposure of normal tissue and the use of higher-energy sources. Modern radiation therapy is associated with a reduced risk of cardiac events, as well as other radiation-related side effects.

** Early experience with trastuzumab-induced cardiac dysfunction suggested spontaneous recovery of LEVF without cardiac medications. However, most cancer survivors receive cardiac medications until the LVEF returns to a normal level.

†† Uterine cancer as a second primary cancer occurs in less than 1% of patients.

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HEALTH PROMOTION

Weight management,[48] increased physical activity,[49] a healthful diet,[50] smoking cessation,[51] and reduced alcohol consumption[52] are the foundation for improved health and wellness for everyone, and especially for cancer survivors. Obesity is a risk factor for the development of several common cancers (e.g., breast, colon, and prostate cancers). It increases mortality among breast-cancer survivors and may increase mortality among survivors of prostate or colon cancer. Randomized trials are testing whether obese survivors of breast cancer who lose weight and increase their physical activity have improved disease-free survival and declines in cancer mortality.[53]

Physical activity improves health-related quality of life and symptom management in cancer survivors, and it may decrease cancer mortality among survivors of some cancers.[49] Tobacco cessation and referral to smoking-cessation programs are essential components of care for survivors. However, cancer survivors are no more likely to quit smoking than the general population, and about half of them do not receive smoking-cessation counseling.[51] Alcohol is a dose-dependent risk factor for the development of multiple cancers, and continued consumption of alcohol appears to increase cause-specific mortality among survivors with various cancers.[52]

PROMOTION OF PSYCHOLOGICAL WELL-BEING

Depression and anxiety,[54] post-traumatic stress disorder (PTSD),[55] fear of recurrence,[56] and return-to-work and financial issues[57] are among the psychological consequences of living beyond cancer. Typically, these conditions are underdiagnosed and undertreated, despite the availability of effective psychosocial and drug interventions (Table 3).

Although cancer survivors, over time, tend to return to former levels of activity and productivity, many experience distress. Distress occurs on a spectrum extending from adjustment disorders that are just below the threshold of mental disorders to diagnosable psychiatric illnesses (e.g., a major depressive episode).[58] Distress screening is one of the mandates of the American College of Surgeons Commission on Cancer for hospital accreditation. There are many instruments for distress screening. The NCCN distress thermometer is a one-item numerical rating scale that has been labeled the "sixth vital sign."[59] As with screening for depression and anxiety, distress screening before a clinic visit is intended to trigger a response from the health care team if a patient's score exceeds a threshold value. Depending on local expertise, the patient should be referred to a social worker, nurse practitioner, psychologist, or another health care professional for assessment and triage.

SPECIAL POPULATIONS

OLDER SURVIVORS

The percentage of cancer survivors over the age of 65 years continues to grow (Fig. 1). This burgeoning population of older cancer survivors poses one of the most important challenges facing the health care system. Efforts are under way to meet this challenge and identify gaps in knowledge (see the Supplementary Appendix for references). In part, these efforts entail the measurement of end points such as active life expectancy, or the time spent living independently with functional status and cognition intact. Older cancer survivors may not have the same goals as younger adult survivors.[60] For younger patients, prolonged survival may be the primary goal, whereas older patients may value independent functioning and preservation of cognition over length of life.[60]

A geriatric assessment can facilitate the care of older cancer survivors. This tool predicts functional status, frailty, coexisting conditions, and risk of death, and the assessment may change decisions regarding the aggressiveness of cancer treatment.[61] Despite all the benefits of the geriatric assessment, its incorporation into routine oncology practice has been slow. The practice demands of busy oncologists make a full geriatric assessment burdensome.

There are many screening tools to identify patients who require a geriatric assessment.[61] According to the International Society of Geriatric Oncology, the Geriatric 8 is the preferred screening tool, but others are validated and recommended (e.g., Vulnerable Elders Survey–13 and the Triage Risk Screening Tool).[61] The Geriatric 8 is an eight-item scale that covers chronologic age, body-mass index, food intake, weight loss,

Table 3. Risk Factors and Interventions for Psychosocial Issues.

Psychosocial Issue	Risk Factors	Frequency	Interventions
Depression[54]	Female sex, higher number of coexisting conditions, negative body image, financial concerns, history of depression, sedentary lifestyle, loneliness	Common	Drugs: SSRIs, SNRIs, atypical antidepressants Nondrug interventions: cognitive behavioral therapy, mindfulness practice and stress-reduction therapy, hypnosis, physical activity, self-directed web-based interventions
Anxiety[54]	Female sex, higher number of coexisting conditions, younger age, shorter time since diagnosis, living alone, financial concerns, history of anxiety, lower functional status	Common	Drugs: anxiolytics, gabapentin Nondrug interventions: largely the same as for depression
Post-traumatic stress disorder[55]	Prior traumatic experience, unemployment, younger age at diagnosis, shorter time since diagnosis, depression, less social support, lower income, greater perceived negative impact of cancer	Common	Drugs: hydrocortisone Nondrug interventions: largely the same as for depression
Fear of recurrence[56]	Increased anxiety, less-effective coping skills, higher reassurance-seeking behaviors, increased family distress, lower educational level, knowledge of a survivor who had a recurrence	Common	Nondrug interventions: largely the same as for depression
Issues concerning return to work[57]	Older age, lower income, lower educational level, lower self-rating of health, chronic pain, depression, greater physical job demands (i.e., heavy labor), cancer treatment that causes physical limitations, cancer site that interferes with work	Common	Nondrug interventions: psychoeducational interventions (patient education and lessons in self-care), vocational services, and physical activity resulting in improved health-related quality of life and a greater likelihood of returning to work

mobility, neuropsychological problems, use of prescription drugs, and self-rating of health status. The survey takes about 4 to 5 minutes to complete and has the highest sensitivity for predicting an abnormal geriatric assessment.[61] The increase in the number of older cancer survivors that is expected over the next 20 years (Fig. 1) necessitates the incorporation of the Geriatric 8 or other screening tools into routine oncology practice to assess frailty, predict the severity of treatment-related side effects, and predict the risk of death.

SURVIVORS OF CHILDHOOD CANCERS

An estimated 80% or more of cancers in children are cured.[62] However, the most pressing problems for childhood-cancer survivors are treatment-related second cancers and coexisting medical conditions.[63] The Children's Oncology Group Long-Term Survivor Study is a wellspring of information about childhood-cancer survivorship,[11] with guidelines for long-term follow-up based on treatment exposure and risk.

Adult survivors of childhood cancers have significant declines in functional status, increased limitations on activity, poorer mental health status, and poorer general health than a matched sibling control cohort.[44] Many adolescent and young adult survivors of childhood cancer are unaware of their increased health risks,[64] and the National Academies of Sciences, Engineering, and Medicine has identified this group as an especially vulnerable survivor population.[3] Common problems of adolescent and young adult survivors are infertility, other reproductive health problems, and psychosocial issues.[65]

CAREGIVERS

The burdens of caregiving are so great that Golant and Haskins have named caregivers the "other cancer survivors."[66] In fact, the problems that caregivers and cancer survivors have are strikingly similar. Fatigue, insomnia, loss of physical strength, loss of appetite and weight, depression, anxiety, PTSD, and lost income are some of the problems associated with caregiving.[67]

A 2015 report by the National Alliance for Caregiving highlights caregivers' burdens.[68] This report summarizes the results of an online survey of 1248 caregivers, with caregivers defined as those who provide unpaid care for family members or friends 18 years of age or older to help

them take care of themselves. This survey was not specific to cancer survivors, but the results are considered to be generalizable.

Key findings from the report include an overall caregiver prevalence of 44 million people, the majority of whom provide care for persons over 50 years of age. Two thirds of the survey respondents were women, and one half said they "had no choice" in becoming a caregiver. Two thirds of the caregivers also reported some interference with their paid work. One third of the respondents reported discussing the needs of the care recipient with the health care team. However, only one sixth of the caregivers had a conversation about their own needs and resources to address those needs. These survey results are a stark reminder that the caregivers are woefully underserved and yet essential as more cancer care is home-based. Making caregivers aware of available resources is important; in addition, psychosocial interventions, including cognitive behavioral therapy, may be helpful.[69]

Another survey, the National Quality of Life Survey for Caregivers, identified more than 1000 caregivers who provided ongoing care for survivors of breast, lung, colorectal, and prostate cancers.[70] The survey population comprised three groups: current caregivers, caregivers whose cancer survivors were in remission, and bereaved caregivers. In multivariate analyses, becoming a bereaved caregiver caused significant declines in mental health scores, as compared with the scores for current caregivers. These findings show that the process of caregiving is not static but is dynamic over time. Caregivers' needs change with the changing needs of the recipient of care.

CARE COORDINATION AND COMMUNICATION

An ASCO position statement, "Achieving High-Quality Cancer Survivorship Care,"[71] identified four critical aspects of survivor care: developing the best models of care for cancer survivors, articulating the purpose of a treatment summary and individualized care plan (referred to as a survivor care plan), identifying gaps in research, and ensuring access to care for survivors. Cancer survivors receive less routine care (non-cancer-related) than healthy controls if the follow-up care is provided by an oncologist, they receive more routine care if they see a primary care provider for follow-up care, and they receive the highest level of care if they see both an oncologist and a primary care provider or participate in a shared-care model[72] (Table 4).

An emerging concept tied to the shared-care model is risk stratification of survivors.[73,77] Survivors are assigned to low-risk, intermediate-risk, and high-risk categories on the basis of the cancer treatment they received and the risk of recurrence. For example, a patient with early-stage lung or colorectal cancer whose primary treatment was surgery alone would be designated as a low-risk survivor, whereas a patient who underwent allogeneic bone marrow transplantation and has risks of multiorgan side effects would be designated as a high-risk survivor.

A systematic review of primary care physicians worldwide revealed that they wished to share care with oncologists but identified several barriers.[75] These include lack of expertise, skills, and knowledge to provide care for cancer survivors and lack of standards for delivering such care. These barriers reflect a lack of communication and care coordination between oncologists and primary care providers. An increased workload with limited time, the increased financial burden of providing care for cancer survivors, inadequate access to mental health services, and medicolegal risks were also cited as barriers.

Another study, which focused on primary care providers located in urban, suburban, and rural regions of the United States, identified two critical barriers to the incorporation of survivor care in routine clinical practice.[76] First, primary care providers did not view cancer survivors as a distinct patient population and had difficulty identifying them in the electronic medical record. Second, primary care providers received limited information regarding the follow-up of cancer survivors. What information they did receive was not useful or was outdated.

To enhance communication among oncologists, primary care providers, and cancer survivors, the National Academies of Sciences, Engineering, and Medicine recommended generating a survivor care plan. Part of the impetus for the care plan was that many cancer survivors do not know what treatments they received and relocate several times during their lifetimes. Survivor care plans enhance communication between oncologists and primary care physicians, and in an

Table 4. Models of Care Delivery for Cancer Survivors.*

Model	Primary Responsibility	Pros	Cons
In-clinic care	Oncologist who provided cancer treatment also provides follow-up care	Patients prefer specialist care	Insufficient preventive health care
Care provided by midlevel clinician (NP or PA) at disease-site clinic	NP or PA provides cancer site–specific care in clinic where survivor received cancer treatment	Provider has experience with the specific cancer and has access to disease-site expert in real time; model is most suited to academic centers with cancer site–specific oncologists and clinics	Not well suited to general oncologists in community practices
Care provided by midlevel practitioner in separate clinic	NP or PA provides care for all cancer survivors in a separate clinic	Most efficient model in terms of use of resources; most suited to general oncologists who practice in academic settings, large community practices, or hospital-based practices	Providers must be familiar with surveillance guidelines and late and long-term effects of different cancers; access to disease-site experts may be limited and not in real time
Shared provision of care[73,74]	PCP and oncologist provide coordinated care	Better communication between the oncologist and PCP results in improved care	Substantial barriers identified by PCPs†
Care provided in multispecialty clinic	Multiple specialists provide care in the same clinic (e.g., mental health practitioners, pain specialists, specialists in rehabilitation, and endocrinologists)	Patients prefer multispecialty care	Most inefficient model in terms of specialists' time

* Information is from Nekhlyudov et al.[73] and Halpern et al.[74] NP denotes nurse practitioner, PA physician assistant, and PCP primary care physician.
† Barriers include lack of expertise, skills, and knowledge to provide care for cancer survivors and lack of standards for delivering such care.[75,76]

interview study, primary care physicians valued the information in the survivor care plan and felt more confident in providing care for cancer survivors.[78] The value of such care plans to cancer survivors is less clear, since randomized, controlled studies with short-term follow-up have thus far failed to show improvement in health-related quality of life or reduction in distress for cancer survivors who received care as part of an individualized survivor care plan versus those who received usual care.[79] Ongoing studies are assessing the value of survivor care plans for primary care providers and cancer survivors.[80]

Table 4 describes the models of care for survivors.[73,74] However, there is a lack of information about which models improve health-related quality of life, reduce distress and coexisting conditions, and increase survival. Also, little is understood about the cost-effectiveness of the models.[81] Nekhlyudov et al. have described various models of care shared by oncologists and primary care providers.[73] These include a model in which primary care providers are integrated into the staff of providers at site-specific cancer clinics and an oncogeneralist model, in which a primary care provider with experience in survivor care sees cancer survivors in consultation.

It is axiomatic that part of survivor care is preventing a recurrence of cancer. Oncologists and primary care providers have a responsibility to communicate effectively.[82] For example, nonadherence and discontinuation of antiestrogen treatments may lead to increases in breast-cancer mortality.[83] Good patient–physician communication and the establishment of realistic expectations about the benefits and side effects of antiestrogen agents in breast-cancer survivors improve treatment adherence.[84] Likewise, good communication fosters adherence to antiandrogen treatment in prostate-cancer survivors.[85]

CONCLUSIONS

The increasing population of cancer survivors presents several challenges and opportunities. Cancer survivors and caregivers have some of the same needs, and their needs change over time. The two most pressing challenges are meeting the needs of the growing population of older cancer survivors and providing care for survivors of childhood cancer who have treatment-related cancers and coexisting medical conditions. Some

models exist for providing survivor care, but there are scant data on their effectiveness in improving survivorship outcomes.

As advances in prevention and treatment lead to reduced cancer mortality, expanded research, funding, and resources will be required for survivor care. Additional research in health disparities among cancer survivors is needed. Finally, increasing efforts in wellness promotion are needed for cancer survivors, their caregivers, and the general population. If we successfully meet these challenges, the community of cancer survivors and caregivers will enjoy a better health-related quality of life and a smoother transition into the mainstream of life.

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