Adolescent and Young Adult (AYA) Oncology, Version 2.2024

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ABSTRACT

This selection from the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology focuses on considerations for the comprehensive care of AYA patients with cancer. Compared with older adults with cancer, AYA patients have unique needs regarding treatment, fertility counseling, psychosocial and behavioral issues, and supportive care services. The complete version of the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology addresses additional aspects of caring for AYA patients, including risk factors, screening, diagnosis, and survivorship.

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Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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The complete NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology are not printed in this issue of JNCCN but can be accessed online at NCCN.org.

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Individual disclosures for the NCCN Adolescent and Young Adult (AYA) Oncology Panel members can be found on page 880. (The most recent version of these guidelines and accompanying disclosures are available at NCCN.org.)

The complete and most recent version of these guidelines is available free of charge at NCCN.org.

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Overview

Advances in cancer treatment have resulted in declining cancer mortality rates among the overall adolescent and young adult (AYA) patient population over the past decade; however, AYA patients continue to face significant challenges in cancer care due to gaps in knowledge regarding etiology, basic biology, treatment, and survivorship. One of the main reasons for these knowledge gaps is that AYA patients have a low rate of participation in clinical trials, reported to consistently remain below 10%. Participation of AYA patients in clinical trials has been decreasing since 2010, with the exception of AYAs with acute lymphoblastic leukemia (ALL). In addition to the low rate of participation in clinical trials, several other factors contribute to poor outcomes in AYA patients, such as differences in disease biology, lack of consistency in treatment approaches, poor adherence or intolerance to therapy, lack of health insurance, delays in diagnosis, and physician’s lack of familiarity with cancer in the AYA population. AYA patients also have unique developmental, medical, and psychosocial issues, which make adjustment to their disease, health maintenance, and financial hardships more challenging.

The biology, epidemiology, and clinical outcomes affecting AYA patients are usually different from those affecting younger and older patients with cancer. In addition, the genetic, physiologic, and pharmacologic changes associated with AYA patients may impact their ability to tolerate cancer therapy and their response to treatment. Moreover, short- and long-term toxicities impacting a young, independent patient—including the impact of treatment on fertility and sexual function—may disincentivize treatment, leading to gaps in adherence and poor outcomes. Addressing these issues and providing options that empower the patient at the time of initial cancer treatment may result in more successful implementation of the planned therapy. Unlike comprehensive geriatric assessment, which is helpful to physicians in developing a coordinated treatment plan and understanding the functional needs of older patients, no similar assessment has been reported for AYA patients. There continue to be fewer evidence-based data to guide the treatment of AYA patients. AYA patients diagnosed with cancer should be recognized as a distinct age group that has unique medical and psychosocial needs. The distinct biology of disease and age-related issues in...
AYA patients (such as fertility, long-term side effects, insurance/financial issues, transportation to clinic appointments, child care, psychosocial support, and adherence to therapy) should be considered in the treatment decision-making process and during the transition of care from pediatric to adult medical teams.1,15,16

Based on the NCI’s Progress Review Group recommendations, an “AYA patient” is generally defined as an individual aged 15 to 39 years at the time of initial cancer diagnosis.2,17 For 2020, the incidence of cancer in the United States in the AYA population was estimated to be 89,500 with 9,270 cancer deaths.1 Globally, up to 1.19 million cancer cases are estimated to be diagnosed in AYA patients annually.18 Compared with children <15 years, 5-year relative survival in AYA patients is worse for those with ALL, acute myeloid leukemia (AML), Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), astrocytomas, Ewing sarcoma, rhabdomyosarcoma, or osteosarcoma.19 Additionally, for Ewing sarcoma, outcomes are worse for patients ≥18 years compared with patients <18 years.20–22

However, 5-year relative survival is better in AYA patients with medulloblastomas and germ cell tumors compared with children with these tumors, possibly reflecting biologic differences in the tumors of each age group. Compared with adults aged ≥40 years, AYA patients tend to have better survival rates, except for those with breast and colorectal cancers.19,23 Increasing age is associated with poorer prognosis in AYA patients with AML, NHL, Burkitt and Burkitt-like lymphoma, or rhabdomyosarcoma.24

The spectrum of cancer types that affect the AYA population is unique and different from those that affect the pediatric and older populations. Thyroid cancers, lymphomas, melanoma, testicular cancer, cervical cancer, bone and soft tissue sarcomas, leukemias, central nervous system (CNS) cancers, breast cancer, and colorectal cancer account for the majority of cancers in this age group.1,25

Quality care for AYA patients with cancer is tied to timely detection and initiation of treatment, adherence to treatment, and access to a multidisciplinary team of health care professionals who are well-versed in the specific age-related/developmental issues relevant to this patient population.26,27 These issues include, but are not limited to, fertility and sexual function; long-term side effects; behavioral, psychosocial, and socioeconomic issues;
transportation to clinic appointments; maintaining school and work obligations; child care; treatment adherence; and the unique biology of the disease. The relative importance of these issues varies considerably across the broad age range defined as AYA. Certain institutions have established centers specialized in accommodating the specific needs of AYA patients. A retrospective analysis in Florida evaluating clinical trial enrollment in a comprehensive care center melanoma program found that AYA patients with advanced disease (ie, nodal or metastatic disease) were more likely to enroll in a clinical trial. Additionally, researchers reported a nonstatistically significant trend of improved 3-year overall survival in AYA patients who presented with advanced disease.28 Referral of patients to AYA centers of excellence, or centers with established social, clinical, therapeutic, and psychosocial support programs, should be encouraged when feasible. Patients who receive AYA-focused care through a comprehensive and multidisciplinary approach have improved outcomes compared with those who do not receive AYA-focused care.29–32

The goals of the NCCN Guidelines for Adolescent and Young Adult Oncology are to identify and increase awareness of issues specific to AYA patients and recommend interventions unique to these patients; educate physicians regarding the prevalence of cancer in the AYA population and its long-term consequences; identify special considerations related to the management of cancer in AYA patients with the aim of improving treatment tolerance, adherence, and clinical outcomes; and promote participation in clinical trials as well as enrollment in tumor banking and biologic protocols.

Comprehensive Care for AYA Patients With Cancer: Special Considerations

AYA patients should be cared for by a multidisciplinary team of providers with expertise in AYA cancer treatment and management of specific developmental issues such as fertility and sexual function, education, career development, employment, family planning, pregnancy, sexually transmitted diseases, and tobacco, alcohol, and substance use disorders. Given the rarity of several tumor types diagnosed in this population, all AYA patients should be encouraged and offered enrollment in tumor banking studies and multicenter clinical trials, when available.
All AYA patients should undergo comprehensive assessment following cancer diagnosis, which should include psychosocial assessment, discussion of the cancer and treatment-related risk on fertility and sexual function, the use of education concerning fertility preservation methods and contraception, evaluation of complete family history, and, if indicated, a subsequent genetic and familial risk assessment by a genetic counselor. Age and developmentally appropriate information related to cancer should be provided. A pregnancy test should be considered prior to each cycle of therapy in accordance with institutional requirements. Consider referral to a fertility preservation or reproductive health program. It is important to speak with each patient individually, without a caregiver or partner present, to solicit any questions or concerns and to give the patient an opportunity to speak freely.

Age-Appropriate Care
AYA patients can be treated either at pediatric or adult cancer centers. Retrospective analyses have shown that AYA patients with certain pediatric-type cancers, such as ALL, rhabdomyosarcoma, and Ewing sarcoma, have superior outcomes when treated with pediatric protocols. Alternatively, there is a lack of compelling evidence that pediatric protocols improve outcomes in AYA patients with AML, HL, and NHL. As aforementioned, the low rate of participation in clinical trials is one of the main reasons for the lack of improvement in outcomes in AYA patients with cancer. A review of 30 studies of adolescents with cancer (aged 15–19 years) showed that 5%–34% of these patients were enrolled in clinical trials. Concerningly, with the exception of AYAs with ALL, participation of AYA patients in clinical trials has been recently decreasing; the decrease in clinical trial accrual from 2010 to 2015 ranged from −10% (aged 15–19 years) to −54% (aged 35–39 years). Care should be provided at medical centers with broad access to clinical trials (standard-of-care registry trials and trials evaluating novel therapies). Pediatric cancer centers enroll more adolescents into clinical trials (35% vs 12% at nonpediatric cancer centers), and AYA patients treated at pediatric cancer centers have a higher rate of clinical trial enrollment (26%) compared with those treated at adult cancer centers (4%). Persons et al reported that AYA patients who are treated by nonpediatric oncologists are less likely to be enrolled in...
clinical trials. Nevertheless, a substantial number of AYA patients with pediatric malignancies are not being treated at pediatric cancer centers. The treatment and appropriate location of care vary with the type of cancer as well as with the availability of family, community, and institutional support. As a study conducted in Pittsburgh evaluated clinical trial enrollment of AYAs following the creation of a dedicated AYA Oncology Program, a joint effort by pediatric and medical oncologists. It was found that AYA clinical trial enrollment increased to 32% in comparison with 4% for historic controls. AYA patients should ideally be evaluated at medical centers with extensive experience in treating cancer in this patient population and at centers that have access to supportive care services (psychosocial/educational support and fertility preservation) specific to the AYA population as well as to medical subspecialty services appropriate to the cancer diagnosis, such as orthopedic surgeons with experience in limb-sparing surgery for patients with extremity sarcomas. In a supportive care needs survey that assessed the information and service needs of young adults with cancer at a single institution, the majority of young adults with cancer identified the following information as most important: information on their specific malignancy, effects of treatment on fertility, information on maintaining a healthy diet, and exercise/physical fitness during cancer treatment.

<table>
<thead>
<tr>
<th>EVALUATION</th>
<th>SUPPORTIVE CARE SERVICES/INTERVENTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Psychosocial factors:</td>
<td>• Refer for neuropsychological assessment if there are concerns regarding the patient’s cognitive function (eg, attention, memory, executive function) and/or prior educational and career transitions, including returning to school/work after treatment.</td>
</tr>
<tr>
<td>† Developmental and cognitive function</td>
<td>If child life specialists or appropriate psychosocial support specialists are present, they can join the team soon after diagnosis to address the patient’s concerns regarding treatment or procedures, and assist with coping mechanisms to reduce anxiety related to procedures.</td>
</tr>
<tr>
<td>● Communication and information delivery preferences</td>
<td>Offer psychosocial support and counseling to help alleviate distress (NCCN Guidelines for Distress Management†).</td>
</tr>
<tr>
<td>◎ Assess health literacy</td>
<td>Consider flexible treatment dates, consultation times, and procedures (evenings/weekends).</td>
</tr>
<tr>
<td>◎ Preferred coping style of patient/family</td>
<td>• Refer for educational and career services to address training, education, employment, disability disclosure, vocational adjustment training, and transition services (ie, social services, vocational counseling, occupational therapy, financial counselors).</td>
</tr>
<tr>
<td>◎ Adjustment to illness</td>
<td>For all AYA patients, offer counseling around sexual health conversations and decision-making regarding the risks of treatment-related fertility impairment and discuss options for fertility preservation prior to the start of therapy. See Fertility, Reproductive Endocrine, and Sexual Health Considerations (AYAO-5).</td>
</tr>
<tr>
<td>○ If interest is expressed, provide opportunity for patient to share their cancer story.</td>
<td>For LGBTQA+ AYAs, offer additional psychosocial support and referrals surrounding stressors, stigma, or rejection related to their sexuality or gender identity.</td>
</tr>
<tr>
<td>◎ See NCCN Guidelines for Distress Management†</td>
<td>Ensure record system accurately states patient’s pronouns and preferred name.</td>
</tr>
<tr>
<td>● Evaluate for current and past psychiatric symptoms, including anxiety, depression, suicidal thoughts, eating disorders, and self-injurious behavior.</td>
<td>For transgender youth, consider referral to a specialized gender clinic for psychosocial support and coordination of gender-affirming medical care at the patient’s discretion.</td>
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<tr>
<td>● Involvement/interruption of school/work</td>
<td>Behavioral factors</td>
</tr>
<tr>
<td>○ Alone</td>
<td>AYAO-8</td>
</tr>
<tr>
<td>○ Spouse/partner</td>
<td>Relationships</td>
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<tr>
<td>○ Friends/roommates</td>
<td>AYAO-9</td>
</tr>
<tr>
<td>○ Parents</td>
<td>Socioeconomic issues</td>
</tr>
<tr>
<td>○ Children</td>
<td>AYAO-11</td>
</tr>
<tr>
<td>○ Homeless or nonstable living environment</td>
<td>Impact of cancer on identity</td>
</tr>
</tbody>
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†To view the most recent version of these guidelines, visit NCCN.org.
AYA patients. Appropriate management of symptoms and side effects to reduce the severity and toxicity of treatment should be an integral part of the comprehensive care of AYA patients. Surgery, radiation therapy (RT), chemotherapy, and hematopoietic cell transplant (HCT) are the main treatment options for patients who are able to tolerate curative treatment. All of these options are associated with both acute and late side effects. Please refer to “Treatment-Related Issues” in the algorithm (page 853) for guidance on screening for treatment-related toxicities.

Surgery plays an important role in the management of cancer in AYA patients, especially in breast cancer, thyroid cancer, melanoma, bone and soft tissue sarcomas, colorectal cancer, and CNS cancers that are more common in this patient population. Adolescent patients, whose bodies are still developing, may be more affected by some surgical procedures than older patients who are already at or near their full body size. The extent of surgery depends on the type and location of cancer. In some cases, extensive surgery requiring removing part of or an entire organ or limb may be necessary. With advances in surgical techniques and chemotherapy, limb-sparing surgery is feasible for most patients with extremity sarcoma and osteosarcoma. Surgery should be performed at high-volume centers by surgeons with expertise in AYA comprehensive care, with access to rehabilitative services to ensure that function is preserved as much as possible.

Radiation Therapy
RT is associated with an increased risk of delayed morbidity and mortality, some of which include development of second malignant neoplasms; pulmonary, cardiac, and thyroid dysfunction; and chronic health conditions and growth abnormalities. AYA patients receiving RT to the testes or ovaries are at risk for developing fertility impairment and reproductive endocrinopathies later in life. Females with HL who receive chest RT between ages 10 and 30 years are at increased risk of developing breast cancer. Cranial RT is associated with short stature, auditory deficits, cognitive processing difficulties, poor physical function, and rarely debilitating migraines, which contribute to lower rates of employment, independent living, and marriage among AYA survivors of childhood cancer.
RT-induced spinal cord dysfunction is thought to be more prevalent in adolescents, presumably because of elongation of the cord during the growth spurt. A multidisciplinary consultation should be considered to determine the optimal method to reduce radiation-induced effects. For patients with a predicted risk of radiation-induced late effects to tissues surrounding but not in targeted tissues, consider a consultation with a radiation oncologist for proton radiotherapy. A dermatology evaluation (ie, annual skin examinations performed by a dermatologist) is also recommended for patients who previously received RT.

**Systemic Therapy**

Pain, fatigue, nausea, vomiting, mucositis, hair loss, infection, and myelosuppression are some of the acute side effects of chemotherapy. Reversible toxicities do not necessarily warrant dose reductions. See the NCCN Guidelines for Supportive Care (available at NCCN.org) for the management of treatment-related toxicities. Every attempt should be made to maintain dose intensity unless it is contraindicated. Dose reductions are often based on avoiding severe, irreversible organ damage. Significant end-organ damage may compromise long-term function and quality of life in AYA patients.

Establish maximum cumulative dosing parameters and monitor cumulative dosing and schedule for certain medications associated with irreversible organ damage and fertility issues when certain lifetime exposure is encountered.

Anticipatory nausea and vomiting (ANV), also known as conditioned, learned, or psychological nausea and vomiting, is reported to occur before chemotherapy in approximately 20% of patients at any one chemotherapy cycle and in 25%–30% of patients by their fourth chemotherapy cycle. Younger patients (<50 years) may be more susceptible to ANV because they generally receive more aggressive chemotherapy and have poorer emesis control than older patients. Other risk factors for ANV include, but are not limited to, female sex, previous ANV, history of motion sickness, and morning sickness during pregnancy. Prevention strategies include behavior therapies, acupuncture, and administration of anxiolytic medications. See the NCCN Guidelines for Antiemesis (available at NCCN.org).

Although limited data are available on the subject, systematic reviews have reported that AYA patients experience more cancer-related fatigue than older patients and that fatigue is one of the most prevalent, severe, and distressing symptoms in this age group. Furthermore,
several studies on the topic have shown benefit of interventions targeting fatigue in AYA patients with cancer or cancer survivors, although further research on effective management strategies is needed.75–78 See the NCCN Guidelines for Cancer-Related Fatigue (available at NCCN.org).

Alkylating agent–based chemotherapy is associated with a higher risk of infertility in patients.61 See “Impact of Cancer and Its Treatment on Fertility” (page 861). Anthracycline-based chemotherapy is associated with irreversible cardiac dysfunction, whereas neurotoxic chemotherapies such as methotrexate and cytarabine can result in CNS dysfunction.58–79 Bleomycin-induced pulmonary toxicity is well-documented in patients with HL treated with bleomycin-containing chemotherapy regimens.80 Higher cumulative doses of cisplatin, ifosfamide, or epipodophyllotoxins are associated with hearing loss, peripheral neuropathy, renal dysfunction, and secondary AML, respectively.81–84 See also the section on “Late Effects in AYA Cancer Survivors” (available in these guidelines, at NCCN.org).

Otototoxicity may occur after treatment with platinum-based chemotherapy agents.85 Although this side effect is not considered life-threatening, it can have a detrimental effect on an AYA patient’s quality of life. In 2022, the FDA approved the use of sodium thiosulfate (STS) for reducing the risk of ototoxicity associated with cisplatin in pediatric patients ≥1 month of age with localized, nonmetastatic solid tumors.86 The approval of this indication was based on data from 2 open-label phase 3 randomized controlled trials in pediatric patients with cancer who were treated with cisplatin; the incidence of hearing loss was lower in those who received STS than in those who did not receive STS.87,88 However, concerns remain regarding the use of STS in the metastatic setting. A posthoc analysis of data from the ACCL0431 trial showed that, among patients with disseminated disease, STS was associated with a significantly lower 3-year overall survival rate compared with those who did not receive STS (45% vs 84%; P=0.009).89

Immunotherapies are becoming an important component of care for patients with cancer. It is possible that there may be long-term toxicity associated with these agents; however, more data in the AYA population are needed to fully understand the effects.

**Hematopoietic Cell Transplant**

HCT is a potentially curative treatment option for an increasing number of AYA patients with leukemias and...
lymphomas.\textsuperscript{90} Graft-versus-host disease (GVHD), chronic immunosuppression, and gonadal dysfunction related to high-dose conditioning chemotherapy and RT are the major posttransplant complications associated with HCT.\textsuperscript{58,59} Chronic GVHD has been identified as the leading cause of nonrelapse mortality in HCT survivors.\textsuperscript{91} AYA patients are at a higher risk of developing chronic GVHD than younger children.\textsuperscript{92} Patients $>$15 years (children $<$5 years had a probability of $<$14\% compared with a probability of 44\% for patients $>$15 years) and the use of total body irradiation was significantly associated with an increased likelihood of developing chronic GVHD following allogeneic HCT.\textsuperscript{93} Patients who receive peripheral stem cells during the transplant procedure have a greater risk of chronic GVHD compared with those who receive bone marrow transplant.\textsuperscript{94} A report from the Bone Marrow Transplant Survival Study showed that chronic GVHD had a significant impact on the overall health status of HCT survivors, particularly in the areas of functional impairment, activity limitation, and pain.\textsuperscript{95} This study also demonstrated that resolution of chronic GVHD resulted in long-term health outcomes that were comparable to survivors who were never diagnosed with chronic GVHD. HCT survivors are also at increased risk for late complications, which include recurrent infections, secondary cancers, cardiac dysfunction, growth failure, weight loss, neurocognitive delay, and other end-organ dysfunction.\textsuperscript{58-59,96} In addition, the incidence of severe or life-threatening chronic health conditions, endocrine complications, or secondary cancers is also higher among HCT survivors than in noncancer populations and patients with cancer who are treated conventionally.\textsuperscript{90} Allogeneic HCT survivors irradiated at $\leq$30 years are at higher risk of developing secondary solid cancers.\textsuperscript{97} These findings highlight the increasingly recognized need for long-term follow-up care that incorporates screening and surveillance of AYA survivors of HCT.

Adherence to Treatment
Adherence is defined as the extent to which a person’s behavior corresponds with agreed recommendations from a healthcare provider. Nonadherence to recommended treatment and follow-up care contributes to poor clinical outcomes in AYA patients with cancer.\textsuperscript{98,99} Nonadherence to appointments can lead to delayed identification of side effects, complications, or secondary cancers.\textsuperscript{5}
Nonadherence to treatment regimens has been an ongoing problem among patients with cancer, and the prevalence of nonadherence has been consistently higher among adolescents compared with younger or older patients with cancer. Nonadherence to oral chemotherapy contributes to reduced treatment efficacy and increased risk of recurrence. Available evidence from clinical trials that have included AYA patients with leukemia and lymphoma suggests that a substantial portion of AYA patients with cancer (27%–63%) have difficulties adhering to their oral treatment regimens. Difficulties with medication adherence also extend to survivorship, with 23.8% of AYA cancer survivors reporting nonadherence compared with 14.3% in the comparison group ($P<.001$). Survivors were also more likely to report that they could not afford their medication, and uninsured survivors were more likely to report nonadherence than those who were privately insured.

Nonadherence to other components of cancer treatment (eg, nonadherence to appointments for treatment or follow-up, refusing medical examinations, not preparing for procedures or therapy) was also identified in AYA patients. Treatment nonadherence in clinical trials can also interfere with adequate evaluation of the efficacy of a given treatment regimen, which in turn can invalidate the results of a clinical trial.

Risk factors for nonadherence among AYA patients include patients’ emotional functioning (depression and poor/low self-esteem), personal beliefs (perceived severity of cancer diagnosis and the necessity of intervention), growing independence, competing obligations (school, work, and family), and lack of insurance and appropriate psychosocial support. In a randomized controlled trial, video game intervention significantly improved treatment adherence to prophylactic antibiotic use among AYAs with acute leukemia, lymphoma, and soft tissue sarcoma. A review aimed to identify and characterize the various digital health interventions available for support of AYAs with cancer. Numerous modalities, including mobile/tablet apps, video games, wearables, virtual reality, social media, and other web-based interventions were found to exist for the purpose of promoting physical activity, assessing pain management, and improving adherence among AYAs. Additional studies evaluating the efficacy of interventions to improve adherence in AYA patients with cancer are needed.

Risk assessment for nonadherence among AYA patients should include consideration of patient maturity, independence, unmet psychosocial and physical needs, and treatment side effects. For AYAs presumed to be at high risk of nonadherence, implementation of individualized interventions such as additional supportive care resources (eg, social work, psychology, palliative care) to promote adherence may improve outcomes in AYA patients with cancer. The patient’s personal support system (family and friends) should be mobilized and educated to assist in relieving some of the burdens of care and to positively encourage the patient to maintain adherence to therapy. In the absence of data from studies evaluating the effect of interventions to improve adherence in AYA patients with cancer, findings from studies involving AYA patients with other chronic diseases may be able to be extrapolated to this patient population.

**NCCN Recommendations on Adherence to Therapy and Safety Plans**

- Educate about the expectations of treatment and explain the patient’s responsibility to adhere to treatment. Engage in collaborative treatment decision-making with the AYA patient.
- Evaluate for any past history or potential barriers to adherence with medical treatment.
- Provide education and/or guidance about each medication prior to the start of treatment and every time there is a change in treatment. Review the list of medications as well as their dose, purpose, and adverse effects.
- Simplify and modify dosing schedule when medically possible, to accommodate an AYA patient’s lifestyle and normal activities.
- Consider the use of technology (eg, smartphone applications).
- Provide access to systematic and standardized symptom management for side effects related to cancer treatment. See the NCCN Guidelines for Supportive Care (available at NCCN.org).

**Impact of Cancer and Its Treatment on Fertility**

Impaired fertility is a major consequence of cancer and its treatment. The impact of cancer treatment on fertility is related to the age of the patient at the time of diagnosis and treatment, and is dependent on the type, duration, and dose intensity of treatment. Alkylating agent–based chemotherapy, high-dose cranial RT that can impair hypothalamic pituitary function, and targeted RT to the uterus, ovaries, or testes are primary risk factors for gonadal dysfunction and decreased fertility. Gonadal exposure to low-dose RT can result in oligospermia or azoospermia in individuals with testes. Higher-dose RT is associated with both ovarian and uterine dysfunction.

Young female patients with HL treated with chemotherapy are at risk for developing premature ovarian failure, irrespective of their age at the time of treatment (38% for those diagnosed between ages 30 and 40 years of age; 37% for those diagnosed between 9 and 29 years). The cumulative risks for premature ovarian failure are much higher after alkylating agent–based chemotherapy. In a large cohort of females treated between ages 15 and 40 years for
HL, the cumulative risk of premature ovarian failure after alkylating agent–based chemotherapy was 60% compared with only 3% or 6% after nonalkylating agent–based chemotherapy.\textsuperscript{117} Independent risk factors for acute ovarian failure include increasing RT doses to the ovaries and exposure to procarbazine and cyclophosphamide at ages 13 to 20 years.\textsuperscript{110} An analysis of 590 female patients who were diagnosed with HL before age 18 years showed that RT to the pelvis was associated with decreased incidence of parenthood (hazard ratio [HR], 0.66; 95% CI, 0.48–0.90; \( P = .01 \)).\textsuperscript{118}

Among young females treated with adjuvant chemotherapy for breast cancer, the risk for premature menopause is significantly higher for those >35 years with newly diagnosed breast cancer treated with chemotherapy.\textsuperscript{119,120} Similarly, among survivors of HL diagnosed between ages 14 and 40 years, those who were aged 22 to 39 years at first treatment were at a higher risk of developing premature menopause after treatment compared with younger patients (aged 14–21 years).\textsuperscript{121} Treatment with MOPP (mechlorethamine, vincristine, procarbazine, and prednisone)/ABV (doxorubicin, bleomycin, and vinblastine) significantly increased the risk of ovarian failure. After 10 years of treatment, the actuarial risk of premature menopause was 64% after high cumulative doses (>8.4 g/m\(^2\)) and 15% after low doses (≤4.2 g/m\(^2\)) of procarbazine.\textsuperscript{121}

In those treated with alkylating agent–based chemotherapy and RT to the testes, germ cell dysfunction with resultant infertility is more common than Leydig cell dysfunction and testosterone insufficiency.\textsuperscript{122} Leydig cell dysfunction is characterized by increased plasma concentrations of luteinizing hormone combined with low levels of testosterone. Germ cell dysfunction is associated with reduced testicular volume, increased follicle-stimulating hormone concentrations, and reduced plasma concentrations of inhibin B. Leydig cell dysfunction occurs at RT doses higher than those associated with germ cell dysfunction. AYA patients treated with testicular RT ≥20 Gy are at high risk for Leydig cell dysfunction, whereas testicular RT ≥2 Gy can impair spermatogenesis resulting in permanent azoospermia.\textsuperscript{122} Total body irradiation used as part of high-dose conditioning therapy before HCT can also affect the testes, resulting in permanent infertility in the majority of AYA patients with testes.\textsuperscript{61}

Azoospermia is associated with chemotherapy and radiation. Whether it is transient or permanent depends on the type of treatment involved, with radiation and alkylating agents posing the greatest risk for long-term damage.\textsuperscript{123} Azoospermia has been reported in more than 90% of males receiving procarbazine–based chemotherapy regimens such as MOPP and may not resolve over time, resulting in permanent infertility.\textsuperscript{124} Alternatively, the ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) regimen has been shown to be less gonadotoxic, with a vast majority of patients regaining normal fertility after completion of treatment.\textsuperscript{125}

Given that gonadal insufficiency/gonadotoxicity is a well-known side effect of cancer therapy,\textsuperscript{126} the Pediatric Initiative Network proposed a standardized risk stratification model that subdivides the risk of gonadal insufficiency/infertility into minimally increased risk, significantly increased risk, and high level of increased risk.\textsuperscript{127} This classification is based on exposure to alkylating agents or heavy metals, HCT, and radiation exposure.\textsuperscript{127} The male model also incorporates the risk of surgery and does not stratify risk according to pubertal status, unlike the female model.\textsuperscript{127} Although limitations exist, this model is meant to estimate and standardize infertility risk and promote conversation concerning fertility preservation. Details regarding the risk assessment can be found under the “Assessment for Gonadal Function” section under “Screening Recommendations for AYA Survivors” in the algorithm (available at NCCN.org).

The NCCN Guidelines recommend discussing the risks of impaired fertility due to cancer and its treatment with all patients at the time of diagnosis, prior to initiating treatment. This is especially important for patients who will be starting therapies with a high risk of affecting fertility, as described above.

Fertility Preservation

As the AYA age range includes the primary reproductive years, fertility preservation is an issue of crucial importance and should be an essential part in the management of the cancer.\textsuperscript{15,61,128–132} ASCO clinical practice guidelines recommend that providers discuss the options for fertility preservation with all new patients with cancer at the time of diagnosis.\textsuperscript{133} Nevertheless, fertility preservation is currently one of the most under-prescribed and least implemented services in AYA patients with cancer.\textsuperscript{61,128,134} A study that reviewed 231 records of AYA patients with leukemia/lymphoma, sarcoma, or breast or testicular cancers showed that infertility risk was discussed 26% of the time, and fertility preservation options were discussed 24% of the time.\textsuperscript{135} However, it is possible that more discussions about infertility occurred without having been documented. Another study that analyzed the electronic medical records of 454 AYA patients at a single cancer center showed that the risk of infertility was discussed with 83% of patients, with females more likely to be informed than males (odds ratio [OR], 3.57; 95% CI, 1.33–9.60; \( P = .01 \)).\textsuperscript{136} A study of 146 adolescent boys at risk for fertility impairment due to cancer treatment across 8 different pediatric oncology centers found that only 53.4% attempted to bank sperm, with 43.8% successfully banking. Parent or medical team recommendation was associated with increased likelihood of sperm banking completion.\textsuperscript{137}

A systemic review reported that the following factors can hinder the decision-making process for females with
cancer: (1) lack of information about fertility preservation options; (2) fear of perceived risks of fertility treatment (eg, delaying cancer treatment, hormone treatment of a hormone-sensitive cancer); (3) lack of physician referral; (4) emotional distress; (5) relationship/parental status; and (6) financial concerns. The American Society of Reproductive Medicine (ASRM) recommends that conversations concerning fertility be undertaken by an interdisciplinary medical team composed of oncologists, reproductive endocrinologists and urologists, and reproductive surgeons trained in fertility preservation methods. The initial step of discussing intended therapies and associated reproductive risks is entrusted to the oncologist, who can subsequently make referrals as appropriate. Psychosocial providers can assist patients and families in the decision-making process about fertility preservation, particularly when AYA patients are distressed about the potential for impaired fertility associated with cancer treatment. The emotional impact of conversations surrounding fertility, especially for the younger AYA patient, must be taken into consideration. Finally, genetic and financial counselors may also be consulted to discuss the risks and probability of heritable disease transmission and review financial options for fertility preservation, respectively.

The Oncofertility Consortium, a group of clinicians and researchers in the United States, was formed in 2007 by the US NIH to address reproductive barriers facing AYA patients and to identify research priorities in this area. Future aims that were developed during a 2011 meeting are as follows:

- Determine optimal techniques for cryopreservation of reproductive tissue and gametes.
- Further investigate in vitro follicle maturation in primates.
- Investigate AYA patients’ psychosocial needs as part of the fertility preservation plan.
- Improve patient–provider communication regarding fertility preservation.
- Develop and carry out multicenter studies, utilizing the preexisting infrastructure of the National Physicians Cooperative.

Ideally, fertility preservation should be initiated before the start of treatment. However, in some situations, when it is impractical or impossible to pursue fertility preservation before starting therapy, it may be appropriate to readdress later in the course of treatment. ASRM recommends that fertility preservation programs be affiliated with an experienced assisted reproductive technology program. Alternatives to fertility preservation, such as the use of donor gametes, embryos, and adoption, should be discussed by the team. For individuals with ovaries scheduled to undergo pelvic RT, the option of gestational surrogacy may also be reviewed. In the case of cryopreservation, appropriate arrangements should be discussed and documented in the case of donor death.

### Options for Individuals With Ovaries

#### Oophoropexy

For individuals scheduled to undergo pelvic RT, oophoropexy or ovarian transposition may be a promising option involving surgical displacement of the ovaries out of the RT field to minimize ovarian damage and preserve ovarian function.

#### Embryo Cryopreservation

Embryo cryopreservation after in vitro fertilization is an option for fertility preservation. This method is an option for postpubertal individuals with ovaries and requires a committed sperm donor who is available with short notice. It has been highly successful in individuals <40 years. According to data published by ASRM on infertile and donor populations, the live birth rate per cycle start for individuals <35 years was 46.8%, while that for those aged 35–37 years was 34.4%, and that for those aged 38–40 years was 21%. In one study that assessed pregnancy outcomes following embryo cryopreservation, letrozole was used in combination with follicle-stimulating hormone to protect patients with breast cancer against the harmful effects of increased estrogen. Of 33 patients, the live birth rate was 45%, with 39% of live births resulting in twins. These rates are not significantly different from those for infertile couples not affected by cancer, except for implantation rate, which was greater in the patients with breast cancer (40.7% vs 26.1%). A little more than half (55%) of the embryos were transferred to a gestational carrier, with no significant differences in outcomes (ie, implantation, live birth, twinning rates) between self-transfers and gestational carriers.

#### Mature Oocyte Cryopreservation

Mature oocyte cryopreservation is an alternative for postpubertal individuals, and, like embryo cryopreservation, requires hormone stimulation and subsequent oocyte retrieval. Evidence from randomized trials and a meta-analysis suggest that in vitro fertilization with cryopreserved oocytes results in fertilization and pregnancy rates similar to that of fresh oocytes. Like embryo cryopreservation, pregnancy rates with mature oocyte cryopreservation also decline with advancing age.

#### Ovarian Tissue Cryopreservation

Cryopreservation of ovarian cortical tissue is a promising strategy for fertility preservation when there is insufficient time for oocyte or embryo cryopreservation and/or the patient is prepubertal. This technique does not require...
hormonal stimulation, so there is no delay in initiation of treatment.61 This procedure would not be appropriate for certain patients with cancer if potential exists for reintroduction of malignant cells with grafting. It is also not recommended for carriers of BRCA mutations due to the increased risk for ovarian cancer. Orthotopic transplantation has been met with success, with 130 live births reported from cryopreserved and thawed ovarian tissue since 2017.139 After transplantation, ovarian tissue is thought to regain function within 60 to 240 days and may last for 7 years.139 Pregnancy and live birth rates are expected to be higher in donors <40 years due to ovarian follicular reserve. It is recommended that transplantation be performed with the purpose of regaining fertility and not gonadal endocrine function.139 While ovarian tissue cryopreservation is still considered investigational at some institutions, it may be discussed as an option for fertility preservation, if available.

Some studies, including randomized trials, have evaluated the role of menstrual suppression with gonadotropin hormone-releasing hormone (GnRH) agonists to preserve ovarian function during chemotherapy.148–156 Some meta-analyses have shown that GnRH agonists may be beneficial for fertility preservation.157–159 However, the impact of such meta-analyses is limited by factors such as only examining those with breast cancer and only including trials that were not adequately powered and did not use blinding and/or a placebo condition, among other flaws.160,161 There are also limited data available on the long-term impact of GnRH on preservation of ovarian function,157 although a 5-year follow-up analysis of a randomized trial showed that administration of a GnRH agonist does not significantly impact premature ovarian failure or future pregnancy rate.156 Therefore, although data suggest that menstrual suppression with GnRH agonists may protect ovarian function, further investigation is needed.

Nevertheless, GnRH agonists and agents such as the progestin medroxyprogesterone and oral contraceptives may be used in patients with hematologic malignancies and thrombocytopenia and/or anemia who are at risk for menorrhagia for the purpose of menstrual suppression.162 However, caution is needed in endometrial cancer survivors where progestin therapy has been associated with high rates of cancer recurrence,163 which may be prevented by combining metformin with medroxyprogesterone.164

**Options for Individuals With Testes**

**Sperm Cryopreservation**

Individuals should also be counseled regarding options for fertility preservation and referral to a reproductive urologist should be considered. Semen cryopreservation before the start of treatment is the most reliable and well-established means of preserving fertility in postpubertal AYA patients with cancer.61–128 The success of sperm banking may be limited in some patients, such as those with HL and testicular cancer, who may already have azoospermia associated with the disease. Depending on the type of chemotherapy, semen collection may be possible after initiation of chemotherapy; however, the impact of chemotherapy and RT on the risk of genetic defects in the offspring remains unknown.165

If the patient has medical, religious, emotional, or developmental issues that preclude traditional ejaculation methods, other options to obtain sperm for cryopreservation may be discussed, including vibratory stimulation, electroejaculation, surgical testicular sperm extraction, the administration of phosphodiesterase type 5 inhibitors, and the use of alpha-agonists. Traditionally more effective in those with neurologic injuries, penile vibratory stimulation may be used to trigger the ejaculatory reflex. Electroejaculation, normally performed under anesthesia, involves the transrectal stimulation of pelvic tissues, including the prostate and seminal vesicles, to yield ejaculate. Surgical testicular sperm extraction is reserved for individuals who have azoospermia and/or are unable to ejaculate via other methods. The use of phosphodiesterase type 5 inhibitors may be used to obtain ejaculate in those experiencing erectile dysfunction; similarly, alpha agonists may be warranted in cases of retrograde ejaculation.139

**Testicular Tissue Cryopreservation**

Cryopreservation and subsequent transplantation of spermatogonial stem cells may be an option for prepubertal and pubertal individuals in whom semen cryopreservation is not possible.61,128 For those with hematologic or testicular malignancies, autologous transplantation of cryopreserved testicular tissue may not be appropriate for fear of reintroduction of tumor cells. However, immature testicular tissue cryopreservation is still considered experimental.139

Similar to the recommendation for those with ovaries, there is limited evidence regarding the efficacy of hormone suppression in reducing the risk of impaired fertility in individuals with testes during chemotherapy.133

**Fertility, Reproductive Endocrine, and Sexual Health Considerations**

The NCCN Guidelines emphasize that fertility preservation and sexual health and function should be an essential component of the comprehensive care of AYA patients with cancer, who may be at risk for impaired fertility and possible sexual dysfunction due to cancer treatments.127,166–168 An assessment of the risk for gonadotoxicity and impaired fertility due to cancer and its therapy should be performed and discussed with patients. Options for fertility preservation...
should be discussed with all patients as soon as possible prior to the start of therapy and throughout the course of therapy. Care should be coordinated by a multidisciplinary team. Providers should initiate referral to fertility preservation clinics within 24 hours for all patients who choose fertility preservation. Consultation with a financial counselor and local or institutional grants may be available to provide financial assistance with fertility preservation needs. Follow-up with a fertility specialist posttreatment may also be helpful for some patients. Referral to a mental health professional is recommended, if needed, to assist with complex decision-making and process any fertility changes/issues related to intimacy. Consider the emotional impact of conversations surrounding fertility preservation, especially for younger AYA patients (and those who might be a sexual & gender minority [SGM]). AYA patients, especially those with caregiver responsibilities, should be provided with support.

All Patients
- After assessing the patient’s risk for impaired fertility and the patient’s preferences for fertility preservation, recommend a form of appropriate fertility preservation and/or make a referral to a fertility preservation specialist.
- Discuss the effects of treatment on sexual function during and after treatment and refer the patient to a specialist if needed.

Individuals With Ovaries
- For individuals who can delay cancer therapy by approximately 3 weeks, oocyte or embryo cryopreservation via immediate (or random start) controlled ovarian stimulation should be discussed.
- For individuals who are unable to delay therapy for oocyte or embryo cryopreservation, discuss or refer the patient for consideration of ovarian tissue cryopreservation.
- Oophoropexy or transposition of the ovaries out of the field of radiation should be considered for individuals for whom the radiation field will include the ovaries.
- The effects of treatment on gonadal hormone function during and after therapy should be discussed with patients. Patients who face premature ovarian failure should be screened and treated by a specialist. Furthermore, patients who do not undergo fertility preservation before starting therapy may still be appropriate candidates for fertility preservation posttherapy and should be screened and referred to a specialist.
- Medroxyprogesterone, oral contraceptives, or GnRH agonists can be used in protocols that are predicted to cause prolonged thrombocytopenia and thus present a risk for menorrhagia.
- GnRH agonists may protect ovarian function; however, other fertility preservation modalities should still be pursued.

Individuals With Testes
- Sperm banking is the preferred choice of fertility preservation for individuals without erection or ejaculation issues. For patients who can delay cancer therapy, consider more than 1 collection of ejaculate before starting treatment. AYA patients can use either a local sperm bank or an available online sperm banking kit. Oncology centers that treat AYA patients should develop a system for offering sperm banking to all AYA patients in a systematic and patient-centered manner.
- Should the patient have any medical, religious, emotional, or developmental issues that preclude traditional ejaculation methods, alternative methods, including phosphodiesterase type 5 inhibitors, vibratory stimulation, electroejaculation, and collection of retrograde ejaculate can be considered.
- Testicular transposition out of the field of radiation can be considered for patients in whom the radiation field will include the testes.
- Surgical sperm extraction, such as the testicular sperm extraction procedure, may be an alternative strategy for those who cannot ejaculate or who have azoospermia or insufficient sperm in the ejaculate to freeze.
- Discuss the effects of treatment on gonadal hormone function. Screen or refer the patient to a specialist as appropriate after completion of therapy.

Contraception in AYA Patients With Cancer
The NCCN Guidelines recommend discussion about sexual function before, during, and after treatment; this should include a discussion on the use of contraception. Condoms may be used safely by AYA patients with cancer. AYA patients with ovaries have unique contraception needs, and the options depend on the type of cancer, its treatment, and treatment-related complications.

Long-acting reversible contraception (LARC) with intrauterine devices (IUDs) or implantable contraceptives are more effective than short-term contraceptive methods, which include the use of estrogen and progestin with various delivery systems. LARC has been shown to be superior to short-acting contraceptives. In a study of 4,167 participants (aged 14–45 years), LARC was associated with higher 12-month adherence rates than oral contraceptive pills (86% vs 55%). In a large, prospective study involving 7,487 participants, the contraceptive failure rate was significantly higher for those using oral contraceptive pills, patch, or ring compared with those using LARC (4.55 vs 0.27), and the failure rates among participants <21 years were twice as great as in those ≥21 years.¹⁷⁹
The Society of Family Planning guidelines recommend the use of IUDs or implantable contraceptives for most females who are receiving treatment for cancer. The use of any method of contraception is recommended for those who have been free of cancer for at least 6 months and have no history of hormonally mediated cancers, chest RT, anemia, osteoporosis, or venous thromboembolism. The use of IUDs is considered the preferred first-line contraceptive option for females with a history of breast cancer, although for those treated with tamoxifen, a levonorgestrel-containing intrauterine system may be preferable because it has been shown to reduce tamoxifen-induced endometrial changes without increasing the risk of breast cancer recurrence. A levonorgestrel-containing intrauterine system may also be used to minimize menstrual blood loss in patients with iron-deficiency anemia.

Due to the risk of venous thromboembolism associated with the use of combined hormonal contraceptive methods, the US CDC recommend that the use of these contraceptive methods should be avoided in patients of childbearing potential with active cancer or who have been treated for cancer in the past 6 months.

Management of Cancer During Pregnancy

All patients of childbearing potential must receive a pregnancy test before starting therapy. Cancer is diagnosed in about 0.1% of pregnant individuals and is the second most common cause of maternal death during pregnancy. Melanoma, breast cancer, cervical cancer, lymphomas, and leukemias are the most common cancer types diagnosed during pregnancy. An analysis of 1963–2007 data from the Swedish Multi-Generation Register and the National Cancer Register showed a lower-than-expected number of cancers diagnosed during pregnancy, and a rebound in the number of cases of melanoma, CNS cancers, breast cancer, and thyroid cancer in postpartum individuals. This rebound may be due to changes in the mammary and thyroid glands being overlooked during the postpartum period. Despite some persisting beliefs, there is no evidence of pregnancy-associated relapse in survivors of HL.

Although limited research is available on the prognosis of cancer during pregnancy, a few meta-analyses and systematic reviews have suggested that the prognosis associated with certain cancers (eg, breast, melanoma, vulvar) may be worse when occurring concurrently with pregnancy compared with the same cancers occurring outside of pregnancy. These results may be confounded by factors related to the patient’s pregnancy, delays in diagnosis, and differences in treatment decisions, making a definitive conclusion difficult. Maternofetal transmission of cancer across the placenta is rare but has been reported for metastatic melanoma, lung cancer, and certain hematologic malignancies.

Accurate diagnosis of the type and stage of cancer using appropriate imaging studies (ultrasound, chest x-ray, and mammogram) with abdominal shielding and limiting fetal exposure to ionizing radiation is an essential step in the management of cancer during pregnancy. When possible, nonradioactive imaging modalities, including MRI and ultrasound, should be used. There is insufficient evidence regarding the safety of gadolinium-based contrast agents in pregnant individuals; however, these agents have been demonstrated to cross the placenta in animal studies. There are currently no available data on the safety of iodinated contrasts during pregnancy. Surgery is possible at any time during pregnancy depending on the anatomic location of the tumor, although it may be beneficial to delay surgery, when possible, until after fetal viability due to the associated risks, including miscarriage, low birth weight, and premature delivery. Selection of an appropriate treatment plan for pregnant individuals is dependent on the cancer type, tumor biology, and tumor stage, similar to the management of cancer in those who are not pregnant. In addition to the disease characteristics in pregnant individuals, the gestational age of the fetus is a significant factor in the selection of treatment.

RT is contraindicated during pregnancy. However, in very rare instances when it is necessary, such as oncologic emergencies like spinal cord compression, superior vena cava compression, and brain metastases, RT may be administered in the lowest effective therapeutic dose (using techniques such as uterine shielding to minimize fetal exposure), with the goal of controlling maternal cancer and providing the fetus with the best chance for survival with normal development. The dose to the fetus can be reduced by using modified RT administration techniques or adding additional shielding between the treatment machine and the patient. Early collaboration among the radiation oncologist, medical physicist, medical and/or surgical oncologist, and obstetrician is essential. The American College of Radiology has developed guidelines with an objective to assist practitioners in identifying pregnancy, preventing unnecessary irradiation of pregnant AYA patients, tailoring examinations to effectively manage RT dose, and developing strategies to quantify and evaluate the potential effects of RT delivered to patients who are pregnant. In 2014, an international consensus panel made up of researchers and clinicians who are experts in cancer treatment during pregnancy developed similar guidelines for RT in individuals who are pregnant.

Chemotherapy should be avoided during the first trimester because of greater risk of teratogenic effects, which include major congenital malformations, impaired organ function, spontaneous abortions, and fetal death. Although the use of chemotherapy during the second and third trimesters has not been associated with significant...
teratogenic effects, it may be associated with maternal and fetal risks including low birth weight, preterm labor, and intrauterine growth restriction. However, a multicenter, prospective case-control study of children born to those with cancer (129 cases, 129 controls) showed no significant impact of chemotherapy treatment on cognitive, cardiac, and general development of the offspring. Potential benefits and risks of chemotherapy for both the pregnant individual and fetus must be carefully evaluated before the start of treatment. Delaying treatment until after fetal maturity, with careful follow-up to rule out disease progression, is a safe option for those diagnosed with early-stage cancers. In some individuals diagnosed with advanced-stage disease with an urgent need to start chemotherapy in the first trimester, pregnancy termination may be considered, and the potential teratogenic risks should be discussed if the individual decides to continue with the pregnancy. Due to the severe teratogenic effects of methotrexate, it should not be used for the treatment of cancer in individuals at any stage of pregnancy. Older-generation alkylating agents (e.g., procarbazine, busulfan), thalidomide, lenalidomide, pomalidomide, and tretnoin are also considered teratogenic and are contraindicated during pregnancy. The safety and efficacy of hormonal agents and targeted therapies have not yet been evaluated in well-controlled studies including those who are pregnant. At the present time, the use of such agents in patients who are pregnant is not recommended.

Supportive care for the management of treatment-related side effects should be integrated into treatment planning based on the trimester of pregnancy. Granulocyte colony-stimulating factors for the management of neutropenia and antiemetics for the management of nausea and vomiting have been used in patients who are pregnant without any significant side effects.

The panel members acknowledge that the management of cancer during pregnancy poses significant diagnostic and therapeutic challenges for the pregnant individual, fetus, and physician. The guidelines recommend that AYA patients diagnosed with cancer during pregnancy receive individualized treatment from a multidisciplinary team involving medical, surgical, radiation, and gynecologic oncologists; obstetricians; and perinatologists as appropriate. Referral to tertiary cancer centers with expertise in the management of high-risk obstetric cases and in the diagnosis of cancer during pregnancy and knowledge of the physiologic changes that occur during pregnancy is strongly encouraged.

Several of the NCCN Guidelines for cancers that are diagnosed more commonly during pregnancy include disease-specific recommendations for managing cancer during pregnancy. For more information, see “Breast Cancer During Pregnancy,” in the NCCN Guidelines for Breast Cancer; “Cervical Cancer and Pregnancy,” in the discussion section of the NCCN Guidelines for Cervical Cancer; “Management of CML During Pregnancy,” in the NCCN Guidelines for Chronic Myeloid Leukemia; and “Special Considerations in the Treatment of Polycythemia Vera (PV) and Essential Thrombocythemia (ET): Pregnancy,” in the NCCN Guidelines for Myeloproliferative Neoplasms (all available at NCCN.org). The American Academy of Dermatology has published recommendations for the diagnosis and management of melanoma during pregnancy. Similarly, the American Cancer Society has published guidelines for the management of HL in pregnancy. Finally, the American Thyroid Association has published guidelines for the diagnosis and management of thyroid disease, including thyroid cancer, during pregnancy.

Psychosocial and Behavioral Issues
AYA patients diagnosed with and treated for cancer have psychosocial and behavioral issues that are distinct from those of pediatric and adult patients. AYA patients aged 20–29 years are significantly less likely to use professional mental health services than teens and older patients aged 30–39 years. AYA patients in the 20- to 29-year-age group are also significantly more likely to report an unmet need with regard to receiving age-appropriate information about their cancer. Some of the challenges faced by AYA patients and survivors include maintaining an active and independent lifestyle, coping with treatment-related side effects and stress, seeking and understanding information, accepting cancer, and maintaining a positive attitude. AYAs go through developmental stages marked by rapid changes in cognitive and emotional growth, and these issues need to be considered while delivering developmentally appropriate psychosocial and supportive care to AYA patients.

Few measurement tools have been developed to better understand health-related quality of life in AYA patients with cancer. Palmer et al developed an AYA Oncology Psychosocial Screening Tool to assist clinicians in supporting psychosocial coping during active treatment and promoting healthy posttreatment survivorship in AYA patients. This screening tool has 4 main areas: a distress thermometer, a checklist of “areas of concern,” a tick box for information provision, and signatures. Further validation of this tool and its use will help clinicians to improve psychosocial care for AYA patients, regardless of where they receive treatment.

Psychosocial needs for AYA patients should be assessed across the following domains: (1) individual function (psychosocial, emotional, and behavioral issues); (2) relationships (family, peers, and health care professionals); and (3) socioeconomic issues. Age-appropriate and developmentally appropriate supportive care services and interventions should be used to address each of these domains.
Individual Function

Psychosocial Issues
AYA patients must cope with cancer treatment while attaining key developmental milestones such as identity development, including sexual identity; peer involvement; initiating intimate and emotional relationships; establishing autonomy from parents; maintaining personal values; fostering self-esteem and resilience; and independently making decisions about their future that involve education, career, or employment.229–232 The impact of diagnosis and treatment of cancer on their physical appearance, sexual development, and sexual function can lead to shame, social isolation, and regressive behaviors if not addressed promptly. Cancer and its often intensive treatments in their normal activities. Interruptions of school or work due to treatment may have negative consequences for their long-term career opportunities, financial status, and lifetime earnings.225 During the treatment period, AYA patients should have the opportunity to live as normal a life as possible, continue their education and/or careers, and participate in the many milestones of their lives.233 Physical and/or occupational therapy may help AYA patients transition back to a lifestyle appropriate for their age group.234

Integral to the comprehensive care of individuals with cancer, including AYA patients, is an assessment for gender expression, gender identity, pronouns, and sexual identity. SGMs, or the lesbian, gay, bisexual, transgender/transsexual, and queer/questioning (LGBTQ) community, are a population that is unrepresented in medicine. This group includes a spectrum of identities; a comprehensive list of acronyms, definitions, and additional resources may be found on the NIH website, overseen by the NIH Sexual & Gender Minority Research Coordinating Committee.235 The terms “lesbian,” “gay,” and “bisexual” denote one’s sexual orientation or attraction.236 According to the NIH, the term “sex” is meant to refer to one’s chromosomal makeup and reproductive anatomy and is most often delineated as either male or female. Intersex refers to those individuals whose sexual anatomy or chromosomal constitution does not adhere to the norm (e.g., Klinefelter syndrome, or the presence of XXY chromosomes).237 Gender, however, is understood to be the integration of social, environmental, cultural, and behavioral factors and encompasses terminologies including gender identity, gender norms, and gender relations.238

Experts estimate that approximately 3.4%–12% of the United States population identifies as LGBTQ. SGMs experience significant disparity related to cancer diagnosis and treatment. Proposed reasons for this incongruity include decreased rates of cancer screening, behavioral risk factors (e.g., increased rates of smoking and alcohol use), obesity and decreased exercise, nulliparity (among SGMs patients assigned female at birth), and receptive anal sex (among SGMs patients assigned male at birth). The SGM population also faces numerous healthcare discrepancies, such as significant discrimination, poorer insurance coverage, and inadequate physician knowledge of specific LGBTQ health needs, leading to psychological ramifications and overall dissatisfaction with treatment.239 In a nationwide online survey of 273 LGBTQ individuals who had been diagnosed with cancer, patients reported to be influenced by provider LGBTQ knowledge and skills, perceived safety of the clinical encounters for the purpose of identity disclosure, and inclusion of members of their support system. SGM patients reported having a variety of clinical experiences and were more likely to be self-advocates of their care.240

The prevalence of cancer risk factors, such as tobacco use, differs among LGBTQ individuals when compared with non-LGBTQ persons. A cross-sectional online survey reported that LGBTQ individuals disclosed higher rates of past 30-day tobacco media exposure and had higher odds of past 30-day use of tobacco products when compared with non-LGBTQ individuals.241 In addition to the increased prevalence of certain risk factors and a greater physical disease burden, SGM individuals are more likely to have mental health concerns. Attributable to a number of factors, when compared with heterosexual persons, SGM individuals are twice as likely to be depressed, 2.5 times as likely to attempt suicide, and are at an increased risk for anxiety disorders and other psychological conditions.242 Similarly, LGBTQ individuals are at an increased risk for self-harm or nonsuicidal self-injury.243

A higher incidence of bullying is reported among youth and AYAs. This figure is even higher among LGBTQ youth, who report more accounts of physical and cyber-bullying. In fact, it has been reported that 80% of LGBTQ adolescents have experienced victimization and harassment by peers.244 Disparity also exists within SGM subpopulations. For instance, nonbinary individuals, or those who do not identify as strictly male or female, reported a higher incidence of bullying (86.7%) and polyvictimization than transgender or LGBTQ cisgender individuals.

Seven cancer sites have been reported to disproportionately affect the LGBTQ population for a variety of theorized reasons: anal, breast, cervical, colorectal, endometrial, lung, and prostate cancers.236 In a survey of 388 oncology providers at a single institution, 91.7% of physicians specializing in the aforementioned 7 cancer sites reported that they would be comfortable treating LGBTQ individuals and would encourage education of unique health matters. However, only 49.5% of providers answered LGBTQ health-related knowledge questions correctly.236 Among 149 respondents to a survey conducted among 450 oncologists from 45 NCI-designated cancer...
centers, although 95.3% reported that they were comfortable treating LGB individuals, only 53.1% were confident in their assessment of the health care needs of the LGB population. The percentage was even lower for oncologists who were comfortable treating transgender patients (82.5%), with only 36.9% confident in their ability to understand the health needs of transgender individuals.239

It is therefore imperative that providers recognize the gravity of their role when caring for SGM AYA patients. Members of the oncology care team must work collaboratively to create an inclusive, safe, and comfortable space to facilitate conversation with LGBTQ individuals surrounding gender, sexual orientation, sexual behaviors, and other relevant experiences.244 Support persons, as identified by SGM patients, may be involved in cancer care as appropriate. Referrals for psychosocial support should be initiated as appropriate, and referrals to a specialized gender clinic should be considered for transgender youth.245,246 Recognizing that members of the SGM population face significant health and healthcare disparities and unique psychosocial issues, providers must develop a thorough and comprehensive understanding of such matters and consider cancer screening as appropriate.247 Research also suggests that LGBTQ individuals must navigate addressing unique survivorship issues, including but not limited to arranging follow-up care and coming out to multiple providers, contemplating the effects of systemic therapy on LGBTQ sexuality, and coping with delicate family and relationship issues.248 Awareness and a thorough understanding of such concerns are required for the care of SGM patients.

**Emotional Issues**

Cancer-related issues such as confrontation with mortality and loss of fertility can result in significant emotional distress and psychiatric symptoms such as depression and anxiety in AYA patients. These feelings are related to patients’ cognitive capacity to understand the severity of their disease while sometimes lacking fully mature cognitive and emotional coping abilities.225 Psychological distress is significantly greater among AYAs compared with older adults249–253 and prescription rates of anxiolytics and hypnotics are higher in AYA survivors compared with their peers, suggesting an increased emotional burden.254 In a longitudinal study that assessed the prevalence of psychological distress in 215 AYA patients with cancer (aged 15–39 years) during the first year following diagnosis, distress symptoms exceeded population norms at diagnosis and at 12-month follow-up.256 In this study, 12% of AYA patients reported clinically significant chronic distress throughout the first 12 months after diagnosis and an additional 15% reported delayed distress. Distress is also prevalent in AYA cancer survivors; however, most AYA survivors with distress reported that they had not spoken with a mental health professional (74.7% with moderate distress, 52.2% with severe distress).255

In addition to distress, depression and anxiety are commonly experienced by AYA cancer survivors. An analysis from the Childhood Cancer Survivor Study showed that survivors of AYA cancer (n=2,589) report higher rates of depression (OR, 1.55; 95% CI, 1.04–2.30) and anxiety (OR, 2.00; 95% CI, 1.17–3.43) compared with their siblings (n=391).256 Another study of 5,341 cancer survivors diagnosed at ≤25 years found that survivors were more likely to be prescribed antidepressants compared with age-and gender-matched controls (26.9/1,000 person-years for survivors vs 22.5/1,000 person-years in controls; HR, 1.19; 95% CI, 1.12–1.28).257

The need for information, counseling, and practical support was reported in 57%, 41%, and 39% of AYA patients, respectively, at 12 months after cancer diagnosis. Kazak et al258 reported that intensive cancer treatments during adolescence are associated with inferior psychosocial outcomes and health beliefs in survivors compared with their age-matched peers. Psychological problems are also associated with an increased risk for obesity and poor health behavior, which may increase future risk for chronic health conditions and secondary neoplasms.259 It is therefore recommended that AYAs diagnosed with cancer meet with child life specialists, if available, soon after diagnosis to address concerns that the patient may have regarding treatment or procedures and assist with coping mechanisms to reduce anxiety.260

**Behavioral Issues**

AYA patients with cancer may engage in risky behaviors (tobacco, alcohol, cannabis, or substance use) that may impair their health. Older age at cancer diagnosis, lower household income, less education, no pulmonary-related cancer treatment, and no brain RT were independently associated with a statistically significant relative risk of smoking initiation.261 The risk factors associated with alcohol use disorders included fair or poor self-assessed health, depression, anxiety, somatization, activity limitations, and cancer-related fears and uncertainty.262 Low perception of susceptibility to late effects, older adolescence compared with early adolescence, and worry about cancer and its treatment were the strongest predictors of substance use disorders.263 Although AYA patients may be aware of the complications associated with tobacco, alcohol, cannabis, or use of other substances during their treatment, they may not avoid them throughout treatment because these habits may make them feel “normal” and like part of their peer group. Clinicians working with this population should be aware of such matters and address these issues in a sensitive and confidential manner.253,254

Studies have shown increased rates of mental illness and cognitive impairment among adolescent cannabis
users compared with adults with similar usage habits. Heavy or regular use of cannabis in adolescents has been associated with impairments in attention, learning, memory, planning, and psychomotor speed. An earlier age of onset of cannabis use exacerbates these adverse effects. If an AYA patient chooses to continue use of cannabis, education on methods for lowering risk of adverse effects is recommended. For example, the patient may be counseled to avoid high tetrahydrocannabinol–content products, avoid synthetic cannabinoids, choose routes of administration other than inhalation of combusted cannabis, limit frequency of use, and never drive while impaired. Additionally, as there are insufficient data, it is uncertain whether cannabis affects the metabolism and efficacy of chemotherapeutic agents.

In 2006, e-cigarettes, or vaping products, were introduced to the United States market. Marketed originally as tools for smoking cessation and safer alternatives to cigarettes, the aerosols of these products are now known to contain active compounds, including nicotine, tetrahydrocannabinol, cannabidiol, vitamin E acetate, and select flavorings and additives. It is reported that among youth, the overall use of nicotine-containing products has increased since the release of e-cigarettes and devices such as the JUUL. Past 30-day vaping among high school students in the United States rose from 1.5% in 2011 to 20.8% in 2018. Alarming, past 30-day e-cigarette use among middle school students in the United States increased from 0.6% in 2011 to 4.9% in 2018. The CDC and US FDA, as well as other health authorities, have reported an extensive number of e-cigarette or vaping use–associated lung injury cases since 2019. Many patients (the majority of whom have been AYAs) have been hospitalized, with several requiring intensive care and respiratory support.

AYA patients are also vulnerable to sexual and reproductive health complications that should be addressed prior to, during, and after completion of treatment. Traditional risk-taking behaviors of AYAs coupled with a compromised immune system may put AYA patients with cancer and survivors at a greater risk of sexually transmitted infections and, in certain cases, malignancy. See the section on "Contraception in AYA Patients with Cancer," (page 865) for more discussion of appropriate contraception choices for patients with cancer and survivors.

Consequent to treatment and lifestyle-related factors, it is reported that AYAs have a 5- to 15-fold increased risk of cardiovascular morbidity when compared with the general population. Therefore, lifestyle and diet modification are key in AYA cancer survivors to increase survival. AYA patients have nutritional concerns that are different from those of children and adults, especially among younger patients in this population. Adolescents are dependent on their families for food preparation and may experience peer pressure when eating at school or with friends. The INAYA trial, consisting of AYAs aged 18 to 39 years, reported improved nutritional behavior among AYAs following intensified individual nutrition counseling during a 3-month period. Diet/nutrition information has thus been reported as an unmet need among AYAs. Promotion of healthy lifestyle behaviors and incorporation of physical activity into treatment regimens and posttreatment follow-up may also produce numerous physical and psychological health benefits. Regular physical activity integrated into AYA cancer care may also decrease cancer-related fatigue.

**NCCN Recommendations for Supportive Care Services/Interventions for Psychosocial and Behavioral Issues**

- Refer AYA patients for neuropsychological assessment if there are concerns regarding cognitive function (eg, attention, memory, executive function) and/or prior to educational and career transitions, including returning to school/work after treatment.
- Child life specialists or appropriate psychosocial support specialists (if available) should meet with the patient soon after diagnosis to address any potential concerns regarding treatment or procedures and assist with coping mechanisms to reduce any potential anxiety.
- Consider a referral to a social worker, mental health provider, and community-based resources serving AYA patients to screen for any symptoms of depression, anxiety, suicidal ideation/behaviors, and self-injurious behavior.
- Offer psychosocial support and counseling to help alleviate distress. See the NCCN Guidelines for Distress Management (available at NCCN.org).
- Consider providing flexible treatment dates, consultation times, and procedures when possible to enable AYA patients to continue with their treatment without interrupting their school/work or other normal activities.
- Refer patients for educational and career services to address training/education, employment, disability disclosure, vocational adjustment training, and transition services (ie, social services, vocational counseling, occupational therapy, financial counselors).
- For all AYA patients, provide counseling around sexual health conversations and decision-making regarding the risks of treatment-related fertility impairment and discuss the options for fertility preservation prior to initiating treatment.
- For lesbian, gay, bisexual, transgender, queer (or questioning), intersex, asexual, 2-spirit (LGBTQIA2S+) AYA patients, consider offering psychosocial support and referrals surrounding stressors, stigma, or rejection related to their sexuality or gender identity.
- Ensure that the record system accurately reflects the patient’s pronouns and correct name. For transgender
youth, consider referring the patient to a specialized gender clinic for psychosocial support and coordination of gender-affirming medical care at the patient’s discretion.

- Refer patients to a smoking cessation program if needed (see NCCN Guidelines for Smoking Cessation; available at NCCN.org).
- Provide education about the impact of early cannabis use on cognitive development and mental health. If the AYA patient chooses to continue use, provide education on the risks and benefits of varying methods of ingestion and dosing.
- Refer patients with signs, symptoms, or a history of a substance use disorder to a risk reduction or substance use counseling program.
- Provide education about the impact of treatment on sexual health, including safe sexual practices in light of risk of infection, risk for bleeding, and prevention of pregnancy.
- Since the incidence of sexually transmitted infections peaks among AYAs aged 15 to 24 years, provide preventive health education about sexually transmitted diseases.
- Provide education about potential diet/nutritional changes associated with cancer treatment and possible interventions. Refer to a registered dietitian-certified specialist in oncology.
- Provide education on physical conditioning and its related health benefits during and after cancer treatment. To address physical impairments and to initiate physical activity interventions, refer AYAs to a rehabilitation specialist (ie, physiatrist, physical therapist, occupational therapist). Note that a medical evaluation and clearance by a physician (such as an oncologist or physiatrist) are recommended before initiating exercise in patients for whom exercise modifications or precautions may be needed.
- Evidence-based integrative therapies/interventions can be considered.
- Refer patients experiencing challenges with their faith or belief in a just or fair world to faith-based resources or activities (eg, church youth groups, mentors). If needed, refer to a chaplain or pastoral counselor.

Relationships

Social, Peer, and Family Relationships
AYA patients often must endure lengthy hospital stays under the supervision of healthcare providers, resulting in significant isolation from family members and/or peer groups. Isolation and alienation are common among AYAs diagnosed with cancer, because they often miss out on the life experiences shared by their non-ill peers. Reinforcing relationships with family members, peers, and health professionals is an important aspect of life for AYA patients.

Although some studies have identified family support and cohesiveness as important contributors to a survivor’s adjustment, others have identified the important role played by same-aged peers (healthy peers as well as other AYA cancer survivors) in helping AYAs cope with cancer and overcome feelings of loneliness. In one study, AYA patients with cancer (aged 16–22 years) identified social support (including family members, friends, healthcare providers, and other patients) as their major coping strategy. In another study, some AYA patients and survivors reported that opportunities to meet other young adult survivors were more important than the support they received from family and peers.

Peer support programs assist AYA patients and survivors in establishing and maintaining relationships with their healthy peers as well as with other AYA patients with cancer, offer opportunities to achieve age-related developmental tasks (building interpersonal and problem-solving skills), and promote positive psychosocial growth. Peer support also provides AYAs with an opportunity to address areas of shared concern, such as uncertainty about the future, establishing autonomy while being increasingly dependent on family and friends, sexual identity, and impaired fertility, thereby reducing feelings of social isolation.

AYA peer support groups have been developed in a variety of formats, including face-to-face meetings, camp style formats, or online support groups. Social networking groups focused on supporting AYA patients are particularly helpful for exchanging support, informational and emotional, through providing advice and empathizing with other AYA patients dealing with cancer. Summer camps and adventure programs where participants are physically challenged have resulted in improvements in self-confidence, independence, and social contacts. Many of the AYA patients may not be interested in conventional cancer support groups but are willing to participate in social networking events involving other AYA patients, survivors, and family members. Indeed, studies of AYA patients and survivors indicated that 73% of patients currently receiving therapy and 74% of off-treatment survivors reported that their needs for retreats and camp programs were unmet.

Communications With Health Care Professionals
Communicating information to AYA patients can be challenging, especially because there are several subgroups within the AYA population with different levels of cognitive and emotional development. It is very important to establish direct communication with the patients on an individual basis, with sufficient sensitivity to each patient’s needs and preferences. Although some
patients prefer not to receive direct communication about their cancer, others may desire a more prominent role in the management of their care. For the latter group, information should be provided directly to patients in a developmentally appropriate manner, allowing time to process the information and delivering information in a caring manner. AYA patients prefer that information about their cancer and cancer-related risks be communicated to them in a manner that is positive, respectful, and nonjudgmental. In a pilot project aimed at eliciting the views of AYA patients with cancer, humor, closely followed by expertise and knowledge, was identified as the most important characteristic that patients would like to see in their nurses. Because there is evidence that AYA patients are willing to use the internet to obtain health information and support, it is also helpful to provide them with a list of recommended and reliable age-appropriate online sources to access information about their cancer, particularly with regard to treatment and late effects, fertility preservation, mental health counseling, peer support groups, diet, and nutrition. See “Online Resources for Patients and Survivors” (available at NCCN.org).

NCCN Recommendations for Supportive Care Services/Interventions for AYA Patient Relationships

- Promote collaborative communication between AYA patients and parents, caregivers, children, spouse/partners, other family members, siblings, friends, and/or social networks.
- Early in the treatment process, encourage the completion of a medical power of attorney/health care proxy and a living will at age of majority.
- Provide access to AYA-specific advanced care planning guides.
- Provide information to identified family members and partners about psychosocial support and supportive services to increase awareness of the possible psychosocial issues associated with cancer diagnosis in AYA patients.
- Provide AYA-specific activities and/or support groups (in person and/or virtually), especially for inpatients, to provide psychosocial support and reduce boredom, anxiety, and depression. Such interventions include AYA support groups, social and recreational programs, and psychoeducational programs.
- Consider family-based intervention models from pediatrics (eg, parent support groups, Impact of Traumatic Stressors Interview Schedule).17
- Provide information about peer support and social networking opportunities and create flexible visiting hours and an environment that will encourage peers to visit AYA patients.
- Establish direct communication with the individual patients, providing developmentally appropriate information about their cancer, treatment options, and potential side effects, thus reinforcing the importance of AYA involvement in decision-making.
- Some AYA patients prefer not to share information about their cancer with their family in an effort to shield their family members from some of the things they themselves worry about. Therefore, obtain their permission to share information with identified family members or other members of their support system, and encourage completion of a Health Insurance Portability and Accountability Act (HIPAA) release form.
- Provide psychoeducation and assistance exploring and documenting advance directive preferences.
- If the AYA patient is >18 years, provide information on and the necessary forms that legally allow medical information to be shared with caregivers of the patient’s choice.
- Always conduct medical and psychosocial care in the language preferred by the patient/family. Use certified interpreters and do not rely on family members, friends, or noncertified medical staff for interpretation.

Socioeconomic Issues

AYA patients ≥26 years, are much more likely to be uninsured or underinsured individuals than adults or children, with many of them in a transition between their parent’s insurance and independent insurance. Young adult survivors of childhood cancers are more likely to report health-related unemployment, lower rates of health insurance coverage, and more difficulties obtaining coverage compared with their siblings. An analysis of 9,353 AYA patients with HL showed that having either public or no health insurance was associated with poorer HL-specific survival, compared with patients with private or military insurance (HR, 2.08; 95% CI, 1.52–2.84). Furthermore, unemployment and lack of health insurance appear to be significant predictors of psychological distress in the childhood cancer survivor population. Uninsured AYA patients are also less likely to participate in clinical trials. As described previously, advanced stage of cancer at diagnosis and lack of health insurance were significantly associated with longer time to cancer diagnosis in AYAs. Greater rates of unemployment and lack of health insurance among AYA patients and survivors are also associated with limited access to long-term follow-up care. Results from the AYA HOPE study, a population-based cohort study of 523 AYA patients with cancer (aged 15–39 years at diagnosis from 2007–2009), suggest that lack of health insurance is also associated with poor health-related quality of life among AYA patients with cancer. Financial toxicity is a concern, because AYA patients with employment also experience problems in obtaining...
affordable health and life insurance due to their pre-existing cancer history. Even those with relatively comprehensive insurance may be liable for substantial out-of-pocket expenses related to treatment, such as transportation costs associated with traveling for treatment, accommodations, meals, and child care, as well as expenses not related to treatment. AYA patients who are financially independent also have to face an additional burden of loss of income because of their inability to work during treatment. Once treatment is completed, AYA patients with cancer also require long-term follow-up care for monitoring and treatment of late effects.

**NCCN Recommendations for Supportive Care Services/Interventions for Socioeconomic Issues**

- Assess AYA patients’ health insurance status and provide information on potential sources of coverage (eg, Medicaid, Health Insurance Marketplace [https://www.healthcare.gov/], parent’s insurance) and other key elements associated with insurance coverage.
- Educate AYA patients about the benefits for which they may qualify (eg, short- or long-term disability, state disability benefits, Social Security benefits, public assistance).
- Provide information regarding drug assistance programs for patients with limited or no insurance. Consider also providing information regarding hospital pharmacy vouchers or low-cost medication programs.
- Provide information on obtaining financial assistance for fertility-based services. Local and institutional grants may be available.
- Provide school support and education services for patients in high school or college.
- Refer patients for career counseling and/or education support as indicated. Encourage discussion with guidance counselors and educators about the impact of cancer care on education.
- Refer to mental health expert as needed to assess the psychosocial impact of financial toxicity (eg, loss of employment, withdrawing from school, not being able to socialize with friends due to decreased income).
- Direct AYA patients to legal resources and/or advocates for assistance with understanding health insurance coverage.
- Provide a referral for transportation assistance programs (eg, van ride programs, voucher programs) for AYA patients who must travel to receive treatment. Identify resources for respite care that would be helpful for those with young children.
- Provide information about recommended and reliable online resources and financial support programs to access information related to their cancer.
- Integrate financial assistance for AYA cancer survivors into their survivorship care plans.
- Consider the need for long-term follow-up care for monitoring and treatment of late effects long after treatment has been completed.

**Summary**

AYA patients with cancer should be recognized as a distinct population that has unique medical, developmental, and psychosocial needs. It is important for physicians to identify issues specific to the AYA population and recommend appropriate interventions with the aim of improving clinical outcomes. Most importantly, all AYA patients should have access to age-appropriate supportive care and medical subspecialty services appropriate for their cancer diagnosis.

**References**


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### Individual Disclosures for the Adolescent and Young Adult (AYA) Oncology Panel

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