NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Adolescent and Young Adult (AYA) Oncology

Version 1.2017 — October 10, 2016

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NCCN Guidelines Panel Disclosures

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

To find clinical trials online at NCCN Member Institutions, click here: nccn.org/clinical_trials/physician.html.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise specified.

See NCCN Categories of Evidence and Consensus.

NCCN Guidelines Version 1.2017 Updates Adolescent and Young Adult Oncology

Updates in Version 1.2017 of the NCCN Guidelines for Adolescent and Young Adult Oncology from Version 1.2016 include:

AYAO-5
- Toxicities: Modified cardiac toxicity from "Regular echocardiograms and electrocardiograms" to "Regular echocardiograms. A baseline electrocardiogram (EKG) is *only* recommended after completion of treatment and then as clinically indicated."

AYAO-6
- Modified "Women are at risk for premature ovarian failure due to chemotherapy" changed to "Women are at risk for premature ovarian failure *following therapy*."
- Under recommendations for Females, removed "embryo cryopreservation is preferred if there is an identified sperm donor."
- Females, menstrual suppression bullets reordered and modified:
  - It is *controversial* ~~inconclusive~~ whether menstrual suppression would protect the ovaries but emerging data suggest that menstrual suppression with GnRH agonists may protect ovaries in young women with breast cancer before the initiation of chemotherapy.

AYAO-7
- Evaluation
  - Changed "Characteristics" to "Psychosocial factors."
  - Moved "Involvement/interruption of school/work to section on psychosocial factors." Removed "childcare" from this bullet.
  - Added Impact of cancer on identity:
    - ◊ Personal values
    - ◊ Self-esteem
    - ◊ Body image and physical changes
    - ◊ Strengths/resilience
    - ◊ Future goals
- Changed "Dietary needs" to "Assess nutritional requirements and potential deficits based on age."
- Supportive Care Services/Intervention
  - Added "Refer to smoking cessation program if needed, see NCCN Guidelines for Smoking Cessation."
  - Added "Refer to registered dietitian-certified specialist in oncology (RD-CSO)."
  - Adherence to therapy
    - ◊ Added "Educate about expectations of treatment and explain patient's responsibility to adhere to therapy."
    - ◊ Changed "Provide" to "*Consider* flexible treatment dates, consultation times, and procedures (evenings/weekends)."

AYAO-10
- Vaccinations
  - HPV vaccine is recommended for males *9-22 years* and females from 9–*27 years of age except in high risk groups*

AYAO-A
- Added "Conventional melanomas in AYA have a similar behavior and a similar genomic signature when compared to melanomas in older patients. These patients should be offered similar treatment options See NCCN Guidelines for Melanoma."
- Removed the following bullets:
  - Principles of pathology for younger patients with consideration to additional testing with comparative genomic hybridization (CGH) or fluorescence in situ hybridization (FISH) may be useful to detect the presence of selected gene mutations for histologically equivocal lesions.
  - Sentinel lymph node biopsy
    - ◊ Higher yield in AYA population
  - Surgical margins have not been established for patients <18 years of age, as they were not included in the trials.

AYAO-B (1 of 3)
- Added "The recommendations listed here include general principles; for more detail refer to the Children's Oncology Group (COG)"

AYAO-B (2 of 3)
- Added "A baseline electrocardiogram (EKG) is only recommended after completion of treatment" to cardiac toxicity screening.

AYAO-B (3 of 3)
- Screening recommendations for females, added *AMH (anti-mullerian hormone).*

AYAO-D
- Updated online resources for AYA patients and survivors.

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DEFINITION OF THE ADOLESCENT AND YOUNG ADULT ONCOLOGY POPULATION

The National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) database defines the Adolescent and Young Adult (AYA) Oncology patient as the one diagnosed at 15–29 years of age.[a] NCI's AYA Oncology Progress Review Group defines AYA as a patient diagnosed at 15–39 years of age.[b] In the NCCN Guidelines, AYA will be defined as patients 15–39 years of age at the time of initial cancer diagnosis.

PURPOSE OF THE NCCN GUIDELINES FOR AYA ONCOLOGY

- **These guidelines have been developed as supportive care guidelines and not as treatment guidelines. The purpose of the guidelines is to increase awareness of unique issues in AYA oncology, identify issues, and recommend interventions unique to the AYA population. In addition, these guidelines will identify resources available to the AYA population, include appropriate tabular materials, and make recommendations per patient management.**
- **AYA patients diagnosed with cancer should be recognized as distinct age groups that have unique medical and psychosocial needs. The frequency of distribution of cancer types is dramatically different across the age spectrum of the AYA population.[c]**
- **The distinct biology of disease as well as other age-related issues in the AYA population (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.**
- **The goal of the NCCN Guidelines for AYA Oncology is to identify issues specific to the AYA population; recommend interventions unique to the AYA population; educate physicians regarding the prevalence of cancer in AYAs; discuss long-term consequences; explain special considerations related to cancer management in AYA patients that aim to improve treatment tolerance, compliance, and clinical outcomes; and promote participation in clinical trials.**
- **Participation in clinical trials should be strongly encouraged in the AYA population.**

[a]Bleyer A, O'Leary M, Barr R, Ries L. Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000. National Cancer Institute, NIH Pub. No. 06-5767 2006.
[b]Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer Report of the Adolescent and Young Adult Oncology Progress Review Group. 2006. http://planning.cancer.gov/library/AYAO_PRG_Report_2006_FINAL.pdf
[c]See Age-Specific SEER Incidences of Cancer by Age Group and Sex in the AYA Population (2008–2012) (AYAO-4).

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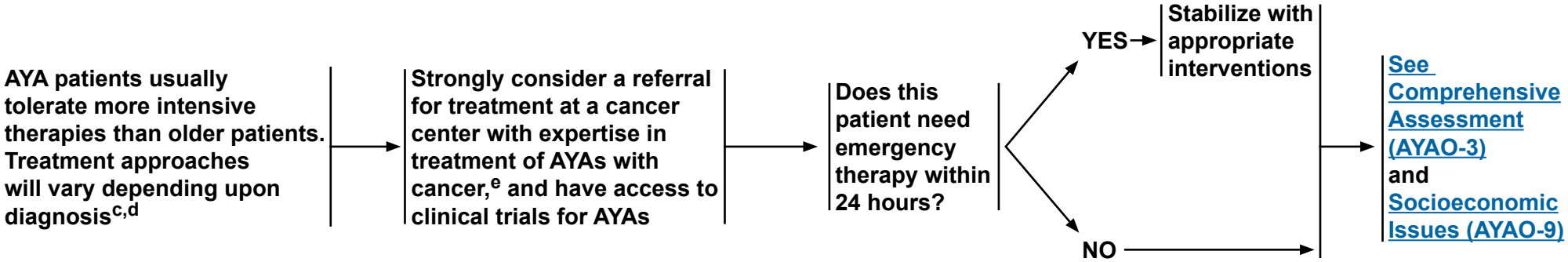
SCREENING, ASSESSMENT, AND EVALUATION



[c]See Age-Specific SEER Incidences of Cancer by Age Group and Sex in the AYA Population (2008–2012) (AYAO-4).
[d]See Definition of AYA Population (AYAO-1).
[e]These centers provide a multidisciplinary approach involving a team of providers with expertise in cancer treatment and management of specific mental health and developmental issues such as fertility, education, career development, employment, family planning, pregnancy, sexually transmitted diseases, smoking, and substance abuse.

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COMPREHENSIVE ASSESSMENT

- **Provide age-appropriate information related to cancer**
  See Online Resources for AYA Patients and Survivors (AYAO-D)
- **Discuss contraception prior to initiating therapy**
- **Discuss risks of infertility due to cancer and its therapy, the use of fertility preservation**
  See Fertility/Endocrine Considerations (AYAO-6)
- **Psychosocial assessment**
  - **See Psychosocial/Behavioral Considerations**
    - ◊ **Individual (AYAO-7)**
    - ◊ **Relationships (AYAO-8)**
    - ◊ **Socioeconomic Issues (AYAO-9)**
  - **See NCCN Guidelines for Distress Management**
- **Referral for genetic and familial risk assessment/counseling (within 2 months after the start of therapy)**
  - **Risk factors for breast cancer**
    - ◊ **Germline mutations of *BRCA1, BRCA2, TP53* (Li-Fraumeni syndrome) or *PTEN* (Cowden syndrome)**
      See NCCN Guidelines for Genetics/Familial High-Risk Assessment: Breast and Ovarian
    - ◊ **Chest irradiation**
  - **Risk factors for colon cancer**
    - ◊ **Mutations in *MMR* genes [hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome)] or *APC* genes [familial adenomatous polyposis (FAP)]**
      See NCCN Guidelines for Colorectal Cancer Screening
  - **Risk factors for sarcomas See NCCN Guidelines for Soft Tissue Sarcoma**
    - ◊ **Li-Fraumeni syndrome**
    - ◊ **Germline mutations in the retinoblastoma (*Rb*) gene or succinate dehydrogenase (*SDH*) gene. Testing for germline mutations in the SDH subunit genes should be considered for AYAs with wild-type gastrointestinal stromal tumors (GIST) (lacking KIT or PDGFRA mutations) or paragangliomas**
    - ◊ **FAP-associated desmoid tumors (aggressive fibromatosis) See NCCN Guidelines for Colorectal Cancer Screening**
    - ◊ **Germline mutations in neurofibromatosis-1 (*NF-1*) gene are associated with malignant peripheral nerve sheath tumor (MPNST)**
  - **Risk Factors for Multiple Endocrine Neoplasms (MEN)**
    - ◊ **See NCCN Guidelines for Neuroendocrine Tumors**

Treatment-related issues → **See AYAO-5**

Fertility/ endocrine → **See Fertility/ Endocrine Considerations (AYAO-6)**

Adherence to treatment → **See Psychosocial/ Behavioral Considerations (AYAO-7)**

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Age-Specific SEER Incidences of Cancer by Age Group and Sex in the AYA Population (2008–2012)[f,g]

Cancer type	Ages 15–19		Ages 20–24		Ages 25–29		Ages 30–34		Ages 35–39	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Bone sarcomas	2.0	1.1	1.2	0.9	0.8	0.8	0.8	0.5	0.8	0.7
Carcinoma of breast				1.3		8.5		26.8	0.2	59.5
CNS cancers	2.2	2.0	2.3	2.2	3.0	2.6	4.0	2.9	4.4	2.9
Carcinoma of cervix and uterus		0.1		1.5		6.6		13.9		21.3
Carcinoma of colon and rectum	0.3	0.4	1.1	0.9	2.4	2.3	5.2	4.7	9.4	9.4
Carcinoma of head and neck	0.5	0.5	0.7	0.8	1.0	1.1	2.0	1.9	4.5	2.9
Carcinoma of respiratory tract		0.1	0.3	0.3	0.5	0.7	1.2	1.2	2.7	2.8
Carcinoma of kidney	0.2	0.2	0.4	0.5	1.2	1.2	3.0	2.2	6.1	3.9
Germ cell neoplasms	4.6	1.2	10.9	1.3	14.8	1.2	13.9	1.0	11.0	0.8
Leukemias	3.6	2.6	3.0	2.2	3.1	2.4	3.7	3.0	4.7	3.9
Lymphomas										
HL	3.0	3.3	4.3	4.6	4.0	4.1	3.8	3.5	3.1	2.5
NHL	2.3	1.2	3.1	1.9	4.0	3.0	5.7	3.9	8.6	6.0
Melanoma	0.9	1.3	2.0	5.2	4.2	9.0	7.2	11.6	10.6	14.9
Soft tissue sarcomas	1.4	1.3	2.1	1.7	3.2	2.1	4.3	2.9	4.9	3.6
Thyroid carcinoma	0.9	4.6	1.7	9.6	2.9	17.0	4.8	24.3	6.8	29.8

[f]These are incidence rates per 100,000.
[g]Data from Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975–2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015.

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TREATMENT-RELATED ISSUES

Dose schedules

- AYA patients usually tolerate more intensive therapies than older patients
  - Dose intensity and dose density are associated with improved outcomes[h]
  - See NCCN Guidelines for Myeloid Growth Factors for growth factor support
- Dose reductions are often based upon avoiding severe, irreversible organ damage
  - Assume that the patient population has a significant long-term survival and that significant end-organ damage may compromise long-term function and quality of life
- Monitoring of cumulative dosing for certain medications associated with irreversible organ damage may be essential when certain lifetime exposure is encountered
  - Anthracycline-based chemotherapy (cardiac dysfunction)
  - Bleomycin (pulmonary toxicity)
  - Cisplatin (hearing impairment and renal dysfunction)
  - Epipodophyllotoxins (secondary acute myeloid leukemia/myelodysplastic syndromes [AML/MDS])
  - Ifosfamide (renal dysfunction)
- Maximum cumulative dosing parameters are often established for a patient to reduce the risk of significant irreversible damage

Toxicities

- Reversible toxicities do not necessarily warrant dose reductions.
  See NCCN Guidelines for Supportive Care for the management of treatment-related toxicities, including:
  - See NCCN Guidelines for Adult Cancer Pain
  - See NCCN Guidelines for Antiemesis
  - See NCCN Guidelines for Cancer- and Chemotherapy-Induced Anemia
  - See NCCN Guidelines for Cancer-Related Fatigue
  - See NCCN Guidelines for Palliative Care
  - See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections
- Intensive screening is recommended for the following treatment-related toxicities:
  - Cardiac toxicity - Regular echocardiograms. A baseline electrocardiogram (EKG) is only recommended after completion of treatment See Screening Recommendations (AYAO-B)
  - Renal toxicity - Regular glomerular filtration rate (GFR) calculations to monitor renal toxicity associated with cisplatin- and ifosfamide-based chemotherapy
  - Neurotoxicity - Regular audiogram to monitor hearing loss associated with cisplatin- or carboplatin-based chemotherapy
  - Routine endocrine, ophthalmology, and dental evaluations for patients with selected radiation exposure and/or total body irradiation (TBI) for stem cell transplant

[h]Womer RB, West DC, Krailo MD, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: a report from the Children's Oncology Group. J Clin Oncol 2012;30:4148-4154.

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FERTILITY/ENDOCRINE CONSIDERATIONS

Fertility and endocrine considerations →

- **Fertility preservation as well as sexual health and function should be an essential part in the management of AYAs with cancer who are at any risk for infertility due to cancer treatments[i]**
- **Discuss risks for infertility due to cancer and its therapy, fertility preservation, and contraception prior to the start of therapy[j]**
  - **Men are at risk for azoospermia following therapy, which may or may not resolve over time**
  - **Women are at risk for premature ovarian failure following therapy**

→

Initiate referral for fertility preservation clinics within 24 hours for all patients who choose the option of fertility preservation
Refer to a mental health professional to assist with complex decision making if needed.
See Psychosocial/ Behavioral Considerations (AYAO-7)

→

Males
- **Discuss the possibility of sperm banking**
- **Suggest a local sperm bank, or available online sperm banking kit**

Females
- **Discuss the possibility of embryo cryopreservation or oocyte cryopreservation**
  - **Initiate if provider deems that therapy can be delayed long enough for a cycle of oocyte stimulation (for low- and intermediate-risk Hodgkin's lymphoma, low-grade sarcomas, and breast cancer)**
- **Oophoropexy**
  - **Ovaries may be surgically moved away from the planned radiation field, either during cancer surgery or in a separate procedure**
- **Menstrual suppression**
  - **Medroxyprogesterone, oral contraceptives, or gonadotropin-releasing hormone (GnRH) agonists may be used in protocols that are predicted to cause prolonged thrombocytopenia and present a risk for menorrhagia**
  - **It is controversial whether menstrual suppression would protect the ovaries, but emerging data suggest that menstrual suppression with GnRH agonists may protect ovaries in young women with breast cancer before the initiation of chemotherapy.[k]**

[i]Levine J, Canada A, Stern CJ. Fertility preservation in adolescents and young adults with cancer. J Clin Oncol 2010;28:4831-4841.

[j]The impact of cancer therapy on fertility is related to the age of the patient at the time of treatment and is dependent on the duration, dose intensity, and type of treatment. See NCCN Guidelines for Breast Cancer for the management of women with breast cancer during pregnancy.

[k]Moore HCF, Unger JM, Phillips K, et al. Phase III trial (Prevention of Early Menopause Study [POEMS]-SWOG S0230) of LHRH analog during chemotherapy (CT) to reduce ovarian failure in early-stage, hormone receptor-negative breast cancer: An international Intergroup trial of SWOG, IBCSG, ECOG, and CALGB (Alliance). J Clin Oncol 32:5s. 2014 (suppl; abstr LBA505).

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PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS

ASSESSMENT → **EVALUATION** → **SUPPORTIVE CARE SERVICES/INTERVENTIONS**

Individual →

- Psychosocial factors:
  - Cognitive function
  - Emotional issues
  - (See NCCN Guidelines for Distress Management)
  - Evaluate for other psychiatric symptoms, depression, and anxiety
  - Involvement/interruption of school/work
  - Living status
    - Alone
    - Spouse/partner
    - Parents
    - Children
  - Impact of cancer on identity
    - Personal values
    - Self-esteem
    - Body image and physical changes
    - Strengths/resilience
    - Future goals
- Behaviors
  - Adherence to therapy
  - Tobacco, alcohol, or substance abuse
  - Sexual behavior/risks/concerns
  - Assess nutritional requirements and potential deficits based on age
  - Exercise needs
- Existential/spiritual issues that could interfere with adherence to therapy

→

- Refer AYA patients with cognitive dysfunction or other psychiatric symptoms (e.g., depression, anxiety) to a mental health provider and community-based resources serving AYA patients.
- Offer psychosocial support and counseling to help alleviate distress. (See NCCN Guidelines for Distress Management)
- Adherence to therapy
  - Educate about the expectations of treatment and explain the patient's responsibility to adhere to therapy.
  - Provide education and/or guidance about each medication prior to the start of treatment and every time there is a change in treatment.
  - Review list of medications and their dose, purpose, and adverse effects.
  - Simplify dosing schedule and change timing and frequency of medication or method of administration, when medically possible, to fit into AYAs' lifestyle and normal activities.
  - Provide access to systematic and standardized symptom management for side effects related to cancer treatment. See NCCN Guidelines for Supportive Care
- Consider flexible treatment dates, consultation times, and procedures (evenings/weekends).
- Refer to smoking cessation program if needed. See NCCN Guidelines for Smoking Cessation
- Refer patients with signs, symptoms, and a history of substance abuse or addiction to a risk reduction or substance abuse management program.
- Provide education about sexual health (including prevention of pregnancy and sexually transmitted infections), diet, and exercise. See WHO recommendations in the Discussion section.
- Refer to registered dietitian-certified specialist in oncology (RD-CSO)
- For all AYA patients, provide counseling around decision-making regarding the risks of treatment-related infertility and discuss options for fertility preservation prior to the start of therapy. See Fertility/Endocrine Considerations (AYAO-6)
- Refer patients experiencing challenges with their faith or belief in a just or fair world to faith-based resources or activities (e.g., church youth groups, mentors). If necessary, refer to a chaplain or pastoral counselor.

Relationships → See AYAO-8

Socioeconomic issues → See AYAO-9

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PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS

ASSESSMENT	EVALUATION	SUPPORTIVE CARE SERVICES/INTERVENTIONS
Relationships →	• Family status ▸ Interaction and relationship with parents ▸ Interaction and relationship with spouse/partner ▸ Patient with young children • Peer relationships • Participation in community and social activities (e.g., religious organizations, clubs, athletics/recreation, music, youth groups) • Communications with health care professionals ▸ Decision-making preferences: family, friend, clinical care team, and/or self ▸ Information and communication preferences (e.g., parents)	• Promote communication between AYA patients and family members. ▸ Parents ▸ Spouse/partners ▸ Siblings • Provide family members and partners with information about psychosocial support and behavioral services. ▸ Increase awareness of the possible psychosocial issues associated with cancer diagnosis in AYAs, so that family members and partners may continue to support the patient. • Family-based intervention models from pediatric studies may have utility for AYAs. ▸ Parent support groups ▸ AYA support groups ▸ Social and recreational programs ▸ Psychoeducational programs • Provide information about peer-support groups to assist AYAs establishing and maintaining relationships with their normal peers as well as with other AYAs with cancer. See Online Resources for AYA Patients and Survivors (AYAO-D) ▸ Face-to-face meetings ▸ Camp and retreat programs ▸ Online support groups • Create flexible visiting hours and an environment that will encourage peers to visit AYA patients. • Health care professionals should establish direct communication with individual patients. ▸ Reinforce the importance of AYA involvement in decision-making. ▸ Ask for permission to share information with family members. ▸ Provide age-appropriate information about their cancer, treatment options, and potential side effects. See Online Resources for AYA Patients and Survivors (AYAO-D)

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PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS

ASSESSMENT	EVALUATION	SUPPORTIVE CARE SERVICES/INTERVENTIONS
Socioeconomic issues →	• Insurance availability and security ▸ Employer-provided ▸ Parent's insurance • Assessment of risk for losing insurance ▸ Loss of employment ▸ Age out of parents' insurance • Risk for financial loss or bankruptcy • Child care • Transportation • Accommodation if traveling to receive treatment • Desires for complementary and alternative medicine (CAM) • Loss of housing →	• Link qualified AYA patients to Medicaid, social security, and/or disability insurance. • Educate AYA patients about benefits they may qualify for, such as short- or long-term disability, state disability benefits, and/or food stamps. • Direct AYA patients to legal resources/advocates for understanding health insurance coverage. • Identify resources for respite care for AYA patients with young children. • Refer to transportation assistance programs (e.g., van ride programs, voucher programs). • Refer to reputable providers of CAM services. • Provide AYAs with a list of recommended and reliable online sources to access information related to their cancer. See Online Resources for AYA Patients and Survivors (AYAO-D) • Financial assistance for AYA cancer survivors needs to be integrated into survivorship plans. • AYAs with cancer need long-term follow-up care for monitoring and treatment of late effects long after completion of treatment.

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SURVIVORSHIP

AYA cancer survivor[l] →

- Develop a "Cancer Treatment Summary and Survivorship Care Plan" See NCCN Guidelines for Survivorship
- Provide a periodic evaluation focusing on history, physical examination, and screening based on treatment exposures and risk for treatment-related late effects
- Vaccinations
  - HPV vaccine is recommended for males 9-22 years and females from 9–27 years of age except in high risk groups[m]
  - Annual influenza vaccine
- Counsel regarding lifestyle practices and methods to reduce risk (e.g., avoiding smoking, increasing level of physical activity)
- Advocate for appropriate health care coverage
- For patients who received chemotherapy and/or radiation therapy (RT), recommend a dental exam and cleaning every 6 months

SELECTED EXPOSURES / SCREENING RECOMMENDATIONS

See Screening Recommendations (AYAO-B)

Cranial or craniospinal radiation →
- Neuroendocrine axis screening
- Neuropsychological evaluation

Chest radiation →
- Females: see breast cancer screening
- Thyroid screening
- Cardiovascular risk assessment and screening
- Screening for cardiomyopathy
- Screening for valvular heart disease
- Pulmonary screening

Abdominal or pelvic radiation →
- Colorectal cancer screening
- Assessment of gonadal function
- Screening for kidney or bladder disease

Alkylating agents →
- Screening for kidney or bladder disease
- Assessment of gonadal function
- Screening for treament-related AML (t-AML) or myelodysplasia
- Pulmonary screening (for selected agents)

Anthracyclines →
- Screening for cardiomyopathy
- Screening for t-AML or myelodysplasia

Bleomycin →
- Pulmonary screening

Cisplatin/ carboplatin →
- Cardiovascular risk assessment
- Screening for kidney and/or bladder disease
- Audiological evaluation
- Screening for t-AML or myelodysplasia

Epipodophyllotoxins →
- Screening for t-AML or myelodysplasia

[l]An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and caregivers are also impacted. Adapted with permission from the National Coalition for Cancer Survivorship as shown in the National Cancer Institute's About Cancer Survivorship Research: Survivorship Definitions webpage.

[m]Further details are here: http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hpv.html

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DISEASE-SPECIFIC ISSUES RELATED TO AGE

Acute Lymphoblastic Leukemia (ALL)

- See NCCN Guidelines for ALL

Bone and Soft Tissue Sarcomas

- See NCCN Guidelines for Bone Cancer and NCCN Guidelines for Soft Tissue Sarcoma
- Rhabdomyosarcoma
  - Uncommon outside of the pediatric population; should be referred to an institution with experience in the management of rhabdomyosarcoma

Colorectal Cancer

- Higher incidence of mucinous histology
- More often right-sided
- Higher incidence of signet ring cells and microsatellite instability (MSI)
- More advanced stage at diagnosis
- Lower incidence of *KRAS* mutations
- Decreased incidence of chromosomal instability
- Consider mismatch repair gene deficiency in these patients
- Increased risk for additional malignancies

Melanoma

- Melanocytic tumors of uncertain malignant potential (MELTUMP) are more frequently seen in younger patients, and when suspected, referral to a pathologist with expertise in atypical melanocytic lesions is recommended.
- Conventional melanomas in AYA have a similar behavior and a similar genomic signature when compared to melanomas in older patients. These patients should be offered similar treatment options See NCCN Guidelines for Melanoma.

Management of Cancer During Pregnancy (See Discussion)

- AYA women diagnosed with cancer during pregnancy should be managed by a multidisciplinary team involving medical, surgical, and radiation oncologists; gynecologic oncologists; obstetricians; and perinatologists as appropriate.
- Selection of an appropriate treatment plan is dependent on individual tumor biology, tumor stage, and most importantly the gestational stage of the fetus.
- Referral to tertiary cancer centers with expertise in diagnosis and treatment of cancer during pregnancy, maternal-fetal medicine, and knowledge of the physiological changes that occur during pregnancy should be strongly encouraged.
- Chemotherapy should be avoided during the first trimester because of greater risk of teratogenic effects and intrauterine fetal death.
- RT is contraindicated during pregnancy. In very rare instances when RT is necessary, it should be delivered in low therapeutic doses with adequate uterine shielding to minimize fetal exposure.

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

The recommendations listed here include general principles; for more detail refer to the Children's Oncology Group (COG)

Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

- The recommendations represent only key aspects; for more detail, refer to the web site, survivorshipguidelines.org.
- See also NCCN Guidelines for Survivorship
- The COG Guidelines are based on exposures used in the treatment for pediatric cancer. As such, the recommendations are applicable to many survivors of cancers that span across adolescence and young adulthood, such as acute leukemias, Hodgkin's and non-Hodgkin's lymphomas, medulloblastomas, and sarcomas. In addition, since the treatment exposures for some young adult cancers, such as male germ cell tumors, are similar to pediatric cancer treatments (e.g., cisplatin, bleomycin, abdominal irradiation), the recommendations may be applicable. In contrast, the COG recommendations are generally not applicable to survivors of typical adult carcinomas occurring during young adulthood, such as breast, colorectal, and ovarian cancers.
- The risk for many late effects may be influenced by family history, lifestyle behaviors, and comorbid health conditions. The following recommendations are based on the treatment exposure; timing and intensity of screening may be adapted based on additional risk factors.
- Most survivors will have multiple treatment exposures, and therefore may have multiple screening needs.

Neuroendocrine axis screening (selected outcomes)

- Growth hormone deficiency
  - High-risk population: radiation dose to hypothalamic-pituitary-adrenal (HPA) axis >18 Gy
  - Screening recommendation: height, weight, and body mass index every 6 months until growth is completed then yearly. Note: most AYA patients will have attained (or nearly attained) final height; the significance and management of growth hormone status among survivors who attained their final height is controversial
  - Consider endocrine consultation for height below the third percentile on the growth curve, or drop of less than second percentile rankings on the growth chart
- Central hypothyroidism
  - High-risk population: total radiation dose to HPA axis >40 Gy
  - Screening recommendation: thyroid-stimulating hormone (TSH) and free T4, yearly
- Gonadotropin deficiency
  - High-risk population: total radiation dose to HPA axis >40 Gy
  - Screening recommendation: follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone (males) and FSH, LH, and estradiol (females) as clinically indicated; semen analysis (males) as requested by patient or for evaluation of fertility
- Central adrenal insufficiency
  - High-risk population: total radiation dose to HPA axis >40 Gy
  - Screening recommendation: 8:00 AM serum cortisol, yearly for at least 15 years after treatment and as clinically indicated

Neuropsychological evaluation

- Severe neurocognitive deficits are uncommon in survivors of AYA cancer, including CNS tumors. However, subtle deficits in executive function, sustained attention, memory, and processing speed may occur with higher-dose cranial radiation (>18 Gy)
- Screening recommendation: In patients with evidence of impaired educational or vocational progress, formal neuropsychological evaluation is recommended

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Breast cancer screening (females)
- High-risk population: chest radiation >20 Gy prior to the age of 30 years
- Screening recommendation: breast MRI and mammogram yearly, starting at age 25 or 8 years after radiation, whichever occurs last

Cardiovascular risk assessment and screening
- High-risk populations: TBI, mediastinal/chest radiation >20 Gy
- Screening recommendation: measure blood pressure and body mass index yearly; fasting glucose, lipid profile every 2 years
- Screening for ischemic coronary artery disease remains controversial; consider cardiology consultation (5–10 years after radiation) in patients who received >40 Gy chest radiation

Screening for cardiomyopathy/asymptomatic heart failure
- High-risk population: cumulative anthracycline dose >300 mg/m^2; chest radiation >30 Gy; combination of anthracycline and chest radiation
- Screening recommendation: echocardiogram (or MUGA scan) every 1–2 years (Note: Frequency of testing is dependent on both age at time of exposure and dose of exposure. The frequency of testing has not been established for breast cancer survivors treated with lower cumulative doses of anthracyclines.) A baseline electrocardiogram (EKG) is only recommended after completion of treatment

Screening for valvular heart disease
- High-risk population: chest radiation >30 Gy
- Screening recommendation: echocardiogram every 1–2 years

Pulmonary screening
- High-risk population: chest radiation >15 Gy (or radiation to large volume of lung), TBI (>6 Gy in single fraction or >12 Gy fractionated), bleomycin >400 U/m^2, combination of chest radiation and bleomycin, and selected alkylating agents (busulfan >500 mg, carmustine >600 mg/m^2)
- Screening recommendation: pulmonary function tests (including diffusion lung capacity for carbon monoxide [DLCO] and spirometry) as a post-therapy baseline and then as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction

Thyroid screening
- Thyroid disorders: hypothyroidism (very common), thyroid cancer (common), and hyperthyroidism (uncommon)
- High-risk population: radiation field includes the thyroid gland (see neuroendocrine axis screening for high-dose cranial radiation)
- Screening recommendation: TSH and thyroid/neck exam, yearly

Colorectal cancer screening
- High-risk population: abdominal or pelvic radiation >30 Gy
- Screening recommendation: colonoscopy starting at age 35 or 10 years after radiation, whichever occurs last

Screening for kidney and/or bladder disease
- Renal insufficiency and secondary renal/renovascular hypertension
  - High-risk population: radiation >10 Gy, combination of radiation with nephrotoxic agents (e.g., cisplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants)
  - Screening recommendation: post-therapy baseline blood urea nitrogen (BUN), creatinine, Na, K, Cl, CO_2, Ca, Mg, and PO_4; repeat as clinically indicated; measure blood pressure yearly; and measure urinalysis yearly

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

- Hemorrhagic cystitis/bladder fibrosis
  - High-risk population: cyclophosphamide >3 gm/m^2, pelvic radiation >30 Gy
  - Screening recommendation: urinalysis, yearly
- Bladder cancer
  - High-risk population: cyclophosphamide combined with pelvic radiation
  - Screening recommendation: urinalysis, yearly

Assessment for gonadal function

- Males
  - Infertility
    - High-risk population: moderate- to high-dose alkylating agent chemotherapy (e.g., MOPP >3 cycles, busulfan >600 mg/m^2, cyclophosphamide cumulative dose >7.5 gm/m^2 or as conditioning for hematopoietic cell transplant, ifosfamide cumulative dose >60 gm/m^2), TBI, testicular irradiation >2 Gy, and any alkylator combined with testicular irradiation or TBI
    - Screening recommendation: semen analysis as requested by patient or for evaluation of infertility; periodic evaluation over time is recommended as resumption of spermatogenesis can occur up to 10 years post therapy
  - Leydig cell dysfunction
    - High-risk population: testicular irradiation >20 Gy
    - Screening recommendation: testosterone as clinically indicated in patients with clinical signs and symptoms of testosterone deficiency
- Females
  - Infertility (acute ovarian failure or premature menopause)
    - High-risk population: moderate- to high-dose alkylating agent chemotherapy (e.g., MOPP >3 cycles, busulfan >600 mg/m^2, cyclophosphamide cumulative dose >7.5 gm/m^2 or as conditioning for hematopoietic cell transplant, ifosfamide cumulative dose >60 gm/m^2), TBI, and abdominal and/or pelvic radiation
    - Screening recommendation: AMH (anti-mullerian hormone), FSH (follicle stimulating hormone), LH (luteinizing hormone) testing, estradiol as indicated in patients with irregular menses, primary or secondary
      amenorrhea, and/or clinical signs and symptoms of estrogen deficiency

Screening for t-AML or myelodysplasia

- High-risk populations: epipodophyllotoxins, alkylating agents, cisplatin, and/or anthracyclines
- Screening recommendation: Complete blood count (CBC)/ differential yearly, up to 10 years after exposure

Audiologic evaluation

- High-risk population: cisplatin >360 mg/m^2, carboplatin conditioning for hematopoietic cell transplant, radiation involving the ear >30 Gy, and combination of cisplatin and cranial/ear radiation
- Screening recommendation: audiology testing as a post-therapy baseline and then as clinically indicated for signs and symptoms of hearing loss

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PALLIATIVE CARE/END-OF-LIFE CONSIDERATIONS

Palliative care used to be synonymous with "end-of-life care." Now, however, palliative care focuses on symptom control and reduction of physical suffering at any stage of a life-threatening disease. Referral to palliative care is appropriate when patients are being treated with curative intent. The WHO definition of palliative care includes palliative care being initiated at diagnosis.[1] A palliative care team is a multidisciplinary team ideally with expertise in understanding the psychosocial, emotional, and developmental issues that are unique to the AYA population.[2] See NCCN Guidelines for Palliative Care

Four main palliative care principles for the AYA population:[1]

1. **Psychosocial needs[3,4]**
   See Psychosocial/Behavioral Considerations (AYAO-7)
   - Psychosocial needs of the patient
     - Needs depend on maturity and level of independence (loss of new-found independence)
     - Peer support - Facilitate peer relationships and interaction with patient's peers as well as other AYAs with cancer
     - Provide physical space in clinic, hospital, etc. for social interactions, web-based peer support, and social networking
     - Provide age-appropriate professional psychosocial support services
   - Psychosocial needs of family and friends
     - Provide family members and friends with information about palliative care services
     - Provide regular counseling and psychosocial support

2. **Physical needs**
   - Lack of communication about illness trajectory is a barrier to transition to palliative care
   - Introduction of palliative care for symptom management can occur early in therapy in order to provide the best possible care for the patient
   - Efforts should be made to normalize palliative care involvement without providing a negative connotation of terminal care

3. **Resources required**
   See Psychosocial/Behavioral Considerations (AYAO-9)
   - Provide flexibility in the health care system for patients to maintain "normalcy"
   - Evidence-based guidelines in AYA palliative care are limited and need to be developed

4. **Advocacy**
   - AYA-specific advocacy groups need to be developed at the state/national/international level to increase awareness
   - It is important to create an AYA team that includes palliative care in order to improve early engagement, research, and patient-centered care[2]

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PALLIATIVE CARE AND END-OF-LIFE CONSIDERATIONS

End-of-life considerations

- **It is imperative for health care professionals not to assume that AYA patients may be less inclined to discuss death and other end-of-life issues.[2]**
- **Discussion about end-of-life preferences should begin early in treatment, but details should be individualized according to the preferences of the AYA patient and family.[5]**
- **Many adolescents indicate a preference for dying at home, yet 80% die in hospitals.[6,7]**
- **Physicians with experience in palliative care should facilitate discussion about end-of-life care issues such as nutrition/hydration, sedation treatment cessation, and place of death.[2]**
- **An advance care planning document is necessary for terminally ill AYA patients with metastatic cancer.[5,8]**
- **Ongoing psychosocial support is extremely important during the transition to end-of-life care. For family and friends, grief from loss may begin before death.**

[1]Pritchard S, Cuvelier G, Harlos M, Barr R. Palliative care in adolescents and young adults with cancer. Cancer 2011;117:2323-2328.
[2]Wein S, Pery S, Zer A. Role of palliative care in adolescent and young adult oncology. J Clin Oncol 2010;28:4819-4824.
[3]D'Agostino NM, Penney A, Zebrack B. Providing developmentally appropriate psychosocial care to adolescent and young adult cancer survivors. Cancer 2011;117:2329-2334.
[4]Zebrack BJ. Psychological, social, and behavioral issues for young adults with cancer. Cancer 2011;117:2289-2294.
[5]Wiener L, Zadeh S, Wexler LH, Pao M. When silence is not golden: Engaging adolescents and young adults in discussions around end-of-life care choices. Pediatric Blood & Cancer 2013;60:715-718.
[6]Bell CJ, Skiles J, Pradhan K, Champion VL. End-of-life experiences in adolescents dying with cancer. Support Care Cancer 2010;18:827-835.
[7]Webb NM, Tucker D. Young adults' opinions about hospice and home death. J Palliat Med 2009;12:337-342.
[8]Wiener L, Ballard E, Brennan T, et al. How I wish to be remembered: the use of an advance care planning document in adolescent and young adult populations. J Palliat Med 2008;11:1309-1313.

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ONLINE RESOURCES FOR AYA PATIENTS AND SURVIVORS - See NCCN Guidelines for Patients: Caring for Adolescents and Young Adults

General Information on Cancer in AYAs:

Critical Mass (The Young Adult Cancer Alliance), "Mission Control":
http://criticalmass.org/missioncontrol/
Comprehensive database to help you find the most up-to-date information on resources that best suit your needs, specific to your diagnosis and location

The 15-40 Connection
http://www.15-40.org/
Not-for-profit organization dedicated to motivating AYAs to take their health and medical care seriously, to take action when they notice changes in their health, and to be strong self-advocates when their instincts tell them something is wrong.

Planet Cancer
http://myplanet.planetcancer.org/
A community of peer support and advocacy for AYAs with cancer, designed to connect and empower AYAs and help them access support and resources.

Seventy K: Survival Up
http://www.seventyk.org/
Not-for-profit organization dedicated to improving cancer care by educating patients, families, and their health care providers about age-appropriate treatment and the unique needs of AYA cancer patients.

Stupid Cancer (The I'm Too Young for This! Cancer Foundation, i[2]y)
http://stupidcancer.org
The nation's largest online support community for AYAs affected by cancer.

Teens Living With Cancer
http://www.13thirty.org
National non-profit organization dedicated to helping teens and young adults live with cancer. This site contains teen-oriented resources designed to help teens cope with their disease and treatment and connect with other teens on the same ride.

Ulman Cancer Fund for Young Adults
http://www.ulmanfund.org/
Grassroots organization dedicated to supporting, educating, connecting, and empowering AYA cancer patients and survivors.

Cancer Diagnosis and Treatment:

American Cancer Society
http://www.cancer.org/Treatment/UnderstandingYourDiagnosis/index
Understanding Your Diagnosis

National Cancer Institute
http://www.cancer.gov/about-cancer/managing-care/services/doctor-facility-fact-sheet
How to Find a Doctor or Treatment Facility if You Have Cancer

National Center for Complementary and Integrative Health
http://www.nccih.nih.gov/

National Comprehensive Cancer Network
http://www.nccn.org/patients/resources/diagnosis/staging.aspx
Cancer Staging Guide

Navigate Cancer Foundation
http://www.navigatecancerfoundation.org/
This free, online program provides consultation services by experienced cancer nurses who can translate pathology reports, scans, and medical documents and help patients find a qualified doctor for a second opinion.

US National Institutes of Health
http://www.clinicaltrials.gov/
Registry and results database of publicly and privately supported clinical studies

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ONLINE RESOURCES FOR AYA PATIENTS AND SURVIVORS - See NCCN Guidelines for Patients: Caring for Adolescents and Young Adults

Fertility Issues:

American Society of Clinical Oncology (ASCO)
http://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/fertility-preservation
What to Know: ASCO's Guideline on Fertility Preservation

Fertile Hope
http://www.livestrong.org/we-can-help/fertility-services/risks/
Fertile Hope is a LIVE**STRONG** initiative dedicated to providing reproductive information, support, and hope to cancer patients and survivors whose
medical treatments present the risk of infertility.

Hope for Two…The Pregnant with Cancer Network
http://www.hopefortwo.org/
Free support for women diagnosed with cancer while pregnant

LiveStrong
https://www.livestrong.org/we-can-help/fertility-services

MyOncofertility.org
http://myoncofertility.org/
Patient education resource provided by the Oncofertility Consortium.

The Oncofertility Consortium
http://oncofertility.northwestern.edu/
Research group dedicated to exploring the relationships between health, disease, survivorship, and fertility preservation in young cancer patients. Site includes information on fertility options and a map of oncofertility centers
across the United States.

Verna's Purse
http://www.vernaspurse.org/
Financial assistance program for those in need of fertility services

Managing Side Effects:

American Institute for Cancer Research Nutrition information:
http://www.aicr.org/reduce-your-cancer-risk/diet/

American Society for Clinical Oncology (ASCO) videos:
Body changes: http://www.cancer.net/navigating-cancer-care/videos/young-adults-cancer/body-changes

American Society of Clinical Oncology (ASCO) Moving Forward Video Series for Young Adults with Cancer:
Diet and exercise
http://www.cancer.net/navigating-cancer-care/videos/young-adults-cancer/diet-and-exercise
Managing pain
http://www.cancer.net/navigating-cancer-care/videos/young-adults-cancer/managing-pain

Look Good, Feel Better
http://lookgoodfeelbetter.org (for women)
http://www.lookgoodfeelbetterformen.org/ (for men)
Program dedicated to improving the self-esteem and quality of life of people undergoing cancer treatment. Includes information on how to manage the appearance-related side effects of treatment.

National Cancer Institute
Coping with Cancer: Managing Physical Effects
http://www.cancer.gov/cancertopics/coping/physicaleffects/
Nutrition in Cancer Care
http://www.cancer.gov/cancertopics/pdq/supportivecare/nutrition/Patient/page1/

National Institute of Health (NIH) Sleep Hygiene Guide
http://www.nhlbi.nih.gov/files/docs/public/sleep/healthysleepfs.pdf

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Navigating Life (During and After Treatment):

American Society of Clinical Oncology (ASCO)
Family life changes http://www.cancer.net/coping-and-emotions/communicating-loved-ones/family-life

American Cancer Society Road to Recovery Program
http://www.cancer.org/treatment/supportprogramsservices/road-to-recovery Provides free ground transportation to patients receiving treatment; Volunteers available based on zip code

Cancer101
http://www.cancer101.org/
CANCER101 helps cancer patients and their families function as active partners in their care. The site offers tools such as the Cancer101 Planner that can help patients navigate their cancer journey.

Cancer and Careers
Empowers and educates people with cancer to thrive in the workplace, by providing expert advice, interactive tools and educational events
http://www.cancerandcareers.org/en

Cancer Care
http://www.cancercare.org/
Provides free professional support services to anyone affected by cancer. All services—including counseling and support groups, education, financial assistance, and practical help—are provided by professional oncology social workers and are completely free of charge.

Cancer in Our Family" (American Cancer Society)
http://acs.bookstore.ipgbook.com/cancer-in-our-family-products-9780944235959.php
Guide that helps parents teach children about the diagnosis, treatment, potential recurrences of the illness, and terminal illness

Cancer.Net
http://www.cancer.net/survivorship/late-effects
Late Effects

CaringBridge.org
http://www.caringbridge.org/
Online space where cancer patients and their friends and family can connect, share, and receive support—kind of like a personalized social network. Available 24/7 to anyone, anywhere at no cost.

Cancer Legal Resource Center (CLRC)
http://www.disabilityrightslegalcenter.org/cancer-legal-resource-center
Telephone assistance line for cancer patients looking for legal information or assistance

Caregiver Action Network
http://caregiveraction.org/
Provides resources for family and caregivers, such as education and peer support

Family Patient Online Patient Update Reports
http://www.familypatient.com/
Website that allows family members to post up-to-date information about the condition of their loved ones.

FinAid! The Smart Student Guide To Financial Aid
http://www.finaid.org/scholarships/cancer.phtml
Information about scholarships for cancer patients, cancer survivors, children of a cancer patient or survivor, students who lost a parent to cancer, and students pursuing careers in cancer treatment.

First Descents
http://firstdescents.org/
Provides free outdoor experiences for young adults with cancer. Helps participants to find support, face fears, and heal

GYST
http://gyst.com/
Online resource to help you take care of important documents such as your will and power or attorney

Imerman Angels
http://www.imermanangels.org/
Pairs individuals touched by cancer with other people who have fought and survived the same type of cancer (a Mentor Angel). These 1-on-1 relationships inspire hope and offer support from someone who is uniquely familiar with the experience of cancer.

Job Accommodation Network
http://www.askjan.org/
Offers tools to help patients understand the types of workplace adjustments that may help them continue working during and after cancer treatment.

LIVE**STRONG**
Late Effects of Cancer Treatment
https://www.livestrong.org/we-can-help/healthy-living-after-treatment/late-effects-of-cancer-treatment
Your Survivorship Care Plan
https://www.livestrong.org/we-can-help/healthy-living-after-treatment/your-survivorship-care-plan

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ONLINE RESOURCES FOR AYA PATIENTS AND SURVIVORS - See NCCN Guidelines for Patients: Caring for Adolescents and Young Adults

LIVE**STRONG Care Plan**
http://www.livestrongcareplan.org/
Interactive program that uses answers to a brief questionnaire to produce a basic survivorship care plan. The LIVE**STRONG** Care Plan is meant to be shared with the oncology team and used as a start for putting together a personal survivorship care plan.

Lotsa Helping Hands
http://www.lotsahelpinghands.com/
Free service designed to help friends and family organize support efforts. Includes a help calendar to schedule and sign up for specific report activities (shopping, rides to medical appointments, meal preparation, etc.) as well as a message board for sharing information.

MyLifeLine.org
http://www.mylifeline.org
Nonprofit organization that encourages cancer patients and caregivers to create free, customized websites to build an online support community of family and friends.

National Cancer Institute
Adolescents and Young Adults with Cancer: Survivorship
http://www.cancer.gov/types/aya#5
Facing Forward: Life after Cancer Treatment
http://www.cancer.gov/cancertopics/coping/life-after-treatment/

National Coalition for Cancer Survivorship
http://www.canceradvocacy.org
The oldest survivor-led cancer advocacy organization in the country, advocating for quality cancer care for all Americans and empowering cancer survivors.

The Patient Access Network Foundation
http://www.panfoundation.org
Provides help to underinsured patients for out-of-pocket expenses for life-saving medications. Patients must complete an application and meet certain insurance and income criteria to qualify for aid.

Patient Advocate Foundation Co-Pay Relief Program
http://www.copays.org/
Provides direct financial support for pharmaceutical co-payments to insured patients who financially and medically qualify.

Patient Advocate Foundation
http://www.patientadvocate.org
Provides professional case managers who serve as advocates for patients in dealing with insurance companies, employers, and/or creditors.

Rx Assist
http://www.rxassist.org/patients
Searchable online database of pharmaceutical companies' patient assistance programs

Surviving And Moving Forward: The SAMFund for Young Adult Survivors of Cancer
http://www.thesamfund.org
Non-profit organization that helps young adult survivors of cancer successfully transition into their post-treatment life, by providing financial support through the distribution of grants and scholarships.

Young Survival Coalition
http://www.youngsurvival.org/
Network of breast cancer survivors and supporters dedicated to the concerns and issues that are unique to young women and breast cancer.

End-of-Life Issues

Aging with Dignity 5 Wishes:
https://www.agingwithdignity.org/five-wishes

Caring Connections
http://www.caringinfo.org/i4a/pages/index.cfm?pageid=1
Provides free resources and information to help people make decisions about end-of-life care and services.

Hospice Education Institute
https://www.hospiceworld.org/
Operates HOSPICELINK, a directory of all hospice and palliative care programs in the United States. HOSPICELINK also provides information about the principles and practices of good hospice and palliative care.

Voicing My Choices Planning Guide for Adolescents and Young Adults
http://www.agingwithdignity.org/voicing-my-choices.php
Planning tool designed to help young people living with a serious illness to communicate their preferences to friends, family, and caregivers.

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Discussion

This discussion is being updated to correspond with the newly updated algorithm. Last updated 09/03/15

NCCN Categories of Evidence and Consensus

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.

Table of Contents

Overview

Over the past 20 years, advances in cancer treatment have significantly improved survival rates for young children and older adults, but there has been no significant improvement in adolescent and young adult (AYA) patients with cancer.[1] One of the main reasons for the lack of improvement in outcomes is that AYA patients have a low rate of participation in clinical trials.[1-4] In the United States, approximately 10% of patients 15 to 19 years of age and 1% to 2% of patients 20 to 39 years of age are enrolled in clinical trials.[5] In addition to the low rate of participation in clinical trials, several other factors contribute to the poor outcome in AYA patients with cancer, such as: differences in disease biology, lack of consistency in treatment approaches, poor compliance with or intolerance to therapy, lack of health insurance, delays in diagnosis, and physician's lack of familiarity with cancer in the AYA population.[6]

The biology, epidemiology, and clinical outcomes affecting AYA patients with cancer are usually different than those of younger and older patients with cancer.[7] In addition, the genetic, physiologic, and pharmacologic changes associated with AYA patients may impact AYA patient's ability to tolerate cancer therapy and response to treatment. 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 are less evidence-based data to guide the treatment of these patients. AYA patients diagnosed with cancer should be recognized as a distinct age group that has unique medical and psychosocial needs.[8] The distinct biology of disease as well as age-related issues in AYA patients should be considered in the treatment decision-making process.[9]

The AYA patient is generally defined as an individual 15 to 39 years of age at the time of initial cancer diagnosis.[10] Nearly 70,000 patients in this age group are diagnosed with cancer each year in the United States, over seven times more patients than those diagnosed who are less than 15 years of age.[10] In 2014, an estimated 5330 adolescents (15–19 years) will be diagnosed with cancer and 610 will die from their disease.[11] Increasing age is associated with poorer prognosis in AYA patients for acute myeloid leukemia; non-Hodgkin's lymphomas, Burkitt and Burkitt-like lymphoma; and rhabdomyosarcoma.[12]

The spectrum of cancer types that affect the AYA population is unique and different from those that affect the pediatric and older population. Cancer is the leading cause of death among the AYA population, excluding homicide, suicide, or unintentional injury.[6,13] Lymphomas, melanoma, testicular cancer, female genital tract malignancies, thyroid cancer, bone and soft tissue sarcomas, leukemias, central nervous system (CNS) cancers, breast cancer, and non-gonadal germ cell tumors account for 95% of the cancers in this age group.[1,11] The frequency and incidence of distribution of cancer types is also dramatically different across the age spectrum of AYA patients. See Table 1.

Quality care for AYA patients with cancer is tied to timely detection and initiation of treatment, compliance with and adherence to treatment, and access to a multidisciplinary team of health care professionals who are well-versed in the specific developmental issues relevant to this patient population.[14,15] These issues include fertility, long-term side effects, psychosocial and socioeconomic issues, transportation to clinic appointments, child care, treatment adherence, and the unique biology of disease.

The goal of the NCCN Guidelines® for Adolescent and Young Adult Oncology is to identify 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, compliance, and clinical outcomes; and promote participation in clinical trials.

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines for Adolescent and Young Adult Oncology, an electronic search of the PubMed database was performed to obtain key literature in Adolescent and Young Adult Oncology published between 04/01/2014 and 03/31/2015, using the following search terms: adolescent young adult cancer, adolescent young adult cancer survivors, psychosocial, infertility, fertility preservation, adherence, supportive care, end of life care, late effects, and long term follow-up. The PubMed database was chosen as it remains the most widely used resource for medical literature and indexes only peer-reviewed biomedical literature.[16]

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies.

The PubMed search resulted in 30 citations and their potential relevance was examined. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these guidelines have been included in this version of the Discussion section (eg, e-publications ahead of print, meeting abstracts). Recommendations for which high-level evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

The complete details of the Development and Update of the NCCN Guidelines are available at www.NCCN.org.

Risk Factors

With rare exceptions, cancer appears to arise sporadically in most AYAs with a negative family history of cancer. There are no established risk factors for the majority of cancer diagnoses before the age of 30.[13] Toxic and environmental exposures that cause cancer in AYAs include chemotherapy and/or radiation therapy (RT) leading to second malignancies in patients treated for cancer during childhood or young adulthood; predisposition to clear cell adenocarcinoma of the vagina or cervix in patients with maternal exposure to diethylstilbestrol; and melanomas induced by ultraviolet light. Infections that predispose AYAs to cancer include cervical carcinoma following exposure to human papillomavirus (HPV), Hodgkin lymphoma (HL) and Burkitt lymphoma following Epstein-Barr virus (EBV) infection, and Kaposi sarcoma and non-Hodgkin's lymphoma (NHL) in patients with human immunodeficiency virus (HIV).[13]

Familial cancer syndromes, associated with germline mutations in a variety of genes, affect only a small minority of AYA patients with cancer. However, these syndromes greatly increase the risk for cancer during adolescence and young adulthood. Referral for genetic and familial risk assessment and counseling (within 2 months after the start of therapy) is recommended.

Young women with germline mutations of *BRCA1/2, TP53* (Li-Fraumeni syndrome), or *PTEN* (Cowden's syndrome), or those who have received

mantle field RT for HL are at an increased risk of developing breast cancer during young adulthood.[1] Screening for breast cancer may be warranted in AYA patients with inherited or familial risk factors. See the NCCN Guidelines for Genetics/Familial High-Risk Assessment: Breast and Ovarian Cancer Screening (available at www.NCCN.org).

In young adults, hereditary polyposis and nonpolyposis syndromes, inflammatory bowel disease, and radiation exposure are predisposing factors for developing colorectal cancer. Hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome) is an autosomal dominant syndrome caused by mutations in one of the four *MMR* genes (*MSH2, MLH1, MSH6, or PMS2*), and is associated with colon cancer developing in the AYA population.[1] Familial adenomatous polyposis (FAP) is an autosomal dominant disease caused by germline mutations in the *APC* gene. This syndrome is associated with thousands of colonic polyps and with the development of colon cancer in most affected patients by age 40. Desmoid tumors are considered to be the most common extracolonic manifestations of FAP, and may be the presenting manifestation of FAP in AYA patients.[17] Screening for colorectal cancers may be warranted in AYA patients with inherited or familial risk factors. See the NCCN Guidelines for Colorectal Cancer Screening (available at www.NCCN.org).

AYA patients with Li-Fraumeni syndrome (resulting from germline mutations in the *TP53* tumor suppressor gene) or germline mutations in the retinoblastoma (*RB*) gene are at a higher risk of developing osteosarcoma and rhabdomyosarcoma.[18] Sarcoma represents 25% of tumors in *TP53* mutation carriers. AYA individuals with germline mutations in the *RB* gene have often been treated for retinoblastoma during early childhood.[19] AYAs with a family history of Li-Fraumeni syndrome have a higher risk of developing not only sarcomas but a wide variety of malignancies, including leukemia, brain tumors, breast cancer, and adrenocortical carcinoma before 40 years of age.[20] See the NCCN Guidelines for Soft Tissue Sarcoma (available at www.NCCN.org).

Patients with mutations in the succinate dehydrogenase (*SDH*) gene are at risk for paraganglioma and pheochromocytoma, gastrointestinal stromal tumors (GISTs), renal clear cell carcinoma, and papillary thyroid carcinoma. Testing for germline mutations in the *SDH* subunit should be considered for AYA patients with wild-type GISTs lacking *KIT* or *PDGFRA* mutations.[21,22] Patients with germline mutations in neurofibromatosis type I *(NF1*) carry a 10% lifetime risk for malignant peripheral nerve sheath tumors, as well as an increased risk for other malignancies including GISTs and early breast cancer in females.[23]

Multiple neuroendocrine neoplasia (MEN) syndromes (MEN1 and MEN2) are autosomal dominant syndromes characterized by the development of endocrine tumors. MEN1 is caused by a germline mutation or inactivation of the tumor suppressor gene *MEN1*, whereas MEN2 is associated with germline tumors in the *RET* proto-oncogene.[24,25] MEN1 is associated with the development of pituitary, parathyroid, and pancreatic neuroendocrine tumors.[26] Testing for MEN1 should be considered for patients with two or more MEN-associated tumors or in patients with one MEN-associated tumor and a relative with MEN1. MEN2 is further subdivided into MEN2A and MEN2B. Both of these subtypes are associated with a high risk of developing medullary thyroid carcinoma (MTC).[27] Most patients with MEN2B have mucosal neuromas or intestinal ganglioneuromas and pheochromocytoma in addition to MTC.[27] Testing for MEN2A should be considered for patients with two or more MEN2A-associated neoplasms or in patients with a close relative with MEN2A-associated neoplasms. Testing for MEN2B should be considered for patients with MTC, pheochromocytoma, mucosal neuromas of the lips and tongue,

medullated corneal nerve fibers, distinctive facies with enlarged lips, “marfanoid” body habitus, or inability to cry tears. See NCCN Guidelines for Neuroendocrine Tumors (available at www.NCCN.org).

HPV infection has been associated with cervical cancer and few other non-cervical cancers including anal and oropharyngeal cancers.[28,29] Recent increase in the incidence of oropharyngeal cancers in the United States has been attributed to HPV infection.[30,31] Randomized clinical trials have demonstrated the efficacy of HPV vaccination against cervical intraepithelial neoplasia, anal intraepithelial neoplasia, and oral HPV infections in women and men 15 to 25 years of age.[32-34] In the PATRICIA trial, the efficacy of HPV vaccine against all cervical intraepithelial neoplasia associated with HPV-16/18 was highest in the 15 to 17 years age group and progressively decreased in the 18 to 20 years and 21 to 25 years age groups, suggesting that early HPV vaccination could substantially reduce the incidence of HPV-associated cancers in the AYA population.[33] HPV immunization (if not previously administered) is recommended for all males and females 9 to 26 years of age since the vaccine has been shown to prevent cervical carcinoma and anal intraepithelial neoplasia.

Screening

AYA patients with cancer should be made aware of the importance of early diagnosis and self-examination of the skin, breasts (for females), and testicles (for males) as recommended by the American Cancer Society. They should also be educated regarding the benefits of early detection and treatment.[6] Cancer screening in some circumstances, particularly in cervical, breast, and colorectal cancers, can significantly reduce mortality if directed at the appropriate age group and if the results are interpreted and followed up appropriately.[35] However, there are no age-specific screening tests that have been developed that would increase early detection in AYA patients with cancer, and in some instances screening tests have been associated with false-positive results leading to false diagnosis and unnecessary treatments.[36] Therefore, it is necessary to assess the potential risks and benefits of cancer screening in the AYA population.

Diagnosis

The onset of new symptoms in AYA patients may not immediately trigger evaluation for malignancy, due to the relatively low incidence of cancer in this age group and the resulting low index of suspicion on the part of patients and primary care providers. AYAs are at a higher risk of delayed cancer diagnosis, which may result in a more advanced stage of cancer that requires more therapy and is associated with a worse prognosis.[6] Some studies have reported that adolescents experience longer lag times (interval between symptom onset and diagnosis) than children.[37-39] Lack of health insurance, inexperienced physicians, and workup that is inappropriate for the patient’s age are some causes of delayed diagnosis in AYA patients with cancer. In a retrospective analysis of 503 patients aged 15 to 29 years with previously untreated cancer, the advanced stage of cancer at diagnosis and lack of health insurance were significantly associated with longer lag times.[40] Those with public or no health insurance had longer lag times than those with private health insurance in most of the cancers evaluated. Patients with leukemia and NHL had shorter lag times (2 to 5 weeks) than those with sarcomas and thyroid cancer (20 to 24 weeks), irrespective of the insurance type. In addition to health insurance, education and employment status are also likely to influence lag time, although these factors were not evaluated in this study.

Management of AYA Patients With Cancer: Special Considerations

All AYA patients should undergo comprehensive assessment following the diagnosis of cancer, which should include psychosocial assessment, discussion of risks of infertility associated with cancer and its treatment, the use of fertility preservation and contraception, and genetic and familial risk assessment (within 2 months after the start of therapy).

Age-appropriate Care

AYA patients with cancer can be treated either at pediatric or at adult cancer centers.[14] Retrospective analyses have shown that AYA patients with certain pediatric-type cancers, such as acute lymphoblastic leukemia (ALL),[12,41-44] rhabdomyosarcoma,[45] and Ewing's sarcoma,[46] 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 acute myeloid leukemia (AML), HL, and NHL.[47-49]

As mentioned earlier, 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.[1-3,12] A review of 30 studies of adolescents with cancer (ages 15–19) showed that 5% to 34% of these patients enrolled in clinical trials.[12] Care should be provided at medical centers with broad access to clinical trials (standard-of-care registry trials and trials evaluating novel therapies).[14] Pediatric cancer centers enroll more adolescents into clinical trials (35% vs.12% at non-pediatric cancer centers), and AYA patients treated at pediatric cancer centers have a higher rate of clinical trial enrollment (26%) compared to those treated at adult cancer centers (4%).[50-52] Parsons et al reported that AYA patients who are treated by non-pediatric oncologists are less likely to be enrolled in clinical trials.[53] Nevertheless, a substantial number of AYA patients with pediatric malignancies are not being treated at pediatric cancer centers.[54,55 12]

The treatment and appropriate location of care vary with the type of cancer as well as with the availability of family, community, and institutional supports.[6,56] Most importantly, AYA patients should 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.[14] 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.[57] Cancer centers should adopt the appropriate evidence-based approach, which includes adult centers implementing treatment based on pediatric protocols that have demonstrated superior outcomes in AYA patients and pediatric centers adopting adult regimens that have demonstrated benefit in this patient population.

AYA patients should be managed by a multidisciplinary team of providers with expertise in cancer treatment and management of specific developmental issues such as fertility, education, career development, employment, family planning, pregnancy, sexually transmitted diseases, and tobacco, alcohol, and substance abuse. Given the rarity of several tumor types diagnosed in this population, all

AYA patients should be offered and encouraged to participate in tumor banking studies and multicenter clinical trials, when available.

Treatment Options

AYA patients usually tolerate more intensive therapies than older patients, since they have fewer comorbid conditions that limit the intensity of treatment in older adults.[6] Dose-intensive and dose-dense treatment is associated with improved outcomes. Every AYA patient with cancer should be treated with aggressive therapy if there are no contraindications.

Treatment-related issues in AYA patients with cancer may differ from those of pediatric or older adult patients due to the distinct biology of the disease.[7] Physical and physiological changes, such as changes in body composition, size and maturity of organs, and hormones associated with the normal pubertal process, may directly affect the drug disposition, drug efficacy, and toxicity of chemotherapy in AYA patients.[58] As mentioned above, AYA patients have fewer comorbid conditions compared to older cancer patients, and thus are usually able to tolerate intense chemotherapy and surgery with less morbidity. Appropriate management of symptoms and side effects to reduce the severity and toxicity of treatment should be an integral part of the management of AYA patients with cancer.[59]

Surgery, RT, chemotherapy, and hematopoietic stem cell transplant (HSCT) 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.[6,60]

Surgery

Surgery plays an important role in the management of cancer in AYA patients, especially in breast and thyroid cancer, melanoma, bone, and soft-tissue sarcomas that are more common in AYA patients. 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.[6] The extent of surgery is dependent on the type and location of cancer. In some cases, extensive surgery requiring removing part or all of an organ or limb may be necessary. With advances in surgical techniques and chemotherapy, limb-sparing surgery is now feasible for the majority of patients with extremity sarcoma and osteosarcoma.[59] It is imperative that surgery should be performed in high-volume centers by surgeons with expertise in the management of AYA patients with cancer.

Radiation Therapy

RT has been associated with an increased risk for late mortality; development of second malignancies; pulmonary, cardiac, and thyroid dysfunction; and chronic health conditions and growth abnormalities.[61] AYA patients with cancer receiving RT to testes or ovaries are at risk of developing infertility later in life.[62] Women with HL who receive chest RT between 10 and 30 years of age are at increased risk of developing breast cancer.[63] Cranial RT is associated with short stature, cognitive processing difficulties, and poor physical function, which contribute to lower rates of employment, independent living, and marriage among AYA cancer survivors.[64] Adolescents are more vulnerable to RT-induced spinal cord dysfunction, presumably because of elongation of the cord during the growth spurt.[65]

Chemotherapy

Alkylating agent-based chemotherapy is associated with a higher risk of infertility in both male and female patients.[62] See the section on *Impact of Cancer and Its Treatment on Fertility*. Anthracycline-based chemotherapy is associated with cardiac dysfunction, whereas neurotoxic chemotherapies such as methotrexate and cytarabine can

result in CNS dysfunction.[59] Bleomycin-induced pulmonary toxicity is well documented in patients with HL treated with bleomycin-containing chemotherapy regimens.[66] Higher cumulative doses of cisplatin, ifosfamide, or epipodophyllotoxin are associated with hearing loss, renal dysfunction, and secondary AML, respectively.[67-70] See also the section on *Late Effects in AYA Cancer Survivors*.

Pain, fatigue, nausea, vomiting, mucositis, hair loss, infection, and myelosuppression are some of the acute side effects of chemotherapy. Reversible toxicities (as mentioned above) do not necessarily warrant dose reductions. See the NCCN Guidelines for Supportive Care (available at www.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. Maximum cumulative dosing parameters are often established for a patient to reduce the risk of significant irreversible damage. Monitoring of cumulative dosing and intensive screening is essential for patients receiving chemotherapy regimens associated with irreversible organ damage.

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% to 30% of patients by their fourth chemotherapy cycle.[71] Younger patients (less than 50 years of age) may be more susceptible to ANV, because they generally receive more aggressive chemotherapy and have poorer emesis control than older patients.[71] Behavioral therapy has been used in patients with ANV.[72] See the NCCN Guidelines for Antiemesis (available at www.NCCN.org).

Hematopoietic Stem Cell Transplant

HSCT is a potentially curative treatment option for an increasing number of AYA patients with leukemias and lymphomas.[73] Graft-versus-host disease (GVHD), chronic immunosuppression, and gonadal dysfunction in males and females related to high-dose conditioning chemotherapy and RT are the major post-transplant complications associated with HSCT.[59,60]

Chronic GVHD has been identified as the leading cause of non-relapse mortality in HSCT survivors.[74] AYA patients are at a higher risk of developing chronic GVHD than younger children. Older patient age at transplantation is associated with an increased risk of chronic GVHD but not acute GVHD.[75] Patient age older than 15 years (children younger than 5 years had a probability of less than 14% compared to a probability of 44% for patients older than 15 years) and the use of total body irradiation (TBI) were significantly associated with an increased possibility of developing chronic GVHD following allogeneic HSCT.[76] Patients receiving peripheral stems cells during their transplant procedure have a greater risk of chronic GVHD compared to those who received bone marrow transplant.[77] A report from the Bone Marrow Transplant Registry demonstrated that chronic GVHD had a significant impact on the overall health status of HSCT survivors, particularly in the areas of functional impairment, activity limitation, and pain.[78] 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.

HSCT 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.[59,60,79] In addition, the incidence of severe or life-threatening chronic health conditions, endocrine complications, or secondary

cancers is also higher among HSCT survivors than in non-cancer populations and patients with cancer who are treated conventionally.[73] Allogeneic HSCT survivors irradiated at 30 years or younger were at higher risk of developing secondary solid cancers.[80]

These findings highlight the increasingly recognized need for long-term follow-up care that incorporates screening and surveillance of AYA survivors of HSCT.

Adherence to Treatment

Adherence is defined as the extent to which a person's behavior corresponds with agreed recommendations from a health care provider. Nonadherence to recommended treatment and follow-up care contributes to poor clinical outcomes in AYA patients with cancer.[81,82] Failure to keep up with appointments can lead to delayed identification of side effects, complications, or secondary cancers.

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 to younger or older patients with cancer.[81] 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% to 63%) have difficulties adhering to their oral treatment regimens.[81,82]

Nonadherence to other components of cancer treatment (eg, failure to keep appointments for treatment or follow-up, refusing medical examinations, preparing for procedures or therapy) was also identified in AYA patients. Treatment nonadherence in clinical trials can 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 with cancer include patients' emotional functioning (depression and 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.[83] In a randomized controlled trial, video game intervention significantly improved treatment adherence to prophylactic antibiotics among adolescents and young adults with acute leukemia, lymphoma, and soft tissue sarcoma.[84] A meta-analysis showed that behavioral and multicomponent interventions have been shown to have a moderate effect on improving treatment adherence in children (2 to 15 years of age) with chronic conditions such as diabetes, asthma, and cystic fibrosis.[85]

Risk assessment for non-adherence among AYA patients should include consideration of patient maturity and independence as well as their psychosocial and physical needs and challenges.[86] Careful assessment of AYA patient's risk for adherence and implementation of individualized interventions to promote adherence may improve outcomes in AYA patients with cancer. Additional studies evaluating the effect of interventions to improve adherence in AYA patients with cancer are needed. In the absence of data from studies evaluating the effect of interventions to improve adherence in AYA patients with cancer, the findings from the studies involving AYA patients with other chronic diseases could be extrapolated to this patient population.

NCCN Recommendations to Promote Adherence

- 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.[81,82]

- Modify treatment protocol (eg, simplify dosing schedule, change timing and frequency of medication or method of administration), when medically possible, to fit into an AYA's lifestyle and normal activities.[81,82]
- Provide access to systematic and standardized symptom management for side effects related to cancer treatment.[81,82] See the NCCN Guidelines for Supportive Care (available at www.NCCN.org).

Impact of Cancer and Its Treatment on Fertility

Infertility is a major consequence of cancer and its treatment in both males and females.[87,88] 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, and testes are primary risk factors for gonadal dysfunction and decreased fertility in both males and females.[89-94] Gonadal exposure to low-dose RT can result in oligospermia or azoospermia in males. Higher-dose RT is associated with both ovarian and uterine dysfunction in women.

Young women with HL treated with chemotherapy are at risk of developing premature ovarian failure, irrespective of their age at the time of treatment (38% for those diagnosed between 30 and 40 years of age; 37% for those diagnosed between 9 and 29 years of age), and the cumulative risks for premature ovarian failure are much higher after alkylating agent-based chemotherapy.[95,96] In a large cohort of women treated between the ages of 15 and 40 years for HL, the cumulative risk of premature ovarian failure after alkylating agent-based chemotherapy was 60% compared to only 3% or 6% after non-alkylating agent-based chemotherapy.[96] Independent risk factors for acute ovarian failure include increasing RT doses to the ovaries and exposure to procarbazine and cyclophosphamide at 13 to 20 years of age.[90]

Among young women treated with adjuvant chemotherapy for breast cancer, the risk for premature menopause is significantly higher for women older than 35 years with newly diagnosed breast cancer treated with chemotherapy.[97,98] Similarly, among female survivors of HL diagnosed between 14 and 40 years of age, women who were 22 to 39 years of age at first treatment were at a higher risk of developing premature menopause after treatment compared to younger patients (14 to 21 years).[99] 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.[99]

In males treated with alkylating agent-based chemotherapy and RT to testes, germ cell dysfunction with resultant infertility is more common than Leydig cell dysfunction and testosterone insufficiency.[100] Leydig cell dysfunction is characterized by increased plasma concentrations of luteinizing hormone (LH) 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 that associated with germ cell dysfunction. AYA men 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.[100] TBI used as part of high-dose

conditioning therapy prior to HSCT can also affect the testes, resulting in permanent infertility in the majority of AYA men.[62]

Azoospermia (which may or may not resolve over time) is more common among men treated with chemotherapy for HL and testicular cancer.[101,102] Azoospermia has been reported in more than 90% of men receiving procarbazine-based chemotherapy regimens and may not resolve over time, resulting in permanent infertility.[102] 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.[101] Cisplatin-based chemotherapy for testicular cancer is associated with temporary azoospermia in most men, with a recovery of spermatogenesis in about 50% to 80% of patients after 2 to 5 years.[101] RT to testes >2 Gy, moderate- to high-dose alkylating agent chemotherapy (MOPP >3 cycles), higher cumulative alkylating agent dose (busulfan >600 mg/m^2, cyclophosphamide >7.5 gm/m^2, or ifosfamide >60 mg/m^2), or any alkylating agent combined with RT to testes or TBI are considered as risk factors for oligospermia and azoospermia.[87,93] Pelvic RT and cumulative cyclophosphamide doses >9.5 g/m^2 are associated with a high risk of permanent infertility in male patients with NHL, Ewing's sarcoma, and soft tissue sarcomas.[103,104] Retroperitoneal lymph node dissection is also associated with infertility in men with testicular cancer.[105]

The NCCN Guidelines recommend discussing the risks of infertility due to cancer and its treatment with all patients at the time of diagnosis, prior to initiating treatment.

Fertility Preservation

Fertility preservation is an issue of crucial importance in AYA patients with cancer and should be an essential part in the management of their cancer.[9,62,106-108]

However, it is currently one of the most under prescribed and least implemented services in AYA patients with cancer.[62,106,109] 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.[110] However, it is possible that more discussions about infertility occurred without having been documented. The ASCO Clinical Practice Guidelines recommend that providers discuss the options for fertility preservation with all new cancer patients at the time of diagnosis.[111] Psychosocial providers can assist patients and families in the decision-making process about fertility preservation, particularly when AYA patients are distressed about the potential infertility associated with cancer treatment.[111]

Options for Females

Ideally, fertility preservation should be initiated prior to the start of treatment. However, in some situations, when it is impractical or impossible to pursue fertility preservation prior to initiating therapy, it may be appropriate to readdress later in the course of treatment.

Oophoropexy and embryo cryopreservation after in vitro fertilization (IVF) are the two established options for fertility preservation in females.[111] Mature oocyte cryopreservation and ovarian tissue grafting and freezing are emerging techniques for fertility preservation in young women.[112]

Oophoropexy involves surgically displacing the ovaries out of the RT field to minimize ovarian damage and has been shown to preserve ovarian function.[113] Embryo cryopreservation after IVF has been highly successful in women younger than 40 years of age.[62,106] However, this method requires a male partner or sperm donor who is available with short notice.

Mature oocyte cryopreservation is a potential alternative for single women, but, like embryo cryopreservation, requires hormone stimulation.[62,106] Evidence from randomized trials [114-117] and a meta-analysis [118] suggest that IVF with cryopreserved oocytes results in fertilization and pregnancy rates similar to that of fresh oocytes. Oocyte cryopreservation is no longer considered investigational in the recently published guidelines from the American Society of Reproductive Medicine.[119] However, the authors also acknowledge that more data are needed to recommend the routine use of oocyte cryopreservation in place of embryo cryopreservation.

Ovarian tissue grafting does not require hormonal stimulation, so there is no long delay in treatment.[62] However, this procedure would not be appropriate for some women with cancer where reintroduction of malignant cells could occur with grafting. Ovarian tissue grafting is still considered investigational.

Some randomized trials have evaluated the role of menstrual suppression with gonadotropin-releasing hormone (GnRH; also known as luteinizing hormone-releasing hormone [LHRH]) agonists to preserve ovarian function during chemotherapy.[120-125] A recent systematic review and meta-analysis of nine randomized trials that evaluated the impact of GnRH analogues delivered during chemotherapy for preservation of ovarian function (N = 765; 401 patients treated with GnRH and 364 controls) showed that GnRH may be beneficial (odds ratio [OR], 0.43; 95% CI, 0.22--0.84; *P* = .013).[126] However, results from earlier meta-analyses were inconsistent, with some demonstrating a potential benefit of GnRH to preservation of ovarian function,[127-129] while other reviews have been unable to come to this conclusion.[130,131] Further, there are little data available on the long-term impact of GnRH on preservation of ovarian function.[126] Data from a recent randomized trial of 218 premenopausal patients with early-stage, hormone receptor-negative breast cancer showed that the GnRH agonist goserelin may prevent ovarian failure (OR, 0.30; 95% CI, 0.09--0.97; *P* = .04) and dysfunction (OR, 0.35; 95% CI, 0.13--0.93; *P* = .03) after two years.[125] Pregnancy occurred more often in patients who received goserelin than patients who received only chemotherapy (OR, 2.45; 95% CI, 1.09--5.51; *P* = .03). Therefore, though recent data suggest that menstrual suppression with GnRH agonists may protect ovarian function, studies are inconclusive.

Options for Males

Semen cryopreservation before the start of treatment is the most reliable and well-established means of preserving fertility in AYA males with cancer.[62,106] 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.[132]

Cryopreservation and subsequent transplantation of spermatogonial stem cells is experimental but may be an alternative option for some patients in whom semen cryopreservation is not possible.[62,106] There is limited evidence regarding the efficacy of hormone suppression in reducing the risk of male infertility during chemotherapy.[111]

Recommendation for Fertility Preservation

The NCCN Guidelines emphasize that fertility preservation, as well as sexual health and function, should be an essential part in the management of AYA patients with cancer, who are at any risk for infertility due to cancer treatments. Options for fertility preservation should be discussed with all patients prior to the start of treatment and providers should initiate referral to fertility preservation clinics within 24 hours for all patients who choose the option of fertility preservation. Referral to a mental health professional to assist with complex decision making is recommended.

Females

- Oophoropexy should be considered for all female patients who will be receiving RT.
- Embryo cryopreservation should be discussed, if it is possible to delay treatment long enough for a cycle of oocyte stimulation, especially for patients with low- and intermediate-risk HL, low-grade sarcomas, and breast cancer.
- Mature oocyte cryopreservation is no longer considered investigational.[119] However, embryo cryopreservation is preferred if there is an identified sperm donor.
- 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.[133]
- Recent data suggest that menstrual suppression with GnRH agonists may protect ovarian function.[125,126] However, menstrual suppression with GnRH agonists is not recommended as an option for fertility preservation since evidence that this procedure protects ovarian function is inconclusive.

Males

- Discuss the possibility of sperm banking at the time of diagnosis. AYA patients can use either a local sperm bank or an available online sperm banking kit.
- The age and comfort level of individual patients and their care givers must be taken into account when discussing sperm banking.
- 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.

Contraception for Women During and After Treatment for Cancer

AYA women with cancer have unique contraception needs and the options are dependent on the type of cancer, its treatment, and treatment-related complications.[134] The NCCN Guidelines recommend discussion about the use of contraception prior to initiating therapy.[134]

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.[135] LARC has been shown to be superior to short-acting contraceptives in AYA women.[136,137] In a study of 4,167 women (14–45 years of age), LARC was associated with higher 12-month compliance rates than oral contraceptive pills (86% vs. 55%).[136] In a large, prospective study involving 7,487 women, the contraceptive failure rate was significantly higher for those using oral contraceptive pills, patch, or ring compared to those using LARC (4.55 vs. 0.27), and the failure rates among women younger than 21 years were twice as great as in women 21 years of age or older.[137]

The Society of Family Planning guidelines recommend the use of IUDs or implantable contraceptives for most women who are receiving

treatment for cancer.[138] The use of any method of contraception is recommended for women 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 (VTE).[138] The use of IUDs is considered the preferred first-line contraceptive option for women with a history of breast cancer, although for women treated with tamoxifen, levonorgestrel-containing intrauterine system (IUS) may be preferable since it has been shown to reduce tamoxifen-induced endometrial changes without increasing the risk of breast cancer recurrence. Levonorgestrel-containing IUS may also be used to minimize menstrual blood loss in women with iron-deficiency anemia.[138]

Due to the risk of VTE associated with the use of combined hormonal contraceptive methods, the WHO and the U.S. Centers for Disease Control and Prevention recommend that the use of these contraceptive methods should be avoided in women of childbearing age with active cancer or who have been treated for cancer in the last 6 months.[139]

Management of Cancer During Pregnancy

Cancer is diagnosed in about 0.1% of pregnant women and is the second most common cause of maternal death during pregnancy.[140] Cervical, breast, thyroid and ovarian cancers, melanoma, lymphoma, and leukemia are the most common cancers diagnosed during pregnancy.[141-143] These are also the most common cancers diagnosed in the AYA population.[144]

Selection of an appropriate treatment plan for pregnant women is dependent on individual tumor biology and tumor stage, similar to the management of cancer in non-pregnant women. Most importantly, in addition to the disease characteristics, in pregnant women, the gestational age of the fetus is a significant factor in the selection of treatment.[145]

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.[145] The American College of Radiology has developed guidelines with an objective to assist practitioners in identifying pregnancy, preventing unnecessary irradiation of pregnant AYA women, 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.[146]

Surgery is possible at any time during pregnancy depending on the anatomical location of the tumor, although it may be beneficial to delay surgery, when possible, until after fetus viability.[145] RT is contraindicated during pregnancy. However, in very rare instances when RT is necessary, it should be delivered in low therapeutic doses (with adequate uterine shielding to minimize fetal exposure) with the goals of controlling maternal cancer and providing the fetus the best chance for survival with normal development.[147] 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.[147] Early collaboration among the radiation oncologist, medical physicist, medical and/or surgical oncologist, and obstetrician is essential.

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.[148-150] While the use of chemotherapy during the second and third trimesters has not been associated with significant teratogenic effects, it may be associated with low birth weight, preterm labor, and intrauterine growth restriction.[143,148,150-153] Potential benefits and risks of chemotherapy for both the mother and fetus must be carefully

evaluated prior to initiation of treatment. Delayed treatment until after fetal maturity, with careful follow-up to rule out disease progression, is a safe option for women diagnosed with early-stage cancers.[154,155] In some women diagnosed with advanced-stage disease with an urgent need to start chemotherapy in the first trimester, potential benefits and risks of chemotherapy for both the mother and fetus must be carefully evaluated prior to initiation of treatment.[143] Due to the severe teratogenic effects of methotrexate, it should not be used for the treatment of cancer in women at any stage of pregnancy.[150] The safety and efficacy of hormonal agents and targeted therapies have not yet been evaluated in well-controlled studies including pregnant women.[145,156,157] At the present time, the use of such agents in pregnant women 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 utilized in pregnant women without any significant side effects.[157-159]

The panel members acknowledged that the management of cancer during pregnancy poses significant diagnostic and therapeutic challenges for both the patient and the physician. The guidelines recommend that AYA women diagnosed with cancer during pregnancy require individualized treatment from a multidisciplinary team involving medical, surgical and radiation oncologists, gynecologic oncologists, obstetricians, and perinatologists as appropriate.[143] Referral to tertiary cancer centers with expertise in the diagnosis of cancer during pregnancy and maternal-fetal medicine and knowledge of the physiological changes that occur during pregnancy should be strongly encouraged.

Psychosocial and Behavioral Issues

AYA patients diagnosed with and treated for cancer have psychosocial issues that are distinct from that of pediatric and adult patients.[160-163] AYA patients 20 to 29 years of age are significantly less likely to use professional mental health services than teens and older patients 30 to 39 years of age. AYA patients in the 20 to 29 years 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 life, coping with treatment-related side effects and stress, seeking and understanding information, accepting cancer, and maintaining a positive attitude.[164] AYA men and women 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 with cancer.[165] Palmer et al have recently developed an AYA Oncology Psychosocial Screening Tool to assist clinicians to support psychosocial coping during active treatment and promote healthy post-treatment survivorship in AYA patients with cancer. This screening tool has four main areas: the distress thermometer, the check list of “areas of concern,” the tick box for information provision, and the signatures. Further validation of this tool and its use will help clinicians to improve psychosocial care for AYA patients with cancer, regardless of treatment location.[166]

Psychosocial needs for AYA patients with cancer should be assessed across the following domains:1) individual function (developmental, emotional, and behavioral issues); 2) relationships (family, peers, and health care professionals); 3) socioeconomic issues; and 4) supportive care services/interventions.

Individual Function

Developmental Issues

AYA patients with cancer have to cope with cancer treatment while accomplishing key developmental tasks such as identity development, including sexual identity; peer involvement; initiating intimate and emotional relationships; establishing autonomy from parents; and independently making decisions about their future that involve education, career, or employment.[167,168] 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 and lengthy treatments put AYA patients at risk for disruptions in their normal activities. Interruptions of school or work due to treatment will have negative consequences for their long-term career opportunities, financial status, and lifetime earnings.[164] 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.[169]

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 matured cognitive and emotional coping abilities.[164] Recent studies suggest that the rates of psychological distress are significantly greater amongst AYAs compared to older adults.[170-175]

In a longitudinal study that assessed the prevalence of psychological distress in 215 AYA patients with cancer (15–39 years of age) during the first year following diagnosis, distress symptoms exceeded population norms at the time of diagnosis and at 12-month follow-up.[173] In this study, 12% of AYA patients reported clinically significant chronic distress throughout the first 12 months following diagnosis and an additional 15% reported delayed distress. The needs for information, counseling, and practical support were reported in 57%, 41%, and 39% of AYA patients, respectively, at 12 months after the diagnosis of cancer.[175] Kazak et al reported that intensive cancer treatments during adolescence are associated with inferior psychosocial outcomes and health beliefs in survivors compared to their age-matched peers.[176] 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.[177]

Behavioral Issues

AYA patients with cancer may also engage in risky behaviors (tobacco, alcohol, or substance abuse) 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.[178] The risk factors associated with heavy drinking included fair or poor self-assessed health, depression, anxiety, somatization, activity limitations, and cancer-related fears and uncertainty.[179] Low perception of susceptibility to late effects, older adolescence compared to early adolescence, and worry were the strongest predictors of substance abuse.[180] While AYA patients may be aware of the complications associated with tobacco, alcohol, or substance abuse during their treatment, they may not avoid them throughout their treatment, as these habits make them feel normal and like part of their peer group. Clinicians working with this population need to be aware of this and address the issues in a sensitive and confidential manner.[169] AYA patients are also vulnerable to reproductive

health complications that should be addressed prior to, during, and after completion of treatment.[134]

NCCN Recommendations For Supportive Care Services/Interventions

- For all AYA patients, provide counseling regarding the risks of infertility associated with cancer and its treatment and the use of fertility preservation and contraception prior to initiating treatment.[181]
- Since the incidence of sexually transmitted infections peaks among AYAs 15 to 24 years of age, provide preventive health education about sexually transmitted diseases.[169]
- Prescribe and provide nutrition and exercise recommendations for all AYA patients.
- Provide AYA patients with flexible treatment dates, consultation times, and procedures to enable them to continue with their treatment without interrupting their school/work or other normal activities.[169]
- Offer psychosocial support and counseling to help alleviate distress. See the NCCN Guidelines for Distress Management (available at www.NCCN.org).
- Refer AYA patients with cognitive dysfunction or other psychiatric symptoms (eg, depression or anxiety) to a mental health provider and community-based resources serving AYA patients.
- Refer patients with signs, symptoms, and a history of substance abuse or addiction to a risk reduction or substance abuse management program.
- 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).[161,182]

Relationships

Social, Peer, and Family Relationships

AYA patients often have to endure lengthy hospital stays under the supervision of health care providers, resulting in significant isolation from their family members and peer group.[169] Isolation and alienation are common among AYA individuals diagnosed with cancer, because they often miss out on the life experiences shared by their non-ill peers. Reinforcing relationships with family, peers, and health professionals is an important aspect of life for AYA patients with cancer.[165,183]

While 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 AYA patients cope with cancer and overcome feelings of loneliness.[161,165] In one study, AYA patients with cancer (16–22 years of age) identified social support (friends and health care providers) as their major coping strategy to deal with cancer, whereas family support was identified as their important source for emotional support.[184] In another study, 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.[181]

Peer support programs assist AYA patients and survivors in establishing and maintaining relationships with their normal 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.[181,185] Peer support also provides AYA patients with an opportunity to address some of their concerns, such as coping with uncertainty about the future, establishing autonomy while being increasingly dependent on family and friends, sexual identity, and infertility, thereby reducing feelings of social isolation.[185]

AYA peer support groups have been developed in a variety of formats, including face-to-face meetings, camp style formats, or online support groups.[186,187] Social networking groups focused on supporting AYA patients with cancer are particularly helpful for exchanging two primary types of support, informational and emotional, through providing advice and empathizing with other AYA patients dealing with cancer.[187] Summer camps and adventure programs where participants are physically challenged have resulted in improvements in self-confidence, independence, and social contacts.[161,186] 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.[161] 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.[188,189]

Communications with Health Care Professionals

Communicating information to AYA patients can be challenging, especially since 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.[14] While some patients prefer not to receive direct communication about their cancer, others may desire to take a more prominent role in the management of their care. For the latter group, information should be provided directly to patients in an age-appropriate manner, allowing time to process the information and deliver information in a caring manner.[190] 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.[169] 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.[191] Since there is evidence that AYA patients are willing to use the internet to get health information and support, it will also be 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.[186,189,192] See *Online Resources for AYA Patients and Survivors* in the guidelines.

NCCN Recommendations For Supportive Care Services/Interventions

- Promote communication between AYA patients and family members (parents, spouse/partners, and siblings).[15]
- Provide information to family members and partners about psychosocial support and behavioral services to increase awareness of the possible psychosocial issues associated with diagnosis of cancer in AYAs.
- Consider family-based intervention models from pediatrics (eg, parent support groups, Impact of Traumatic Stressors Interview Schedule).[10]
- Establish direct communication with the individual patients, providing age-appropriate information about their cancer, treatment options, and potential side effects, thus reinforcing the importance of AYA involvement in decision-making.[14,181]
- 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 other family members.

- Provide information about peer support groups and create flexible visiting hours and an environment that will encourage peers to visit AYA patients.[169]

Socioeconomic Issues

AYA patients are much more likely to be uninsured or underinsured individuals than adults or children, with many of them in a transition between their parents' insurance and their independent insurance.[10] 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 to their siblings.[193] Furthermore, unemployment and lack of health insurance appear to be significant predictors of psychological distress in the childhood cancer survivor population.[194] Uninsured AYA patients are also less likely to participate in clinical trials.[53] As described above, advanced stage of cancer at diagnosis and lack of health insurance were significantly associated with longer time to cancer diagnosis in AYAs.[40] 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.[164] Recent results from the AYA HOPE study, a population-based cohort study of 523 AYA patients with cancer (15–39 years of age 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.[195]

AYA patients with employment also experience problems in obtaining health and life insurance due to their pre-existing cancer history.[161] 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 childcare as well as expenses not related to treatment.[161] 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 the treatment is over, AYA patients with cancer also need long-term follow-up care for monitoring and treatment of late effects.

NCCN Recommendations For Supportive Care Services/Interventions

- Assess AYA patients' health insurance status and provide information on potential sources of coverage (eg, Medicaid, Social Security, Disability 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, food stamps).
- Provide a referral for transportation assistance programs (eg, van ride programs, voucher programs) for AYA patients who have to travel to receive treatment. Identify resources for respite care that would be helpful for those with young children.
- For those who desire to receive complementary and alternative medicine, refer them to reputable providers of these services.
- Provide information about reliable online sources to access age-appropriate information related to their cancer. See *Online Resources for AYA Patients and Survivors* in the guidelines.
- Educate AYA patients with cancer about their long-term follow-up care for monitoring and treatment of late effects, long after completion of treatment.
- Integrate financial assistance for AYA cancer survivors into their survivorship plans.

Survivorship Issues

Late Effects In AYA Cancer Survivors

AYA cancer survivors are at increased risk for late effects related to cancer treatment, and the risk for long-term effects is dependent on the age at initial diagnosis and the type of treatment.[196-198] In addition, the risk for many late effects may also be influenced by family history, lifestyle behaviors, and comorbid health conditions. Age at treatment exposure modifies the risk of some late effects (eg, breast cancer following chest RT, cardiomyopathy following anthracycline chemotherapy) but not others (eg, ischemic coronary artery disease following chest RT).[199,200]

Much of the understanding of the long-term outcomes of AYA cancer survivors comes from the Childhood Cancer Survivor Study (CCSS), which includes long-term survivors of childhood and adolescent cancers who were diagnosed prior to age 21.[201,202] No such large cohort studies have addressed the survivorship issues related to cancer diagnosed in young adult patients between the ages of 22 and 39 years. Outcomes from the CCSS among those diagnosed between the ages of 15 and 20 are particularly relevant for the NCCN Guidelines for AYA Oncology. Among adult survivors of childhood and adolescent cancer, Oeffinger et al reported that by 30 years after the cancer diagnosis, the cumulative incidence of a chronic health condition was 73%, with a cumulative incidence of 42% for severe, disabling, or life-threatening conditions or death. Importantly, the risk for a chronic health condition (ie, long-term or late effect) was similar for those diagnosed with the primary cancer in adolescence and in childhood.[201]

More recent reports have also documented the prevalence of treatment-related adverse health status and the risk of late morbidity leading to hospitalizations among AYA cancer survivors.[203-206]

A report that examined the health status of 4054 AYA cancer survivors revealed a significantly higher prevalence of current smoking (26% vs. 18%); obesity (31% vs. 27%); cardiovascular disease (14% vs. 7%); hypertension (35% vs. 29%); asthma (15% vs. 8%); disability (36% vs. 18%); and poor mental health (20% vs. 10%) and physical health (24% vs. 10%) among AYA cancer survivors compared to those who had no history of cancer.[203] In another large cohort study that included adult cancer survivors (245 patients 15–19 years of age and 12 patients 20–24 years of age at the time of diagnosis), impaired organ dysfunction (pulmonary, auditory, endocrine, and nervous system) was the most prevalent of all the adverse health outcomes.[204] In a recent retrospective analysis of 5-year survivors of young adult cancer (n = 902), the presence of at least one late morbidity leading to hospitalization was higher in survivors than in the control group (50.4% and 37.9%, respectively), and the adjusted risk of this morbidity for survivors was 1.4 times higher than for the control group.[205] In another report that evaluated the quality-of-life outcomes in 8375 AYA cancer survivors (diagnosed with cancer between 15–39 years) relative to the same aged controls, AYA cancer survivors were 2 times more likely to report fair or poor general health than the control group. The limitations in quality of life persisted across gender, race, ethnicity, and age.[206]

While several single cancer studies have assessed long-term outcomes among HL and testicular cancer survivors across the AYA age range, the long-term outcomes of survivors of other cancers occurring in young adulthood, such as breast, ovarian, and thyroid cancers or melanoma, remain understudied. Since there is a paucity of literature on survivorship issues related to cancer diagnosed during adolescence

and young adulthood, the findings from the CCSS and similar studies focusing on childhood and adolescent cancer survivors could be extrapolated to the survivors of AYA cancers, albeit with caution. Increased adherence to long-term follow-up guidelines may contribute to improvement in health status of AYA cancer survivors.[203]

Some of the more common late effects among AYA cancer survivors are discussed below.

Secondary Cancers

AYA cancer survivors (between 15–39 years of age at the time of diagnosis) are at significant risk of developing a variety of secondary cancers compared to the general population.[207] The risk and specific types of secondary cancers are widely dependent on the type of initial cancer diagnosis and treatment exposure.[208-210] Older age at diagnosis (15–21 years) was associated with increased risk for breast cancer, nonmelanoma skin cancers, and other solid organ cancers (including head and neck, small intestine, and colorectal cancers).[210,211]

AYA survivors of HL diagnosed between 21 to 39 years of age are at increased risk of developing secondary cancers.[209] The most frequently observed secondary cancers are breast, lung, thyroid, and gastrointestinal cancers.[199] AYA women with HL treated with chest RT are at significantly increased risk of developing secondary breast cancer, and the risk for secondary breast cancer among HL survivors is strongly associated with age at diagnosis and mediastinal RT dose.[63,212-214] In a cohort of 770 female survivors who had been diagnosed with HL before age 41 years, the risk of developing breast cancer increased with increasing RT dose (38.5 Gy or more).[212] In an international, population-based study of 3,817 female survivors of HL diagnosed at age 30 years or younger, Travis et al reported that for women treated at age 25 years with a chest RT dose of at least 40 Gy without alkylating agents, the estimated cumulative absolute risks of developing breast cancer by age 35, 45, and 55 years were 1.4%, 11.1%, and 29.0%, respectively.[213]

Alkylating agent-based chemotherapy for HL has been associated with a modestly increased risk for secondary lung cancers in patients diagnosed at 40 years or younger, and the risk increased with both increasing number of cycles of alkylating agents and the cumulative dose.[215] In this study, the risk of secondary lung cancer was substantially higher among survivors who smoked (9.6% due to treatment alone compared to 63.3% due to the combination of treatment and smoking). In a collaborative British Cohort study that assessed the risk of developing secondary cancers in 5,798 patients diagnosed with HL between 15 and 34 years of age, the 20-year cumulative risk of second cancer was 13% and 18%, respectively, for chemotherapy alone and combined modality therapy.[216] Risks for secondary lung cancer, NHL, and leukemia were significantly higher after treatment with chemotherapy alone, whereas combined modality therapy was associated with a higher risk for these and several other cancers.[216]

AYA survivors of testicular cancer are also at significantly increased risk of developing secondary cancers, including contralateral testicular cancer, leukemia, malignant mesothelioma, and cancers of the lung, colon, esophagus, stomach, and pancreas.[217,218] In a population-based study of 29,515 testicular cancer survivors, the 15-year cumulative risk of developing contralateral testicular cancer was almost 2%, which is 12-fold higher than that of the general population.[219] In an international, population-based study of 40,576 testicular cancer survivors, the cumulative risk of developing solid tumors by age 75 years was slightly higher for patients with seminomas than for patients without seminomas who were diagnosed at 35 years of age (36% and 31%, respectively).[220] The combination of chemotherapy and RT was associated with a larger

risk of secondary solid tumors than RT alone, although the difference was not statistically significant.[220] Secondary leukemia related to chemotherapy with topoisomerase II inhibitors and alkylating agents has also been reported in testicular cancer survivors. In one study, the cumulative incidence of secondary AML was 0.5% at 2 years after treatment with high-dose chemotherapy (with a median cumulative etoposide dose of 4.9 g/m^2) and autologous HSCT.[221] In another study involving 42,722 one-year survivors of testicular cancer, the estimated excess cumulative leukemia risk was 0.23% at 30 years after testicular cancer diagnosis.[222] The risk for secondary AML was higher for patients treated with chemotherapy compared to those treated with radiotherapy alone.

The risk for secondary malignancies among survivors of cervical and breast cancers, NHL, and melanoma has been assessed in only a few cohort studies.[223-225] Among 104,760 one-year survivors of cervical cancer, patients heavily treated with RT were at increased risk for secondary cancers at sites in close proximity to the cervix beyond 40 years of follow-up. The 40-year cumulative risk for any second cancer was higher among women diagnosed before age 50 than among women diagnosed after age 50 (22.2% and 16.4%, respectively).[223] In a population-based cohort of 376,825 one-year survivors of breast cancer from the Scandinavian cancer registries, women diagnosed at 40 years or younger with localized disease were particularly at risk of developing a second cancer at 30 or more years after breast cancer diagnosis.[224] In an analysis of 28,131 patients from the Swedish Cancer Registry, the risk of developing subsequent solid tumors after NHL during the first decade was higher among patients diagnosed between 20 and 39 years of age compared to those who were age 40 years or older at the time of diagnosis.[225] In the SEER database analysis of 89,515 melanoma survivors, patients diagnosed at younger than 30 years of age had the highest risk of developing secondary cancers (breast, prostate, and NHL being the most common cancers) at more than 20 years after initial diagnosis. HSCT and RT to head and neck also increased the risk of subsequent cancers in the oral cavity.[226]

Long-term AYA survivors of pediatric-predominant cancers, including ALL, AML, CNS tumors, and bone and soft tissue sarcomas, are also at risk of developing secondary cancers. Among the survivors of ALL and AML, CNS was the most common secondary cancer (24%) followed by thyroid cancer (22%). For patients who survived for at least 5 years after the diagnosis, the cumulative incidences of secondary cancers at 30 years was 3.9% and 4.3%, respectively, for ALL and AML.[227]

The risk is especially higher among patients diagnosed at a younger age (17 years or younger for ALL and CNS tumors; 18 years or younger for bone and soft tissue sarcomas).[207] Among long-term survivors of bone cancers at 25 years after diagnosis, the cumulative incidence of subsequent cancers is higher for those diagnosed with Ewing's sarcoma compared to those diagnosed with osteosarcoma (9.0% and 5.4%, respectively).[228,229]

Clinicians who provide care for the majority of AYA cancer survivors must implement and evaluate methods for improving awareness of secondary cancers. They must also implement appropriate surveillance strategies for early detection of these malignancies.[230] An annual mammogram and breast MRI are recommended for women treated with a chest RT ≥20 Gy prior to 30 years of age.[231] A colonoscopy is recommended starting at age 35 years or 10 years after completion of RT, whichever occurs last, for patients treated with abdominal or pelvic RT ≥30 Gy. Routine endocrine, ophthalmology, and dental evaluation (dental exam and cleaning every 6 months) is recommended for long-term AYA cancer survivors treated with chemotherapy and/or RT

or those treated with TBI for HSCT.[226] Screening for secondary AML or myelodysplasia may be done by assessing complete blood count (CBC)/differential annually up to 10 years after exposure, though currently available data do not support routine screening in this manner.

Cardiovascular Complications

Cardiovascular complications (congestive heart failure [CHF], myocardial infarction [MI], pericardial disease, and valvular abnormalities) are the leading non-malignant cause of death among survivors of AYA cancers, compared to the general population.[232-235]

Mediastinal RT and anthracycline-based chemotherapy are the strongest risk factors for late cardiovascular complications in AYA survivors of HL.[200,236,237] In the British Cohort Study of 7,033 patients with HL, the risk of death from MI was highest for patients younger than 35 years at the time of treatment with supradiaphragmatic RT.[237] Patients treated with anthracyclines were at increased risk for MI within one year after first treatment, whereas the risk for MI among patients treated with supradiaphragmatic RT and vincristine without anthracyclines increased sharply after the first year of follow-up.[237] In another study of 1,474 survivors of HL younger than 41 years at the time of treatment, mediastinal RT increased the risk of MI, CHF, and valvular disorders, whereas the addition of anthracyclines to RT elevated the risks for CHF and valvular disorders.[200] The 25-year cumulative incidence of CHF after mediastinal RT and anthracyclines was 8%.

Cisplatin-based chemotherapy is associated with long-term risk for cardiovascular complications in testicular cancer survivors.[238,239 240] In a Dutch study of 2,512 testicular cancer survivors, nonseminoma testicular cancer survivors younger than 30 years at diagnosis treated with mediastinal RT and chemotherapy with cisplatin, vinblastine, and bleomycin were at increased risk for MI within 20 years of treatment.[238] Haugnes et al reported that treatment with cisplatin, bleomycin, and etoposide and/or RT was associated with increased risks for cardiovascular disease in testicular cancer survivors; chemotherapy alone or in combination with RT significantly increased the risk for MI.[239]

Survivors of brain tumors, leukemia, NHL, and bone and soft tissue sarcomas treated with anthracyclines and cardiac irradiation are also at significantly higher risk of adverse cardiovascular complications. However, the majority of patients included in these studies were younger than 21 years at the time of diagnosis.[241] A more recent report from the Finnish Cancer Registry, that included 5-year survivors (n = 13,860; younger than 35 years of age at diagnosis), has also documented increased cardiovascular complications among survivors of lymphoma, brain tumor, leukemia, and testicular cancer.[233]

Pulmonary Complications

Chemotherapy, chest RT, and craniospinal irradiation are associated with pulmonary toxicity and can compromise pulmonary function in AYA cancer survivors.[240,242,243]

Age at diagnosis (15– 21 years compared with age younger than 15 years) and pulmonary toxic chemotherapy alone or combined with chest RT were associated with a significantly increased relative risk of lung fibrosis and pleurisy.[242] The cumulative incidence increased up to 15 to 20 years after diagnosis. Other complications include recurrent pneumonia, chronic cough, supplemental oxygen use, and shortness of breath.

A large international study reported a significant increase in mortality from respiratory diseases among testicular cancer survivors treated with chemotherapy compared to the general population.[244] Risk factors for pulmonary toxicity include age at diagnosis, cumulative bleomycin dose,

reduced glomerular filtration rate, renal dysfunction, and stage IV disease at presentation.[245] Haugnes et al reported that among 1,049 testicular cancer survivors, those treated with chemotherapy combined with pulmonary surgery or large cumulative cisplatin doses had significantly reduced pulmonary function compared with those treated with surgery alone.[246] Bleomycin dose was not associated with restrictive lung disease. Instead, in a multivariate model, cisplatin dose (P = .007) and age at diagnosis (P = .008) were associated with the risk for restrictive lung disease.

Neurological Complications

AYA survivors of brain tumors treated with cranial RT are at increased risk for neurologic complications, including hearing impairments, cataracts and other vision problems, seizure disorders, and coordination and motor control problems.[247,248] However, these findings are relevant to survivors diagnosed at 21 years of age or younger.

Long-term AYA survivors of testicular cancer who were treated with cisplatin-based chemotherapy are at risk for neurological complications such as sensory neuropathy, tinnitus, hearing impairment, and Raynaud's phenomena (white or cold hands or feet on cold exposure).[240] Among 1,814 survivors of testicular cancer included in a Norwegian observational study, Raynaud-like phenomena were the most frequently reported complications (39% of men), followed by paresthesia of the hands or feet (29%), and tinnitus and hearing impairment (22% and 21%, respectively) by men treated with chemotherapy compared to those not treated with chemotherapy.[249] The incidences of paresthesia of the feet were also higher among men treated with RT.

Stroke, although relatively uncommon, is a devastating neurological complication in AYA survivors of brain tumors and leukemia treated with cranial RT and survivors of HL treated with mantle field RT.[250,251] In a retrospective cohort study of 2201 5-year survivors of HL, those treated with RT to the neck and mediastinum were particularly at increased risk for stroke and transient ischemic attack.[252] The incidences were higher among patients diagnosed at younger than 21 years than those diagnosed between 21 and 30 years of age. The standardized incidence ratio was 3.8 and 3.1, respectively.

Nephrotoxicity

Long-term renal dysfunction has been reported in survivors of testicular cancer treated with infradiaphragmatic RT and cisplatin-based chemotherapy. In one study with a long-term follow-up, renal impairment was observed in 8% of patients treated with abdominal RT alone compared to a 14% reduction in patients with chemotherapy with or without RT. Age at treatment and type of treatment were associated with impaired renal function.

Endocrine Complications

Cranial or spinal RT, TBI, and targeted RT to neck, abdomen, pelvis, and testes are associated with endocrine late effects in survivors of AYA cancers.[100] The most common endocrine complications include growth hormone (GH) deficiency, thyroid gland abnormalities, gonadal dysfunction, and decreased fertility.[59,91] AYA cancer survivors treated with RT dose of ≥18 Gy to the hypothalamic-pituitary-adrenal (HPA) axis are at high risk for GH deficiency, whereas those treated with RT dose of ≥40 Gy to the HPA axis are at risk of developing central hypothyroidism, gonadotropin deficiency, and central adrenal insufficiency.

GH deficiency can be observed within 5 years after treatment with RT doses higher than 30 Gy, whereas in patients treated with lower doses (18–24 Gy) it may not be evident for 10 years or more.[100] Secondary

thyroid cancers, hypothyroidism, and, to a lesser extent, hyperthyroidism are more common among AYA survivors of brain tumors, ALL, HL, and those who underwent HSCT.[247,253,254] Testicular cancer survivors treated with chemotherapy and RT are at greater risk for hypogonadism.[240] Low testosterone levels and testosterone replacement have been reported in 34% and 4% of testicular cancer survivors, respectively.[255]

Long-term Follow-up

As discussed above, AYA cancer survivors have a high risk of developing a wide range of late effects. AYA cancer survivors may benefit from regular screening and early intervention for cardiovascular disease.[256] Continued follow-up of AYA cancer survivors is needed to monitor the pulmonary complications.[257] Development of a "Cancer Treatment Summary and Survivorship Care Plan," including periodic evaluation with focused history, physical examination, and screening based on treatment exposures, and risk for treatment-related late effects, should be an integral part of management of AYA cancer survivors.[197,258,259] Issues related to insurance, clinical team composition (presence of a provider knowledgeable in childhood cancer), scheduling (availability of flexible scheduling), and comprehensive nature of the care provided were identified as patient-perceived facilitators for the transition of survivorship care in young adult survivors of childhood cancer.[260]

The models for AYA survivorship care include cancer center follow-up (primary treatment team or specialized long-term follow-up clinics), follow-up by the patient's primary care physician, or a combination of both (shared care model).[259,261] Some studies have shown that a shared care model involving both the primary oncology team and the primary care physician is feasible and can facilitate appropriate care in childhood cancer survivors.[262-264]

Risk stratification of survivors based on the current medical issues and prior treatments may be helpful to determine the different levels of follow-up in the shared care model.[261,265,266] Survivors at low risk for late effects (treated with surgery alone and/or chemotherapy with no RT, not including alkylating agents, anthracycline, bleomycin, or epipodophyllotoxin) can be transitioned to their primary care physician soon after completion of therapy. Survivors at moderate risk for late effects (treated with low- or moderate-dose chemotherapy with no RT, chemotherapy-containing alkylating agents, anthracycline, bleomycin, or epipodophyllotoxin) can be evaluated by their oncology team or primary care physician on alternating years. Survivors at high risk for late effects, such as those treated for CNS cancers or those treated with HSCT, any RT, high-dose alkylating agents, anthracycline, bleomycin, or epipodophyllotoxin, should be followed annually by their oncology team and continue follow-up care with their primary care physician.

The screening recommendations included in the NCCN Guidelines for AYAO are adapted from the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers, available at survivorshipguidelines.org.[230] See *Screening Recommendations for AYA Survivors* in the guidelines for specific recommendations based on the treatment exposure and timing and intensity of screening. These recommendations may be adapted based on additional risk factors.

Palliative and End-of-life Care

Palliative care is interdisciplinary care of patients with life-threatening illnesses, malignant as well as non-malignant. The goal of palliative care in patients with cancer is to control symptoms, relieve emotional

and physical suffering from adverse effects of treatment, and improve quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies.[267] See the NCCN Guidelines for Palliative Care (available at www.NCCN.org).

Palliative care services for AYA patients should be provided by a multidisciplinary team ideally with expertise in understanding the psychosocial, emotional, developmental, and financial issues that are unique to this age group.[267,268] Introduction of palliative care for symptom management and psychosocial support should occur before the patients are considered "palliative" in order to provide the best possible care.[269] Palliative care is appropriate even when patients are being treated with curative intent, and there is growing consensus that AYA patients should have access to palliative care services from the time of diagnosis until the time of death or cure.[269] Patients, caregivers, and health care professionals should be taught that palliative care is an integral part of their comprehensive cancer care.[268] AYA patients usually are not making decisions in isolation. While some AYA patients have the ability to make life and death decisions independently, many are either not the primary decision maker or they rely intensely on input from parents, spouses, significant others, and other family members.[267] Palliative care services should also consider the psychosocial needs of the patient's family, friends, and caregivers.[269] Social support is required for almost all AYA patients receiving palliative care, including attention to patients' goals, hopes, dreams, and the desire to leave a legacy.[268]

End-of-life care involves the management of delirium, existential distress, discussion about the place of death, and support of family.[267,268] It is imperative for health care professionals not to assume that AYA patients may be less inclined to discuss death and other end-of-life issues.[267] In an exploratory study of 50 adolescent patients (15–21 years of age) with and without chronic illnesses, adolescents were willing to discuss end-of-life decision making by taking part in a one-on-one survey administered by a researcher.[270] The quality of life of AYA patients should be heeded by the care team.[268] During palliative and end-of-life care, AYA patients may be able to and wish to continue to engage in their day-to-day activities, even if some activities are in discord with medical advice (eg, participating in strenuous physical activity).

Discussion about end-of-life preferences should begin at the time of initiating treatment, but details should be individualized according to the preferences of the AYA patient and family.[271] AYA patients' opinions about end-of-life care vary across this age group. Exploring individual preferences for end-of-life care and providing interventions specific to the needs of this patient population could significantly improve end-of-life care.[271,272] In one retrospective review, a significant number of adolescents dying of cancer felt that discussions about end-of-life occurred very close to death, thus allowing very little time to psychologically prepare for death.[273] Physicians with expertise in palliative care should facilitate difficult end-of-life issues such as nutrition/hydration, sedation, treatment cessation, and place of death.[267] An advance care planning document is necessary for terminally ill AYA patients with metastatic cancer.[271,274] Ongoing psychosocial support is extremely important during the transition to end-of-life care.

Summary

AYA patients with cancer should be recognized as a distinct age group that has unique medical 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 as well as medical subspecialty services appropriate for their cancer diagnosis.

Table 1. Age-specific SEER incidences of cancer by cancer site and sex in the AYA population (2008–2012)[1,2]

Cancer type	Ages 15–39 (Females)
Carcinoma of breast	20.7
Thyroid carcinoma	17.4
Carcinoma of cervix and uterus	9.1
Melanoma	8.6
Carcinoma of colon and rectum	3.7
HL	3.5
NHL	3.3
Leukemias	2.9
CNS cancers	2.5
Soft tissue sarcomas	2.4
Carcinoma of the kidney	1.7
Carcinoma of head and neck	1.5
Germ cell neoplasms	1.1

Cancer type	Ages 15–39 (Males)
Germ cell neoplasms	11.0
Melanoma	5.2
NHL	4.9
Carcinoma of colon and rectum	3.9
Leukemias	3.7
HL	3.6
Thyroid carcinoma	3.5
Soft tissue sarcomas	3.2
CNS cancers	3.2
Carcinoma of the kidney	2.3
Carcinoma of head and neck	1.8
Bone sarcomas	1.1

[1.] These are incidence rates are per 100,000.

[2.] Data from Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2013 SEER data submission, posted to the SEER website, April 2015.

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