National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Poland Edition

Adolescent and Young Adult (AYA) Oncology

Version 2.2025 — April 8, 2025

NCCN.org

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.

NCCN Guidelines for Patients® available at www.nccn.org/patients

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[NCCN Guidelines Panel Disclosures]

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ξ Bone marrow transplantation
‡ Hematology/Hematology oncology
† Medical oncology
€ Pediatric oncology
§ Radiation oncology
θ Psychiatry and psychology, including health behavior
£ Supportive care including palliative, pain management, pastoral care, and oncology social work
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Find an NCCN Member Institution: https://www.nccn.org/home/member-institutions.

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

See NCCN Categories of Evidence and Consensus.

See International Adaptations Table of Contents for other NCCN Guidelines: Poland Edition. Most recent version of the NCCN Guidelines is available at www.NCCN.org.

RECOMMENDATIONS ARE REPRESENTED AS FOLLOWS:
Black Text: Recommendations that are widely applicable
Italicized Blue Text: Country/region-specific modifications that are appropriate and/or feasible
Gray Text: Recommendations that may be costly, technically challenging, and/or not widely available in the specific country/region*
Gray Text with ~~Strikethrough~~: Recommendations that are not feasible or available in the specific country/region**

* Recommendations that are considered clinically appropriate by national/regional experts but are not currently available due to lack of reimbursement by the national/regional healthcare financing system.
**Recommendations that are considered as inconsistent with national/regional medical practice.

Note: Drugs and biologics included in the NCCN Guidelines® are approved by the United States Food and Drug Administration (FDA). Alternate agents based on the local regulations and availability may be substituted provided evidence supports their efficacy and safety. Generic drugs should be used only when studies have proven bioequivalence and the drugs have met the same standards for identity, strength, purity, and quality as the innovator drugs. The WHO Model Lists of Essential Medicines can be found here: http://www.who.int/medicines/publications/essentialmedicines/en/.

PRINCIPLES OF CANCER CARE

- ***Standards of care are based on best reported achievable outcomes. Multidisciplinary care is always recommended.***
- ***Delays in treatment reduce the effectiveness of treatment, so efforts should be made to expedite investigations and referrals to reduce waiting time before treatment initiation.***

DEFINITION OF THE ADOLESCENT AND YOUNG ADULT ONCOLOGY POPULATION

The adolescent and young adult (AYA) oncology patient is defined as an individual aged 15–39 years at the time of initial cancer diagnosis. This definition is based on the National Cancer Institute (NCI) Progress Review Group recommendations for a national agenda to advance AYA oncology.

PURPOSE OF THE NCCN GUIDELINES FOR AYA ONCOLOGY

AYA patients with cancer have a number of unique medical and psychosocial concerns that have been identified by panels of experts, including (although not limited to) fertility preservation, parenting, education, and employment attainment and retention. The relative importance of these issues understandably varies markedly across the broad age range defined. These issues should be considered as part of the overall therapeutic plan for the patient. Specific recommendations are highlighted in the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology. Many centers have established AYA centers to accommodate the specific needs of patients with cancer in this age group. Consideration should be given to referring such patients to one of these AYA centers of excellence if feasible. Available literature demonstrate improved outcomes in patients receiving AYA-focused care through a comprehensive and multidisciplinary approach. AYA patients are encouraged to seek care at centers with established social, clinical, therapeutic, and psychosocial support programs.

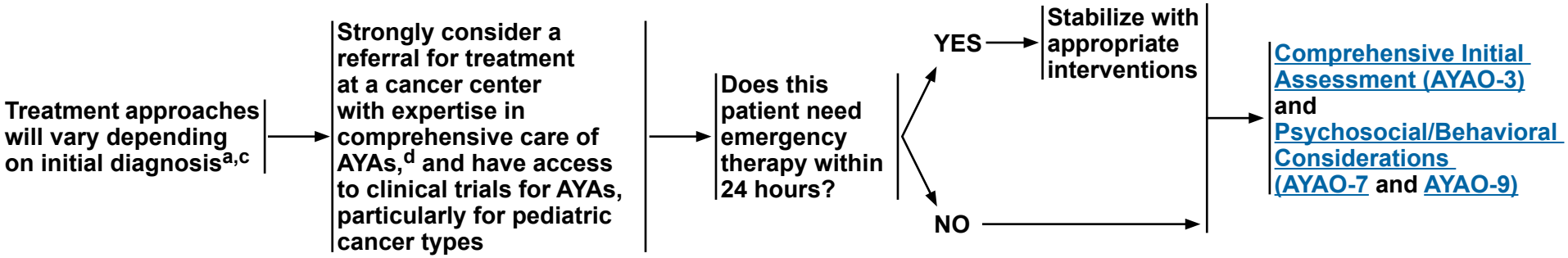
The NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology have been developed as supportive care guidelines and not as treatment guidelines. The purpose of the guidelines is to identify and increase awareness of unique issues in AYA oncology. In addition, these guidelines will identify resources available to the AYA population, include appropriate tabular materials, and make recommendations for patient care.

- **AYA patients diagnosed with cancer should be recognized as a distinct age group that has unique medical and psychosocial needs. The distribution of cancer types is dramatically different across the age spectrum of the AYA population.[a]**
- **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 and during the transition of care from pediatric to adult medical teams.[b]**
- **Participation in clinical trials as well as enrollment on tumor banking and biologic protocols should be strongly encouraged in the AYA population.**

[a] Howlader N, et al (eds). SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2017, based on November 2019 SEER data submission, posted to the SEER website, April 2020.
[b] Perez GK, et al. Am Soc Clin Oncol Educ Book 2020;40:1-15.

Note: All recommendations are category 2A unless otherwise indicated. This is the NCCN Guidelines: Poland Edition. For definitions, see page DEF-1.

SCREENING, ASSESSMENT, AND EVALUATION



[a] Howlader N, et al (eds). SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2017, based on November 2019 SEER data submission, posted to the SEER website, April 2020.

[c] Definition of AYA Population (AYAO-1).

[d] These centers provide a multidisciplinary approach involving a team of providers with expertise in AYA 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 use disorders.

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COMPREHENSIVE INITIAL ASSESSMENT*

- It is important to speak with the patient individually to solicit questions/concerns without a caregiver/partner present so the patient can speak freely.
- Provide age-appropriate information related to cancer.
  See Online Resources for AYA Patients and Survivors**
- Consider a pregnancy test prior to each cycle of therapy in accordance with institutional requirements.
  - Discuss contraception prior to initiating therapy.
    - Consult with OB/GYN for patients with ovaries/uterus ~~and consult the CDC Summary Chart of U.S. Medical Eligibility Criteria~~ to assist with the safety and efficacy of selection of appropriate contraception for individuals at risk of pregnancy.
  - Discuss risks of impaired fertility due to cancer and its therapy, as well as fertility preservation options, and consider referral to a fertility preservation/reproductive health program.
    See Fertility, Reproductive Endocrine, and Sexual Health Considerations (AYAO-5)
- Psychosocial assessment
  - See Comprehensive Psychosocial/Behavioral Considerations
    - Individual (AYAO-7 and AYAO-8)
    - Relationships (AYAO-9)
    - Socioeconomic Issues (AYAO-11)
  - See NCCN Guidelines for Distress Management
- As part of an initial evaluation, a complete family history should be taken. If indicated, refer for subsequent evaluation by a genetic counselor for genetic and familial risk assessment/counseling. Approximately 8%–9% of all patients with cancer will have a germline mutation in a cancer-predisposing gene.[e]
  - Risk factors for breast cancer
    - See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic
    - Chest irradiation
  - Risk factors for colon cancer
    - See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
  - Risk factors for sarcomas
    - See NCCN Guidelines for Soft Tissue Sarcoma
    - See NCCN Guidelines for Bone Cancer
  - Risk factors for multiple endocrine neoplasia (MEN)
    - See NCCN Guidelines for Neuroendocrine and Adrenal Tumors

→ Treatment-related issues → Treatment-Related Issues (AYAO-4)

→ Fertility/endocrine → Fertility, Reproductive Endocrine, and Sexual Health Considerations (AYAO-5)

→ Adherence to treatment → Psychosocial/Behavioral Considerations (AYAO-7 and AYAO-9)

** The conditions of Polish clinical practice and the reimbursement state should be taken into account while using the recommendations outlined in other NCCN Guidelines referenced on this page.*

*** The conditions of Polish clinical practice and the reimbursement state should be taken into account while using these resources.*

[e] Parsons DW, et al. JAMA Oncol 2016;2:616-624; Zhang J, et al. N Engl J Med 2015;373:2336-2346; Gröbner SN, et al. Nature 2018;555:321-327.

Note: All recommendations are category 2A unless otherwise indicated. This is the NCCN Guidelines: Poland Edition. For definitions, see page DEF-1.

TREATMENT-RELATED ISSUES

Dose schedules

- AYA patients should be offered enrollment in open clinical trials for their specific disease when available and appropriate and supportive care should follow well-established guidelines such as those available at www.NCCN.org.*
- Dose reductions may be appropriate and are often based on 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.
- Establish maximum cumulative dosing parameters and monitor cumulative dosing and schedule for certain medications associated with irreversible organ damage and fertility issues when certain lifetime exposure is encountered. See AYAO-10 for specific agents.

Toxicities

- Reversible toxicities do not necessarily warrant dose reductions.
  See NCCN Guidelines for Supportive Care for the management of treatment-related toxicities,* including:
  - NCCN Guidelines for Adult Cancer Pain
  - NCCN Guidelines for Antiemesis
  - NCCN Guidelines for Cancer-Related Fatigue
  - NCCN Guidelines for Palliative Care
  - NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections
  - See NCCN Guidelines for Hematopoietic Growth Factors for growth factor support and management of cancer- and chemotherapy-induced anemia for those who refuse blood transfusions.
- Screening is recommended for the following treatment-related toxicities:
  - Cardiac toxicity - Provide periodic echocardiograms for select patients.[f] A post-treatment baseline electrocardiogram (ECG) is recommended after completion of treatment. See Screening Recommendations for AYA Survivors (AYAO-B). Consider adding a cardioprotectant (eg, dexrazoxane) for anthracycline doses exceeding 250 mg/m^2;[g] however, there may be variability depending on institutional guidelines.
  - Renal toxicity - Provide periodic monitoring of renal function and electrolytes in patients treated with platinum-based therapies and ifosfamide-based chemotherapy.
  - Ototoxicity - Conduct routine evaluations for tinnitus and periodic audiogram to monitor hearing loss associated with platinum-based chemotherapy. Consider sodium thiosulfate (STS) to reduce the risk of ototoxicity associated with cisplatin in patients with localized, non-metastatic, solid tumors. There are concerns about the use of STS in the metastatic setting.[h]
  - Neurotoxicity - Conduct routine evaluation for symptoms of peripheral neuropathy.
  - Routine endocrine, ophthalmology, and dental evaluations are recommended for patients with selected radiation exposure and/or total body irradiation (TBI) for hematopoietic cell transplant (HCT).
  - Fertility impairment - See Screening Recommendations (AYAO-B 4 of 6)
  - Pulmonary toxicity - See Screening Recommendations (AYAO-B 3 of 6)
  - Radiation-related effects - Consider multidisciplinary consultation, which includes a radiation oncologist for the optimal method to reduce radiation-induced late effects.
  - Immunotherapy-induced toxicity - There may be long-term toxicity, but more data on the AYA population are needed.
  - Osteoporosis and osteopenia in selected populations[i]
  - Dermatologic side effects
  - Hair loss and recommendation for management

** The conditions of Polish clinical practice and the reimbursement state should be taken into account while using the recommendations outlined in other NCCN Guidelines referenced on this page.*

[f] Ehrhardt MJ, et al. Lancet Oncol 2023;24:e108-e120.
[g] de Baat EC, et al. Lancet Child Adolesc Health 2022;6:885-894.
[h] Orgel E, et al. Lancet Oncol 2022;23:570-572.
[i] van Atteveld JE, et al. Lancet Diabetes Endocrinol 2021;9:622-637.

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FERTILITY, REPRODUCTIVE ENDOCRINE, AND SEXUAL HEALTH CONSIDERATIONS

- **Addressing fertility and sexual health and function should be an essential part of the care of AYAs with cancer who are at any level of risk for impaired fertility or sexual dysfunction due to cancer treatments, regardless of gender identity, sexual orientation, or financial status.[j]**
- **Perform an assessment of the risk for gonadotoxicity and impaired fertility due to cancer and its treatment and discuss that assessment and options for fertility preservation with the patient. Do this as soon as possible prior to the start of therapy and throughout the course of treatment.[k]**

→

- **Initiate referral for fertility preservation clinics and/or provide resources for off-site/remote sperm banking as soon as possible for all patients who are interested in discussing fertility preservation.**
- **Consider the emotional impact of conversations surrounding fertility preservation, especially for the younger AYA and sexual gender minority (SGM) patient. See Comprehensive Psychosocial/Behavioral Considerations (AYAO-7).**
- **Provide AYA patients with financial resources for fertility preservation.**

→ **Fertility, Reproductive Endocrine, and Sexual Health Considerations (AYAO-6)**

[ji] Meacham LR, et al. J Adolesc Young Adult Oncol 2020;9:662-666; Mulder RL, et al. Lancet Oncol 2021;22:e68-e80; Mulder RL, et al. Lancet Oncol 2021;22:e57-e67; Mulder R, et al. Lancet Oncol 2021;22:e45-e56.
[k] Green DM, et al. Pediatr Blood Cancer 2014;61:53-67.

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FERTILITY, REPRODUCTIVE ENDOCRINE, AND SEXUAL HEALTH CONSIDERATIONS

General[l]

- After assessing the patient's risk for impaired fertility, and the patient's preferences for fertility preservation, recommend a form of appropriate fertility preservation and/or make a referral to a fertility preservation specialist.[m]
- Discuss effects of treatment on sexual function during and after treatment. Consider referral to a specialist as appropriate. See NCCN Guidelines for Survivorship.*
- Discuss contraception before, during, and after treatment.
  - Consult with OB/GYN for patients with ovaries/uterus ~~and consult the CDC Summary Chart of U.S. Medical Eligibility Criteria~~ to assist with the safety and efficacy of selection of appropriate contraception for individuals at risk of pregnancy.

Individuals with Testes

- Sperm banking is the preferred choice for patients without erection or ejaculation issues. For patients who can delay cancer treatment, consider more than one collection of ejaculate prior to initiating treatment.
  - Suggest a local sperm bank ~~or available online sperm banking kit.~~[n]
  - A semen analysis should be performed by the sperm bank, which should be assessed to ensure viable sperm has been frozen before starting cancer treatment, if time allows.
- For patients with erection or ejaculation issues, there are other options available,[o] including:
  - PDE5 inhibitors
  - Vibratory stimulation†
  - Electro-ejaculation†
  - ~~Collection of retrograde ejaculate~~
- ~~Testicular transposition out of the field of radiation can be considered for patients in whom the radiation field will include the testes.~~
- For those who cannot ejaculate, or who now have azoospermia or insufficient sperm in the ejaculate to freeze, discuss surgical sperm extraction as an alternative strategy, such as the testicular sperm extraction (TESE) procedure.[o]
- Discuss effects of treatment on gonadal hormone function. After completion of treatment, screen or refer the patient to a specialist as appropriate.[p,‡]

Individuals with Ovaries

- For patients who can delay cancer treatment for approximately 3 weeks, discuss oocyte or embryo cryopreservation via immediate (or random start) controlled ovarian stimulation (COS).
- For patients who cannot delay treatment for oocyte or embryo cryopreservation, *ovarian tissue cryopreservation (OTC) can be considered after receiving ethical approval and in a research context. OTC should not be offered to patients with low ovarian reserve* ~~discuss or refer the patient for consideration of ovarian tissue cryopreservation~~.
- For patients in whom the radiation field will include the ovaries, discuss oophoropexy or transposition of the ovaries out of the field of radiation.
- Discuss effects of treatment on gonadal hormone function during and after treatment. Some individuals face primary ovarian insufficiency and should be screened and treated by a specialist. Additionally, for individuals who did not undergo fertility preservation prior to treatment, some may still be eligible for fertility preservation after treatment is completed. After completion of treatment, screen or refer the patient to a specialist as appropriate.[q]
- Menstrual suppression
  - Progestin-only methods, combined hormonal 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. *Gonadotropin-releasing hormone (GnRH) agonists, progestin-only methods, or combined hormonal contraceptives may be used in protocols that are predicted to cause prolonged thrombocytopenia and present a risk for menorrhagia. Estrogen-containing contraceptives (particularly prolonged use of transdermal patches) should be avoided due to the increased risk of thromboembolic events. The decision to use estrogen-containing contraceptives in patients with cancer should be tailored to the individual patient's risk-benefit ratio.* It is controversial whether menstrual suppression provides adequate protection for the ovaries. GnRH agonists may protect ovarian function[r];** however, other fertility preservation modalities should still be considered and, if possible, pursued.

FOOTNOTES ON AYAO-6A

Note: All recommendations are category 2A unless otherwise indicated. This is the NCCN Guidelines: Poland Edition. For definitions, see page DEF-1.

FOOTNOTES

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*** Out of label use*

† These methods are not easily accessible, and it would be advisable to propose a permanent collaboration with a fertility treatment clinic willing to handle this.

‡ According to the ministerial program for the Treatment of Infertility, including medically assisted procreation procedures such as in vitro fertilization, for the years 2024–2028, patients may qualify for the fertility preservation program if they are undergoing or about to undergo oncological treatment with potential fertility-impairing effects. Eligibility criteria (as of the date of application—the first visit to the program provider) are: women from puberty up to the age of 40 and men from puberty up to the age of 45. Qualified patients will be able to undergo gamete retrieval procedures for storage purposes.

[l] Creating safe spaces to disclose gender identity and sexual orientation can mitigate and provide community partnership/resources for fertility and psychosocial experts in sexual and gender minorities (GLMA directory): https://www.glma.org/find_a_provider.php

[m] Practice Committee of the American Society for Reproductive Medicine. Fertil Steril 2019;112:1022-1033; Oktay K, et al. J Clin Oncol 2018;36:1994-2001; Mulder RL, et al. Lancet Oncol 2021;22:e57-e67; Mulder RL, et al. Lancet Oncol 2021;22:e45-e56.

[n] Lee JS, et al. J Clin Oncol 2006;24:2917-2931; Loren AW, et al. J Clin Oncol 2013;31:2500-2510; Oktay K, et al. J Clin Oncol 2018;36:1994-2001.

[o] Practice Committee of the American Society for Reproductive Medicine. Fertil Steril 2019;112:1022-1033.

[p] Skinner R, et al. Lancet Oncol 2017;18:e75-e90.

[q] van Dorp W, et al. J Clin Oncol 2016;34:3440-3450.

[r] Lambertini M, et al. J Natl Cancer Inst 2022;114:400-408.

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COMPREHENSIVE PSYCHOSOCIAL CONSIDERATIONS THROUGHOUT TREATMENT: INDIVIDUAL

EVALUATION

- Psychosocial factors:
  - Evaluate for current and past trauma history (eg, adverse childhood experiences [ACEs], medical-related trauma, abusive relationships)
  - Developmental and cognitive function
  - Communication and information delivery preferences
    - ◊ Assess health literacy
  - Preferred coping style of patient/family/caregiver
  - Adjustment to illness
    - ◊ If interest is expressed, provide opportunity for patient to share their cancer story
  - See NCCN Guidelines for Distress Management*
  - Evaluate for current and past psychiatric symptoms, including anxiety, depression, suicidal thoughts, eating disorders, and self injurious behavior
  - Involvement/interruption of school/work
  - Living status
    - ◊ Alone
    - ◊ Spouse/partner
    - ◊ Friends/roommates
    - ◊ Parents
    - ◊ Children
    - ◊ Homeless or nonstable living environment
  - Impact of cancer on identity
    - ◊ Personal values
    - ◊ Self-esteem
    - ◊ Relational identity
    - ◊ Body image and physical changes
    - ◊ Strengths/resilience
    - ◊ Future goals
  - Impact of cancer on support network
    - ◊ Social isolation
    - ◊ Lack of will to discuss diagnosis due to feelings of shame or embarrassment
    - ◊ Loss of family, caregiver, or friends
  - Assess for gender expression, gender identity, chosen name, pronouns, and sexual orientation
  - Patient or family/caregiver involvement with criminal justice system or family court system
  - Patient or family/caregiver living in the United States without legal status/ documentation
  - Patient preference for information sharing and involvement of certain biological or chosen family members in care (and exclusion of others)

SUPPORTIVE CARE SERVICES/INTERVENTIONS

- Refer for neuropsychological assessment if there are concerns regarding the patient's cognitive function (eg, attention, memory, executive function) and/ or prior to educational and career transitions, including returning to school/ work after treatment.
- If child life specialists or appropriate psychosocial support specialists are present, have them meet with the patient soon after diagnosis to address the patient's concerns regarding treatment or procedures, and assist with coping mechanisms to reduce anxiety related to procedures.
- Refer AYA patients to a social worker, mental health provider, and community-based resources serving AYA patients to screen for symptoms of depression, anxiety, suicidal ideation/behaviors, and self-injurious behavior.
- Offer psychosocial support and counseling to help alleviate distress (NCCN Guidelines for Distress Management).*
- Consider flexible treatment dates, consultation times, and procedures ~~(evenings/weekends)~~.
- ~~Refer for educational and career services to address training/education, employment, disability disclosure, vocational adjustment training, and transition services (ie, social services, vocational counseling, occupational therapy, financial counselors).~~
- For all AYA patients, provide counseling around sexual health conversations and decision-making regarding the risks of treatment-related fertility impairment and discuss options for fertility preservation prior to the start of therapy. See Fertility, Reproductive Endocrine, and Sexual Health Considerations (AYAO-5).
- For LGBTQIA2S+ AYAs, offer additional psychosocial support and referrals surrounding stressors, stigma, or rejection related to their sexuality or gender identity.
- Ensure record system accurately states patient's pronouns and preferred name.
  - ◊ ~~For transgender youth, consider referral to a specialized gender clinic for psychosocial support and coordination of gender-affirming medical care at the patient's discretion.~~
- Refer patients to legal services (if applicable) for estate or legacy planning, child custody concerns, or other legal issues.

Behavioral factors → AYAO-8
Relationships → AYAO-9
Socioeconomic issues → AYAO-11

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COMPREHENSIVE BEHAVIORAL CONSIDERATIONS THROUGHOUT TREATMENT: INDIVIDUAL

EVALUATION

- Behavioral factors:
  - Adherence to therapy
  - Tobacco, vaping, alcohol, cannabis, or other substance use
  - ~~Assess for access to firearms or other dangerous objects in the home~~
  - Sexual behavior/risks/concerns
  - Assess nutritional requirement and potential deficits based on age
  - Exercise needs, hobbies, and recreational activities
  - Sleep patterns
- Use of both integrative therapies and ~~complementary and~~ alternative medicine ~~(CAM)~~
- ~~Existential/spiritual issues~~

Relationships (AYAO-9)
Socioeconomic issues (AYAO-11)

SUPPORTIVE CARE SERVICES/INTERVENTIONS

- Adherence to therapy and safety plans
  - Educate about the expectations of treatment and explain the patient's responsibility to adhere to therapy.
  - Evaluate for any past history or potential barriers to adherence with medical treatment.
  - Provide education and/or guidance about all medications and their dose, purpose, and adverse effects prior to the start of treatment and every time there is a change in treatment.
  - Simplify and modify dosing schedule, when medically possible, to fit into AYA's lifestyle and normal activities.
  - ~~Consider the use of technology (eg, smartphone applications).~~
  - Provide access to systematic and standardized symptom management for side effects related to cancer treatment (NCCN Guidelines for Supportive Care).*
- Refer to smoking cessation program if needed (NCCN Guidelines for Smoking Cessation).*
- Provide education about the impact of early cannabis use on cognitive development and mental health.
  - ~~If AYA chooses to continue use, provide education on risks and benefits of varying methods of ingestion and dosing.~~
- Refer patients with signs, symptoms, or a history of a substance use disorder to a risk reduction or substance use counseling program.
- Provide education about the impact of treatment on sexual health, including safe sexual practices in light of risk of infection, risk for bleeding, prevention of pregnancy, and sexually transmitted diseases.
- Provide education about potential diet/nutritional changes associated with cancer treatment and possible interventions. Refer to a registered dietitian-certified specialist in oncology (RD-CSO).
- Provide education on physical conditioning and related health benefits during and following cancer treatment. Refer to a rehabilitation specialist (ie, physiatrist, physical therapist, occupational therapist) to address physical impairments and initiate physical activity interventions. Medical evaluation and clearance by a physician (such as an oncologist or a physiatrist) are recommended prior to initiating exercise in patients in whom exercise modifications or precautions might be needed.
- Consider evidence-based integrative therapies/interventions.
- 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). Refer to a chaplain or spiritual counselor.
- If appropriate, consider referral to palliative care.

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COMPREHENSIVE PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS THROUGHOUT TREATMENT: RELATIONSHIPS

EVALUATION

- Family/caregiver status
  - Interaction and relationship with parents/caregivers
  - Interaction and relationship with spouse/partner
    - ◊ Dating and intimacy
  - Interaction and relationship with sibling(s) and other family members/caregivers
  - Patient with young children
- Peer relationships
- Gender identification and sexual orientation
- Participation in community and social activities (eg, religious organizations, clubs, athletics/recreation, music, youth groups)
- Communications with health care professionals
  - Assistance with preparation of advance directive
    - ◊ Assistance with end-of-life planning and goal setting (eg, what the patient would like to achieve prior to death)
  - Addressing issues related to privacy and confidentiality:
    - ◊ ~~Encouragement of completion of HIPAA release form when the patient is of age of majority~~
  - Ongoing consideration for the level of information the AYA patient wishes to have and share regarding disease and/or treatment
  - Consideration of patient's heritage, culture, and familial structure when addressing psychosocial concerns and needs, including decision-making and end-of-life care

→ Supportive Cancer Services/ Interventions (AYAO-10)

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COMPREHENSIVE PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS THROUGHOUT TREATMENT: RELATIONSHIPS

SUPPORTIVE CARE SERVICES/INTERVENTIONS

- **Promote collaborative communication between AYA patients:**
  - **Parents/caregivers**
  - **Children**
  - **Spouse/partner**
  - **Siblings and other family members/caregivers**
  - **Friends**
  - **Social network**
- **Early in the treatment process encourage education and the completion of a medical power of attorney and a living will at age of majority.**
  - **Provide access to AYA-specific advanced care planning guides to determine a health care proxy.**
- **Provide identified family members/caregivers and partners with information about psychosocial support and behavioral services.**
  - **Increase awareness of and normalize the possible psychosocial issues associated with cancer diagnosis in AYAs, so that family members/caregivers and partners may continue to support the patient.**
- **Provide AYA-specific activities and/or support groups (in person and/or virtual), especially for inpatients to provide psychosocial support and reduce boredom, anxiety, and depression. Such interventions include:**
  - **Parent/caregiver support groups**
  - **AYA support groups**
  - **Social and recreational programs**
  - **Psychoeducational programs**
- **Provide information about peer support to assist AYAs establishing and maintaining relationships with their peers as well as with other AYAs with cancer (Online Resources for AYA Patients and Survivors).***
  - **Face-to-face meetings**
  - **Camp and retreat programs**
  - **Online support groups**
  - **Social networking opportunities**
- **Create flexible visiting hours and an environment that will encourage peers to visit AYA patients.**
- **Communicate directly with individual patients.**
  - **Provide psychoeducation and assistance exploring and documenting advance directive preferences.**
  - **Ask for permission to share information with identified family members/caregivers or supports.**
  - **Provide developmentally appropriate information about their cancer, treatment options, and potential side effects (Online Resources for AYA Patients and Survivors).***
  - **If AYA patient is >18 years of age, provide information on and necessary forms that legally allow medical information to be shared with caregivers of patient's choice.**
  - **Always conduct medical and psychosocial care in the language preferred by the patient/family/caregiver. Use certified interpreters and do not rely on family members/caregivers, friends, or non-certified medical staff for interpretation.**

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COMPREHENSIVE PSYCHOSOCIAL/BEHAVIORAL CONSIDERATIONS THROUGHOUT TREATMENT: SOCIOECONOMIC ISSUES

EVALUATION

- Insurance availability and security
  - Employer-provided
  - Parent's insurance
  - ~~Medicaid~~
- ~~Health insurance marketplace~~
- *Additional health insurance*
- Assessment of risk for losing insurance
  - Loss of employment
  - Age out of parent's insurance
- Assessment of financial toxicity
- Risk for financial loss ~~or bankruptcy~~
- Child care
- Transportation
- Accommodation if traveling to receive treatment
- Stability of housing and basic household socioeconomic needs

SUPPORTIVE CARE SERVICES/INTERVENTIONS

- Link qualified AYA patients to ~~Medicaid,~~ Social Security, and/or disability insurance.
  - Provide information regarding drug assistance programs for patients with limited or no insurance.
  - ~~Provide information regarding hospital pharmacy vouchers or low-cost medication programs.~~
- Educate AYA patients about benefits for which they may qualify, such as short- or long-term disability, state disability benefits, and public assistance.
- Provide information on obtaining financial assistance for fertility-based services. Local and institutional grants may be available.
- Provide school support and education services for patients *during education* ~~in high school or college~~.
- Refer for career counseling and/or education support as indicated.
- Encourage discussion with guidance counselors and educators about impact of cancer care on education.
- Refer to mental health expert as needed to assess the psychosocial impact of financial toxicity (eg, loss of employment, withdrawing from school, not being able to socialize with friends due to decreased income).
- Direct AYA patients to legal resources~~/advocates~~ for assistance with understanding health insurance coverage.
- Identify resources for respite care for AYA patients with young children.
- Refer to transportation assistance programs ~~(eg, van ride programs, voucher programs)~~.
- Provide AYAs with a list of recommended and reliable online sources and financial support programs to access information related to their cancer.
  See Online Resources for AYA Patients and Survivors.*
- *Encourage AYA to seek socioeconomic assistance in appropriate institutions as a part of survivorship care plan* ~~Integrate financial assistance into AYA survivorship care plans~~.
- Consider need for 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[s] →

- **Develop a "Cancer Treatment Summary and Survivorship Care Plan." See NCCN Guidelines for Survivorship.***
- ***Fullfil individualized survivorship passport (ONKOPAS) dedicated to all patients after therapy with curative intent or long-term remission.*****
- **Always conduct medical and psychosocial care in the language preferred by the patient/family/caregiver. Use certified interpreters and do not rely on family members/caregivers, friends, or non-certified medical staff for interpretation.**
- **Provide a periodic evaluation focusing on history, physical examination, and screening based on treatment exposures and risk for treatment-related late effects.**
- **Encourage relationship with primary health care provider for routine health issues.**
- **Provide assistance in establishing care with primary health care provider.** ***For basic guidelines for primary care providers, please see https://www.pto.med.pl/zalecenia.***
- **Ensure patient is provided continuous access to mental health support (eg, support groups, individual therapy, AYA-specific organizations).†**
- **Recommend vaccinations:**
  - **HPV vaccine is recommended for all survivors aged 9–26 years and may be given through age 45 (however, best protection is achieved at earlier ages). Clinicians should discuss HPV vaccination with survivors aged 27–45 years, and determine on an individual basis whether or not vaccination may be of benefit for individual survivors within this age group.[t,‡]**
  - ***COVID-19 vaccination depending on the epidemiological situation.*** ~~**Please see the CDC for Use of COVID-19 Vaccines in the US.**~~
  - **Annual influenza vaccine**
  - **See NCCN Guidelines for Survivorship* for additional guidance on vaccines.**
- **Counsel regarding striving to meet physical activity guidelines and methods to reduce risk of long-term chronic health problems, recurrence, or new tumors (eg, avoiding smoking, increasing level of physical activity).**
- ***In Poland, there is equal access to healthcare services under the National Health Fund.*** ~~**Advocate for appropriate health care coverage.**~~
- **Due to the transient lifestyle of the AYA population (ie, attending college far from home, traveling to different locations to establish careers), it is imperative for the initial care team to communicate with the new care team (once established).****
- **Young cancer survivors should be screened for risky behavior (ie, substance use, tobacco/nicotine use, binge drinking/excessive alcohol use) on a regular basis and counseled on cessation.****
- **Young cancer survivors should be educated on safe sex practices/contraceptive options if they are not trying to actively conceive regardless of their infertility risk post treatment.****
- **AYAs should also be asked about sexual dysfunction on a routine basis and how it may be impacting interpersonal relationships/self-image.**

→ **Exposure and Recommendations Table (AYAO-13)**

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*** At the time of publication of the guidelines, work is underway on a survivorship passport that will address these issues.*

† Limited access

‡ Refund for children aged 9 to 14

[s] An individual is considered a cancer survivor from the time of diagnosis, through the balance of their 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: https://cancercontrol.cancer.gov/ocs/about/staff.html.

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

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SURVIVORSHIP

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.

EXPOSURE	RECOMMENDATION Screening Recommendations (AYAO-B)	
Any exposure	• Recommend a dental exam and cleaning every 6 mo for patients who received chemotherapy and/or radiation therapy (RT) to head or upper neck regions	
Total body irradiation (TBI)	• Thyroid disease screening • Cardiovascular risk factor screening (dyslipidemia) when TBI >10 Gy • Ocular screening (cataracts)	• Screening for secondary malignant neoplasms (SMNs) • Impaired glucose metabolism screening when TBI >10 Gy • Gonadal dysfunction screening
Cranial or craniospinal radiation	• Neuroendocrine axis screening • Neuropsychological evaluation • Ocular screening • Gonadal dysfunction screening	• Audiological evaluation for cranial radiation doses ≥30 Gy • Colorectal cancer screening (for lumbar, sacral, or whole spine)
Chest radiation	• Individual assigned female at birth: see NCCN Guidelines for Breast Cancer Screening and Diagnosis* • Cardiovascular risk assessment and screening	• Screening for cardiomyopathy • Screening for valvular heart disease • Pulmonary function screening
Neck radiation	• Thyroid disease screening	• Consider carotid artery screening
Abdominal or pelvic radiation	• Colorectal cancer screening • Assessment of gonadal and sexual function/ dyspareunia • Screening for dyslipidemia (for abdominal radiation)	• Assessment for bowel dysfunction • Screening for kidney or bladder disease • Screening for impaired glucose metabolism (for abdominal radiation) • Consider screening for cardiac disease (cardiopathy and vascular disease) if RT to upper abdomen)
Limb radiation	• Physical therapy to address muscle fibrosis	• Orthopedic screening to assess fragility fractures • Avascular necrosis
Intrathecal chemotherapy and high CNS penetrating systemic chemotherapy (high-dose methotrexate, Ara-C)	• Neuropsychological evaluation	

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SURVIVORSHIP

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.

EXPOSURE	RECOMMENDATION Screening Recommendations (AYAO-B)
Corticosteroid	• Osteoporosis screening • ***Screening for metabolic syndrome (the screening measures: waistline, blood pressure, HDL cholesterol level, triglyceride level, and fasting blood sugar)***
Alkylating agents	• Screening for kidney or bladder disease • Assessment of gonadal function • Screening for treatment-related acute myeloid leukemia (t-AML) or myelodysplasia • Pulmonary function screening (for selected agents)
Anthracyclines	• Screening for cardiomyopathy • Screening for t-AML or myelodysplasia
Bleomycin	• Pulmonary function screening
Cisplatin/ carboplatin	• Cardiovascular risk assessment • Screening for kidney and/or bladder disease • Audiologic evaluation • Screening for t-AML or myelodysplasia • Screening for peripheral neuropathy • Screening for gonadal function
Epipodophyllotoxins	• Screening for t-AML or myelodysplasia
Vinca alkaloid	• Screening for peripheral neuropathy

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DISEASE-SPECIFIC ISSUES RELATED TO AGE*

In the case of diseases listed below, consider referring the patient to a medical center specialized in diagnosing and treating this disease and conduct diagnostic and therapeutic procedures according to the Polish standards of clinical treatment.

~~Consider referral to an institution with multidisciplinary expertise in the management of the disease types specified below.~~

Acute Lymphoblastic Leukemia (ALL)
- NCCN Guidelines for ALL
- NCCN Guidelines for Pediatric ALL

Lymphomas
- NCCN Guidelines for Hodgkin Lymphoma
- NCCN Guidelines for Pediatric Hodgkin Lymphoma
- NCCN Guidelines for B-Cell Lymphoma
- NCCN Guidelines for Pediatric Aggressive Mature B-Cell Lymphomas

Central Nervous System (CNS) Tumors
- NCCN Guidelines for CNS Cancers**

Bone and Soft Tissue Sarcomas
- NCCN Guidelines for Bone Cancer and NCCN Guidelines for Soft Tissue Sarcoma
- Rhabdomyosarcoma
  - Uncommon outside of the pediatric population
  - Rhabdomyosarcoma in AYA patients often has high-risk features and may be associated with inferior outcomes. Consider referral to a center familiar with rhabdomyosarcoma therapy depending on the clinical situation[1,2]
- Ewing sarcoma
  - Inferior outcomes for patients >18 years of age[3]

Colorectal Cancer
- NCCN Guidelines for Colon Cancer and NCCN Guidelines for Rectal Cancer**
- Higher incidence of mucinous histology
- Higher incidence of signet ring cells and microsatellite instability (MSI)
- More likely advanced stage at diagnosis
- Greater mutation frequency of *BRCA2*, *ATM*, *MSH2*, and *ATR*[4]
- Decreased incidence of chromosomal instability
- Consider mismatch repair gene deficiency in these patients
- Increased risk for additional malignancies

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*** See International Adaptations Table of Contents for specific NCCN Guidelines: Poland Edition.*

[1] Ferrari A, et al. Lancet Child Adolesc Health 2022;6:545-554.
[2] Harrison DJ, et al. Pediatr Blood Cancer 2024;71:e30847.
[3] Leavey PJ, et al. J Clin Oncol 2021;39:4029-4038.
[4] Tricoli JV, et al. Cancer 2018;124:1070-1082.

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DISEASE-SPECIFIC ISSUES RELATED TO AGE*

Melanoma

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

Management of Cancer During Pregnancy (Discussion)

- While cancer in pregnancy is relatively uncommon, it complicates about one out of 1000 pregnancies.
- Cervical and breast cancer account for about 50% of cancers diagnosed during pregnancy and hematologic cancers account for about 25% of cancers during pregnancy. Other cancers less commonly seen include melanoma, ovarian, thyroid, and colon. Other cancers are exceedingly rare.
- Individuals diagnosed with cancer during pregnancy should be treated 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 the cancer type, tumor biology, tumor stage, and gestational age 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 physiologic changes that occur during pregnancy should be strongly encouraged.
- Cancer therapy during the first trimester is associated with the highest risk.
- If feasible, chemotherapy should be avoided during the first trimester because of greater risk of teratogenic effects and intrauterine fetal death.
- Certain chemotherapeutic agents are safer than others depending on the agent's mutagenic effect, ability to cross the placental barrier, and side effect profile.
- RT is contraindicated during pregnancy. In very rare instances when RT is necessary, it should be delivered in the lowest effective therapeutic doses using techniques to minimize fetal exposure.[5]
- Risk of transplacental transfer of cancer is diagnosis dependent.
- Most cancers can be adequately treated with medication that is safe for both the pregnant patient and the fetus. However, full counseling about all options regarding the pregnancy, including termination per patient preference or to expedite use of necessary teratogenic medication should be incorporated in all cancer treatment discussions for pregnant AYA patients.
- For disease-specific recommendations on management of cancer during pregnancy, see:*
  - NCCN Guidelines for Breast Cancer**
  - NCCN Guidelines for Cervical Cancer**
  - ~~NCCN Guidelines for Chronic Myeloid Leukemia~~
  - ~~NCCN Guidelines for Hodgkin Lymphoma~~
  - ~~NCCN Guidelines for Myeloproliferative Neoplasms~~
- *In the case of diseases listed below, consider referring the patient to a medical center specialized in diagnosing and treating this disease and conduct diagnostic and therapeutic procedures according to the Polish standards of clinical treatment:*
  - *Chronic Myeloid Leukemia*
  - *Hodgkin Lymphoma*
  - *Myeloproliferative Neoplasms*

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[5] Silverstein J, et al. JCO Oncol Pract 2020;16:545-557.

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.*

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

- The recommendations represent only key aspects; for more information, refer to the Children's Oncology Group (COG) website, www.survivorshipguidelines.org.
- ***See also the NCCN Guidelines for Survivorship,* European recommendations for short-term surveillance, and Polish Oncological Society (at a national level).***
- 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 and non-Hodgkin lymphomas, medulloblastomas, and sarcomas. In addition, since the treatment exposures for some young adult cancers, such as germ cell tumors in individuals with testes, are similar to pediatric cancer treatments (eg, 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 (BMI) 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.
- Central hypothyroidism
  - High-risk population: total radiation dose to HPA axis ≥30 Gy
  - Screening recommendation: thyroid-stimulating hormone (TSH) and free T4, yearly
- Gonadotropin deficiency
  - High-risk population: total radiation dose to HPA axis ≥30 Gy
  - Screening recommendation: follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone for individuals with testes and FSH, LH, anti-Müllerian hormone (AMH), and estradiol for individuals with ovaries, as clinically indicated. Referral to a reproductive endocrinologist is recommended.
- Central adrenal insufficiency
  - High-risk population: total radiation dose to HPA axis ≥30 Gy
  - Screening recommendation: 8:00 AM serum cortisol, yearly after treatment. Refer to endocrinology for further testing if level is <13 mcg/dL or <365 nmol/L.

Dermatology Evaluation

- High-risk population: patients who previously received RT
- Screening recommendation: annual skin examinations performed by a dermatologist

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.*

Neuropsychological Evaluation

- The risk of neuropsychological deficits is related to tumor location and specific treatment interventions (radiation dose, radiation treatment volume, and surgical intervention). However, subtle deficits in executive function, sustained attention, memory, and processing speed may occur with cranial radiation, particularly in higher doses given to treat brain tumors and head/neck tumors.
  - Include information/education regarding neuropsychological evaluations, and/or cognitive screening for AYA survivors. Neuropsychological evaluations and/or cognitive screening may be warranted regardless of treatment history and should be offered if patient raises concerns.
- Screening recommendation: All AYA survivors of cancer should undergo routine screening for difficulties in school or work during follow-up so that providers can identify the need for referral early in the survivorship phase.[1] In particular, patients with brain tumors and those treated with cranial/craniospinal radiation, intrathecal chemotherapy, and/or high-dose methotrexate (eg, osteosarcoma therapy) should be referred for neuropsychological evaluation.
  - The goal is to reinforce screening for subtle neurocognitive deficits in AYA survivors including those treated for non-CNS tumors in long-term follow-up, so that those in need of neurocognitive/neuropsychological interventions can be referred for treatment.

Breast Cancer Screening

- High-risk population: See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic*
- Screening recommendation: See NCCN Guidelines for Breast Cancer Screening and Diagnosis*
- Survivors <30 years who receive thoracic RT should be considered for enhanced screening.

Cardiovascular Risk Assessment and Screening

- High-risk population: ≥15 Gy combined with anthracycline or mediastinal/chest radiation ≥35 Gy alone, or abdominal radiation, or TBI
- Screening recommendation: optimize cardiovascular risk factors, including blood pressure, lipid profile, and blood glucose
- Baseline ECG post treatment: not for treatment decision, but definitely for when there is a subsequent issue for comparison
- Screening for ischemic coronary artery disease remains controversial; consider cardiology consultation (5–10 years after radiation) in patients who received ≥35 Gy chest radiation

Screening for Cardiomyopathy/Asymptomatic Heart Failure[2]

- High-risk population: cumulative anthracycline dose ≥250 mg/m^2, doxorubicin equivalent dose; chest radiation ≥30 Gy; combination of anthracycline ≥100 mg/m^2 and chest irradiation ≥15 Gy
- Moderate-risk population: cumulative anthracycline dose ≥100 mg/m^2 and <250 mg/m^2 with <15 Gy or no chest radiation; or chest radiation alone at dose of 15–30 Gy
- Screening recommendation: echocardiogram every 2 years for patients who are high risk and every 5 years for patients who are moderate risk. (Note: Frequency of testing is dependent on dose of exposure. The frequency of testing has not been established for breast cancer survivors treated with lower cumulative doses of anthracyclines.) A baseline ECG is recommended at entry into long-term follow-up if anthracycline exposure or chest radiation ≥15 Gy; repeat as clinically indicated.

Screening for Valvular Heart Disease

- High-risk population: chest radiation ≥35 Gy
- Low-risk population: chest radiation 15–35 Gy
- Screening recommendation: echocardiogram every 2 years for patients who are high risk and every 5 years for patients who are lower risk

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.*

Pulmonary Function 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, combination of chest radiation and bleomycin, and selected alkylating agents (ie, busulfan, carmustine)
- Screening recommendation: pulmonary function tests (including diffusing capacity of the lung 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 Disease Screening

- Thyroid disorders: hypothyroidism (very common), thyroid cancer (common), and hyperthyroidism (uncommon)
- High-risk population: radiation field includes or is in close proximity to the thyroid gland (Neuroendocrine Axis Screening [AYAO-B 1 of 6] for high-dose cranial radiation)
- Use of immune checkpoint inhibitors
- Screening recommendation: TSH, free T4, and thyroid/neck exam yearly

Colorectal Cancer Screening

- High-risk population: all patients who received any abdominal or pelvic radiation or TBI or spinal radiation (lumbar, sacral, or whole spine)
- Screening recommendation: colorectal cancer screening, ie, colonoscopy every 5 years or multitarget stool DNA test every 3 years, based on informed decision-making between survivor and clinician starting at age 30 or 5 years after radiation, whichever occurs last
- For patients with known colorectal cancer predisposition syndromes, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal*

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 (eg, cisplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants, history of HCT), and history of nephrectomy
  - 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
- Hemorrhagic cystitis/bladder fibrosis
  - High-risk population: cyclophosphamide >3 gm/m^2, ifosfamide, and pelvic radiation ≥30 Gy
  - Screening of pertinent urinary tract symptoms is recommended
- Bladder cancer
  - High-risk population: cyclophosphamide combined with pelvic radiation
  - Screening of pertinent urinary tract symptoms is recommended

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.*

Assessment for Gonadal Function

- See also the NCCN Guidelines for Survivorship*
- Individuals with testes
  - Individuals with bilateral orchiectomy will have both impaired fertility and Leydig cell dysfunction and will need referral for hormonal replacement therapy.
  - Impaired fertility: Temporary azoospermia or oligospermia can occur for variable periods of time post-therapy. Below are risk assessments according to the Pediatric Initiative Network (PIN) Risk Stratification System for Treatment-Related Gonadal Insufficiency and Infertility in Childhood Adolescent and Young Adult Cancer[3]:
    - ◊ High level of increased risk:
      - – Alkylator: ≥4 g/m^2 cyclophosphamide equivalent dose (CED)[4]
      - – HCT: including alkylator ± TBI; myeloablative and reduced-intensity regimens
      - – Radiation to testes: ≥6.0 Gy[a,5,6,7,8]
      - – Radiation to hypothalamus: >40 Gy
    - ◊ Significantly increased risk:
      - – Cisplatin: >500 mg/m^2
      - – Radiation to testes: 0.7–5.9 Gy
      - – Radiation to hypothalamus: 30–39.9 Gy
      - – Retroperitoneal lymph node dissection
    - ◊ Minimally increased risk:
      - – Alkylator: <4 g/m^2 CED
      - – Carboplatin or cisplatin: any dose <500 mg/m^2
      - – Radiation to testes: 0.2–0.6 Gy
      - – Radiation to hypothalamus: 26–29.9 Gy
    - ◊ Screening recommendation: semen analysis as requested by patient or evaluation of impaired fertility; periodic evaluation over time is recommended as resumption of spermatogenesis can occur post therapy[9,10]
  - Leydig cell dysfunction
    - ◊ High-risk population: testicular irradiation combined with head/brain irradiation, testicular radiation dose ≥12 Gy in combination with alkylating agents, cyclophosphamide conditioning for HCT, or unilateral orchiectomy[5,6,8,10-13]
    - ◊ Screening recommendation: early morning testosterone as clinically indicated in patients with clinical signs and symptoms of testosterone deficiency

** The conditions of Polish clinical practice and the reimbursement state should be taken into account while using the recommendations outlined in other NCCN Guidelines referenced on this page.*

[a] Radiation dose to testes (≤6 Gy azoospermia may be transient, ≥6 Gy azoospermia likely permanent and especially testicular dose ≥20 Gy), combination with alkylating agents, and/or genitourinary surgery.

Note: All recommendations are category 2A unless otherwise indicated. This is the NCCN Guidelines: Poland Edition. For definitions, see page DEF-1.

Continued

SCREENING RECOMMENDATIONS FOR AYA SURVIVORS

Care for patients after oncology treatment requires the establishment of appropriate organizational frameworks in Poland. The recommended management plan for each patient will be included in the survivorship passport. General recommendations for survivorship are presented below.*

- Individuals with ovaries
  - Individuals with bilateral oophorectomy will have both impaired fertility and ovarian hormone deficiency and will need referral for hormonal replacement therapy.**
  - Impaired fertility (acute ovarian insufficiency or primary ovarian insufficiency): When marked depletion of the ovarian reserve occurs secondary to cancer therapy, ovarian insufficiency can develop soon after the completion of therapy. However, there may be a reproductive window before the onset of primary ovarian insufficiency. Below are risk assessments according to the PIN Risk Stratification System for Treatment-Related Gonadal Insufficiency and Infertility in Childhood Adolescent and Young Adult Cancer[3]:
    - ◊ High level of risk
      - – Alkylator: prepubertal (>12 g/m² CED); pubertal (>8 g/m² CED)
      - – HCT: including alkylator ± TBI; myeloablative and reduced-intensity regimens
      - – Radiation to ovary: prepubertal (≥15 Gy); pubertal (≥10 Gy)
      - – Radiation to hypothalamus: >40 Gy
    - ◊ Significantly increased risk
      - – Alkylator: prepubertal (8–12 g/m² CED); pubertal (4–8 g/m² CED)
      - – Radiation to ovary: prepubertal (<15 Gy); pubertal (<10 Gy)
      - – Radiation to hypothalamus: 30–39.9 Gy
    - ◊ Minimally increased risk:
      - – Alkylator: prepubertal (<8 g/m² CED); pubertal (<4 g/m² CED)
      - – Carboplatin or cisplatin: Any dose
      - – Radiation to hypothalamus: 22–29.9 Gy
    - ◊ Screening recommendation: Annual history and physical (H&P) (menstrual and pregnancy history, history of hormonal therapy, Tanner staging) only. Laboratory screening (ie, FSH, estradiol, AMH) for those with menstrual cycle dysfunction or those who desire information about future fertility. Bone density evaluation (dual-energy x-ray absorptiometry [DEXA]) at baseline (entry to long-term follow-up) for those who had corticosteroids and/or HCT only.[14]
    - ◊ Referral to reproductive endocrinology is recommended for antral follicle count, ovarian reserve evaluation, and consultation regarding assisted reproductive technologies in patients at risk who desire information about potential fertility and interventions to preserve future fertility.
    - ◊ Referral to gynecology, reproductive medicine, or endocrinology is recommended for post-pubertal survivors treated with potentially gonadotoxic chemotherapy and/or radiotherapy who desire information regarding potential fertility and/or interventions to preserve future fertility.
  - Pregnancy in cancer survivors: Referral is recommended for patients with cardiomyopathy, cardiovascular risk factors, and history of pelvic radiation to maternal-fetal medicine.
  - Patients with uterine radiation exposure are at increased risk for uterine vascular insufficiency, resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth-weight infant, fetal malposition, and premature labor. Factors associated with increased risk: Wilms tumor and associated Müllerian anomalies (ie, agenesis, hypoplasia), TBI, higher radiation dose to pelvis, and radiation dose ≥30 Gy.[15-17]
  - Monitor for (intervening if necessary) vaginal stenosis that can develop after radiation.[18]

Screening for t-AML or Myelodysplasia

- High-risk populations: epipodophyllotoxins, alkylating agents, heavy metals, and/or anthracyclines; autologous HCT
- Screening recommendation: Complete blood count (CBC) and bone marrow exam as clinically indicated based on symptoms

Audiologic Evaluation

- High-risk population: cisplatin ≥360 mg/m², carboplatin conditioning for HCT, radiation involving the ear for doses ≥30 Gy, and combination of cisplatin and cranial/ear radiation
- Screening recommendation: audiology testing as a post-therapy baseline and then every 5 years
- Cancer survivors with hearing impairment should be provided with psychoeducational evaluation and support related to educational, psychological, and social function.

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***Hormonal replacement therapy is not recommended for breast cancer patients.*

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SCREENING RECOMMENDATIONS FOR AYA SURVIVORS – REFERENCES

[1] Thornton CP, Ruble K, Jacobson LA. Beyond risk-based stratification: impacts of processing speed and executive function on adaptive skills in adolescent and young adult cancer survivors. J Adolesc Young Adult Oncol 2021;10:288-295.
[2] Ehrhardt MJ, Leerink JM, Mulder RL, et al. Systematic review and updated recommendations for cardiomyopathy surveillance for survivors of childhood, adolescent, and young adult cancer from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2023;24:e108-e120.
[3] Meacham LR, Burns K, Orwig KE, Levine J. Standardizing risk assessment for treatment-related gonadal insufficiency and infertility in childhood adolescent and young adult cancer: The Pediatric Initiative Network Risk Stratification System. J Adolesc Young Adult Oncol 2020;9:662-666.
[4] Green DM, Nolan VG, Goodman PJ, et al. The cyclophosphamide equivalent dose as an approach for quantifying alkylating agent exposure: a report from the Childhood Cancer Survivor Study. Pediatr Blood Cancer 2014;61:53-67.
[5] Kenney LB, Antal Z, Ginsberg JP, et al. Improving male reproductive health after childhood, adolescent, and young adult cancer: Progress and future directions for survivorship research. J Clin Oncol 2018;36:2160-2168.
[6] Sprauten M, Brydøy M, Haugnes HS, et al. Longitudinal serum testosterone, luteinizing hormone, and follicle-stimulating hormone levels in a population-based sample of long-term testicular cancer survivors. J Clin Oncol 2014;32:571-578.
[7] Wasilewski-Masker K, Seidel KD, Leisenring W, et al. Male infertility in long-term survivors of pediatric cancer: A report from the childhood cancer survivor study. J Cancer Surviv 2014;8:437-447.
[8] Chematilly W, Liu Q, van Iersel L, et al. Leydig cell function in male survivors of childhood cancer: A report from the St Jude Lifetime Cohort Study. J Clin Oncol 2019 37:3018-3031.
[9] Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Pediatric, Adolescent, and Young Adult Cancers. Accessed 2020 from: www.survivorshipguidelines.org.
[10] Skinner R, Mulder RL, Kremer LC, et al. Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. Lancet Oncol 2017;18:e75-e90. Erratum in Lancet Oncol 2017;18:e196.
[11] Lopez R, Plat G, Bertrand Y, et al. Testosterone deficiency in men surviving childhood acute leukemia after treatment with hematopoietic stem cell transplantation or testicular radiation: An L.E.A study. Bone Marrow Transplant 2021;56:1422-1425.
[12] Mostoufi-Moab S, Seidel K, Leisenring WM, et al. Endocrine abnormalities in aging survivors of childhood cancer: A report from the childhood cancer survivor study. J Clin Oncol 2016;34:3240-3247.
[13] Wilhelmsson M, Vatanen A, Borgstrom B, et al. Adult testicular volume predicts spermatogenic recovery after allogenic HSCT in childhood and adolescence Pediatr Blood Cancer 2014;61:1094-1100.
[14] van Atteveld JE, Mulder RL, van den Heuvel-Eibrink MM, et al. Bone mineral density surveillance for childhood, adolescent, and young adult cancer survivors: evidence-based recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Diabetes Endocrinol 2021;9:622-637.
[15] Gao W, Liang JX, Yan Q: Exposure to radiation therapy is associated with female reproductive health among childhood cancer survivors: a meta-analysis study. J Assist Reprod Genet 2015;32:1179-1186.
[16] Rozen G, Rogers P, Chander S, et al. Clinical summary guide: reproduction in women with previous abdominopelvic radiotherapy or total body irradiation. Hum Reprod Open 2020;4:hoaa045.
[17] van de Loo LEXM, van den Berg MH, Overbeek A, et al. Uterine function, pregnancy complications, and pregnancy outcomes among female childhood cancer survivors. Fertil Steril 2019;111:372-380.
[18] Morris L, Do V, Chard J, et al. Radiation-induced vaginal stenosis: current perspectives. Int J Womens Health 2017;9:273-279.

de Beijer IAE, Skinner R, Haupt R, et al. European recommendations for short-term surveillance of health problems in childhood, adolescent and young adult cancer survivors from the end of treatment to 5 years after diagnosis: a PanCare guideline. J Cancer Surviv. 2023 Dec 4. doi: 10.1007/s11764-023-01493-z.

Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer. PanCare website. Available at: https://www.pancare.eu/guidelines/. Accessed March 26, 2025.

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PALLIATIVE CARE ACROSS THE DISEASE CONTINUUM

Palliative care focuses on symptom control, reduction of physical suffering or discomfort, and optimizing quality of life at any stage of a life-threatening disease (NCCN Guidelines for Palliative Care).* ~~Referral to palliative care is appropriate when patients are being treated with curative intent and can be initiated at the time of initial diagnosis.[1,2,3]~~ *When caring for a patient, raise the issue of access to palliative care.* A palliative care team is one with resources and expertise to address the psychosocial, emotional, and physical challenges relevant to the patient.[4,5] Strategies to support a patient, particularly in the AYA population, must be individualized in the context of the family dynamic, including maturity of the patient and level of independence (both desired and actual).

END-OF-LIFE CONSIDERATIONS

- **Palliation of symptoms is an important aspect of care.[6]**
- **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.[7,8,9,10]**
- **Consideration to include palliative care team or hospice services should be discussed early in treatment if prognosis is poor in order to provide the continuity of care and support for both patient and family/caregiver throughout their cancer experience.[1,2]**
- **Discussion about end-of-life preferences and the formulation of an advance care planning document should begin early in treatment, but details should be individualized according to the preferences of the AYA patient and family/caregiver.[7,11,12]**
- **Involve child life specialists and/or psychosocial team member to discuss legacy projects and memory work with patient and family/caregiver.**
- **Individual, family/caregiver, and cultural differences influence the preferred location of death. While many adolescents indicate a preference for dying at home, 80% die in hospitals.[13,14,15] Other AYAs and families choose to die in the hospital due to regional scarcities of home hospice, caregiver demand at the end of life, or personal preference. Every effort should be made to query and support AYA's preferred location of death. Clinicians with experience in end-of-life care should facilitate discussion about medical interventions such as nutrition/hydration, sedation, treatment cessation, and place of death.[5]**
- **Ongoing psychosocial support is extremely important during the transition to end-of-life care. For family/caregiver and friends, grief from loss may begin before death.**
- **Clinical teams should be aware of and work with their palliative care teams regarding local guidelines for concurrent palliative and cancer-directed care.**

** The conditions of Polish clinical practice and the reimbursement state should be taken into account while using the recommendations outlined in other NCCN Guidelines referenced on this page.*

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PALLIATIVE CARE ACROSS THE DISEASE CONTINUUM – REFERENCES

[1] Pritchard S, Cuvelier G, Harlos M, Barr R. Palliative care in adolescents and young adults with cancer. Cancer 2011;117:2323-2328.
[2] Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline update. J Clin Oncol 2017;35:96-112.
[3] Feudtner C, Friebert S, Jewell J, et al. Pediatric palliative care and hospice care commitments, guidelines, and recommendations. Pediatrics 2013;132:966-972.
[4] National Consensus Project for Quality Palliative Care. Clinical Practice Guidelines for Quality Palliative Care, 4th edition. Richmond, VA: National Coalition for Hospice and Palliative Care; 2018. https://www.nationalcoalitionhpc.org/ncp.
[5] Wein S, Pery S, Zer A. Role of palliative care in adolescent and young adult oncology. J Clin Oncol 2010;28:4819-4824.
[6] Steineck A, Bradford MC, O'Daffer A, et al. Quality of life in adolescents and young adults: The role of symptom burden. J Pain Symptom Manage 2022;64:244-253.e2.
[7] Jacobs S, Perez J, Cheng YI, et al. Adolescent end of life preferences and congruence with their parents' preferences: results of a survey of adolescents with cancer. Pediatr Blood Cancer 2015;62:710-714.
[8] Pousset G, Bilsen J, De Wilde J, et al. Attitudes of adolescent cancer survivors toward end-of-life decisions for minors. Pediatrics 2009;124:e1142-e1148.
[9] Weaver MS, Baker JN, Gattuso JS, et al. Adolescents' preferences for treatment decisional involvement during their cancer. Cancer 2015;121:4416-4424.
[10] Wiener L, Zadeh S, Battles H, et al. Allowing adolescents and young adults to plan their end-of-life care. Pediatrics 2012;130:897-905.
[11] 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. Pediatr Blood Cancer 2013;60:715-718.
[12] 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.
[13] Odejide O, Fisher L, Kushi LH, et al. Patient, family, and clinician perspectives on location of death for adolescents and young adults with cancer. JCO Oncol Pract 2022;18:e1621-e1629.
[14] Rajeshuni N, Johnston EE, Saynina O, et al. Disparities in location of death of adolescents and young adults with cancer: A longitudinal, population study in California. Cancer 2017;123:4178-4184.
[15] Mack JW, Chen K, Boscoe FP, et al. High intensity of end-of-life care among adolescent and young adult cancer patients in the New York State Medicaid program. Med Care 2015;53:1018-1026.

Fekete Z, Fekete A, Kacsó G. Treatment Classification by Intent in Oncology—The Need for Meaningful Definitions: Curative, Palliative and Potentially Life-Prolonging. Journal of Personalized Medicine. 2024; 14(9):932. https://doi.org/10.3390/jpm14090932.

Crawford GB, Dzierżanowski T, Hauser K, et al; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Care of the adult cancer patient at the end of life: ESMO Clinical Practice Guidelines. ESMO Open. 2021 Aug;6(4):100225. doi: 10.1016/j.esmoop.2021.100225.

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ABBREVIATIONS

ACE	adverse childhood experience
ALL	acute lymphoblastic leukemia
AMH	anti-Müllerian hormone
AYA	adolescent and young adult
BMI	body mass index
BUN	blood urea nitrogen
CAM	complementary and alternative medicine
CBC	complete blood count
CED	cyclophosphamide equivalent dose
CNS	central nervous system
COG	Children's Oncology Group
COS	controlled ovarian stimulation
DEXA	dual-energy x-ray absorptiometry
DLCO	diffusing capacity of the lung for carbon monoxide
ECG	electrocardiogram
FSH	follicle-stimulating hormone
GnRH	gonadotropin-releasing hormone
H&P	history and physical
HCT	hematopoietic cell transplant
HIPAA	Health Insurance Portability and Accountability Act
HPA	hypothalamic-pituitary-adrenal
HPV	human papillomavirus
LGBTQIA2S+	lesbian, gay, bisexual, transgender, queer and/or questioning, intersex, asexual, two-spirit, and additional sexual orientation and gender identities
LH	luteinizing hormone
MELTUMP	melanocytic tumors of uncertain malignant potential
MEN	multiple endocrine neoplasia
MSI	microsatellite instability
PIN	Pediatric Initiative Network
RD-CSO	registered dietitian-certified specialist in oncology
SGM	sexual gender minority
SMN	secondary malignant neoplasm
t-AML	treatment-related acute myeloid leukemia
TBI	total body irradiation
TESE	testicular sperm extraction
TSH	thyroid-stimulating hormone

NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus (≥50%, but <85% support of the Panel) 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 indicated.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025
Adolescent and Young Adult (AYA) Oncology

Discussion

This discussion corresponds to the NCCN Guidelines for Adolescent and Young Adult Oncology. Last updated on September 24, 2024.

Table of Contents

Overview

Advances in cancer treatment have resulted in declining cancer mortality rates among the overall adolescent and young adult (AYA) patient population over the last decade; however, AYA patients continue to face significant challenges in cancer care due to gaps in knowledge regarding etiology, basic biology, treatment, and survivorship.[1] One of the main reasons for these knowledge gaps is that AYA patients have a low rate of participation in clinical trials, reported to consistently remain below 10%.[2-4] Participation of AYA patients in clinical trials has been decreasing since 2010, with the exception of AYAs with acute lymphoblastic leukemia (ALL).[4] In addition to the low rate of participation in clinical trials, several other factors contribute to poor outcomes in AYA patients, such as: differences in disease biology, lack of consistency in treatment approaches, poor adherence or intolerance to therapy, lack of health insurance, delays in diagnosis, and physician's lack of familiarity with cancer in the AYA population.[5,6] AYA patients also have unique developmental, medical, and psychosocial issues, which make adjustment to their disease, health maintenance, and financial hardships more challenging.[2,7-10]

The biology, epidemiology, and clinical outcomes affecting AYA patients are usually different from those affecting younger (<15 years) and older patients (>39 years) with cancer.[11,12] In addition, the genetic, physiologic, and pharmacologic changes associated with AYA patients may impact their ability to tolerate cancer therapy and their response to treatment. Moreover, short- and long-term toxicities impacting a young, independent patient—including the impact of treatment on fertility and sexual function—may disincentivize treatment, leading to gaps in adherence and poor outcomes. Addressing these issues and providing options that empower the patient at the time of initial cancer treatment may result in more successful implementation of the planned therapy. Unlike comprehensive geriatric assessment, which is helpful to physicians in developing a coordinated treatment plan and understanding the functional needs of older patients, no similar assessment has been reported for AYA patients. There continues to remain fewer evidence-based data to guide the treatment of AYA patients. AYA patients diagnosed with cancer should be recognized as a distinct age group that has unique medical and psychosocial needs.[13,14] The distinct biology of disease as well as age-related issues in AYA patients (such as fertility, long-term side effects, insurance/financial issues, transportation to clinic appointments, child care, psychosocial support, and adherence to therapy) should be considered in the treatment decision-making process and during the transition of care from pediatric to adult medical teams.[15,16]

Based on the National Cancer Institute's (NCI's) Progress Review Group recommendations, the AYA patient is generally defined as an individual aged 15 to 39 years at the time of initial cancer diagnosis.[2,17] For 2024, the incidence of cancer in the United States in the AYA population is estimated to be 84,100 with 8890 cancer deaths.[18] Globally, up to 1.19 million cancer cases are estimated to be diagnosed in AYAs annually.[19] Compared to children <15 years, 5-year relative survival in AYA patients is worse for those with ALL, acute myeloid leukemia (AML), Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), astrocytomas, Ewing sarcoma, rhabdomyosarcoma, or osteosarcoma.[20] Additionally, for Ewing sarcoma, outcomes are worse for patients ≥18 years.[21-23] However, 5-year relative survival is better in AYA patients with medulloblastomas and germ cell tumors compared to in children with these tumors, possibly reflecting biologic differences in the tumors of each age group. Compared to adults aged ≥40 years, AYA patients tend to have better survival rates, except for those with breast and colorectal cancers.[20,24] Increasing age is associated with poorer prognosis in AYA patients with AML, NHL, Burkitt and Burkitt-like lymphoma, or rhabdomyosarcoma.[25]

The spectrum of cancer types that affect the AYA population is unique and different from those that affect the population outside of AYA. Thyroid cancers, lymphomas, melanoma, testicular cancer, cervical cancer, bone and soft tissue sarcomas, leukemias, central nervous system (CNS) cancers, breast cancer, and colorectal cancer account for the majority of cancers in this age group.[1,26]

Quality care for AYA patients with cancer is tied to timely detection and initiation of treatment, adherence to treatment, and access to a multidisciplinary team of health care professionals who are well-versed in the specific age-related/developmental issues relevant to this patient population.[27,28] These issues include, but are not limited to, fertility and sexual function; long-term side effects; behavioral, psychosocial, and socioeconomic issues; transportation to clinic appointments; maintaining school and work obligations; child care; treatment adherence; and the unique biology of the disease. The relative importance of these issues varies considerably across the broad age range defined as AYA. Certain institutions have established centers specialized in accommodating the specific needs of AYA patients. A retrospective analysis in Florida evaluating clinical trial enrollment in a comprehensive care center melanoma program found that AYAs with advanced disease (ie, nodal or metastatic disease) were more likely to enroll in a clinical trial. Additionally, researchers reported a nonstatistically significant trend of improved 3-year overall survival in AYA patients whose disease was advanced.[29] Referral of patients to AYA centers of excellence, or centers with established social, clinical, therapeutic, and psychosocial support programs, should be encouraged when feasible. Patients who receive AYA-focused care through a comprehensive and multidisciplinary approach have improved outcomes compared to those who do not receive AYA-focused care.[30-33]

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

Guidelines Update Methodology

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

Literature Search Criteria

Prior to the update 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, using the following search terms: cancer infertility, cancer fertility, cancer AND adolescent, or cancer AND young adult. The PubMed database was chosen because it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.[34]

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; Meta-Analysis; Practice Guideline; Randomized Controlled Trial; Systematic Reviews; and Validation Studies. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these guidelines as discussed by the Panel during the Guidelines update have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the Panel's review of lower-level evidence and expert opinion.

Sensitive/Inclusive Language Usage

NCCN Guidelines strive to use language that advances the goals of equity, inclusion, and representation.[35] NCCN Guidelines endeavor to use language that is person-first; not stigmatizing; anti-racist, anti-classist, anti-misogynist, anti-ageist, anti-ableist, and anti-weight-biased; and inclusive of individuals of all sexual orientations and gender identities. NCCN Guidelines incorporate non-gendered language, instead focusing on organ-specific recommendations. This language is both more accurate and more inclusive and can help fully address the needs of individuals of all sexual orientations and gender identities. NCCN Guidelines will continue to use the terms *men, women, female*, and *male* when citing statistics, recommendations, or data from organizations or sources that do not use inclusive terms. Most studies do not report how sex and gender data are collected and use these terms interchangeably or inconsistently. If sources do not differentiate gender from sex assigned at birth or organs present, the information is presumed to predominantly represent cisgender individuals. NCCN encourages researchers to collect more specific data in future studies and organizations to use more inclusive and accurate language in their future analyses.

Risk Factors

With rare exceptions, cancer appears to arise sporadically in most AYAs with a negative family history of cancer. Toxic and environmental exposures that cause cancer in AYAs include, but are not limited to, chemotherapy and/or radiation therapy (RT) leading to second malignant neoplasms (SMNs) in patients treated for cancer during childhood or young adulthood[36-38]; predisposition to clear cell adenocarcinoma of the vagina or cervix in patients with maternal exposure to diethylstilbestrol; and melanomas induced by ultraviolet light/sun exposure. Infections that predispose AYAs to cancer include cervical carcinoma following exposure to human papillomavirus (HPV), HL and Burkitt lymphoma following Epstein-Barr virus (EBV) infection, and Kaposi sarcoma and NHL in people with HIV.[39]

Familial cancer syndromes, associated with germline mutations in a variety of genes, affect only a minority of AYA patients. However, these syndromes greatly increase the risk for cancer during adolescence and young adulthood. Approximately 8% to 9% of all patients with cancer will have a germline mutation in a cancer-predisposing gene.[40-42]

Young individuals with germline mutations of *BRCA1/2* are predisposed to hereditary breast and ovarian cancer syndrome, while those with mutations in *TP53* (Li-Fraumeni syndrome), *PTEN* (Cowden syndrome), or *ATM* (ataxia-telangiectasia), or those who have received mantle field RT for HL are at an increased risk of developing breast cancer during young adulthood.[2,43,44] Screening for breast cancer may be warranted in AYA patients with inherited or familial risk factors. See the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

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 mismatch repair (MMR) genes (*MSH2, MLH1, MSH6,* or *PMS2*), and is associated with early-onset colorectal cancer.[2,6] Familial adenomatous polyposis (FAP) is an autosomal dominant disease caused by germline mutations in the *APC* gene. This syndrome is associated with the presence of thousands of colonic polyps and with the development of colon cancer in most affected patients by age 40 years. Desmoid tumors are considered to be the most common extracolonic manifestations of FAP and may be the presenting manifestation of FAP in AYA patients.[45] Screening for colorectal cancers may be warranted in AYA patients with inherited or familial risk factors. See the NCCN Guidelines for Colorectal Cancer Screening.

AYA patients with Li-Fraumeni syndrome (resulting from germline mutations in the *TP53* tumor suppressor gene) or germline mutations in the *RB* gene are at higher risk of developing osteosarcoma and rhabdomyosarcoma.[46] Sarcomas represent 25% of tumors in *TP53* mutation carriers. AYAs with germline mutations in the *RB* gene have often been treated for retinoblastoma during early childhood.[47] 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 age 40 years.[48] Rhabdomyosarcoma in AYA patients has high-risk features and may be associated with inferior outcomes. Referral to a center familiar with rhabdomyosarcoma therapy should be considered depending on the clinical situation.[49,50] See the NCCN Guidelines for Soft Tissue Sarcoma.

Patients with mutations in the *SDH* gene are at risk for paraganglioma and pheochromocytoma, gastrointestinal stromal tumors (GIST), 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 GIST lacking *KIT* or *PDGFRA* mutations.[51,52] Patients with germline mutations in *NF1* carry a 10% lifetime risk for malignant peripheral nerve sheath tumors, as well as an increased risk for other malignancies including GIST and early breast cancer.[53]

Multiple neuroendocrine neoplasia (MEN) syndromes (MEN1 and MEN2) are autosomal dominant syndromes characterized by the development of multiple endocrine tumors. MEN1 is caused by a germline mutation or inactivation of the tumor suppressor gene *MEN1*, whereas MEN2 is associated with germline mutations in the *RET* proto-oncogene.[54] MEN1 is associated with the development of pituitary, parathyroid, and pancreatic neuroendocrine tumors.[54] 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).[55] Most patients with MEN2B have mucosal neuromas or intestinal ganglioneuromas and pheochromocytoma in addition to MTC.[55] 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 the NCCN Guidelines for Neuroendocrine and Adrenal Tumors for more information. HPV infection has been associated with cervical cancer and few other non-cervical cancers, including anal and oropharyngeal cancers.[56,57] Randomized clinical trials have demonstrated the efficacy of HPV vaccination against cervical intraepithelial neoplasia, anal intraepithelial neoplasia, and oral HPV infections in patients aged 15 to 25 years.[58-60] 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-year-age group and progressively decreased in the 18- to 20-year and 21- to 25-year-age groups, suggesting that early HPV vaccination could substantially reduce the incidence of HPV-associated cancers in the AYA population.[59] However, studies have shown that survivors of childhood or AYA cancers have lower rates of HPV vaccination compared to their peers.[61,62] Furthermore, recommendation for HPV vaccination from the survivor’s medical team was positively associated with vaccination,[61,62] highlighting the importance of recommending the HPV vaccine to AYA patients and their caregivers. HPV immunization (if not previously administered) is recommended by the Advisory Committee on Immunization Practices (ACIP) for all adolescents aged 11 or 12 years and can be administered in patients as young as 9 years. Catch-up vaccination is recommended in both sexes until age 26 years, since the vaccine has been shown to prevent cervical carcinoma

and anal intraepithelial neoplasia.[63-65] The American Cancer Society recommends HPV vaccination for all adolescents between ages 9 and 12 years to promote on-time vaccination rates. Health care providers are also encouraged to start offering the HPV vaccine at age 9 or 10 years.[66] ACIP also recommends that individuals with specific risk factors, including those who are transgender, or those who have immunocompromising medical conditions (such as cancer) be vaccinated through age 26 years.[63,64]

Screening

AYA patients, especially those with risk factors, should be made aware of the importance of early diagnosis and self-examination of the skin, breasts, and testicles as recommended by the American Cancer Society. They should also be educated regarding the benefits of early detection and treatment.[67] 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.[68] 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.[69] 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, their families, 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.[67] Some studies have reported that adolescents experience longer lag times (interval between symptom onset and diagnosis) than children.[70-72] 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, although more research is needed on these contributing factors.[2] Passage of the Affordable Care Act in 2010, which included provisions extending dependent health care coverage up to age 26 years, has improved insurance rates for young adults through age 25 years, although lack of insurance remains a problem for AYA patients who are >26 years.[73] 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.[74] Those with public or no health insurance had longer lag times than those with private health insurance in most of the cancers evaluated. 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.

Comprehensive Care for AYA Patients with Cancer: Special Considerations

AYA patients should be cared for by a multidisciplinary team of providers with expertise in AYA cancer treatment and comprehensive care of specific developmental issues such as fertility and sexual function, education, career development, employment, family planning, pregnancy, sexually transmitted diseases, and tobacco, alcohol, and substance use. Given the rarity of several tumor types diagnosed in this population, all AYA patients should be encouraged and offered enrollment in tumor banking studies and multicenter clinical trials, when available.

All AYA patients should undergo comprehensive assessment following cancer diagnosis, which should include a comprehensive psychosocial assessment, discussion of the cancer and treatment-related risk on fertility and sexual function, the use of education concerning fertility preservation

methods and contraception, evaluation of complete family history, and, if indicated, a subsequent genetic and familial risk assessment by a genetic counselor. Age and developmentally appropriate information related to cancer should be provided. A pregnancy test should be considered prior to each cycle of therapy in accordance with institutional requirements. Consult with an OB/GYN for patients with ovaries/uterus and consult the CDC Summary Chart of U.S. Medical Eligibility Criteria to assist with the safety and efficacy of selection of appropriate contraception for individuals at risk of pregnancy. Consider referral to a fertility preservation or reproductive health program. It is important to speak with each patient individually, without a caregiver or partner present, to solicit any questions or concerns and to give the patient an opportunity to speak freely.

Age-Appropriate Care

AYA patients can be treated either at pediatric or adult cancer centers.[27] Retrospective analyses have shown that AYA patients with certain pediatric-type cancers, such as ALL,[25,75-77] rhabdomyosarcoma,[78] and Ewing sarcoma,[79,80] have superior outcomes when treated with pediatric protocols. Alternatively, there is a lack of compelling evidence that pediatric protocols improve outcomes in AYA patients with AML, HL, and NHL.[81-83]

As aforementioned, the low rate of participation in clinical trials is one of the main reasons for the lack of improvement in outcomes in AYA patients with cancer.[3,25,84-86] A review of 30 studies of adolescents with cancer (aged 15–19 years) showed that 5% to 34% of these patients were enrolled in clinical trials.[25] Concerningly, with the exception of AYAs with ALL, participation of AYA patients in clinical trials has been decreasing; the decrease in clinical trial accrual from 2010 to 2015 ranged from -10% (aged 15–19 years) to -54% (aged 35–39 years).[4] Care should be provided at medical centers with broad access to clinical trials (standard-of-care registry trials and trials evaluating novel therapies).[27] 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%).[87-89] Parsons et al reported that AYA patients who are treated by non-pediatric oncologists are less likely to be enrolled in clinical trials.[90] Nevertheless, a substantial number of AYA patients with pediatric malignancies are not being treated at pediatric cancer centers.[25,91,92]

The treatment and appropriate location of care vary with the type of cancer as well as with the availability of family, community, and institutional support.[67,93] A study conducted in Pittsburgh evaluated clinical trial enrollment of AYAs following the creation of a dedicated AYA Oncology Program, a joint effort by pediatric and medical oncologists. It was found that AYA clinical trial enrollment increased to 32% in comparison to 4% for historic controls.[94] AYA patients should ideally be evaluated at medical centers with extensive experience in treating cancer in this patient population and at centers that have access to supportive care services (psychosocial/educational support and fertility preservation) specific to the AYA population as well as to medical subspecialty services appropriate to the cancer diagnosis, such as orthopedic surgeons with experience in limb-sparing surgery for patients with extremity sarcomas.[27] 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.[95]

Treatment Options

Select AYA patients may tolerate more intensive therapies than older patients, as they have fewer comorbid conditions that limit the intensity of

treatment in some older adults.[67] Dose-intensive and dose-dense treatments are associated with improved outcomes in certain malignancies.[21,96,97] Therefore, more intensive therapy may be considered for some AYA patients if such a regimen exists for that particular disease and there are no contraindications. When possible, AYA patients should be enrolled in clinical trials for their specific disease.

Treatment-related issues in AYA patients may differ from those of populations outside of AYA due to the distinct biology of the disease.[11] Physical and physiologic 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.[98] Appropriate management of symptoms and side effects to reduce the severity and toxicity of treatment should be an integral part of the comprehensive care of AYA patients.[99] Surgery, RT, chemotherapy, and hematopoietic cell transplant (HCT) are the main treatment options for patients who are able to tolerate curative treatment. All of these options are associated with both acute and late side effects.[67,100] Please refer to *Treatment-Related Issues* in the algorithm for guidance on screening for treatment-related toxicities.

Surgery

Surgery plays an important role in the management of cancer in AYA patients, especially in breast cancer, thyroid cancer, melanoma, bone and soft tissue sarcomas, colorectal cancer, and CNS cancers that are more common in this patient population. Adolescent patients, whose bodies are still developing, may be more affected by some surgical procedures than older patients who are already at or near their full body size.[67] The extent of surgery is dependent on the type and location of cancer. In some instances, extensive surgery requiring removing part of or an entire organ or limb may be necessary. With advances in surgical techniques and chemotherapy, limb-sparing surgery is feasible for the majority of patients with extremity sarcoma and osteosarcoma.[80] Surgery should be performed at high-volume centers by surgeons with expertise in AYA comprehensive care, with access to rehabilitative services to ensure that function is preserved as much as possible.

Radiation Therapy

RT is associated with an increased risk of delayed morbidity and mortality; development of SMNs; pulmonary, cardiac, and thyroid dysfunction; and chronic health conditions and growth abnormalities.[101] AYA patients receiving RT to the testes or ovaries are at risk of developing fertility impairment and reproductive endocrinopathies later in life.[102] Females with HL who receive chest RT between ages 10 and 30 years are at increased risk of developing breast cancer.[103] Cranial RT is associated with short stature, auditory deficits, cognitive processing difficulties, poor physical function, and rarely debilitating migraines, which contribute to lower rates of employment, independent living, and marriage among AYA survivors of childhood cancer.[104-106] RT-induced spinal cord dysfunction is thought to be more prevalent in adolescents, presumably because of elongation of the cord during the growth spurt.[107] A multidisciplinary consultation should be considered to determine the optimal method to reduce radiation-induced effects. For patients with a predicted risk of radiation-induced late effects to tissues surrounding but not in targeted tissues, consider a consultation with a radiation oncologist for proton radiotherapy.[108-112] A dermatology evaluation (ie, annual skin examinations performed by a dermatologist) is also recommended for patients who previously received RT.[113]

Systemic Therapy

Pain, fatigue, nausea, vomiting, mucositis, hair loss, infection, and myelosuppression are some of the acute side effects of chemotherapy. Reversible toxicities do not necessarily warrant dose reductions. See the NCCN Guidelines® for Supportive Care (available at 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. Establish maximum cumulative dosing parameters and monitor cumulative dosing and schedule for certain medications associated with irreversible organ damage and fertility issues when certain lifetime exposure is encountered.

Anticipatory nausea and vomiting (ANV), also known as conditioned, learned, or psychological nausea and vomiting, is reported to occur before chemotherapy in approximately 20% of patients at any one chemotherapy cycle and in 25% to 30% of patients by their fourth chemotherapy cycle.[114] Younger patients (<50 years) may be more susceptible to ANV, because they generally receive more aggressive chemotherapy and have poorer emesis control than older patients.[114] Other risk factors for ANV include, but are not limited to, female sex, previous ANV, history of motion sickness, and morning sickness during pregnancy. Prevention strategies include behavior therapies, acupuncture, and administration of anxiolytic medications.[115] See the NCCN Guidelines for Antiemesis.

Although there are limited data on the subject, systematic reviews have reported that AYA patients experience more cancer-related fatigue than older patients[116] and that fatigue is one of the most prevalent, severe, and distressing symptoms in this age group.[117] Furthermore, several studies on the topic have shown benefit of interventions targeting fatigue in AYA patients with cancer or cancer survivors, although further research on effective management strategies is needed.[116-119] See the NCCN Guidelines for Cancer-Related Fatigue.

Alkylating agent-based chemotherapy is associated with a higher risk of infertility in patients.[102] See the section on *Impact of Cancer and Its Treatment on Fertility* in this Discussion. Anthracycline-based chemotherapy is associated with irreversible cardiac dysfunction, whereas neurotoxic chemotherapies such as methotrexate and cytarabine can result in CNS dysfunction.[99,120] Bleomycin-induced pulmonary toxicity is well-documented in patients with HL treated with bleomycin-containing chemotherapy regimens.[121] Higher cumulative doses of cisplatin, ifosfamide, or epipodophyllotoxins are associated with hearing loss, peripheral neuropathy, renal dysfunction, and secondary AML, respectively.[122-125] See also the section on *Late Effects in AYA Cancer Survivors*.

Ototoxicity may occur following treatment with platinum-based chemotherapy agents.[126] Although this side effect is not considered life-threatening, it can have a detrimental effect on an AYA patient's quality of life. In 2022, the FDA approved the use of sodium thiosulfate (STS) for reducing the risk of ototoxicity associated with cisplatin in pediatric patients ≥1 month of age with localized, non-metastatic solid tumors.[127] The approval of this indication was based on data from two open-label, phase 3, randomized controlled trials in pediatric patients with cancer who were treated with cisplatin; the incidence of hearing loss was lower in those who received STS than those who did not receive STS.[128,129] However, concerns remain regarding the use of STS in the metastatic setting. A post-hoc analysis of data from the ACCL0431 trial showed that, among patients with disseminated disease, STS was associated with a significantly lower 3-year overall survival rate compared with those who did not receive STS (45% vs. 84%; P = .009).[130]

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

AYA cancer survivors are at increased risk for reduced bone mineral density, alopecia, and other dermatologic side effects. Due to the risk of osteoporosis and osteopenia bone mineral density surveillance is recommended upon entry into long-term follow-up with repeat testing once the patient is 25 years old.[131] Chemotherapy-induced alopecia, hair loss, is common as the treatment targets rapidly growing cells and therefore damages hair follicles.[132,133] Hair loss can have long-term psychosocial and behavioral effects on patients. A randomized control trial investigating the use of scalp cooling to increase hair thickness and density has found promising results in patients with breast cancer, but the long-term effects are still under investigation.[134] Additionally, various dermatologic side effects from cancer treatments include scarring, irritated skin, hyperpigmentation, and hirsutism, and these conditions can have a significant impact on a patient's quality of life.[135,136]

Hematopoietic Cell Transplant

HCT is a potentially curative treatment option for an increasing number of AYA patients with leukemias and lymphomas.[137] Graft-versus-host disease (GVHD), chronic immunosuppression, and gonadal dysfunction related to high-dose conditioning chemotherapy and RT are the major post-transplant complications associated with HCT.[99,100]

Chronic GVHD has been identified as the leading cause of non-relapse mortality in HCT survivors.[138] AYA patients are at a higher risk of developing chronic GVHD than younger children.[139] Patients >15 years (children <5 years had a probability of <14% compared to a probability of 44% for patients >15 years) and the use of total body irradiation (TBI) were significantly associated with an increased likelihood of developing chronic GVHD following allogeneic HCT.[140] Patients who receive peripheral stem cells during their transplant procedure have a greater risk of chronic GVHD compared to those who received bone marrow transplant.[141] A report from the Bone Marrow Transplant Survival Study demonstrated that chronic GVHD had a significant impact on the overall health status of HCT survivors, particularly in the areas of functional impairment, activity limitation, and pain.[142] This study also demonstrated that resolution of chronic GVHD resulted in long-term health outcomes that were comparable to survivors who were never diagnosed with chronic GVHD.

HCT survivors are also at increased risk for late complications, which include recurrent infections, secondary cancers, cardiac dysfunction, growth failure, weight loss, neurocognitive delay, and other end-organ dysfunction.[99,100,143] In addition, the incidence of severe or life-threatening chronic health conditions, endocrine complications, or secondary cancers is also higher among HCT survivors than in non-cancer populations and patients with cancer who are treated conventionally.[137] Allogeneic HCT survivors irradiated at ≤30 years are at higher risk of developing secondary solid cancers.[144]

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

Adherence to Treatment

Adherence is defined as the extent to which a person's behavior corresponds with agreed recommendations from a health care provider. Nonadherence to recommended treatment and follow-up care contributes to poor clinical outcomes in AYA patients with cancer.[145,146] Non-adherence to appointments can lead to delayed identification of side effects, complications, or secondary cancers.[5]

Nonadherence to treatment regimens has been an ongoing problem among patients with cancer, and the prevalence of nonadherence has been consistently higher among adolescents compared to younger or older patients with cancer.[145] Nonadherence to oral chemotherapy

contributes to reduced treatment efficacy and increased risk of recurrence. Available evidence from clinical trials that have included AYA patients with leukemia and lymphoma suggests that a substantial portion of AYA patients with cancer (27%–63%) have difficulties adhering to their oral treatment regimens.[145,146] Difficulties with medication adherence also extend to survivorship, with 23.8% of AYA cancer survivors reporting nonadherence compared to 14.3% in the comparison group ($P < .001$). Survivors were also more likely to report that they could not afford their medication, and uninsured survivors were more likely to report nonadherence than those who were privately insured.[147]

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

Risk factors for nonadherence among AYA patients include patients' emotional functioning (depression and poor/low self-esteem), personal beliefs (perceived severity of cancer diagnosis and the necessity of intervention), growing independence, competing obligations (school, work, and family), and lack of insurance and appropriate psychosocial support.[148] In a randomized controlled trial, video game intervention significantly improved treatment adherence to prophylactic antibiotic use among AYAs with acute leukemia, lymphoma, and soft tissue sarcoma.[149] A review aimed to identify and characterize the various digital health interventions available for support of AYAs with cancer. Numerous modalities, including mobile/tablet apps, video games, wearables, virtual reality, social media, and other web-based interventions were found to be in existence for the purpose of promoting physical activity, assessing pain management, and improving adherence among AYAs.[150] Additional studies evaluating the efficacy of interventions to improve adherence in AYA patients with cancer are needed.[2]

Risk assessment for non-adherence among AYA patients should include consideration of patient maturity, independence, unmet psychosocial and physical needs, and treatment side effects.[151] For AYAs presumed to be at high risk of nonadherence, implementation of individualized interventions such as additional supportive care resources (eg, social work, psychology, palliative care) to promote adherence may improve outcomes in AYA patients with cancer. The patient's personal support system (family, friends, or caregiver) should be mobilized and educated to assist in relieving some of the burdens of care and to positively encourage the patient to maintain adherence to therapy. In the absence of data from studies evaluating the effect of interventions to improve adherence in AYA patients with cancer, findings from studies involving AYA patients with other chronic diseases may be able to be extrapolated to this patient population.[5]

NCCN Recommendations on Adherence to Therapy and Safety Plans

- Educate about the expectations of treatment and explain the patient's responsibility to adhere to treatment. Engage in collaborative treatment decision-making with the AYA patient.
- Evaluate for any past history or potential barriers to adherence with medical treatment.
- Provide education and/or guidance about each medication prior to the start of treatment and every time there is a change in treatment. Review the list of medications as well as their dose, purpose, and adverse effects.[145,146]
- Simplify and modify dosing schedule when medically possible, to accommodate an AYA patient's lifestyle and normal activities.[145,146]
- Consider the use of technology (eg, smartphone applications).

- Provide access to systematic and standardized symptom management for side effects related to cancer treatment.[145,146] See the NCCN Guidelines for Supportive Care (available at www.NCCN.org).

Impact of Cancer and Its Treatment on Fertility

Impaired fertility is a major consequence of cancer and its treatment.[152-155] The impact of cancer treatment on fertility is related to the age of the patient at the time of diagnosis and treatment, and is dependent on the type, duration, and dose intensity of treatment. Alkylating agent-based chemotherapy, high-dose cranial RT that can impair hypothalamic pituitary function, and targeted RT to the uterus, ovaries, or testes are primary risk factors for gonadal dysfunction and decreased fertility.[156-161] Gonadal exposure to low-dose RT can result in oligospermia or azoospermia in individuals with testes. Higher-dose RT is associated with both ovarian and uterine dysfunction.

Young females with HL treated with chemotherapy are at risk of developing primary ovarian insufficiency, irrespective of their age at the time of treatment (38% for those diagnosed between ages 30 and 40 years; 37% for those diagnosed between 9 and 29 years of age).[162] The cumulative risks for primary ovarian insufficiency are much higher after alkylating agent-based chemotherapy.[162,163] In a large cohort of females treated between ages 15 and 40 years for HL, the cumulative risk of premature ovarian insufficiency after alkylating agent-based chemotherapy was 60% compared to only 3% or 6% after non-alkylating agent-based chemotherapy.[163] Independent risk factors for acute ovarian insufficiency include increasing RT doses to the ovaries and exposure to procarbazine and cyclophosphamide at ages 13 to 20 years.[157] An analysis of 590 females who were diagnosed with HL before age 18 years showed that RT to the pelvis was associated with decreased incidence of parenthood (hazard ratio [HR], 0.66; 95% CI, 0.48–0.90; P = .01).[164]

Among young females treated with adjuvant chemotherapy for breast cancer, the risk for premature menopause is significantly higher for those >35 years with newly diagnosed breast cancer treated with chemotherapy.[165,166] Similarly, among survivors of HL diagnosed between ages 14 and 40 years, those who were aged 22 to 39 years at first treatment were at a higher risk of developing premature menopause after treatment compared to younger patients (aged 14–21 years).[167] Treatment with MOPP (mechlorethamine, vincristine, procarbazine, and prednisone)/ABV (doxorubicin, bleomycin, and vinblastine) significantly increased the risk of ovarian insufficiency. 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.[167]

In those treated with alkylating agent-based chemotherapy and RT to the testes, germ cell dysfunction with resultant infertility is more common than Leydig cell dysfunction and testosterone insufficiency.[168] 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 (FSH) concentrations, and reduced plasma concentrations of inhibin B. Leydig cell dysfunction occurs at RT doses higher than those associated with germ cell dysfunction. AYA patients treated with testicular RT ≥20 Gy are at high risk for Leydig cell dysfunction, whereas testicular RT ≥2 Gy can impair spermatogenesis resulting in permanent azoospermia.[168] TBI used as part of high-dose conditioning therapy prior to HCT can also affect the testes, resulting in permanent infertility in the majority of AYA patients with testes.[102]

Azoospermia is associated with chemotherapy and radiation. Whether it is transient or permanent depends on the type of treatment involved, with radiation and alkylating agents posing the greatest risk for long-term damage.[169] Azoospermia has been reported in >90% of males receiving

procarbazine-based chemotherapy regimens such as MOPP and may not resolve over time, resulting in permanent infertility.[170] 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.[171]

Given that gonadal insufficiency/gonadotoxicity is a well-known side effect of cancer therapy,[172] the Pediatric Initiative Network (PIN) proposed a standardized risk stratification model, which subdivides the risk of gonadal insufficiency/infertility into minimally increased risk, significantly increased risk, and high level of increased risk.[173] This classification is based on exposure to alkylating agents or heavy metals, HCT, and radiation exposure.[173] The male model also incorporates the risk of surgery and does not stratify risk according to pubertal status, unlike the female model.[173] Although limitations exist, this model is meant to estimate and standardize infertility risk and promote conversation concerning fertility preservation. Details regarding the risk assessment can be found under the "Assessment for Gonadal Function" section under *Screening Recommendations for AYA Survivors* in the algorithm.

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

Fertility Preservation

As the AYA age range includes the primary reproductive years, fertility preservation is an issue of crucial importance and should be an essential part in the management of the cancer.[15,102,174-178] The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines recommend that providers discuss the options for fertility preservation with all new patients with cancer at the time of diagnosis.[179] Nevertheless, fertility preservation is currently one of the most under-prescribed and least implemented services in AYA patients with cancer.[102,174,180] 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.[181] However, it is possible that more discussions about infertility occurred without having been documented. Another study that analyzed the electronic medical records of 454 AYA patients at a single cancer center showed that the risk of infertility was discussed with 83% of patients, with females more likely to be informed than males (odds ratio [OR], 3.57; 95% CI, 1.33–9.60; $P = .01$).[182] A study of 146 adolescent males at risk for fertility impairment due to cancer treatment across eight different pediatric oncology centers found that only 53.4% attempted to bank sperm, with 43.8% successfully banking. Parent or medical team recommendation was associated with increased likelihood of sperm banking completion.[183]

A systemic review reported that the following factors can hinder the decision-making process for females with cancer: 1) lack of information about fertility preservation options; 2) fear of perceived risks of fertility treatment (eg, delaying cancer treatment, hormone treatment for a hormone-sensitive cancer); 3) lack of physician referral; 4) emotional distress; 5) relationship/parental status; and 6) financial concerns.[184] The American Society for Reproductive Medicine (ASRM) recommends that conversations concerning fertility be undertaken by an interdisciplinary medical team composed of oncologists, reproductive endocrinologists and urologists, and reproductive surgeons trained in fertility preservation methods. The initial step of discussing intended therapies and associated reproductive risks is entrusted to the oncologist, who can subsequently make referrals as appropriate.[185] Psychosocial providers can assist patients and families in the decision-making process about fertility preservation, particularly when AYA patients are distressed about the

potential for impaired fertility associated with cancer treatment.[179] The emotional impact of conversations surrounding fertility, especially for the younger AYA patient, must be taken into consideration. Finally, genetic and financial counselors may also be consulted to discuss the risks and probability of heritable disease transmission and review financial options for fertility preservation, respectively.[185]

The Oncofertility Consortium, a group of clinicians and researchers in the United States, was formed in 2007 by the U.S. National Institutes of Health (NIH) to address reproductive barriers facing AYA patients and to identify research priorities in this area.[186] Future aims that were developed during a 2011 meeting are as follows:

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

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. ASRM recommends that fertility preservation programs be affiliated with an experienced assisted reproductive technology (ART) program. Alternatives to fertility preservation, such as the use of donor gametes, embryos, and adoption, should be discussed by the team. For individuals with ovaries scheduled to undergo pelvic RT, the option of gestational surrogacy may also be reviewed. In the case of cryopreservation, appropriate arrangements should be discussed and documented in the case of donor death.[185]

Options for Individuals with Ovaries

Oophoropexy

For individuals scheduled to undergo pelvic RT, oophoropexy or ovarian transposition may be a promising option involving surgical displacement of the ovaries out of the RT field to minimize ovarian damage and preserve ovarian function.[187]

Embryo Cryopreservation

Embryo cryopreservation after in vitro fertilization (IVF) is an option for fertility preservation.[179] This method is an option for post-pubertal individuals with ovaries and requires a committed sperm donor who is available with short notice. It has been highly successful in individuals <40 years.[102,174] According to data published by ASRM on infertile and donor populations, the live birth rate per cycle start for individuals <35 years was 46.8%, while that for those aged 35 to 37 years was 34.4%, and that for those aged 38 to 40 years was 21%.[185] In one study that assessed pregnancy outcomes following embryo cryopreservation, letrozole was used in combination with FSH to protect patients with breast cancer against the harmful effects of increased estrogen.[188] Out of 33 patients, the live birth rate was 45%, with 39% of live births resulting in twins. These rates are not significantly different from those for infertile couples not affected by cancer, except for implantation rate, which was greater in the patients with breast cancer (40.7% vs. 26.1%). A little more than half (55%) of the embryos were transferred to a gestational carrier, with no significant differences in outcomes (ie, implantation, live birth, twinning rates) between self-transfers and gestational carriers.

Mature Oocyte Cryopreservation

Mature oocyte cryopreservation is an alternative for post-pubertal individuals, and, like embryo cryopreservation, requires hormone stimulation and subsequent oocyte retrieval.[102,174] Evidence from randomized trials[189-192] and a meta-analysis[193] suggest that IVF with cryopreserved oocytes results in fertilization and pregnancy rates similar to that of fresh oocytes. Like embryo cryopreservation, pregnancy rates with mature oocyte cryopreservation also decline with advancing age.[185]

Ovarian Tissue Cryopreservation

Cryopreservation of ovarian cortical tissue is a promising strategy for fertility preservation when there is insufficient time for oocyte or embryo cryopreservation and/or the patient is prepubertal. This technique does not require hormonal stimulation, so there is no delay in initiation of treatment.[102] This procedure would not be appropriate for certain patients with cancer if potential exists for reintroduction of malignant cells with grafting. It is also not recommended for carriers of *BRCA* mutations due to the increased risk for ovarian cancer. Orthotopic transplantation has been met with success, with 130 live births reported from cryopreserved and thawed ovarian tissue since 2017.[185] Following transplantation, ovarian tissue is thought to regain function within 60 to 240 days and may last for 7 years.[185] Pregnancy and live birth rates are expected to be higher in donors <40 years due to ovarian follicular reserve. It is recommended that transplantation be performed with the purpose of regaining fertility and not gonadal endocrine function.[185] While ovarian tissue cryopreservation is still considered investigational at some institutions, it may be discussed as an option for fertility preservation, if available.

Some studies, including randomized trials, have evaluated the role of menstrual suppression with gonadotropin hormone-releasing hormone (GnRH) agonists to preserve ovarian function during chemotherapy.[194-202] Some meta-analyses have shown that GnRH agonists may be beneficial for fertility preservation.[203-205] However, the impact of such meta-analyses is limited by factors such as only examining those with breast cancer and only including trials that were not adequately powered and did not use blinding and/or a placebo condition, among other flaws.[206,207] There are also limited data available on the long-term impact of GnRH on preservation of ovarian function,[203] although a 5-year follow-up analysis of a randomized trial showed that administration of a GnRH agonist does not significantly impact primary ovarian insufficiency or future pregnancy rate.[202] Therefore, although data suggest that menstrual suppression with GnRH agonists may protect ovarian function, further investigation is needed.

Nevertheless, GnRH agonists and agents such as the progestin medroxyprogesterone and oral contraceptives may be used in patients with hematologic malignancies and thrombocytopenia and/or anemia who are at risk for menorrhagia for the purpose of menstrual suppression.[208] However, caution is needed in endometrial cancer survivors where progestin therapy has been associated with high rates of cancer recurrence,[209] which may be prevented by combining metformin with medroxyprogesterone.[210]

Options for Individuals with Testes

Sperm Cryopreservation

Individuals should also be counseled regarding options for fertility preservation and referral to a reproductive urologist should be considered. Semen cryopreservation before the start of treatment is the most reliable and well-established means of preserving fertility in post-pubertal AYA patients with cancer.[102,174] 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.[211]

If the patient has medical, religious, emotional, or developmental issues that preclude traditional ejaculation methods, other options to obtain sperm for cryopreservation may be discussed, including: vibratory stimulation, electroejaculation, surgical testicular sperm extraction (TESE), the administration of phosphodiesterase type 5 (PDE5) inhibitors, and the use of alpha-agonists. Traditionally more effective in those with neurologic injuries, penile vibratory stimulation may be used to trigger the ejaculatory reflex. Electroejaculation, normally performed under anesthesia, involves the transrectal stimulation of pelvic tissues, including the prostate and seminal vesicles, to yield ejaculate. Surgical TESE is reserved for individuals who have azoospermia and/or are unable to ejaculate via other methods. The use of PDE5 inhibitors may be used to obtain ejaculate in those experiencing erectile dysfunction; similarly, alpha agonists may be warranted in cases of retrograde ejaculation.[185]

Testicular Tissue Cryopreservation

Cryopreservation and subsequent transplantation of spermatogonial stem cells may be an option for prepubertal and pubertal individuals in whom semen cryopreservation is not possible.[102,174] For those with hematologic or testicular malignancies, autologous transplantation of cryopreserved testicular tissue may not be appropriate for fear of reintroduction of tumor cells. However, immature testicular tissue cryopreservation is still considered experimental.[185]

Similar to the recommendation for those with ovaries, there is limited evidence regarding the efficacy of hormone suppression in reducing the risk of impaired fertility in individuals with testes during chemotherapy.[179]

Fertility, Reproductive Endocrine, and Sexual Health Considerations

The NCCN Guidelines emphasize that fertility preservation and sexual health and function should be an essential component of the comprehensive care of AYA patients with cancer who are at any level of risk for impaired fertility and possible sexual dysfunction due to cancer treatments, regardless of gender identity, sexual orientation, or financial status.[173,212-214] An assessment of the risk for gonadotoxicity and impaired fertility due to cancer and its therapy should be performed and discussed with patients. Options for fertility preservation should be discussed with all patients as soon as possible prior to the start of therapy and throughout the course of therapy.[215] Care should be coordinated by a multidisciplinary team. Providers should initiate referral to fertility preservation clinics and/or provide resources for off-site/remote sperm banking as soon as possible for all patients who are interested in discussing fertility preservation.[216-218] Consultation with a financial counselor and local or institutional grants may be available to provide financial assistance with fertility preservation needs. Follow-up with a fertility specialist post-treatment may also be helpful for some patients. Consider the emotional impact of conversations surrounding fertility preservation, especially for the younger AYA patient and sexual gender minority (SGM) patients. Creating safe spaces to disclose gender identity and sexual orientation can mitigate and provide community partnership or resources for fertility and psychosocial experts in sexual and gender minorities (GLMA directory).

All Patients

- After assessing the patient's risk for impaired fertility and the patient's preferences for fertility preservation, recommend a form of appropriate fertility preservation and/or make a referral to a fertility preservation specialist.[185,212,219]

- Discuss the effects of treatment on sexual function during and after treatment and refer the patient to a specialist as appropriate. See NCCN Guidelines for Survivorship.
- Discuss contraception before, during, and after treatment. Consult with an OB/GYN for patients with ovaries/uterus and consult the CDC Summary Chart of U.S. Medical Eligibility Criteria to assist with the safety and efficacy of selection of appropriate contraception for individuals at risk of pregnancy.

Individuals with Ovaries

- For individuals who can delay cancer treatment by approximately 3 weeks, oocyte or embryo cryopreservation via immediate (or random start) controlled ovarian stimulation (COS) should be discussed.
- For individuals who are unable to delay treatment for oocyte or embryo cryopreservation, discuss or refer the patient for consideration of ovarian tissue cryopreservation.
- Oophoropexy or transposition of the ovaries out of the field of radiation should be considered for individuals for whom the radiation field will include the ovaries.
- The effects of treatment on gonadal hormone function during and after treatment should be discussed with patients. Patients who face primary ovarian insufficiency should be screened and treated by a specialist. Furthermore, patients who do not undergo fertility preservation prior to initiating treatment may still be appropriate candidates for fertility preservation post-treatment and should be screened and referred to a specialist.[220]
- Progestin-only methods, combined hormonal contraceptives, or GnRH agonists can be used in protocols that are predicted to cause prolonged thrombocytopenia and thus present a risk for menorrhagia.[208]
- GnRH agonists may protect ovarian function[221]; however, other fertility preservation modalities should still be considered and, if possible, pursued.

Individuals with Testes

- Sperm banking is the preferred choice of fertility preservation for individuals without erection or ejaculation issues. For patients who can delay cancer treatment, consider >1 collection of ejaculate, prior to initiating treatment. AYA patients can use either a local sperm bank or an available online sperm banking kit.[179,219,222] A semen analysis should be performed by the sperm bank, which should be assessed to ensure viable sperm has been frozen before starting cancer treatment, if time allows. Oncology centers that treat AYA patients should develop a system for offering sperm banking to all AYA patients in a systematic and patient-centered manner.
- Should the patient have any medical, religious, emotional, or developmental issues that preclude traditional ejaculation methods, alternative methods, including PDE5 inhibitors, vibratory stimulation, electro-ejaculation, and collection of retrograde ejaculate can be considered.[185]
- Testicular transposition out of the field of radiation can be considered for patients in whom the radiation field will include the testes.[223]
- Surgical sperm extraction, such as the TESE procedure, may be an alternative strategy for those who cannot ejaculate or who have azoospermia or insufficient sperm in the ejaculate to freeze.[185]
- Discuss the effects of treatment on gonadal hormone function. Screen or refer the patient to a specialist as appropriate after completion of treatment.[224]

Contraception in AYA Patients with Cancer

The NCCN Guidelines recommend discussion about sexual function before, during, and after treatment; this should include a discussion on the use of contraception.[225,226] Condoms may be used safely by AYAs with cancer.[227] AYAs with ovaries have unique contraception needs and the options are dependent on the type of cancer, its treatment, and treatment-related complications.[225]

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.[228] LARC has been shown to be superior to short-acting contraceptives.[229,230] In a study of 4167 participants (aged 14–45 years), LARC was associated with higher 12-month adherence rates than oral contraceptive pills (86% vs. 55%).[229] In a large, prospective study involving 7487 participants, 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 progression rates among participants <21 years were twice as great as in those ≥21 years.[230]

The Society of Family Planning guidelines recommend the use of IUDs or implantable contraceptives for most females who are receiving treatment for cancer.[231] The use of any method of contraception is recommended for those who have been free of cancer for at least 6 months and have no history of hormonally mediated cancers, chest RT, anemia, osteoporosis, or venous thromboembolism (VTE).[231] The use of IUDs is considered the preferred first-line contraceptive option for females with a history of breast cancer, although for those treated with tamoxifen, a levonorgestrel-containing intrauterine system (IUS) may be preferable since it has been shown to reduce tamoxifen-induced endometrial changes without increasing the risk of breast cancer recurrence. A levonorgestrel-containing IUS may also be used to minimize menstrual blood loss in patients with iron-deficiency anemia.[231]

Due to the risk of VTE associated with the use of combined hormonal contraceptive methods, the U.S. Centers for Disease Control and Prevention (CDC) recommend that the use of these contraceptive methods should be avoided in patients of childbearing potential with active cancer or who have been treated for cancer in the last 6 months.[232,233]

Management of Cancer During Pregnancy

All patients of childbearing potential must receive a pregnancy test prior to initiating therapy. Cancer is diagnosed in about 0.1% of pregnant individuals and is the second most common cause of maternal death during pregnancy.[234] Melanoma, breast cancer, cervical cancer, lymphomas, and leukemias are the most common cancer types diagnosed during pregnancy.[235-239] HL is the most common hematologic malignancy diagnosed during pregnancy, and accounts for 6% of cancers occurring in pregnancy.[237] An analysis of 1963–2007 data from the Swedish Multi-Generation Register and the National Cancer Register showed a lower-than-expected number of cancers diagnosed during pregnancy, and a rebound in the number of instances of melanoma, CNS cancers, breast cancer, and thyroid cancer in postpartum individuals.[238] This rebound may be due to changes in the mammary and thyroid glands being overlooked during the postpartum period. Despite some persisting beliefs, there is no evidence of pregnancy-associated relapse in survivors of HL.[240]

While there is limited research on the prognosis of cancer during pregnancy, a few meta-analyses and systematic reviews have suggested that the prognosis of certain cancers (eg, breast, melanoma, vulvar) may be worse when occurring concurrently with pregnancy compared to the same cancers occurring outside pregnancy.[241-244] These results may be confounded by factors related to the patient's pregnancy, delays in

diagnosis, and differences in treatment decisions, making a definitive conclusion difficult. Maternofetal transmission of cancer across the placenta is rare, but has been reported for metastatic melanoma,[245] lung cancer, and certain hematologic malignancies.[239,246-249] Most cancers can be adequately treated with medication that is safe for both the pregnant patient and the fetus. However, full counseling about all options regarding the pregnancy, including termination per patient preference or to expedite use of necessary teratogenic medication should be incorporated in all cancer treatment discussions for pregnant AYA patients.

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.[250-252] When possible, non-radioactive imaging modalities, including MRI and ultrasound, should be used.[239] There is insufficient evidence regarding the safety of gadolinium-based contrast agents in pregnant individuals; however, these agents have been demonstrated to cross the placenta in animal studies.[239,252] There are currently no available data on the safety of iodinated contrasts during pregnancy. Surgery is possible at any time during pregnancy depending on the anatomical location of the tumor, although it may be beneficial to delay surgery, when possible, until after fetal viability due to the associated risks including miscarriage, low birth weight, and premature delivery.[239,250,252] Selection of an appropriate treatment plan for pregnant individuals is dependent on the cancer type, tumor biology, and tumor stage, similar to the management of cancer in those who are not pregnant. In addition to the disease characteristics in pregnant individuals, the gestational age of the fetus is a significant factor in the selection of treatment.[250]

RT is contraindicated during pregnancy.[253] However, in very rare instances when it is necessary, such as oncologic emergencies like spinal cord compression, superior vena cava compression, and brain metastases,[254,255] RT may be administered in the lowest effective therapeutic dose (using techniques such as uterine shielding to minimize fetal exposure), with the goal of controlling maternal cancer and providing the fetus with the best chance for survival with normal development.[256] 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.[256] Early collaboration among the radiation oncologist, medical physicist, medical and/or surgical oncologist, and obstetrician is essential. The American College of Radiology has developed guidelines with an objective to assist practitioners in identifying pregnancy, preventing unnecessary irradiation of pregnant AYAs, 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.[257] In 2014, an international consensus panel made up of researchers and clinicians who are experts in cancer treatment during pregnancy developed similar guidelines for RT in individuals who are pregnant.[251]

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.[252,258-261] While the use of chemotherapy during the second and third trimesters has not been associated with significant teratogenic effects, it may be associated with maternal and fetal risks including low birth weight, preterm labor, and intrauterine growth restriction.[237,258,260,262-264] However, a multicenter, prospective case-control study of children born to those with cancer (129 cases, 129 controls) showed no significant impact of chemotherapy treatment on cognitive, cardiac, and general development of the offspring.[265] Potential benefits and risks of chemotherapy for both the pregnant individual and fetus must be carefully evaluated prior to initiation of treatment. Delaying treatment until after fetal maturity, with

careful follow-up to rule out disease progression, is a safe option for those diagnosed with early-stage cancers.[266,267] In some individuals diagnosed with advanced-stage disease with an urgent need to start chemotherapy in the first trimester, pregnancy termination may be considered and the potential teratogenic risks should be discussed if the pregnant individual decides to continue with the pregnancy.[237,239] Due to the severe teratogenic effects of methotrexate, it should not be used for the treatment of cancer in individuals at any stage of pregnancy.[260] Older-generation alkylating agents (eg, procarbazine, busulfan), thalidomide, lenalidomide, pomalidomide, and tretinoin are also considered teratogenic and are contraindicated during pregnancy.[251] The safety and efficacy of hormonal agents and targeted therapies have not yet been evaluated in well-controlled studies including those who are pregnant.[250-252,268-270] At the present time, the use of such agents in patients who are pregnant is not recommended.

Supportive care for the management of treatment-related side effects should be integrated into treatment planning based on the trimester of pregnancy. Granulocyte colony-stimulating factors for the management of neutropenia and antiemetics for the management of nausea and vomiting have been used in patients who are pregnant without any significant side effects.[251,269,271,272]

The Panel members acknowledge that the management of cancer during pregnancy poses significant diagnostic and therapeutic challenges for the pregnant individual, fetus, and physician. The guidelines recommend that AYA patients diagnosed with cancer during pregnancy receive individualized treatment from a multidisciplinary team involving medical, surgical, radiation and gynecologic oncologists; obstetricians; and perinatologists as appropriate.[237,251] Referral to tertiary cancer centers with expertise in the comprehensive care of high-risk obstetric cases and in the diagnosis of cancer during pregnancy and knowledge of the physiologic changes that occur during pregnancy is strongly encouraged.

Several of the NCCN Guidelines for cancers that are diagnosed more commonly during pregnancy include disease-specific recommendations for managing cancer during pregnancy. For more information, see *Breast Cancer During Pregnancy* in the NCCN Guidelines for Breast Cancer; *Cervical Cancer and Pregnancy* in the discussion section of the NCCN Guidelines for Cervical Cancer; *Management of CML During Pregnancy* in the NCCN Guidelines for Chronic Myeloid Leukemia; and *Special Considerations in the Treatment of Polycythemia Vera and Essential Thrombocythemia: Pregnancy* in the NCCN Guidelines for Myeloproliferative Neoplasms. The American Academy of Dermatology has published recommendations for the diagnosis and management of melanoma during pregnancy.[273] Similarly, the American Cancer Society has published guidelines for the management of HL in pregnancy.[274] Finally, the American Thyroid Association has published guidelines for the diagnosis and management of thyroid disease, including thyroid cancer, during pregnancy.[275]

Comprehensive Psychosocial and Behavioral Issues

AYA patients diagnosed with and treated for cancer have psychosocial and behavioral issues that are distinct from those of pediatric and adult patients.[2,7-10] AYA patients aged 20 to 29 years are significantly less likely to use professional mental health services than teens and patients aged 30 to 39 years. AYA patients in the 20- to 29-year-age group are also significantly more likely to report an unmet need with regard to receiving age-appropriate information about their cancer. Some of the challenges faced by AYA patients and survivors include maintaining an active and independent lifestyle, coping with treatment-related side effects and stress, seeking and understanding information, accepting cancer, and maintaining a positive attitude.[276,277] AYAs go through developmental

stages marked by rapid changes in cognitive and emotional growth, and these issues need to be considered while delivering developmentally appropriate psychosocial and supportive care to AYA patients.[278]

Few measurement tools have been developed to better understand health-related quality of life in AYA patients with cancer.[2] Palmer and colleagues developed an AYA Oncology Psychosocial Screening Tool to assist clinicians in supporting psychosocial coping during active treatment and promoting healthy post-treatment survivorship in AYA patients. This screening tool has four main areas: a distress thermometer, a checklist of "areas of concern," a tick box for information provision, and signatures. Further validation of this tool and its use will help clinicians to improve psychosocial care for AYA patients, regardless of where they receive treatment.[279]

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

Individual Function

Psychosocial Issues

AYA patients have to cope with cancer treatment while attaining key developmental milestones such as identity development, including sexual identity; peer involvement; initiating intimate and emotional relationships; establishing autonomy from parents; maintaining personal values; fostering self-esteem and resilience; and independently making decisions about their future that involve education, career, or employment.[280-283] 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 may have negative consequences for their long-term career opportunities, financial status, and lifetime earnings.[276] 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.[284] Physical and/or occupational therapy may help AYA patients transition back to a lifestyle appropriate for their age group.[285] Additionally, patients should be evaluated for past trauma history, including adverse childhood experiences (ACEs), medical-related trauma, and abusive relationships.

Integral to the comprehensive care of individuals with cancer, including AYAs, is an assessment for gender expression, gender identity, preferred pronouns, and sexual identity. SGMs, or the lesbian, gay, bisexual, transgender/transsexual, and queer/questioning (LGBTQ) community, are a population that is unrepresented in medicine. This group includes a spectrum of identities; a comprehensive list of acronyms, definitions, and additional resources may be found on the NIH website (https://www.edi.nih.gov/our-communities/sexual-and-gender-minority), overseen by the NIH Sexual & Gender Minority Research Coordinating Committee. The terms "lesbian," "gay," and "bisexual" denote one's sexual orientation or attraction.[286] According to the NIH, the term "sex" is meant to refer to one's chromosomal makeup and reproductive anatomy and is most often delineated as either male or female. Intersex refers to those individuals whose sexual anatomy or chromosomal constitution does not adhere to the norm (eg, Klinefelter syndrome, or the presence of XXY chromosomes).[287] Gender, however, is understood to be the integration of social, environmental, cultural, and behavioral factors and encompasses terminologies including gender identity, gender norms, and gender relations.[288]

It is estimated that approximately 3.4% to 12% of the U.S. population identifies as LGBTQ. SGMs experience significant inequity related to cancer diagnosis and treatment. Proposed reasons for this incongruity include decreased rates of cancer screening, behavioral risk factors (eg, increased rates of smoking and alcohol use), obesity and decreased exercise, nulliparity (among SGM assigned female at birth [AFAB]), and receptive anal sex (among SGM assigned male at birth [AMAB]). The SGM population also faces numerous health care discrepancies, such as significant discrimination, poorer insurance coverage, and inadequate physician knowledge of specific LGBTQ health needs, leading to psychological ramifications and overall dissatisfaction with treatment.[289] In a nationwide online survey of 273 LGBTQ individuals who had been diagnosed with cancer, patients reported to be influenced by provider LGBTQ knowledge and skills, perceived safety of the clinical encounters for the purpose of identity disclosure, and inclusion of members of their support system. SGM patients reported having a variety of clinical experiences and were more likely to be self-advocates of their care.[290]

The prevalence of cancer risk factors, such as tobacco use, differs among LGBTQ individuals when compared to non-LGBTQ persons. A cross-sectional online survey reported that LGBTQ individuals disclosed higher rates of past 30-day tobacco media exposure and had higher odds of past 30-day use of tobacco products when compared to non-LGBTQ individuals.[291] In addition to the increased prevalence of certain risk factors and a greater physical disease burden, SGM individuals are more likely to have mental health concerns. Attributable to a number of factors, when compared to heterosexual persons, SGM individuals are twice as likely to be depressed, 2.5 times as likely to attempt suicide, and are at an increased risk for anxiety and other psychological conditions.[292] Similarly, LGBTQ individuals are at an increased risk for self-harm or non-suicidal self-injury.[293]

A higher incidence of bullying is reported among youth and AYAs. This figure is even higher among LGBTQ youth, who report more accounts of physical and cyberbullying. In fact, it has been reported that 80% of LGBTQ adolescents have experienced victimization and harassment by peers.[294] Inequity also exists within SGM subpopulations. For instance, nonbinary individuals, or those who do not identify as strictly male or female, reported a higher incidence of bullying (86.7%) and polyvictimization than transgender or LGBTQ cisgender individuals.

Seven cancer sites have been reported to disproportionately affect the LGBTQ population for a variety of theorized reasons: anal, breast, cervical, colorectal, endometrial, lung, and prostate cancers.[286] In a survey of 388 oncology providers at a single institution, 91.7% of physicians specializing in the aforementioned seven cancer sites reported that they would be comfortable treating LGBTQ individuals and would encourage education of unique health matters. However, only 49.5% of providers answered LGBTQ health-related knowledge questions correctly.[286] Among 149 respondents to a survey conducted among 450 oncologists from 45 NCI-Designated Cancer Centers, while 95.3% reported that they were comfortable treating lesbian, gay, bisexual (LGB) individuals, only 53.1% were confident in their assessment of the health care needs of the LGB population. The percentage was even lower for oncologists who were comfortable treating transgender patients (82.5%), with only 36.9% being confident in their ability to understand the health needs of transgender individuals.[289]

It is therefore imperative that providers recognize the gravity of their role when caring for SGM AYAs. Members of the oncology care team must work collaboratively to create an inclusive, safe, and comfortable space to facilitate conversation with LGBTQ individuals surrounding gender, sexual orientation, sexual behaviors, and other relevant experiences.[294] Support persons, as identified by SGM patients, may be involved in cancer care as

appropriate. Referrals for psychosocial support should be initiated as appropriate and referrals to a specialized gender clinic should be considered for transgender youth.[295,296] Recognizing that members of the SGM population face significant health and health care inequities and unique psychosocial issues, providers must develop a thorough and comprehensive understanding of such matters and consider cancer screening as appropriate.[297] Research also suggests that LGBTQ individuals have to navigate addressing unique survivorship issues, including but not limited to arranging follow-up care and coming out to multiple providers, contemplating the effects of systemic therapy on LGBTQ sexuality, and coping with delicate family and relationship issues.[298] Awareness and a thorough understanding of such concerns are required for the care of SGMs.

Emotional Issues

Cancer-related issues such as confrontation with mortality and loss of fertility can result in significant emotional distress and psychiatric symptoms such as depression and anxiety in AYA patients. These feelings are related to patients' cognitive capacity to understand the severity of their disease while sometimes lacking fully mature cognitive and emotional coping abilities.[276] Psychological distress is significantly greater among AYAs compared with older adults[299-303] and prescription rates of anxiolytics and hypnotics are higher in AYA survivors compared to their peers, suggesting an increased emotional burden.[304]

In a longitudinal study that assessed the prevalence of psychological distress in 215 AYA patients with cancer (aged 15–39 years) during the first year following diagnosis, distress symptoms exceeded population norms at the time of diagnosis and at 12-month follow-up.[300] 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. Distress is also prevalent in AYA cancer survivors; however, most AYA survivors with distress reported that they had not spoken with a mental health professional (74.7% with moderate distress, 52.2% with severe distress).[305]

In addition to distress, depression and anxiety are commonly experienced by AYA cancer survivors. An analysis from the Childhood Cancer Survivor Study (CCSS) showed that survivors of AYA cancer (n = 2589) report higher rates of depression (OR, 1.55; 95% CI, 1.04–2.30) and anxiety (OR, 2.00; 95% CI, 1.17–3.43) compared to their siblings (n = 391).[306] Another study of 5341 cancer survivors diagnosed at ≤25 years found that survivors were more likely to be prescribed antidepressants compared to age- and gender-matched controls (26.9/1000 person-years for survivors vs. 22.5/1000 person-years in controls; HR, 1.19; 95% CI, 1.12–1.28).[307]

The need for information, counseling, and practical support was reported in 57%, 41%, and 39% of AYA patients, respectively, at 12 months after cancer diagnosis.[302] Kazak and colleagues reported that intensive cancer treatments during adolescence are associated with inferior psychosocial outcomes and health beliefs in survivors compared to their age-matched peers.[308] 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.[309] It is therefore recommended that AYAs diagnosed with cancer meet with child life specialists, if available, soon after diagnosis to address concerns that the patient may have regarding treatment or procedures and assist with coping mechanisms to reduce anxiety.[310]

Behavioral Issues

AYA patients with cancer may engage in risky behaviors (tobacco, alcohol, cannabis, or substance use) that may impair their health. Advanced 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.[311] The risk factors associated with alcohol use included fair or poor self-assessed health, depression, anxiety, somatization, activity limitations, and cancer-related fears and uncertainty.[312] Low perception of susceptibility to late effects, older adolescence compared to early adolescence, and worry about cancer and its treatment were the strongest predictors of substance use.[313] While AYA patients may be aware of the complications associated with tobacco, alcohol, cannabis, or use of other substances during their treatment, they may not avoid them throughout treatment as these habits may make them feel "normal" and like part of their peer group. Clinicians working with this population should be aware of such matters and address these issues in a sensitive and confidential manner.[284,314]

Studies have shown increased rates of mental illness and cognitive impairment among adolescent cannabis users compared to adults with similar usage habits.[315] Heavy or regular use of cannabis in adolescents has been associated with impairments in attention, learning, memory, planning, and psychomotor speed. An earlier age of onset of cannabis use exacerbates these adverse effects. If an AYA patient chooses to continue use of cannabis, education on methods for lowering risk of adverse effects is recommended. For example, the patient may be counseled to avoid high tetrahydrocannabinol (THC)-content products, avoid synthetic cannabinoids, choose routes of administration other than inhalation of combusted cannabis, limit frequency of use, and never drive while impaired.[316] Additionally, as there are insufficient data, it is uncertain whether cannabis affects the metabolism and efficacy of chemotherapeutic agents.

In 2006, e-cigarettes, or vaping products, were introduced to the U.S. market.[317] Marketed originally as tools for smoking cessation and safer alternatives to cigarettes, the aerosols of these products are now known to contain active compounds, including nicotine, THC, cannabidiol, vitamin E acetate, and select flavorings and additives. It is reported that among youth, the overall use of nicotine-containing products has increased since the release of e-cigarettes and devices such as the JUUL. Past 30-day vaping among U.S. high school students rose from 1.5% in 2011 to 20.8% in 2018. Alarmingly, past 30-day e-cigarette use among U.S. middle school students increased from 0.6% in 2011 to 4.9% in 2018.[318] The CDC and U.S. Food and Drug Administration (FDA), as well as other health authorities, have reported an extensive number of e-cigarette or vaping use-associated lung injury (EVALI) cases since 2019. Many patients (the majority of whom have been AYAs) have been hospitalized, with several requiring intensive care and respiratory support.[319,320]

AYA patients are also vulnerable to sexual and reproductive health complications that should be addressed prior to, during, and after completion of treatment.[225] Traditional risk-taking behaviors of AYAs coupled with a compromised immune system may put AYA patients with cancer and survivors at a greater risk of sexually transmitted infections and, in certain cases, malignancy. See the section on *Contraception in AYA Patients with Cancer* for more discussion of appropriate contraception choices for patients with cancer and survivors.

Consequent to treatment and lifestyle-related factors, it is reported that AYAs have a 5- to 15-fold increased risk of cardiovascular morbidity when compared to the general population.[321] Therefore, lifestyle and diet modification are key in AYA cancer survivors to increase survival. AYA patients have nutritional concerns that are different from those of children and adults, especially among younger patients in this population. Adolescents are dependent on their families for food preparation and may experience peer pressure when eating at school or with friends. The INAYA trial, consisting of AYAs aged 18 to 39 years, reported improved nutritional behavior among AYAs following intensified individual nutrition counseling during a 3-month period. Diet/nutrition information has thus

been reported as an unmet need among AYA patients.[8] Promotion of healthy lifestyle behaviors and incorporation of physical activity into treatment regimens and post-treatment follow-up may also produce numerous physical and psychological health benefits.[322,323] Regular physical activity integrated into AYA cancer care may also decrease cancer-related fatigue.[324]

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

- Refer AYA patients for neuropsychological assessment if there are concerns regarding cognitive function (eg, attention, memory, executive function) and/or prior to educational and career transitions, including returning to school/work after treatment.
- Child life specialists or appropriate psychosocial support specialists (if available) should meet with the patient soon after diagnosis to address any potential concerns regarding treatment or procedures and assist with coping mechanisms to reduce any potential anxiety.
- Consider a referral to a social worker, mental health provider, and community-based resources serving AYA patients to screen for any symptoms of depression, anxiety, suicidal ideation/behaviors, and self-injurious behavior.
- Offer psychosocial support and counseling to help alleviate distress. See the NCCN Guidelines for Distress Management.
- Consider providing flexible treatment dates, consultation times, and procedures when possible to enable AYA patients to continue with their treatment without interrupting their school/work or other normal activities.[284]
- Refer patients for educational and career services to address training/education, employment, disability disclosure, vocational adjustment training, and transition services (ie, social services, vocational counseling, occupational therapy, financial counselors).
- For all AYA patients, provide counseling around sexual health conversations and decision-making regarding the risks of treatment-related fertility impairment and discuss the options for fertility preservation prior to initiating treatment.[325]
- For lesbian, gay, bisexual, transgender, queer (or questioning), intersex, asexual, two-spirit (LGBTQIA2S+) AYAs, consider offering psychosocial support and referrals surrounding stressors, stigma, or rejection related to their sexuality or gender identity.
- Ensure that the record system accurately reflects the patient's pronouns and preferred name. For transgender youth, consider referring the patient to a specialized gender clinic for psychosocial support and coordination of gender-affirming medical care at the patient's discretion.
- Refer patients to legal services, if applicable, for estate or legacy planning, child custody concerns, or other legal issues.
- Refer patients to a smoking cessation program if needed (see NCCN Guidelines for Smoking Cessation).
- Provide education about the impact of early cannabis use on cognitive development and mental health. If the AYA patient chooses to continue use, provide education on the risks and benefits of varying methods of ingestion and dosing.
- Refer patients with signs, symptoms, or a history of a substance use to a risk reduction or substance use counseling program.
- Provide education about the impact of treatment on sexual health, including safe sexual practices in light of risk of infection, risk for bleeding, and prevention of pregnancy.
- Since the incidence of sexually transmitted infections peaks among AYAs aged 15 to 24 years, provide preventive health education about sexually transmitted diseases.[284]

- Provide education about potential diet/nutritional changes associated with cancer treatment and possible interventions. Refer to a Registered Dietitian-Certified Specialist in Oncology (RD-CSO).[326]
- Provide education on physical conditioning and its related health benefits during and following cancer treatment. To address physical impairments and to initiate physical activity interventions, refer AYAs to a rehabilitation specialist (ie, physiatrist, physical therapist, occupational therapist). Note that a medical evaluation and clearance by a physician (such as an oncologist or physiatrist) are recommended before initiating exercise in patients for whom exercise modifications or precautions may be needed.
- Evidence-based integrative therapies/interventions can be considered.
- Refer patients experiencing challenges with their faith or belief in a just or fair world to faith-based resources or activities (eg, church youth groups, mentors).[9,327] Refer to a chaplain or spiritual counselor.
- If appropriate, consider referral to palliative care.

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, caregiver, and/or peer group.[284,328] Isolation and alienation are common among AYAs diagnosed with cancer, because they often miss out on the life experiences shared by their non-ill peers. Reinforcing relationships with family members, caregivers, peers, and health professionals is an important aspect of life for AYA patients.[278,329]

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.[9,278] In one study, AYA patients with cancer (aged 16–22 years) identified social support (including family members, friends, health care providers, and other patients) as their major coping strategy.[330] In another study, some AYA patients and survivors reported that opportunities to meet other young adult survivors were more important than the support they received from family and peers.[325]

Peer support programs assist AYA patients and survivors in establishing and maintaining relationships with their healthy peers as well as with other AYA patients with cancer, offer opportunities to achieve age-related developmental tasks (building interpersonal and problem-solving skills), and promote positive psychosocial growth.[325,331] Peer support also provides AYA patients with an opportunity to address areas of shared concern, such as uncertainty about the future, establishing autonomy while being increasingly dependent on family and friends, sexual identity, and impaired fertility, thereby reducing feelings of social isolation.[331]

AYA peer support groups have been developed in a variety of formats, including face-to-face meetings, camp style formats, or online support groups.[332,333] Social networking groups focused on supporting AYA patients are particularly helpful for exchanging support, informational and emotional, through providing advice and empathizing with other AYA patients dealing with cancer.[333] Summer camps and adventure programs where participants are physically challenged have resulted in improvements in self-confidence, independence, and social contacts.[9,332] 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.[9] 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.[334,335]

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.[27] While some patients prefer not to receive direct communication about their cancer, others may desire a more prominent role in their comprehensive care. For the latter group, information should be provided directly to patients in a developmentally appropriate manner, allowing time to process the information and deliver information in a caring manner.[336] 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.[284] 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.[337] Since there is evidence that AYA patients are willing to use the internet to obtain health information and support, it is also helpful to provide them with a list of recommended and reliable age-appropriate online sources to access information about their cancer, particularly with regard to treatment and late effects, fertility preservation, mental health counseling, peer support groups, diet, and nutrition.[332,335,338] See *Online Resources for Patients and Survivors*.

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

- Promote collaborative communication between AYA patients and parents, caregivers, children, spouse/partners, other family members, siblings, friends, and/or social network.[28]
- Encourage early in the treatment process the completion of a medical power of attorney/health care proxy and a living will at age of majority.
- Provide access to AYA-specific advanced care planning guides to determine a health care proxy.
- Provide information to identified family members, caregivers, and partners about psychosocial support and supportive services to increase awareness of the possible psychosocial issues associated with cancer diagnosis in AYAs.
- Provide AYA-specific activities and/or support groups (in person and/or virtual), especially for inpatients, to provide psychosocial support and reduce boredom, anxiety, and depression. Such interventions include AYA support groups, social and recreational programs, and psychoeducational programs.
- Consider family-based intervention models from pediatrics (eg, parent support groups, Impact of Traumatic Stressors Interview Schedule).[17]
- Provide information about peer support and social networking opportunities and create flexible visiting hours and an environment that will encourage peers to visit AYA patients.[284]
- Establish direct communication with the individual patients, providing developmentally appropriate information about their cancer, treatment options, and potential side effects, thus reinforcing the importance of AYA involvement in decision-making.[27,325]
- Some AYA patients prefer not to share information about their cancer with their family in an effort to shield their family members or caregivers from some of the things they themselves worry about. Therefore, obtain their permission to share information with identified family members or other members of their support system, and encourage completion of a health insurance portability and accountability act (HIPAA) release form.
- Provide psychoeducation and assistance exploring and documenting advance directive preferences.

- If the AYA patient is >18 years, provide information on and the necessary forms that legally allow medical information to be shared with caregivers of the patient's choice.
- Always conduct medical and psychosocial care in the language preferred by the patient, family, or caregiver. Use certified interpreters and do not rely on family members, caregivers, friends, or non-certified medical staff for interpretation.

Socioeconomic Issues

AYA patients, ≥26 years, are much more likely to be uninsured or underinsured individuals than adults or children, with many of them in a transition between their parent's insurance and their independent insurance.[17,73] 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.[339] An analysis of 9353 AYA patients with HL showed that having either public or no health insurance was associated with poorer HL-specific survival, compared to patients with private or military insurance (HR, 2.08; 95% CI, 1.52–2.84).[340] Furthermore, unemployment and lack of health insurance appear to be significant predictors of psychological distress in the childhood cancer survivor population.[341] Uninsured AYA patients are also less likely to participate in clinical trials.[90] 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.[74] 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.[276] Results from the AYA HOPE study, a population-based cohort study of 523 AYA patients with cancer (aged 15–39 years at diagnosis from 2007–2009), suggest that lack of health insurance is also associated with poor health-related quality of life among AYA patients with cancer.[342]

Financial toxicity is a concern, as AYA patients with employment also experience problems in obtaining affordable health and life insurance due to their pre-existing cancer history.[9] Even those with relatively comprehensive insurance may be liable for substantial out-of-pocket expenses related to treatment, such as transportation costs associated with traveling for treatment, accommodations, meals, and child care as well as expenses not related to treatment.[9] AYA patients who are financially independent also have to face an additional burden of loss of income because of their inability to work during treatment. Once treatment is completed, AYA patients with cancer also require long-term follow-up care for monitoring and treatment of late effects.

NCCN Recommendations for Supportive Care Services/Interventions for Socioeconomic Issues

- Assess AYA patients' health insurance status and provide information on potential sources of coverage (eg, Medicaid, Health Insurance Marketplace [https://www.healthcare.gov/], parent's insurance) and other key elements associated with insurance coverage.
- Educate AYA patients about the benefits for which they may qualify (eg, short- or long-term disability, state disability benefits, Social Security benefits, public assistance).
- Provide information regarding drug assistance programs for patients with limited or no insurance. Consider also providing information regarding hospital pharmacy vouchers or low-cost medication programs.
- Provide information on obtaining financial assistance for fertility-based services. Local and institutional grants may be available.
- Provide school support and education services for patients in high school or college.
- Refer patients for career counseling and/or education support as indicated. Encourage discussion with guidance counselors and educators about the impact of cancer care on education.

- Refer to mental health expert as needed to assess the psychosocial impact of financial toxicity (eg, loss of employment, withdrawing from school, not being able to socialize with friends due to decreased income).
- Direct AYA patients to legal resources and/or advocates for assistance with understanding health insurance coverage.
- Provide a referral for transportation assistance programs (eg, van ride programs, voucher programs) for AYA patients who have to travel to receive treatment. Identify resources for respite care that would be helpful for those with young children.
- Provide information about recommended and reliable online resources and financial support programs to access information related to their cancer.
- Integrate financial assistance for AYA cancer survivors into their survivorship care plans.
- Consider the need for long-term follow-up care for monitoring and treatment of late effects long after treatment has been completed.

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.[343-345] 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).[346,347] Improvements in RT and surgical techniques may help reduce late effects.[348]

Much of the understanding of the long-term outcomes of AYA cancer survivors comes from the Childhood Cancer Survivors Study, which includes long-term survivors of childhood and adolescent cancers who were diagnosed prior to age 21 years.[349,350] 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 ages 15 and 20 years are particularly relevant for the NCCN Guidelines for Adolescent and Young Adult Oncology. Among adult survivors of childhood and adolescent cancer, Oeffinger and colleagues 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.[349]

Other 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.[351-354] In a 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.[353] Other analyses of survivors of young adult cancers showed that hospitalization rates are highest for survivors of upper gastrointestinal cancer, leukemia, urologic malignancies, brain cancer, and HL.[355,356]

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.[351] In another large cohort study that included adult cancer survivors (245 patients, aged 15–19 years and 12 patients, aged 20–24 years at the time of diagnosis), impaired organ dysfunction (pulmonary, auditory, endocrine, and nervous system) was the most prevalent of all the adverse health outcomes.[352] In a report that evaluated the quality-of-life outcomes in 8375 AYA cancer survivors (diagnosed with cancer between ages 15–39 years) relative to the same aged controls, AYA cancer survivors were two 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.[354]

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.[351]

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

Secondary Cancers

AYA cancer survivors (aged 15–39 years at the time of diagnosis) are at significant risk of developing a variety of secondary cancers compared to the general population,[36,357] as well as cancer survivors diagnosed during either childhood or older adulthood.[37] Although secondary cancers may be caused by a hereditary syndrome, they are thought to be largely caused by treatment exposure.[348] The risk and specific types of secondary cancers are widely dependent on the type of initial cancer diagnosis and treatment exposure,[358-360] although the most common secondary malignancies are breast cancer, gastrointestinal cancer, genital cancers, and melanoma.[37] RT exposure is particularly associated with risk of secondary cancers.[37,357] In a retrospective matched cohort study consisting of 10,574 AYA cancer survivors, the 20-year cumulative incidence of SMN was found to be 12.5%. An elevated risk for SMN in the same site as the primary neoplasm was noted in AYA survivors of breast cancer, melanoma, and testicular cancer. In this study, risk factors for SMN were found to be older age at diagnosis, female sex, white race/ethnicity, advanced stage at first cancer diagnosis, and treatment with RT. Finally, AYA cancer survivors diagnosed with SMNs were found to have a 7-fold increased mortality risk compared with those who did not develop SMNs, highlighting the importance of SMN surveillance as appropriate in the AYA population.[38]

AYA survivors of HL diagnosed between ages 21 and 39 years are at an increased risk of developing secondary cancers.[359] The most frequently observed secondary cancers are breast, lung, thyroid, and gastrointestinal cancers.[346] AYA patients 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.[103,361-363] In a cohort of 770 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).[361] In an international, population-based study of 3817 HL survivors diagnosed at ≤30 years of age, Travis and colleagues reported that for those treated at age 25 years with a chest RT dose of at least 40 Gy without alkylating agents, the estimated cumulative absolute risk of

developing breast cancer by age 35, 45, and 55 years was 1.4%, 11.1%, and 29.0%, respectively.[362]

Alkylating agent-based chemotherapy for HL has been associated with a modestly increased risk for secondary lung cancers in patients diagnosed at ≤40 years, and the risk increased with both increasing number of cycles of alkylating agents and the cumulative dose.[364] 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 5798 patients diagnosed with HL between 15 and 34 years of age, the 20-year cumulative risk of secondary cancer was 13% and 18%, respectively, for chemotherapy alone and combined modality therapy.[365] 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.[365]

AYA survivors of testicular cancer are also at a significantly increased risk of developing secondary cancers, including contralateral testicular cancer, leukemia, malignant mesothelioma, and cancers of the lung, colon, esophagus, stomach, and pancreas.[366,367] 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.[368] 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 age 35 years (36% and 31%, respectively).[369] 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.[369] 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 HCT.[370] 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.[371] 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.[372-374] 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 secondary cancer was higher among patients diagnosed before age 50 years than among those diagnosed after age 50 years (22.2% and 16.4%, respectively).[372] In a population-based cohort of 376,825 one-year survivors of breast cancer from the Scandinavian cancer registries, patients diagnosed at ≤40 years with localized disease were particularly at risk of developing a secondary cancer at 30 or more years after breast cancer diagnosis.[373] 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 ≥40 years at the time of diagnosis.[374] In the Surveillance, Epidemiology, and End Results (SEER) database analysis of 89,515 melanoma survivors, patients diagnosed at <30 years had the highest risk of developing secondary cancers (with breast, prostate, and NHL being the most common cancers) at more than 20 years after initial diagnosis. HCT and RT to head and neck also increased the risk of subsequent cancers in the oral cavity.[375]

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 tumors were the most common secondary cancers (24%) followed by thyroid cancer (22%). For patients who survived for at least 5 years after initial diagnosis, the cumulative incidence of secondary cancer at 30 years was 3.9% and 4.3%, respectively, for ALL and AML.[376]

The risk is especially higher among patients diagnosed at a younger age (≤17 years for ALL and CNS tumors; ≤18 years for bone and soft tissue sarcomas).[377] 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 sarcoma compared to those diagnosed with osteosarcoma (9.0% and 5.4%, respectively).[378,379]

Clinicians who provide care for AYA cancer survivors must implement and evaluate methods for improving awareness of SMNs. They must also implement appropriate surveillance strategies for early detection of these malignancies.[380] An annual mammogram and breast MRI for the purpose of secondary breast cancer screening are recommended for survivors treated with a chest RT ≥10 Gy, including those <30 years of age.[381,382] Refer to the NCCN Guidelines for Breast Cancer Screening and Diagnosis for information about breast cancer screening recommendations and the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic for information about individuals who may be at high risk for breast cancer. A colonoscopy, for the purpose of secondary colorectal cancer screening, is recommended (ie, every 5 years or multitarget stool DNA test every 3 years), based on informed decision-making, starting at age 30 years or 5 years after completion of RT, whichever occurs last, for patients treated with abdominal or pelvic RT or TBI. Screening for secondary AML or myelodysplasia should be done by assessing complete blood count (CBC) and bone marrow examination as clinically indicated based on symptoms. Routine endocrine, ophthalmology, and dental evaluation (dental examination and cleaning every 6 months) are recommended for long-term AYA cancer survivors following any treatment exposure to the head or upper neck regions.[375]

Cardiovascular Complications

Cardiovascular complications (including, but not limited to, 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.[383-386] Additionally, lifestyle factors, including poor physical activity and dietary habits, unique to the AYA population increase the risk of cardiovascular mortality.[321] A retrospective cohort study comparing 5673 two-year AYA survivors of cancer to 57,617 controls showed that the cancer survivors were more likely to develop cardiovascular disease (adjusted incidence rate ratio [IRR], 2.37; 95% CI, 1.93–2.93), with risk being highest among survivors of breast cancer (adjusted IRR, 3.63; 95% CI, 2.41–5.47) and leukemia (adjusted IRR, 4.23; 95% CI, 1.73–10.31).[387] A systematic review and meta-analysis of 64 studies of specific cardiovascular late effects in 143,606 survivors of childhood or adolescent cancer reported that the weighted average prevalence was 19.7% for hypertension and 2.3% for stroke in this population.[388]

Mediastinal RT and anthracycline-based chemotherapy are the strongest risk factors for late cardiovascular complications in AYA survivors of HL.[347,389,390] The Children's Oncology Group (COG) Long-Term Follow-Up Guidelines recommend cardiac imaging as appropriate according to the cumulative anthracycline and/or RT dose.[380] In a British cohort study of 7033 patients with HL, the risk of death from MI was highest for patients <35 years at the time of treatment with supradiaphragmatic RT.[390] Patients treated with anthracyclines were at increased risk for MI within 1 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.[390] In another study of 1474 survivors of HL <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.[347] The 25-year cumulative incidence of CHF after mediastinal RT and anthracyclines was 8%. An analysis of 15,815 survivors of childhood cancer, including participants from the CCSS (*n* = 12,407), showed that the anthracycline daunorubicin may be less cardiotoxic than doxorubicin (HR, 0.45; 95% CI, 0.23–0.73).[391] Methods to mitigate anthracycline toxicity include the administration of dexrazoxane, a cardioprotective agent, as well as the use of continuous infusion therapy rather than bolus treatments, the preference for epirubicin or liposomal doxorubicin, and the use of beta-blockers and angiotensin-converting enzyme inhibitors as appropriate.[392-396]

Cisplatin-based chemotherapy is associated with long-term risk for cardiovascular complications in testicular cancer survivors.[397-399,] In a Dutch study of 2512 testicular cancer survivors, non-seminomatous testicular cancer survivors <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.[397] Haugnes and colleagues reported that treatment with cisplatin, bleomycin, and etoposide and/or RT was associated with increased risk for cardiovascular disease in testicular cancer survivors; chemotherapy alone or in combination with RT significantly increased the risk for MI.[398]

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 <21 years at the time of diagnosis.[400] Other reports have also documented increased cardiovascular complications among survivors of lymphoma, brain tumor, leukemia, and testicular cancer.[384,401]

Pulmonary Complications

Analysis of data from the CCSS showed that pulmonary complications (eg, asthma, chronic cough, emphysema, lung fibrosis) are more frequent in survivors (*n* = 20,690) than in sibling controls (*n* = 4027).[402] AYAs must therefore be counseled regarding avoidance of tobacco and smoking cessation as appropriate. Chemotherapy (eg, bleomycin and alkylating agents such as busulfan, carmustine, and lomustine), chest RT, and craniospinal irradiation are associated with pulmonary toxicity and can compromise pulmonary function in AYA cancer survivors.[380,399,403,404] Age at diagnosis (15–21 years compared with age <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.[403] 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.[405] Risk factors for pulmonary toxicity include age at diagnosis, cumulative bleomycin dose, reduced glomerular filtration rate, renal dysfunction, and stage IV disease at presentation.[406] Haugnes and colleagues reported that among 1049 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.[407] 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. Therefore, AYA cancer survivors, particularly those who

received RT and chemotherapeutic agents known to cause pulmonary toxicity, are advised to undergo baseline and interim pulmonary function screening as recommended by the COG Long-Term Follow-Up Guidelines.[408]

Neurologic Complications

AYA survivors of brain tumors and those treated with intrathecal chemotherapy, high-CNS penetrating chemotherapy, and/or cranial RT are at increased risk for neurologic and/or neuropsychological complications, including hearing impairments, cataracts and other vision problems, seizure disorders, migraines, and coordination and motor control problems.[409-416] However, these findings are relevant to survivors diagnosed at ≤21 years. Neuropsychological screening for difficulties in school or work is recommended for all AYA survivors of cancer so that providers identify the need for referral early in the survivorship phase.[417] In particular, patients with brain tumors, or those treated with cranial/craniospinal radiation, intrathecal chemotherapy, and/or high-dose methotrexate, should be referred for neuropsychological evaluation.

Long-term AYA survivors of testicular cancer who were treated with cisplatin-based chemotherapy are at risk for neurologic complications such as sensory neuropathy, tinnitus, hearing impairment, and Raynaud's disease.[399] Among 1814 survivors of testicular cancer included in a Norwegian observational study, Raynaud-like phenomena were the most frequently reported complications (39%), followed by paresthesia of the hands or feet (29%), and tinnitus and hearing impairment (22% and 21%, respectively) by patients treated with chemotherapy compared to those not treated with chemotherapy.[418] The incidences of paresthesia of the feet were also higher among patients treated with RT.

Patients treated with vincristine, docetaxel, or paclitaxel are also at risk for long-term peripheral neuropathy.[419] A cross-sectional study of 80 ALL survivors who had been treated with vincristine found that 33.75% had neuropathy as measured electrophysiologically, although the study reported significant improvement over time.[420] Another study of 37 ALL survivors who had been treated with vincristine reported that 29.7% of patients showed abnormalities in nerve conduction studies.[421] A study of 605 breast cancer survivors at least 2 years out from diagnosis reported that survivors treated with docetaxel or paclitaxel were more likely to experience peripheral neuropathy (31% for docetaxel, 44% for paclitaxel) than those who were not treated with these chemotherapies (17% for no chemotherapy, 20% for other chemotherapies).[422] Routine evaluation for symptoms of peripheral neuropathy is recommended.

Stroke, although relatively uncommon, is a devastating neurologic complication in AYA survivors of brain tumors and leukemia treated with cranial RT and survivors of HL treated with mantle field RT.[413,423-425] In a retrospective cohort study of 5-year survivors of HL (*N* = 2201), those treated with RT to the neck and mediastinum were particularly at increased risk for stroke and transient ischemic attack.[426] The incidences were higher among patients diagnosed at <21 years than those diagnosed between 21 and 30 years. The standardized incidence ratio was 3.8 and 3.1, respectively. In an analysis of CCSS data, out of 271 survivors who reported a stroke, 26% reported a second stroke.[425] Predictors of recurrent stroke included history of brain tumor, exposure to cranial RT (total dose ≥50 Gy), older age at first stroke, and hypertension.[425]

Nephrotoxicity

Long-term renal dysfunction has been reported in survivors of testicular cancer treated with infra-diaphragmatic RT and cisplatin-based chemotherapy. In one study with 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. Screening for renal insufficiency and other renal complications is recommended for those at high risk.

Bladder and Bowel Symptoms

Cancer survivors treated with pelvic RT, especially those administered concurrent cyclophosphamide, are more likely to experience bladder and bowel symptoms. Hemorrhagic cystitis may occur consequent to RT and/or cyclophosphamide administration (now coadministered with mesna in high-dose protocols) and may progress to long-term bladder fibrosis and contracture in some cases.[427] A study of 104 survivors of cervical or endometrial cancer found that the severity of bladder and bowel symptoms were significantly associated with pelvic RT treatment.[428] Two studies of long-term gynecologic cancer survivors (N = 77 and N = 519) found that approximately 12% to 17% of survivors treated with pelvic RT develop symptoms of bowel incontinence.[429,430] Bowel incontinence was associated with the mean radiation dose, with the larger study reporting that mean doses >50 Gy carry the greatest risk.[429] Cancer survivors who experienced bladder and/or bowel incontinence as a result of pelvic RT therapy have reported considerable distress and a decreased quality of life as a result of their symptoms.[428,431] Screening of urinary bladder function may be performed as appropriate.

Endocrine Complications

Cranial and/or spinal RT, TBI, and targeted RT to the neck, abdomen, pelvis, and testes are associated with neuroendocrine late effects in survivors of AYA cancers.[168] The most common endocrine complications include growth hormone (GH) deficiency, thyroid gland abnormalities, gonadal dysfunction, obesity, diabetes mellitus, and decreased fertility.[99,158,432] AYA cancer survivors treated with an RT dose of ≥18 Gy to the hypothalamic-pituitary-adrenal (HPA) axis are at high risk for GH deficiency, whereas those treated with an 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 >30 Gy, whereas in patients treated with lower doses (18–24 Gy) it may not be evident for 10 years or more.[168] Secondary thyroid cancers, hypothyroidism, and, to a lesser extent, hyperthyroidism are more common among AYA survivors of brain tumors, ALL, HL, and those who have undergone HCT.[409,433,434] Testicular cancer survivors treated with chemotherapy and RT are at greater risk for hypogonadism.[399] Low testosterone levels and testosterone replacement have been reported in 34% and 4% of testicular cancer survivors, respectively.[435] In a study of semen variables in 214 adult cancer survivors following alkylating agent administration (measured in cyclophosphamide equivalent doses [CED]), a negative correlation was discerned between increasing CED and sperm concentration. Additional findings included the possibility of azoospermia, oligospermia, and normospermia with CED.[436] Risk of endocrine complications may increase over time, indicating a need for lifelong evaluation and screening as appropriate.[432,437]

Long-Term Follow-up

As discussed above, AYA cancer survivors have a high risk of developing a wide range of late effects. Development of a “Cancer Treatment Summary and Survivorship Care Plan,” including periodic evaluation with focused history, physical examination, and screening based on treatment exposure, and risk for treatment-related late effects, should be an integral part of caring for AYA cancer survivors.[344,438,439] Medical and psychosocial care should be conducted in the language preferred by the patient, their family, or caregiver. Certified interpreters should be used; do not rely on non-certified medical staff or family members, caregivers, or friends for interpretation. Vaccinations are recommended for AYA cancer survivors;

please refer to the NCCN Guidelines for Survivorship for additional guidance on vaccines.

As aforementioned, the screening recommendations included in the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology are adapted from the COG Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers, available at survivorshipguidelines.org.[380] See *Screening Recommendations for AYA Survivors* in the algorithm for specific recommendations based on the treatment exposure and timing and intensity of screening. These recommendations may be adapted based on additional risk factors.

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.[440] 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).[439,441] Some studies have suggested that a shared care model involving both the primary oncology team and the primary care physician is feasible and may facilitate appropriate care in childhood cancer survivors.[442-444] A relationship between the AYA cancer survivor and their primary health care provider for routine health issues is encouraged. Due to the transient lifestyle of the AYA population (ie, attending college far from home, traveling to different locations to establish careers), it is imperative for the initial care team to communicate with the new care team (once established). Young cancer survivors should be screened for risky behavior such as substance use, tobacco/nicotine use, and binge drinking/excessive alcohol use on a regular basis and counseled on cessation. Young cancer survivors should be educated on safe sex practices/contraceptive options if they are not trying to actively conceive regardless of their infertility risk post treatment. AYAs should also be asked about sexual dysfunction on a routine basis and how it may impact interpersonal relationships or self-image.

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.[441,445,446] Survivors at low risk for late effects (treated with surgery alone and/or chemotherapy with no RT, not including alkylating agents, anthracyclines, 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, anthracyclines, 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 HCT, 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 regularly. Cancer survivors with cardiomyopathy, cardiovascular risk factors, and a history of pelvic radiation who become pregnant should be referred to maternal-fetal medicine. The International Late Effects of Childhood Cancer Guideline Harmonization Group has developed additional recommendations on counseling and surveillance of obstetric-related risks in childhood, adolescent, and young adult cancer survivors.[447]

Palliative and End-of-Life Care

Palliative care is interdisciplinary care of patients with life-threatening illnesses, and malignant as well as non-malignant cancer. 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.[448,449] See the NCCN Guidelines for Palliative Care.

Palliative care services for AYA patients should be provided by a team with expertise in understanding the psychosocial, emotional, developmental, and financial issues that are unique to this age group.[448,450-452] Introduction of palliative care for symptom management and psychosocial support should occur before the patient's condition is considered "palliative" in order to provide the best possible care.[453-455] 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.[453] Patients, caregivers, and health care professionals should be taught that palliative care is an integral part of their comprehensive cancer care.[451] AYA patients usually do not make 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, caregivers and/or other family members.[448] Palliative care services should also consider the psychosocial needs of the patient's family members, friends, and caregivers.[453] Patients' goals, dreams, and desires to leave a legacy are important considerations to address.[451]

End-of-life care involves the palliation of symptoms, management of delirium, existential distress, discussion about the place of death, and support of family.[448,451] 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.[456-459] In an exploratory study of 50 adolescent patients (aged 15–21 years) with and without chronic illness, adolescents were willing to discuss end-of-life decision-making by taking part in a one-on-one survey administered by a researcher.[460] The quality of life of AYA patients should be heeded by the care team.[451] 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).

If prognosis is poor, consider initiating a discussion with a palliative care team or hospice services early in treatment to provide continuity of care and support for both the patient and family throughout the cancer experience.[453,454] Discussion about end-of-life preferences and the formulation of an advance directive/advance care planning document should begin at the time of initiating treatment, but details should be individualized according to the preferences of the AYA patient and family.[461] Several retrospective studies have shown that >50% of AYA patients with cancer receive medically intensive care at the end of life, indicating a need for better understanding of care preferences in these patients.[462-464] In one of these studies, a review of the health records of 12,938 deceased AYA patients with cancer showed that 59% of patients received at least one intensive intervention at the end of life and 30% received two or more. Patients treated at non-specialty cancers were more likely to receive two or more intensive interventions than those at specialty centers.[462]

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.[461,465] In one retrospective review, a significant number of adolescents dying of cancer felt that discussions about end of life occurred very close to death, allowing very little time to psychologically prepare for death.[466] Involve child life specialists and/or psychosocial team members to discuss legacy projects and memory work with the patient, their family, or caregivers. Note that the preferred location

of death may be influenced by individual, family, and cultural differences.[467] While many adolescents indicate a preference for dying at home, the majority die in hospitals.[468-470] Others may choose to die in the hospital due to regional scarcities of home hospice, caregiver demand at the end of life, or personal preference.[471] It is critical to make every effort to query and support the patient's preferred location of death.

Clinicians with expertise in end-of-life care should facilitate discussion of difficult medical issues such as nutrition/hydration, sedation, treatment cessation, and place of death.[448] Ongoing psychosocial support is extremely important during the transition to end-of-life care. Clinical teams need to be aware of and work with their palliative care teams with regard to local guidelines for concurrent palliative and cancer-directed care.

Summary

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

References

1. Miller KD, Fidler-Benaoudia M, Keegan TH, et al. Cancer statistics for adolescents and young adults, 2020. CA Cancer J Clin 2020;70:443-459. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32940362.
2. Smith AW, Seibel NL, Lewis DR, et al. Next steps for adolescent and young adult oncology workshop: An update on progress and recommendations for the future. Cancer 2016;122:988-999. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26849003.
3. Wolfson JA, Richman JS, Sun CL, et al. Causes of inferior outcome in adolescents and young adults with acute lymphoblastic leukemia: Across oncology services and regardless of clinical trial enrollment. Cancer Epidemiol Biomarkers Prev 2018;27:1133-1141. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30262597.
4. Bleyer A, Tai E, Siegel S. Role of clinical trials in survival progress of American adolescents and young adults with cancer-and lack thereof. Pediatr Blood Cancer 2018;65:e27074. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29667766.
5. Coccia PF. Don't give up - they eventually grow up: issues in AYA medicine. J Natl Compr Canc Netw 2012;10:1059-1060. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22956804.
6. Tricoli JV, Boardman LA, Patidar R, et al. A mutational comparison of adult and adolescent and young adult (AYA) colon cancer. Cancer 2018;124:1070-1082. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29194591.
7. Abrams AN, Hazen EP, Penson RT. Psychosocial issues in adolescents with cancer. Cancer Treat Rev 2007;33:622-630. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17434265.
8. Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. Cancer 2013;119:201-214. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22744865.
9. Zebrack BJ. Psychological, social, and behavioral issues for young adults with cancer. Cancer 2011;117:2289-2294. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523748.
10. Zebrack B, Butler M. Context for understanding psychosocial outcomes and behavior among adolescents and young adults with cancer. J Natl Compr Canc Netw 2012;10:1151-1156. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22956811.
11. Bleyer A, Barr R, Hayes-Lattin B, et al. The distinctive biology of cancer in adolescents and young adults. Nat Rev Cancer 2008;8:288-298. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18354417.
12. Tricoli JV, Blair DG, Anders CK, et al. Biologic and clinical characteristics of adolescent and young adult cancers: Acute lymphoblastic leukemia, colorectal cancer, breast cancer, melanoma, and sarcoma. Cancer 2016;122:1017-1028. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26849082.
13. Ramphal R, Meyer R, Schacter B, et al. Active therapy and models of care for adolescents and young adults with cancer. Cancer 2011;117:2316-2322. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523752.
14. Bleyer A, Barr R, Ries L, et al., eds. Cancer in adolescents and young adults (ed 2). Switzerland AG: Springer International Publishing; 2017.
15. Nass SJ, Beaupin LK, Demark-Wahnefried W, et al. Identifying and addressing the needs of adolescents and young adults with cancer: summary of an Institute of Medicine workshop. Oncologist 2015;20:186-195. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25568146.
16. Perez GK, Salsman JM, Fladeboe K, et al. Taboo topics in adolescent and young adult oncology: Strategies for managing challenging but important conversations central to adolescent and young adult cancer survivorship. Am Soc Clin Oncol Educ Book 2020;40:1-15. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32324424.
17. 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: U.S. department of health and human services, national institutes of health, national cancer institute, livestrong™ young adult alliance 2006. Available at: https://www.cancer.gov/types/aya/research/ayao-august-2006.pdf.
18. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance research program [Cited 2024 September 10] National Cancer Institute; 2024. Available at: https://seer.cancer.gov/statistics-network/explorer/.
19. Collaborators GBDAYAC. The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Oncol 2022;23:27-52. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34871551.

20. Trama A, Botta L, Foschi R, et al. Survival of European adolescents and young adults diagnosed with cancer in 2000-07: population-based data from EUROCARE-5. Lancet Oncol 2016;17:896-906. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27237614.
21. 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. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23091096.
22. Lee J, Hoang BH, Ziogas A, Zell JA. Analysis of prognostic factors in Ewing sarcoma using a population-based cancer registry. Cancer 2010;116:1964-1973. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20151425.
23. Verma V, Denniston KA, Lin CJ, Lin C. A comparison of pediatric vs. Adult patients with the ewing sarcoma family of tumors. Front Oncol 2017;7:82. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28534008.
24. Weinberg BA, Marshall JL, Salem ME. The growing challenge of young adults with colorectal cancer. Oncology (Williston Park) 2017;31:381-389. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28516436.
25. Tai E, Buchanan N, Westervelt L, et al. Treatment setting, clinical trial enrollment, and subsequent outcomes among adolescents with cancer: a literature review. Pediatrics 2014;133 Suppl 3:S91-97. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24918213.
26. American Cancer Society Inc Surveillance Research. Cancer facts & figures 2020. Special section: Cancer in adolescents and young adults; 2020. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/special-section-cancer-in-adolescents-and-young-adults-2020.pdf.
27. Ferrari A, Thomas D, Franklin AR, et al. Starting an adolescent and young adult program: some success stories and some obstacles to overcome. J Clin Oncol 2010;28:4850-4857. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20479411.
28. Zebrack B, Mathews-Bradshaw B, Siegel S, Alliance LYA. Quality cancer care for adolescents and young adults: a position statement. J Clin Oncol 2010;28:4862-4867. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20855821.
29. Sreeraman Kumar R, Thapa R, Kim Y, et al. Higher than reported adolescent and young adult clinical trial enrollment during the "Golden Age" of melanoma clinical trials. Cancer Med 2018;7:991-996. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29478277.
30. Alvarez E, Spunt SL, Malogolowkin M, et al. Treatment at specialized cancer centers is associated with improved survival in adolescent and young adults with soft tissue sarcoma. J Adolesc Young Adult Oncol 2022;11:370-378. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34910881.
31. Alvarez EM, Malogolowkin M, Hoch JS, et al. Treatment complications and survival among children and young adults with acute lymphoblastic leukemia. JCO Oncol Pract 2020;16:e1120-e1133. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32525752.
32. Wolfson J, Sun CL, Kang T, et al. Impact of treatment site in adolescents and young adults with central nervous system tumors. J Natl Cancer Inst 2014;106:dju166. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25178694.
33. Wolfson J, Sun CL, Wyatt L, et al. Adolescents and young adults with acute lymphoblastic leukemia and acute myeloid leukemia: Impact of care at specialized cancer centers on survival outcome. Cancer Epidemiol Biomarkers Prev 2017;26:312-320. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28209594.
34. PubMed Overview. Available at: https://pubmed.ncbi.nlm.nih.gov/about/.
35. Freedman-Cass DA, Fischer T, Alpert AB, et al. The value and process of inclusion: Using sensitive, respectful, and inclusive language and images in nccn content. J Natl Compr Canc Netw 2023;21:434-441. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37156485.
36. Bright CJ, Reulen RC, Winter DL, et al. Risk of subsequent primary neoplasms in survivors of adolescent and young adult cancer (teenage and young adult cancer survivor study): A population-based, cohort study. Lancet Oncol 2019;20:531-545. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30797674.
37. Lee JS, DuBois SG, Coccia PF, et al. Increased risk of second malignant neoplasms in adolescents and young adults with cancer. Cancer 2016;122:116-123. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26441212.

38. Chao C, Bhatia S, Xu L, et al. Incidence, risk factors, and mortality associated with second malignant neoplasms among survivors of adolescent and young adult cancer. JAMA Netw Open 2019;2:e195536. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31173129.
39. Bleyer A, Viny A, Barr R. Cancer in 15- to 29-year-olds by primary site. Oncologist 2006;11:590-601. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16794238.
40. Grobner SN, Worst BC, Weischenfeldt J, et al. The landscape of genomic alterations across childhood cancers. Nature 2018;555:321-327. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29489754.
41. Parsons DW, Roy A, Yang Y, et al. Diagnostic yield of clinical tumor and germline whole-exome sequencing for children with solid tumors. JAMA Oncol 2016;2:616-624. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26822237.
42. Zhang J, Walsh MF, Wu G, et al. Germline mutations in predisposition genes in pediatric cancer. N Engl J Med 2015;373:2336-2346. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26580448.
43. Jerzak KJ, Mancuso T, Eisen A. Ataxia-telangiectasia gene (ATM) mutation heterozygosity in breast cancer: a narrative review. Curr Oncol 2018;25:e176-e180. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29719442.
44. Samadder NJ, Giridhar KV, Baffy N, et al. Hereditary cancer syndromes-a primer on diagnosis and management: Part 1: Breast-ovarian cancer syndromes. Mayo Clin Proc 2019;94:1084-1098. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31171119.
45. Koskenvuo L, Peltomaki P, Renkonen-Sinisalo L, et al. Desmoid tumor patients carry an elevated risk of familial adenomatous polyposis. J Surg Oncol 2016;113:209-212. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26663236.
46. Ognjanovic S, Olivier M, Bergemann TL, Hainaut P. Sarcomas in TP53 germline mutation carriers: a review of the IARC TP53 database. Cancer 2012;118:1387-1396. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21837677.
47. Kamihara J, Bourdeaut F, Foulkes WD, et al. Retinoblastoma and neuroblastoma predisposition and surveillance. Clin Cancer Res 2017;23:e98-e106. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28674118.
48. Mai PL, Best AF, Peters JA, et al. Risks of first and subsequent cancers among TP53 mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort. Cancer 2016;122:3673-3681. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27496084.
49. Ferrari A, Chisholm JC, Jenney M, et al. Adolescents and young adults with rhabdomyosarcoma treated in the European paediatric Soft tissue sarcoma Study Group (EpSSG) protocols: a cohort study. Lancet Child Adolesc Health 2022;6:545-554. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35690071.
50. Harrison DJ, Qumseya A, Xue W, et al. Adolescents and young adults with rhabdomyosarcoma: A report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group. Pediatr Blood Cancer 2024;71:e30847. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38282125.
51. Miettinen M, Wang ZF, Sarlomo-Rikala M, et al. Succinate dehydrogenase-deficient GISTs: a clinicopathologic, immunohistochemical, and molecular genetic study of 66 gastric GISTs with predilection to young age. Am J Surg Pathol 2011;35:1712-1721. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21997692.
52. Janeway KA, Kim SY, Lodish M, et al. Defects in succinate dehydrogenase in gastrointestinal stromal tumors lacking KIT and PDGFRA mutations. Proc Natl Acad Sci U S A 2011;108:314-318. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21173220.
53. Friedman JM. Neurofibromatosis 1. In: Pagon RA, Bird TD, Dolan CR, Stephens K, eds. GeneReviews [Internet]. Seattle, WA: University of Washington, Seattle, WA 2009: Initial Posting: October 2, 1998; Last Update: June 1992, 2009.
54. Gaztambide S, Vazquez F, Castano L. Diagnosis and treatment of multiple endocrine neoplasia type 1 (MEN1). Minerva Endocrinol 2013;38:17-28. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23435440.
55. Moline J, Eng C. Multiple endocrine neoplasia type 2: an overview. Genet Med 2011;13:755-764. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21552134.
56. Herrero R, Castellsague X, Pawlita M, et al. Human papillomavirus and oral cancer: The international agency for research on cancer multicenter study. J Natl Cancer Inst 2003;95:1772-1783. Available at: https://www.ncbi.nlm.nih.gov/pubmed/14652239.

57. Chaturvedi AK. Beyond cervical cancer: burden of other HPV-related cancers among men and women. J Adolesc Health 2010;46:S20-26. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20307840.
58. Palefsky JM, Giuliano AR, Goldstone S, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med 2011;365:1576-1585. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22029979.
59. Lehtinen M, Paavonen J, Wheeler CM, et al. Overall efficacy of HPV-16/18 AS04-adjuvanted vaccine against grade 3 or greater cervical intraepithelial neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol 2012;13:89-99. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22075171.
60. Herrero R, Quint W, Hildesheim A, et al. Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica. PLoS One 2013;8:e68329. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23873171.
61. Klosky JL, Favaro B, Peck KR, et al. Prevalence and predictors of human papillomavirus (HPV) vaccination among young women surviving childhood cancer. J Cancer Surviv 2016;10:449-456. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26572902.
62. Klosky JL, Hudson MM, Chen Y, et al. Human papillomavirus vaccination rates in young cancer survivors. J Clin Oncol 2017;35:3582-3590. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28837404.
63. Markowitz LE, Dunne EF, Saraiya M, et al. Human papillomavirus vaccination: Recommendations of the advisory committee on immunization practices (ACIP). MMWR Recomm Rep 2014;63:1-30. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25167164.
64. Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination - updated recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep 2016;65:1405-1408. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27977643.
65. Meites E, Szilagyi PG, Chesson HW, et al. Human papillomavirus vaccination for adults: Updated recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep 2019;68:698-702. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31415491.
66. Saslow D, Andrews KS, Manassaram-Baptiste D, et al. Human papillomavirus vaccination 2020 guideline update: American Cancer Society guideline adaptation. CA Cancer J Clin 2020;70:274-280. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32639044.
67. Bleyer A. Young adult oncology: the patients and their survival challenges. CA Cancer J Clin 2007;57:242-255. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17626120.
68. Smith RA, Andrews KS, Brooks D, et al. Cancer screening in the United States, 2018: A review of current American Cancer Society guidelines and current issues in cancer screening. CA Cancer J Clin 2018;68:297-316. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29846940.
69. Bryant H. Screening for cancer in children, adolescents, and young adults: questions--and more questions. Cancer 2011;117:2275-2280. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523746.
70. Pollock BH, Krischer JP, Vietti TJ. Interval between symptom onset and diagnosis of pediatric solid tumors. J Pediatr 1991;119:725-732. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1941378.
71. Klein-Geltink J, Pogany L, Mery LS, et al. Impact of age and diagnosis on waiting times between important healthcare events among children 0 to 19 years cared for in pediatric units: the canadian childhood cancer surveillance and control program. J Pediatr Hematol Oncol 2006;28:433-439. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16825989.
72. Dang-Tan T, Trottier H, Mery LS, et al. Delays in diagnosis and treatment among children and adolescents with cancer in Canada. Pediatr Blood Cancer 2008;51:468-474. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18454472.
73. Parsons HM, Schmidt S, Tenner LL, et al. Early impact of the Patient Protection and Affordable Care Act on insurance among young adults with cancer: Analysis of the dependent insurance provision. Cancer 2016;122:1766-1773. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26998967.
74. Martin S, Ulrich C, Munsell M, et al. Delays in cancer diagnosis in underinsured young adults and older adolescents. Oncologist 2007;12:816-824. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17673613.

75. Stock W, Luger SM, Advani AS, et al. A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: results of CALGB 10403. Blood 2019;133:1548-1559. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30658992.
76. Siegel SE, Advani A, Seibel N, et al. Treatment of young adults with Philadelphia-negative acute lymphoblastic leukemia and lymphoblastic lymphoma: Hyper-CVAD vs. pediatric-inspired regimens. Am J Hematol 2018;93:1254-1266. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30058716.
77. Siegel SE, Stock W, Johnson RH, et al. Pediatric-inspired treatment regimens for adolescents and young adults with philadelphia chromosome-negative acute lymphoblastic leukemia: A review. JAMA Oncol 2018;4:725-734. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29450465.
78. Ferrari A, Dileo P, Casanova M, et al. Rhabdomyosarcoma in adults. A retrospective analysis of 171 patients treated at a single institution. Cancer 2003;98:571-580. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12879475.
79. Scurr M, Judson I. How to treat the Ewing's family of sarcomas in adult patients. Oncologist 2006;11:65-72. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16401715.
80. Reed DR, Hayashi M, Wagner L, et al. Treatment pathway of bone sarcoma in children, adolescents, and young adults. Cancer 2017;123:2206-2218. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28323337.
81. Tai E, Pollack LA, Townsend J, et al. Differences in non-Hodgkin lymphoma survival between young adults and children. Arch Pediatr Adolesc Med 2010;164:218-224. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20194253.
82. Sandlund JT. Should adolescents with NHL be treated as old children or young adults? Hematology Am Soc Hematol Educ Program 2007:297-303. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18024643.
83. Burkhardt B, Oschlies I, Klapper W, et al. Non-Hodgkin's lymphoma in adolescents: experiences in 378 adolescent NHL patients treated according to pediatric NHL-BFM protocols. Leukemia 2011;25:153-160. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21030984.
84. 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. Available at: http://www.seer.cancer.gov/publications/aya/.
85. Burke ME, Albritton K, Marina N. Challenges in the recruitment of adolescents and young adults to cancer clinical trials. Cancer 2007;110:2385-2393. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17918260.
86. Ferrari A, Montello M, Budd T, Bleyer A. The challenges of clinical trials for adolescents and young adults with cancer. Pediatr Blood Cancer 2008;50:1101-1104. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18360838.
87. Bleyer WA, Tejeda H, Murphy SB, et al. National cancer clinical trials: children have equal access; adolescents do not. J Adolesc Health 1997;21:366-373. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9401854.
88. Shochat SJ, Fremgen AM, Murphy SB, et al. Childhood cancer: patterns of protocol participation in a national survey. CA Cancer J Clin 2001;51:119-130. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11577480.
89. Downs-Canner S, Shaw PH. A comparison of clinical trial enrollment between adolescent and young adult (AYA) oncology patients treated at affiliated adult and pediatric oncology centers. J Pediatr Hematol Oncol 2009;31:927-929. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19855302.
90. Parsons HM, Harlan LC, Seibel NL, et al. Clinical trial participation and time to treatment among adolescents and young adults with cancer: does age at diagnosis or insurance make a difference? J Clin Oncol 2011;29:4045-4053. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21931022.
91. Howell DL, Ward KC, Austin HD, et al. Access to pediatric cancer care by age, race, and diagnosis, and outcomes of cancer treatment in pediatric and adolescent patients in the state of Georgia. J Clin Oncol 2007;25:4610-4615. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17925556.

92. Albritton KH, Wiggins CH, Nelson HE, Weeks JC. Site of oncologic specialty care for older adolescents in Utah. J Clin Oncol 2007;25:4616-4621. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17925557.
93. Bleyer A. The Quid Pro Quo of pediatric versus adult services for older adolescent cancer patients. Pediatr Blood Cancer 2010;54:238-241. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19813248.
94. Shaw PH, Boyiadzis M, Tawbi H, et al. Improved clinical trial enrollment in adolescent and young adult (AYA) oncology patients after the establishment of an AYA oncology program uniting pediatric and medical oncology divisions. Cancer 2012;118:3614-3617. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22213134.
95. Gupta AA, Edelstein K, Albert-Green A, D'Agostino N. Assessing information and service needs of young adults with cancer at a single institution: the importance of information on cancer diagnosis, fertility preservation, diet, and exercise. Support Care Cancer 2013;21:2477-2484. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23604520.
96. DeAngelo DJ, Stevenson KE, Dahlberg SE, et al. Long-term outcome of a pediatric-inspired regimen used for adults aged 18-50 years with newly diagnosed acute lymphoblastic leukemia. Leukemia 2015;29:526-534. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25079173.
97. Gerber NK, Wexler LH, Singer S, et al. Adult rhabdomyosarcoma survival improved with treatment on multimodality protocols. Int J Radiat Oncol Biol Phys 2013;86:58-63. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23414767.
98. Veal GJ, Hartford CM, Stewart CF. Clinical pharmacology in the adolescent oncology patient. J Clin Oncol 2010;28:4790-4799. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20439647.
99. Oeffinger KC, Mertens AC, Hudson MM, et al. Health care of young adult survivors of childhood cancer: a report from the childhood cancer survivor study. Ann Fam Med 2004;2:61-70. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15053285.
100. Oeffinger KC, Hudson MM. Long-term complications following childhood and adolescent cancer: foundations for providing risk-based health care for survivors. CA Cancer J Clin 2004;54:208-236. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15253918.
101. Armstrong GT, Stovall M, Robison LL. Long-term effects of radiation exposure among adult survivors of childhood cancer: results from the childhood cancer survivor study. Radiat Res 2010;174:840-850. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21128808.
102. Levine J, Canada A, Stern CJ. Fertility preservation in adolescents and young adults with cancer. J Clin Oncol 2010;28:4831-4841. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20458029.
103. Travis LB, Hill DA, Dores GM, et al. Breast cancer following radiotherapy and chemotherapy among young women with Hodgkin disease. JAMA 2003;290:465-475. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12876089.
104. Janson C, Leisenring W, Cox C, et al. Predictors of marriage and divorce in adult survivors of childhood cancers: a report from the Childhood Cancer Survivor Study. Cancer Epidemiol Biomarkers Prev 2009;18:2626-2635. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19815636.
105. Singh AK, Tantiwongkosi B, Moise AM, Altmeyer WB. Stroke-like migraine attacks after radiation therapy syndrome: Case report and review of the literature. Neuroradiol J 2017;30:568-573. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28643603.
106. Strojan P, Hutcheson KA, Eisbruch A, et al. Treatment of late sequelae after radiotherapy for head and neck cancer. Cancer Treat Rev 2017;59:79-92. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28759822.
107. Bleyer A, Choi M, Wang SJ, et al. Increased vulnerability of the spinal cord to radiation or intrathecal chemotherapy during adolescence: A report from the Children's Oncology Group. Pediatr Blood Cancer 2009;53:1205-1210. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19821538.
108. ASTRO model policies: Proton beam therapy (PBT). 2017. Available at: https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/ASTROPBTModelPolicy.pdf. Accessed September 6, 2024.
109. Bishop AJ, Livingston JA, Ning MS, et al. Young adult populations face yet another barrier to care with insurers: Limited access to proton therapy. Int J Radiat Oncol Biol Phys 2021;110:1496-1504. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33677051.
110. Dabaja BS, Hoppe BS, Plastaras JP, et al. Proton therapy for adults with mediastinal lymphomas: the International Lymphoma Radiation

Oncology Group guidelines. Blood 2018;132:1635-1646. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30108066.
111. Lim PS, Tran S, Kroeze SGC, et al. Outcomes of adolescents and young adults treated for brain and skull base tumors with pencil beam scanning proton therapy. Pediatr Blood Cancer 2020;67:e28664. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32881313.
112. Mizumoto M, Fuji H, Miyachi M, et al. Proton beam therapy for children and adolescents and young adults (AYAs): JASTRO and JSPHO Guidelines. Cancer Treat Rev 2021;98:102209. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33984606.
113. Importance of skin cancer screening after radiation therapy. Journal of the American Academy of Dermatology 2016;74:AB199. Available at: https://doi.org/10.1016/j.jaad.2016.02.782.
114. Roscoe JA, Morrow GR, Aapro MS, et al. Anticipatory nausea and vomiting. Support Care Cancer 2011;19:1533-1538. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20803345.
115. Figueroa-Moseley C, Jean-Pierre P, Roscoe JA, et al. Behavioral interventions in treating anticipatory nausea and vomiting. J Natl Compr Canc Netw 2007;5:44-50. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17239325.
116. Nowe E, Stobel-Richter Y, Sender A, et al. Cancer-related fatigue in adolescents and young adults: A systematic review of the literature. Crit Rev Oncol Hematol 2017;118:63-69. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28917270.
117. Spathis A, Booth S, Grove S, et al. Teenage and young adult cancer-related fatigue is prevalent, distressing, and neglected: It is time to intervene. A systematic literature review and narrative synthesis. J Adolesc Young Adult Oncol 2015;4:3-17. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25852970.
118. Hauken MA, Holsen I, Fismen E, Larsen TM. Working toward a good life as a cancer survivor: a longitudinal study on positive health outcomes of a rehabilitation program for young adult cancer survivors. Cancer Nurs 2015;38:3-15. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24921193.
119. Rabin C, Dunsiger S, Ness KK, Marcus BH. Internet-based physical activity intervention targeting young adult cancer survivors. J Adolesc Young Adult Oncol 2011;1:188-194. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23610737.
120. Suter TM, Ewer MS. Cancer drugs and the heart: importance and management. Eur Heart J 2013;34:1102-1111. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22789916.
121. Huang TT, Hudson MM, Stokes DC, et al. Pulmonary outcomes in survivors of childhood cancer: a systematic review. Chest 2011;140:881-901. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21415131.
122. Schell MJ, McHaney VA, Green AA, et al. Hearing loss in children and young adults receiving cisplatin with or without prior cranial irradiation. J Clin Oncol 1989;7:754-760. Available at: https://www.ncbi.nlm.nih.gov/pubmed/2715805.
123. Skinner R, Cotterill SJ, Stevens MC. Risk factors for nephrotoxicity after ifosfamide treatment in children: a UKCCSG Late Effects Group study. United Kingdom Children's Cancer Study Group. Br J Cancer 2000;82:1636-1645. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10817497.
124. Knight KR, Kraemer DF, Neuwelt EA. Ototoxicity in children receiving platinum chemotherapy: underestimating a commonly occurring toxicity that may influence academic and social development. J Clin Oncol 2005;23:8588-8596. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16314621.
125. Hijiya N, Ness KK, Ribeiro RC, Hudson MM. Acute leukemia as a secondary malignancy in children and adolescents: current findings and issues. Cancer 2009;115:23-35. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19072983.
126. Langer T, am Zehnhoff-Dinnesen A, Radtke S, et al. Understanding platinum-induced ototoxicity. Trends Pharmacol Sci 2013;34:458-469. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23769626.
127. Drugs@FDA: FDA-approved drugs. U.S. Food & Drug Administration; Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed September 6, 2024.
128. Freyer DR, Chen L, Krailo MD, et al. Effects of sodium thiosulfate versus observation on development of cisplatin-induced hearing loss in children with cancer (ACCL0431): a multicentre, randomised, controlled, open-label, phase 3 trial. Lancet Oncol 2017;18:63-74. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27914822.
129. Brock PR, Maibach R, Childs M, et al. Sodium Thiosulfate for Protection from Cisplatin-Induced Hearing Loss. N Engl J Med

2018;378:2376-2385. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29924955.
130. Orgel E, Villaluna D, Krailo MD, et al. Sodium thiosulfate for prevention of cisplatin-induced hearing loss: updated survival from ACCL0431. Lancet Oncol 2022;23:570-572. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35489339.
131. van Atteveld JE, Mulder RL, van den Heuvel-Eibrink MM, et al. Bone mineral density surveillance for childhood, adolescent, and young adult cancer survivors: evidence-based recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Diabetes Endocrinol 2021;9:622-637. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34339631.
132. Watanabe T, Yagata H, Saito M, et al. A multicenter survey of temporal changes in chemotherapy-induced hair loss in breast cancer patients. PLoS One 2019;14:e0208118. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30625139.
133. Shaw J, Baylock B, O'Reilly A, et al. Scalp cooling: a qualitative study to assess the perceptions and experiences of Australian patients with breast cancer. Support Care Cancer 2016;24:3813-3820. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27061409.
134. Kang D, Cho J, Zhao D, et al. Scalp Cooling in Preventing Persistent Chemotherapy-Induced Alopecia: A Randomized Controlled Trial. J Clin Oncol 2024;42:3115-3122. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38843479.
135. Rose L, Mallela T, Waters M, et al. Cosmetic considerations after breast cancer treatment. Arch Dermatol Res 2024;316:223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38787423.
136. Almeida V, Pires D, Silva M, et al. Dermatological Side Effects of Cancer Treatment: Psychosocial Implications-A Systematic Review of the Literature. Healthcare (Basel) 2023;11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37830658.
137. Armenian SH, Sun CL, Kawashima T, et al. Long-term health-related outcomes in survivors of childhood cancer treated with HSCT versus conventional therapy: a report from the bone marrow transplant survivor study (BMTSS) and childhood cancer survivor study (CCSS). Blood 2011;118:1413-1420. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21652685.
138. Wingard JR, Majhail NS, Brazauskas R, et al. Long-term survival and late deaths after allogeneic hematopoietic cell transplantation. J Clin Oncol 2011;29:2230-2239. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21464398.
139. Flowers ME, Inamoto Y, Carpenter PA, et al. Comparative analysis of risk factors for acute graft-versus-host disease and for chronic graft-versus-host disease according to National Institutes of Health consensus criteria. Blood 2011;117:3214-3219. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21263156.
140. Zecca M, Prete A, Rondelli R, et al. Chronic graft-versus-host disease in children: incidence, risk factors, and impact on outcome. Blood 2002;100:1192-1200. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12149197.
141. Anasetti C, Logan BR, Lee SJ, et al. Peripheral-blood stem cells versus bone marrow from unrelated donors. N Engl J Med 2012;367:1487-1496. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23075175.
142. Fraser CJ, Bhatia S, Ness K, et al. Impact of chronic graft-versus-host disease on the health status of hematopoietic cell transplantation survivors: A report from the bone marrow transplant survivor study. Blood 2006;108:2867-2873. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16788100.
143. Inaba H, Yang J, Kaste SC, et al. Longitudinal changes in body mass and composition in survivors of childhood hematologic malignancies after allogeneic hematopoietic stem-cell transplantation. J Clin Oncol 2012;30:3991-3997. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23032628.
144. Rizzo JD, Curtis RE, Socie G, et al. Solid cancers after allogeneic hematopoietic cell transplantation. Blood 2009;113:1175-1183. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18971419.
145. Butow P, Palmer S, Pai A, et al. Review of adherence-related issues in adolescents and young adults with cancer. J Clin Oncol 2010;28:4800-4809. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20212260.
146. Kondryn HJ, Edmondson CL, Hill J, Eden TO. Treatment non-adherence in teenage and young adult patients with cancer. Lancet Oncol 2011;12:100-108. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20580606.

147. Kaul S, Avila JC, Mehta HB, et al. Cost-related medication nonadherence among adolescent and young adult cancer survivors. Cancer 2017;123:2726-2734. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28542734.
148. Windebank KP, Spinetta JJ. Do as I say or die: compliance in adolescents with cancer. Pediatr Blood Cancer 2008;50:1099-1100. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18360837.
149. Kato PM, Cole SW, Bradlyn AS, Pollock BH. A video game improves behavioral outcomes in adolescents and young adults with cancer: a randomized trial. Pediatrics 2008;122:e305-317. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18676516.
150. McCann L, McMillan KA, Pugh G. Digital Interventions to Support Adolescents and Young Adults With Cancer: Systematic Review. JMIR Cancer 2019;5:e12071. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31368438.
151. Rosenberg AR, Macpherson CF, Kroon L, Johnson R. Rethinking Adherence: A Proposal for a New Approach to Risk Assessment. J Adolesc Young Adult Oncol 2013;2:83-86. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23781406.
152. Kenney LB, Cohen LE, Shnorhavorian M, et al. Male reproductive health after childhood, adolescent, and young adult cancers: a report from the children's oncology group. J Clin Oncol 2012;30:3408-3416. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22649147.
153. Metzger ML, Meacham LR, Patterson B, et al. Female reproductive health after childhood, adolescent, and young adult cancers: Guidelines for the assessment and management of female reproductive complications. J Clin Oncol 2013;31:1239-1247. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23382474.
154. Gunnes MW, Lie RT, Bjorge T, et al. Reproduction and marriage among male survivors of cancer in childhood, adolescence and young adulthood: a national cohort study. Br J Cancer 2016;114:348-356. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26794280.
155. Chow EJ, Stratton KL, Leisenring WM, et al. Pregnancy after chemotherapy in male and female survivors of childhood cancer treated between 1970 and 1999: A report from the childhood cancer survivor study cohort. Lancet Oncol 2016;17:567-576. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27020005.
156. Wallace WH, Anderson RA, Irvine DS. Fertility preservation for young patients with cancer: who is at risk and what can be offered? Lancet Oncol 2005;6:209-218. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15811616.
157. Chemaitilly W, Mertens AC, Mitby P, et al. Acute ovarian failure in the childhood cancer survivor study. J Clin Endocrinol Metab 2006;91:1723-1728. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16492690.
158. Darzy KH. Radiation-induced hypopituitarism after cancer therapy: who, how and when to test. Nat Clin Pract Endocrinol Metab 2009;5:88-99. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19165221.
159. Green DM, Sklar CA, Boice JD, Jr., et al. Ovarian failure and reproductive outcomes after childhood cancer treatment: Results from the childhood cancer survivor study. J Clin Oncol 2009;27:2374-2381. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19364956.
160. Green DM, Kawashima T, Stovall M, et al. Fertility of male survivors of childhood cancer: A report from the childhood cancer survivor study. J Clin Oncol 2010;28:332-339. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19949008.
161. Barton SE, Najita JS, Ginsburg ES, et al. Infertility, infertility treatment, and achievement of pregnancy in female survivors of childhood cancer: A report from the childhood cancer survivor study cohort. Lancet Oncol 2013;14:873-881. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23856401.
162. Haukvik UKH, Dieset I, Bjøro T, et al. Treatment-related premature ovarian failure as a long-term complication after Hodgkin's lymphoma. Ann Oncol 2006;17:1428-1433. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16831852.
163. van der Kaaij MA, Heutte N, Meijnders P, et al. Premature ovarian failure and fertility in long-term survivors of Hodgkin's lymphoma: a European Organisation for Research and Treatment of Cancer Lymphoma Group and Groupe d'Etude des Lymphomes de l'Adulte Cohort Study. J Clin Oncol 2012;30:291-299. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22184372.
164. Bramswig JH, Riepenhausen M, Schellong G. Parenthood in adult female survivors treated for Hodgkin's lymphoma during childhood and adolescence: a prospective, longitudinal study. Lancet Oncol

2015;16:667-675. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25959806.
165. Bines J, Oleske DM, Cobleigh MA. Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer. J Clin Oncol 1996;14:1718-1729. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8622093.
166. Goodwin PJ, Ennis M, Pritchard KI, et al. Risk of menopause during the first year after breast cancer diagnosis. J Clin Oncol 1999;17:2365-2370. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10561298.
167. De Bruin ML, Huisbrink J, Hauptmann M, et al. Treatment-related risk factors for premature menopause following Hodgkin lymphoma. Blood 2008;111:101-108. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17890454.
168. Chemaitilly W, Sklar CA. Endocrine complications in long-term survivors of childhood cancers. Endocr Relat Cancer 2010;17:R141-159. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20453080.
169. Meistrich ML. Effects of chemotherapy and radiotherapy on spermatogenesis in humans. Fertil Steril 2013;100:1180-1186. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24012199.
170. Sieniawski M, Reineke T, Josting A, et al. Assessment of male fertility in patients with Hodgkin's lymphoma treated in the German Hodgkin Study Group (GHSG) clinical trials. Ann Oncol 2008;19:1795-1801. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18544558.
171. Howell SJ, Shalet SM. Spermatogenesis after cancer treatment: damage and recovery. J Natl Cancer Inst Monogr 2005:12-17. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15784814.
172. Salama M, Isachenko V, Isachenko E, et al. Advances in fertility preservation of female patients with hematological malignancies. Expert Rev Hematol 2017;10:951-960. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28828900.
173. Meacham LR, Burns K, Orwig KE, Levine J. Standardizing risk assessment for treatment-related gonadal insufficiency and infertility in childhood adolescent and young adult cancer: The pediatric initiative network risk stratification system. J Adolesc Young Adult Oncol 2020;9:662-666. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32456570.
174. Wallace WH. Oncofertility and preservation of reproductive capacity in children and young adults. Cancer 2011;117:2301-2310. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523750.
175. Redig AJ, Brannigan R, Stryker SJ, et al. Incorporating fertility preservation into the care of young oncology patients. Cancer 2011;117:4-10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21235031.
176. Fernbach A, Lockart B, Armus CL, et al. Evidence-based recommendations for fertility preservation options for inclusion in treatment protocols for pediatric and adolescent patients diagnosed with cancer. J Pediatr Oncol Nurs 2014;31:211-222. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24799444.
177. Benedict C, Thom B, D NF, et al. Young adult female cancer survivors' unmet information needs and reproductive concerns contribute to decisional conflict regarding posttreatment fertility preservation. Cancer 2016;122:2101-2109. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27213483.
178. Waks AG, Partridge AH. Fertility preservation in patients with breast cancer: Necessity, methods, and safety. J Natl Compr Canc Netw 2016;14:355-363. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26957619.
179. Loren AW, Mangu PB, Beck LN, et al. Fertility preservation for patients with cancer: American society of clinical oncology clinical practice guideline update. J Clin Oncol 2013;31:2500-2510. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23715580.
180. Johnson RH, Kroon L. Optimizing fertility preservation practices for adolescent and young adult cancer patients. J Natl Compr Canc Netw 2013;11:71-77. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23307983.
181. Quinn GP, Block RG, Clayman ML, et al. If you did not document it, it did not happen: rates of documentation of discussion of infertility risk in adolescent and young adult oncology patients' medical records. J Oncol Pract 2015;11:137-144. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25549654.
182. Salsman JM, Yanez B, Smith KN, et al. Documentation of fertility preservation discussions for young adults with cancer: Examining compliance with treatment guidelines. J Natl Compr Canc Netw

2016;14:301-309. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26957616.
183. Klosky JL, Wang F, Russell KM, et al. Prevalence and predictors of sperm banking in adolescents newly diagnosed with cancer: Examination of adolescent, parent, and provider factors influencing fertility preservation outcomes. J Clin Oncol 2017;35:3830-3836. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28976795.
184. Jones G, Hughes J, Mahmoodi N, et al. What factors hinder the decision-making process for women with cancer and contemplating fertility preservation treatment? Hum Reprod Update 2017;23:433-457. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28510760.
185. Practice Committee of the American Society for Reproductive Medicine. Electronic address aao. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril 2019;112:1022-1033. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31843073.
186. Waimey KE, Duncan FE, Su HI, et al. Future directions in oncofertility and fertility preservation: A report from the 2011 oncofertility consortium conference. J Adolesc Young Adult Oncol 2013;2:25-30. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23610740.
187. Terenziani M, Piva L, Meazza C, et al. Oophoropexy: a relevant role in preservation of ovarian function after pelvic irradiation. Fertil Steril 2009;91:935 e915-936. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18951125.
188. Oktay K, Turan V, Bedoschi G, et al. Fertility preservation success subsequent to concurrent aromatase inhibitor treatment and ovarian stimulation in women with breast cancer. J Clin Oncol 2015;33:2424-2429. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26101247.
189. Cobo A, Kuwayama M, Perez S, et al. Comparison of concomitant outcome achieved with fresh and cryopreserved donor oocytes vitrified by the Cryotop method. Fertil Steril 2008;89:1657-1664. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17889865.
190. Cobo A, Meseguer M, Remohi J, Pellicer A. Use of cryo-banked oocytes in an ovum donation programme: a prospective, randomized, controlled, clinical trial. Hum Reprod 2010;25:2239-2246. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20591872.
191. Rienzi L, Romano S, Albricci L, et al. Embryo development of fresh 'versus' vitrified metaphase II oocytes after ICSI: a prospective randomized sibling-oocyte study. Hum Reprod 2010;25:66-73. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19861328.
192. Parmegiani L, Cognigni GE, Bernardi S, et al. Efficiency of aseptic open vitrification and hermetical cryostorage of human oocytes. Reprod Biomed Online 2011;23:505-512. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21843968.
193. Cobo A, Diaz C. Clinical application of oocyte vitrification: a systematic review and meta-analysis of randomized controlled trials. Fertil Steril 2011;96:277-285. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21718983.
194. Del Mastro L, Boni L, Michelotti A, et al. Effect of the gonadotropin-releasing hormone analogue triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer: a randomized trial. JAMA 2011;306:269-276. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21771987.
195. Behringer K, Wildt L, Mueller H, et al. No protection of the ovarian follicle pool with the use of GnRH-analogues or oral contraceptives in young women treated with escalated BEACOPP for advanced-stage Hodgkin lymphoma. Final results of a phase II trial from the German Hodgkin Study Group. Ann Oncol 2010;21:2052-2060. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20305034.
196. Gerber B, von Minckwitz G, Stehle H, et al. Effect of luteinizing hormone-releasing hormone agonist on ovarian function after modern adjuvant breast cancer chemotherapy: the GBG 37 ZORO study. J Clin Oncol 2011;29:2334-2341. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21537042.
197. Demeestere I, Brice P, Peccatori FA, et al. Gonadotropin-releasing hormone agonist for the prevention of chemotherapy-induced ovarian failure in patients with lymphoma: 1-year follow-up of a prospective randomized trial. J Clin Oncol 2013;31:903-909. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23129737.
198. Elgindy EA, El-Haieg DO, Khorshid OM, et al. Gonadatrophin suppression to prevent chemotherapy-induced ovarian damage: a randomized controlled trial. Obstet Gynecol 2013;121:78-86. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23262931.
199. Moore HC, Unger JM, Phillips KA, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. N Engl J Med

2015;372:923-932. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25738668.
200. Bildik G, Akin N, Senbabaoglu F, et al. GnRH agonist leuprolide acetate does not confer any protection against ovarian damage induced by chemotherapy and radiation in vitro. Hum Reprod 2015;30:2912-2925. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26466909.
201. Blumenfeld Z, Zur H, Dann EJ. Gonadotropin-releasing hormone agonist cotreatment during chemotherapy may increase pregnancy rate in survivors. Oncologist 2015;20:1283-1289. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26463871.
202. Demeestere I, Brice P, Peccatori FA, et al. No evidence for the benefit of gonadotropin-releasing hormone agonist in preserving ovarian function and fertility in lymphoma survivors treated with chemotherapy: Final long-term report of a prospective randomized trial. J Clin Oncol 2016;34:2568-2574. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27217453.
203. Del Mastro L, Ceppi M, Poggio F, et al. Gonadotropin-releasing hormone analogues for the prevention of chemotherapy-induced premature ovarian failure in cancer women: systematic review and meta-analysis of randomized trials. Cancer Treat Rev 2014;40:675-683. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24360817.
204. Lambertini M, Ceppi M, Poggio F, et al. Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients: a meta-analysis of randomized studies. Ann Oncol 2015;26:2408-2419. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26347105.
205. Munhoz RR, Pereira AA, Sasse AD, et al. Gonadotropin-releasing hormone agonists for ovarian function preservation in premenopausal women undergoing chemotherapy for early-stage breast cancer: A systematic review and meta-analysis. JAMA Oncol 2016;2:65-73. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26426573.
206. Rodriguez-Wallberg K, Turan V, Munster P, Oktay K. Can ovarian suppression with gonadotropin-releasing hormone analogs (GnRHa) preserve fertility in cancer patients? Ann Oncol 2016;27:357. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26609009.
207. Oktay K, Turan V. Failure of ovarian suppression with gonadotropin-releasing hormone analogs to preserve fertility: An assessment based on the quality of evidence. JAMA Oncol 2016;2:74-75. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26426406.
208. Bates JS, Buie LW, Woodis CB. Management of menorrhagia associated with chemotherapy-induced thrombocytopenia in women with hematologic malignancy. Pharmacotherapy 2011;31:1092-1110. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22026397.
209. Park JY, Nam JH. Progestins in the fertility-sparing treatment and retreatment of patients with primary and recurrent endometrial cancer. Oncologist 2015;20:270-278. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25673106.
210. Mitsuhashi A, Sato Y, Kiyokawa T, et al. Phase II study of medroxyprogesterone acetate plus metformin as a fertility-sparing treatment for atypical endometrial hyperplasia and endometrial cancer. Ann Oncol 2016;27:262-266. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26578736.
211. Williams DH. Sperm banking and the cancer patient. Ther Adv Urol 2010;2:19-34. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21789080.
212. Mulder RL, Font-Gonzalez A, Green DM, et al. Fertility preservation for male patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2021;22:e57-e67. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33539754.
213. Mulder RL, Font-Gonzalez A, Hudson MM, et al. Fertility preservation for female patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2021;22:e45-e56. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33539753.
214. Mulder RL, Font-Gonzalez A, van Dulmen-den Broeder E, et al. Communication and ethical considerations for fertility preservation for patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2021;22:e68-e80. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33539755.

215. Green DM, Nolan VG, Goodman PJ, et al. The cyclophosphamide equivalent dose as an approach for quantifying alkylating agent exposure: A report from the childhood cancer survivor study. Pediatr Blood Cancer 2014;61:53-67. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23940101.
216. Nahata L, Liles SM, Gerhardt CA, et al. Clinicians' perspectives on barriers and facilitators to sperm banking in adolescent males with cancer: a mixed-methods study. J Assist Reprod Genet 2023;40:2809-2817. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37730946.
217. Nahata L, Dattilo TM, Olsavsky AL, et al. Impact of a novel family-centered values clarification tool on adolescent sperm banking attempts at the time of a new cancer diagnosis. J Assist Reprod Genet 2021;38:1561-1569. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33564937.
218. Flynn JS, Russell KM, Lehmann V, et al. Parent recommendation to bank sperm among at-risk adolescent and young adult males with cancer. Pediatr Blood Cancer 2020;67:e28217. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32453503.
219. Oktay K, Harvey BE, Partridge AH, et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 2018;36:1994-2001. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29620997.
220. van Dorp W, Mulder RL, Kremer LC, et al. Recommendations for premature ovarian insufficiency surveillance for female survivors of childhood, adolescent, and young adult cancer: A report from the international late effects of childhood cancer guideline harmonization group in collaboration with the pancaresurfup consortium. J Clin Oncol 2016;34:3440-3450. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27458300.
221. Lambertini M, Boni L, Michelotti A, et al. Long-term outcomes with pharmacological ovarian suppression during chemotherapy in premenopausal early breast cancer patients. J Natl Cancer Inst 2022;114:400-408. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34850043.
222. Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 2006;24:2917-2931. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16651642.
223. Le Bon M, Lejeune H, Helfre S, et al. Testicular transposition in children before scrotal external radiotherapy. Pediatr Blood Cancer 2020;67:e28526. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32618059.
224. Skinner R, Mulder RL, Kremer LC, et al. Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. Lancet Oncol 2017;18:e75-e90. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28214419.
225. Murphy D, Klosky JL, Termuhlen A, et al. The need for reproductive and sexual health discussions with adolescent and young adult cancer patients. Contraception 2013;88:215-220. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23040131.
226. Britton L. Unintended pregnancy: A systematic review of contraception use and counseling in women with cancer. Clin J Oncol Nurs 2017;21:189-196. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28315546.
227. Laurence V, Gbolade BA, Morgan SJ, Glaser A. Contraception for teenagers and young adults with cancer. Eur J Cancer 2004;40:2705-2716. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15571952.
228. Committee on Adolescent Health Care Long-Acting Reversible Contraception Working Group TACoO, Gynecologists. Committee opinion no. 539: adolescents and long-acting reversible contraception: implants and intrauterine devices. Obstet Gynecol 2012;120:983-988. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22996129.
229. Peipert JF, Zhao Q, Allsworth JE, et al. Continuation and satisfaction of reversible contraception. Obstet Gynecol 2011;117:1105-1113. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21508749.
230. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. N Engl J Med 2012;366:1998-2007. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22621627.
231. Patel A, Schwarz EB, Society of Family P. Cancer and contraception. Release date May 2012. SFP guideline #20121. Contraception 2012;86:191-198. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22682881.
232. Curtis KM, Tepper NK, Jatlaoui TC, et al. Centers for disease control and prevention. U.S. Medical eligibility criteria for contraceptive

use, 2016. MMWR Recomm Rep. Vol. 65(No. RR-3); 2016:1-104. Available at: https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6503.pdf.
233. Centers for disease control and prevention. U.S. Medical eligibility criteria for contraceptive use, 2010. Adapted from the world health organization medical eligibility criteria for contraceptive use, 4th edition. MMWR 2010. Vol. 59 (No. RR-4):1-85. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr59e0528.pdf.
234. Pavlidis NA. Coexistence of pregnancy and malignancy. Oncologist 2002;7:279-287. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12185292.
235. Azim HA, Jr., Pavlidis N, Peccatori FA. Treatment of the pregnant mother with cancer: a systematic review on the use of cytotoxic, endocrine, targeted agents and immunotherapy during pregnancy. Part II: Hematological tumors. Cancer Treat Rev 2010;36:110-121. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20018452.
236. Azim HA, Jr., Peccatori FA, Pavlidis N. Treatment of the pregnant mother with cancer: a systematic review on the use of cytotoxic, endocrine, targeted agents and immunotherapy during pregnancy. Part I: Solid tumors. Cancer Treat Rev 2010;36:101-109. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20015593.
237. Van Calsteren K, Heyns L, De Smet F, et al. Cancer during pregnancy: an analysis of 215 patients emphasizing the obstetrical and the neonatal outcomes. J Clin Oncol 2010;28:683-689. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19841323.
238. Andersson TM, Johansson AL, Fredriksson I, Lambe M. Cancer during pregnancy and the postpartum period: A population-based study. Cancer 2015;121:2072-2077. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25737403.
239. Hepner A, Negrini D, Hase EA, et al. Cancer during pregnancy: The oncologist overview. World J Oncol 2019;10:28-34. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30834049.
240. Weibull CE, Eloranta S, Smedby KE, et al. Pregnancy and the risk of relapse in patients diagnosed with hodgkin lymphoma. J Clin Oncol 2016;34:337-344. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26668344.
241. Kyrgidis A, Lallas A, Moscarella E, et al. Does pregnancy influence melanoma prognosis? A meta-analysis. Melanoma Res 2017;27:289-299. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28430756.
242. Hartman EK, Eslick GD. The prognosis of women diagnosed with breast cancer before, during and after pregnancy: a meta-analysis. Breast Cancer Res Treat 2016;160:347-360. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27683280.
243. Azim HA, Jr., Santoro L, Russell-Edu W, et al. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. Cancer Treat Rev 2012;38:834-842. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22785217.
244. Matsuo K, Whitman SA, Blake EA, et al. Feto-maternal outcome of pregnancy complicated by vulvar cancer: a systematic review of literature. Eur J Obstet Gynecol Reprod Biol 2014;179:216-223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24768232.
245. Alexander A, Samlowski WE, Grossman D, et al. Metastatic melanoma in pregnancy: risk of transplacental metastases in the infant. J Clin Oncol 2003;21:2179-2186. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12775744.
246. Catlin EA, Roberts JD, Jr., Erana R, et al. Transplacental transmission of natural-killer-cell lymphoma. N Engl J Med 1999;341:85-91. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10395632.
247. Isoda T, Ford AM, Tomizawa D, et al. Immunologically silent cancer clone transmission from mother to offspring. Proc Natl Acad Sci U S A 2009;106:17882-17885. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19822752.
248. Maruko K, Maeda T, Kamitomo M, et al. Transplacental transmission of maternal B-cell lymphoma. Am J Obstet Gynecol 2004;191:380-381. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15295401.
249. Yagasaki H, Ohashi H, Ito M, et al. A novel mechanism of transplacental cancer transmission: natural killer/T-cell lymphoma in the paratesticular region is of maternal origin. Blood 2011;117:6046-6047. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21636718.
250. Pentheroudakis G, Orecchia R, Hoekstra HJ, et al. Cancer, fertility and pregnancy: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 Suppl 5:v266-273. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20555095.
251. Lishner M, Avivi I, Apperley JF, et al. Hematologic malignancies in pregnancy: Management guidelines from an international consensus

meeting. J Clin Oncol 2016;34:501-508. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26628463.
252. Loibl S, Schmidt A, Gentilini O, et al. Breast cancer diagnosed during pregnancy: Adapting recent advances in breast cancer care for pregnant patients. JAMA Oncol 2015;1:1145-1153. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26247818.
253. Silverstein J, Post AL, Chien AJ, et al. Multidisciplinary management of cancer during pregnancy. JCO Oncol Pract 2020;16:545-557. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32910882.
254. Chen Z, King W, Pearcey R, et al. The relationship between waiting time for radiotherapy and clinical outcomes: a systematic review of the literature. Radiother Oncol 2008;87:3-16. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18160158.
255. Peccatori FA, Azim HA, Jr., Orecchia R, et al. Cancer, pregnancy and fertility: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 Suppl 6:vi160-170. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23813932.
256. Martin DD. Review of radiation therapy in the pregnant cancer patient. Clin Obstet Gynecol 2011;54:591-601. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22031249.
257. American College of Radiology. ACR-SPR practice parameter for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation-Revised 2018 (Resolution 39). Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Pregnant-Pts.pdf.
258. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. Lancet Oncol 2004;5:283-291. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15120665.
259. Brewer M, Kueck A, Runowicz CD. Chemotherapy in pregnancy. Clin Obstet Gynecol 2011;54:602-618. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22031250.
260. Koren G, Carey N, Gagnon R, et al. RETIRED: Cancer chemotherapy and pregnancy. J Obstet Gynaecol Can 2013;35:263-278. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23470115.
261. Pinnix CC, Osborne EM, Chihara D, et al. Maternal and fetal outcomes after therapy for hodgkin or non-hodgkin lymphoma diagnosed during pregnancy. JAMA Oncol 2016;2:1065-1069. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27227654.
262. Cardonick E, Usmani A, Ghaffar S. Perinatal outcomes of a pregnancy complicated by cancer, including neonatal follow-up after in utero exposure to chemotherapy: results of an international registry. Am J Clin Oncol 2010;33:221-228. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19745695.
263. Amant F, Han SN, Gziri MM, et al. Chemotherapy during pregnancy. Curr Opin Oncol 2012;24:580-586. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22581358.
264. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol 2012;13:887-896. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22902483.
265. Amant F, Vandenbroucke T, Verheecke M, et al. Pediatric outcome after maternal cancer diagnosed during pregnancy. N Engl J Med 2015;373:1824-1834. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26415085.
266. Duggan B, Muderspach LI, Roman LD, et al. Cervical cancer in pregnancy: reporting on planned delay in therapy. Obstet Gynecol 1993;82:598-602. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8377988.
267. Cold S, During M, Ewertz M, et al. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). Br J Cancer 2005;93:627-632. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16136052.
268. Amant F, Loibl S, Neven P, Van Calsteren K. Breast cancer in pregnancy. Lancet 2012;379:570-579. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22325662.
269. Brenner B, Avivi I, Lishner M. Haematological cancers in pregnancy. Lancet 2012;379:580-587. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22325663.
270. Palani R, Milojkovic D, Apperley JF. Managing pregnancy in chronic myeloid leukaemia. Ann Hematol 2015;94 Suppl 2:S167-176. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25814083.
271. Einarson A, Maltepe C, Navioz Y, et al. The safety of ondansetron for nausea and vomiting of pregnancy: a prospective comparative study.

BJOG 2004;111:940-943. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15327608.
272. Matok I, Gorodischer R, Koren G, et al. The safety of metoclopramide use in the first trimester of pregnancy. N Engl J Med 2009;360:2528-2535. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19516033.
273. Melanoma during pregnancy: what it means for you and your baby. American Academy of Dermatology; Available at: https://www.aad.org/public/diseases/skin-cancer/types/common/melanoma/during-pregnancy. Accessed September 6, 2024.
274. Hodgkin lymphoma treatment during pregnancy. American Cancer Society, Inc.; Available at: https://www.cancer.org/cancer/hodgkin-lymphoma/treating/hodgkin-disease-in-pregnancy.html. Accessed September 6, 2024.
275. Alexander EK, Pearce EN, Brent GA, et al. 2017 guidelines of the american thyroid association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid 2017;27:315-389. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28056690.
276. Zebrack B, Isaacson S. Psychosocial care of adolescent and young adult patients with cancer and survivors. J Clin Oncol 2012;30:1221-1226. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22412147.
277. Sodergren SC, Husson O, Robinson J, et al. Systematic review of the health-related quality of life issues facing adolescents and young adults with cancer. Qual Life Res 2017;26:1659-1672. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28251543.
278. D'Agostino NM, Penney A, Zebrack B. Providing developmentally appropriate psychosocial care to adolescent and young adult cancer survivors. Cancer 2011;117:2329-2334. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523754.
279. Palmer S, Patterson P, Thompson K. A national approach to improving adolescent and young adult (AYA) oncology psychosocial care: the development of AYA-specific psychosocial assessment and care tools. Palliat Support Care 2014;12:183-188. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23659778.
280. Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. Am Psychol 2000;55:469-480. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10842426.
281. Zeltzer LK. Cancer in adolescents and young adults psychosocial aspects. Long-term survivors. Cancer 1993;71:3463-3468. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8490896.
282. Evan EE, Kaufman M, Cook AB, Zeltzer LK. Sexual health and self-esteem in adolescents and young adults with cancer. Cancer 2006;107:1672-1679. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16906508.
283. Ishibashi A, Okamura J, Ueda R, et al. Psychosocial strength enhancing resilience in adolescents and young adults with cancer. J Pediatr Oncol Nurs 2016;33:45-54. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25862715.
284. Morgan S, Davies S, Palmer S, Plaster M. Sex, drugs, and rock 'n' roll: caring for adolescents and young adults with cancer. J Clin Oncol 2010;28:4825-4830. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20498401.
285. Sleight AG, Duker LI. Toward a broader role for occupational therapy in supportive oncology care. Am J Occup Ther 2016;70:7004360030p7004360031-7004360038. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27295001.
286. Tamargo CL, Quinn GP, Sanchez JA, Schabath MB. Cancer and the LGBTQ population: Quantitative and qualitative results from an oncology providers' survey on knowledge, attitudes, and practice behaviors. J Clin Med 2017;6:93. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28991160.
287. Quinn GP, Sanchez JA, Sutton SK, et al. Cancer and lesbian, gay, bisexual, transgender/transsexual, and queer/questioning (LGBTQ) populations. CA Cancer J Clin 2015;65:384-400. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26186412.
288. Clayton JA, Tannenbaum C. Reporting sex, gender, or both in clinical research? JAMA 2016;316:1863-1864. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27802482.
289. Schabath MB, Blackburn CA, Sutter ME, et al. National survey of oncologists at national cancer institute-designated comprehensive cancer centers: Attitudes, knowledge, and practice behaviors about

LGBTQ patients with cancer. J Clin Oncol 2019;37:547-558. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30650044.
290. Kamen CS, Alpert A, Margolies L, et al. "Treat us with dignity": a qualitative study of the experiences and recommendations of lesbian, gay, bisexual, transgender, and queer (LGBTQ) patients with cancer. Support Care Cancer 2019;27:2525-2532. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30411237.
291. Emory K, Buchting FO, Trinidad DR, et al. Lesbian, gay, bisexual, and transgender (LGBT) view it differently than Non-LGBT: Exposure to tobacco-related couponing, e-cigarette advertisements, and anti-tobacco messages on social and traditional media. Nicotine Tob Res 2019;21:513-522. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29546337.
292. Gordon JR, Baik SH, Schwartz KTG, Wells KJ. Comparing the mental health of sexual minority and heterosexual cancer survivors: A systematic review. LGBT Health 2019;6:271-288. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31314662.
293. Jackman K, Honig J, Bockting W. Nonsuicidal self-injury among lesbian, gay, bisexual and transgender populations: an integrative review. J Clin Nurs 2016;25:3438-3453. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27272643.
294. Gower AL, Rider GN, McMorris BJ, Eisenberg ME. Bullying victimization among LGBTQ youth: Current and future directions. Curr Sex Health Rep 2018;10:246-254. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31057341.
295. Society for Adolescent H, Medicine. Recommendations for promoting the health and well-being of lesbian, gay, bisexual, and transgender adolescents: a position paper of the Society for Adolescent Health and Medicine. J Adolesc Health 2013;52:506-510. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23521897.
296. Society for Adolescent H, Medicine. Promoting health equality and nondiscrimination for transgender and gender-diverse youth. J Adolesc Health 2020;66:761-765. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32473724.
297. Gibson AW, Radix AE, Maingi S, Patel S. Cancer care in lesbian, gay, bisexual, transgender and queer populations. Future Oncol 2017;13:1333-1344. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28589734.
298. Kamen C. Lesbian, gay, bisexual, and transgender (LGBT) survivorship. Semin Oncol Nurs 2018;34:52-59. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29275016.
299. Stava CJ, Lopez A, Vassilopoulou-Sellin R. Health profiles of younger and older breast cancer survivors. Cancer 2006;107:1752-1759. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16967441.
300. Kwak M, Zebrack BJ, Meeske KA, et al. Trajectories of psychological distress in adolescent and young adult patients with cancer: a 1-year longitudinal study. J Clin Oncol 2013;31:2160-2166. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23650425.
301. Kwak M, Zebrack BJ, Meeske KA, et al. Prevalence and predictors of post-traumatic stress symptoms in adolescent and young adult cancer survivors: a 1-year follow-up study. Psychooncology 2013;22:1798-1806. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23135830.
302. Zebrack BJ, Corbett V, Embry L, et al. Psychological distress and unsatisfied need for psychosocial support in adolescent and young adult cancer patients during the first year following diagnosis. Psychooncology 2014;23:1267-1275. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24664958.
303. Burgoyne MJ, Bingen K, Leuck J, et al. Cancer-related distress in young adults compared to middle-aged and senior adults. J Adolesc Young Adult Oncol 2015;4:56-63. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26812552.
304. Johannsdottir IM, Loge JH, Kiserud CE, et al. Increased prescription rates of anxiolytics and hypnotics to survivors of cancer in childhood, adolescence, and young adulthood-A population-based study. Pediatr Blood Cancer 2018;65. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29077266.
305. Kaul S, Avila JC, Mutambudzi M, et al. Mental distress and health care use among survivors of adolescent and young adult cancer: A cross-sectional analysis of the National Health Interview Survey. Cancer 2017;123:869-878. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27859009.
306. Prasad PK, Hardy KK, Zhang N, et al. Psychosocial and neurocognitive outcomes in adult survivors of adolescent and early young adult cancer: A report from the childhood cancer survivor study. J Clin Oncol 2015;33:2545-2552. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26150441.

307. Johannsdottir IM, Karlstad O, Loge JH, et al. Prescriptions of antidepressants to survivors of cancer in childhood, adolescence, and young adulthood: A population-based study. J Adolesc Young Adult Oncol 2017;6:120-126. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27841952.
308. Kazak AE, Derosa BW, Schwartz LA, et al. Psychological outcomes and health beliefs in adolescent and young adult survivors of childhood cancer and controls. J Clin Oncol 2010;28:2002-2007. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20231679.
309. Krull KR, Huang S, Gurney JG, et al. Adolescent behavior and adult health status in childhood cancer survivors. J Cancer Surviv 2010;4:210-217. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20383785.
310. Committee on Hospital C, Child Life C. Child life services. Pediatrics 2014;133:e1471-1478. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24777212.
311. Emmons K, Li FP, Whitton J, et al. Predictors of smoking initiation and cessation among childhood cancer survivors: a report from the childhood cancer survivor study. J Clin Oncol 2002;20:1608-1616. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11896111.
312. Lown EA, Goldsby R, Mertens AC, et al. Alcohol consumption patterns and risk factors among childhood cancer survivors compared to siblings and general population peers. Addiction 2008;103:1139-1148. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18554347.
313. Cox CL, McLaughlin RA, Steen BD, Hudson MM. Predicting and modifying substance use in childhood cancer survivors: application of a conceptual model. Oncol Nurs Forum 2006;33:51-60. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16470234.
314. Rosenberg AR, Bona K, Ketterl T, et al. Intimacy, substance use, and communication needs during cancer therapy: A report from the "resilience in adolescents and young adults" study. J Adolesc Health 2017;60:93-99. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27769762.
315. Lubman DI, Cheetham A, Yucel M. Cannabis and adolescent brain development. Pharmacol Ther 2015;148:1-16. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25460036.
316. Fischer B, Russell C, Sabioni P, et al. Lower-risk cannabis use guidelines: A comprehensive update of evidence and recommendations. Am J Public Health 2017;107:e1-e12. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28644037.
317. Fadus MC, Smith TT, Squeglia LM. The rise of e-cigarettes, pod mod devices, and JUUL among youth: Factors influencing use, health implications, and downstream effects. Drug Alcohol Depend 2019;201:85-93. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31200279.
318. Cullen KA, Ambrose BK, Gentzke AS, et al. Notes from the field: Use of electronic cigarettes and any tobacco product among middle and high school students - United States, 2011-2018. MMWR Morb Mortal Wkly Rep 2018;67:1276-1277. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30439875.
319. Hartnett KP, Kite-Powell A, Patel MT, et al. Syndromic surveillance for e-cigarette, or vaping, product use-associated lung injury. N Engl J Med 2020;382:766-772. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31860794.
320. Werner AK, Koumans EH, Chatham-Stephens K, et al. Hospitalizations and deaths associated with EVALI. N Engl J Med 2020;382:1589-1598. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32320569.
321. Quidde J, von Grundherr J, Koch B, et al. Improved nutrition in adolescents and young adults after childhood cancer - INAYA study. BMC Cancer 2016;16:872. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27825320.
322. Spreafico F, Murelli M, Timmons BW, et al. Sport activities and exercise as part of routine cancer care in children and adolescents. Pediatr Blood Cancer 2019;66:e27826. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31115152.
323. Wurz A, Brunet J. Exploring the feasibility and acceptability of a mixed-methods pilot randomized controlled trial testing a 12-week physical activity intervention with adolescent and young adult cancer survivors. Pilot Feasibility Stud 2019;5:154. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31890266.
324. Munsie C, Ebert J, Joske D, Ackland T. The benefit of physical activity in adolescent and young adult cancer patients during and after treatment: A systematic review. J Adolesc Young Adult Oncol 2019;8:512-524. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31090475.

325. Zebrack B, Bleyer A, Albritton K, et al. Assessing the health care needs of adolescent and young adult cancer patients and survivors. Cancer 2006;107:2915-2923. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17103383.
326. Ward EJ, Henry LM, Friend AJ, et al. Nutritional support in children and young people with cancer undergoing chemotherapy. Cochrane Database Syst Rev 2015;2015:CD003298. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26301790.
327. Proserpio T, Ferrari A, Veneroni L, et al. Spiritual aspects of care for adolescents with cancer. Tumori 2014;100:130e-135e. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25296603.
328. Pahl DA, Wieder MS, Steinberg DM. Social isolation and connection in adolescents with cancer and survivors of childhood cancer: A systematic review. J Adolesc 2021;87:15-27. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33450464.
329. Albritton K, Barr R, Bleyer A. The adolescence of young adult oncology. Semin Oncol 2009;36:478-488. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19835743.
330. Kyngas H, Mikkonen R, Nousiainen EM, et al. Coping with the onset of cancer: coping strategies and resources of young people with cancer. Eur J Cancer Care (Engl) 2001;10:6-11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11827269.
331. Zebrack BJ, Oeffinger KC, Hou P, Kaplan S. Advocacy skills training for young adult cancer survivors: the Young Adult Survivors Conference at Camp Mak-a-Dream. Support Care Cancer 2006;14:779-782. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16482447.
332. Treadgold CL, Kuperberg A. Been there, done that, wrote the blog: the choices and challenges of supporting adolescents and young adults with cancer. J Clin Oncol 2010;28:4842-4849. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20351337.
333. Love B, Crook B, Thompson CM, et al. Exploring psychosocial support online: a content analysis of messages in an adolescent and young adult cancer community. Cyberpsychol Behav Soc Netw 2012;15:555-559. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22970826.
334. Zebrack B. Information and service needs for young adult cancer patients. Support Care Cancer 2008;16:1353-1360. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18386075.
335. Zebrack B. Information and service needs for young adult cancer survivors. Support Care Cancer 2009;17:349-357. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18543006.
336. Palmer S, Mitchell A, Thompson K, Sexton M. Unmet needs among adolescent cancer patients: a pilot study. Palliat Support Care 2007;5:127-134. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17578063.
337. Fallon S, Smith J, Morgan S, et al. 'Pizza, patients and points of view': Involving young people in the design of a post registration module entitled the adolescent with cancer. Nurse Educ Pract 2008;8:140-147. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17919977.
338. Rabin C, Simpson N, Morrow K, Pinto B. Behavioral and psychosocial program needs of young adult cancer survivors. Qual Health Res 2011;21:796-806. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20705863.
339. Kirchhoff AC, Leisenring W, Krull KR, et al. Unemployment among adult survivors of childhood cancer: a report from the childhood cancer survivor study. Med Care 2010;48:1015-1025. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20940653.
340. Keegan TH, DeRouen MC, Parsons HM, et al. Impact of treatment and insurance on socioeconomic disparities in survival after adolescent and young adult hodgkin lymphoma: A population-based study. Cancer Epidemiol Biomarkers Prev 2016;25:264-273. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26826029.
341. Zeltzer LK, Recklitis C, Buchbinder D, et al. Psychological status in childhood cancer survivors: a report from the childhood cancer survivor study. J Clin Oncol 2009;27:2396-2404. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19255309.
342. Smith AW, Bellizzi KM, Keegan TH, et al. Health-related quality of life of adolescent and young adult patients with cancer in the United States: the Adolescent and Young Adult Health Outcomes and Patient Experience study. J Clin Oncol 2013;31:2136-2145. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23650427.
343. Soliman H, Agresta SV. Current issues in adolescent and young adult cancer survivorship. Cancer Control 2008;15:55-62. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18094661.

344. Oeffinger KC, Tonorezos ES. The cancer is over, now what?: Understanding risk, changing outcomes. Cancer 2011;117:2250-2257. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523742.
345. Woodward E, Jessop M, Glaser A, Stark D. Late effects in survivors of teenage and young adult cancer: does age matter? Ann Oncol 2011;22:2561-2568. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21427066.
346. Dores GM, Metayer C, Curtis RE, et al. Second malignant neoplasms among long-term survivors of Hodgkin's disease: a population-based evaluation over 25 years. J Clin Oncol 2002;20:3484-3494. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12177110.
347. Aleman BM, van den Belt-Dusebout AW, De Bruin ML, et al. Late cardiotoxicity after treatment for Hodgkin lymphoma. Blood 2007;109:1878-1886. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17119114.
348. Bhatia S, Armenian SH, Armstrong GT, et al. Collaborative research in childhood cancer survivorship: The current landscape. J Clin Oncol 2015;33:3055-3064. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26304891.
349. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med 2006;355:1572-1582. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17035650.
350. Armstrong GT, Liu Q, Yasui Y, et al. Late mortality among 5-year survivors of childhood cancer: A summary from the childhood cancer survivor study. J Clin Oncol 2009;27:2328-2338. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19332714.
351. Tai E, Buchanan N, Townsend J, et al. Health status of adolescent and young adult cancer survivors. Cancer 2012;118:4884-4891. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22688896.
352. Hudson MM, Ness KK, Gurney JG, et al. Clinical ascertainment of health outcomes among adults treated for childhood cancer. JAMA 2013;309:2371-2381. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23757085.
353. Zhang Y, Lorenzi MF, Goddard K, et al. Late morbidity leading to hospitalization among 5-year survivors of young adult cancer: a report of the childhood, adolescent and young adult cancer survivors research program. Int J Cancer 2014;134:1174-1182. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24037993.
354. Kirchhoff AC, Spraker-Perlman HL, McFadden M, et al. Sociodemographic disparities in quality of life for survivors of adolescent and young adult cancers in the behavioral risk factor surveillance system. J Adolesc Young Adult Oncol 2014;3:66-74. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24940530.
355. Richardson DP, Daly C, Sutradhar R, et al. Hospitalization rates among survivors of young adult malignancies. J Clin Oncol 2015;33:2655-2659. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26169617.
356. Rugbjerg K, Olsen JH. Long-term risk of hospitalization for somatic diseases in survivors of adolescent or young adult cancer. JAMA Oncol 2016;2:193-200. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26584448.
357. Turcotte LM, Whitton JA, Friedman DL, et al. Risk of subsequent neoplasms during the fifth and sixth decades of life in the childhood cancer survivor study cohort. J Clin Oncol 2015;33:3568-3575. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26261260.
358. Ng AK, Travis LB. Subsequent malignant neoplasms in cancer survivors. Cancer J 2008;14:429-434. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19060610.
359. Ng AK, Kenney LB, Gilbert ES, Travis LB. Secondary malignancies across the age spectrum. Semin Radiat Oncol 2010;20:67-78. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19959033.
360. Friedman DL, Whitton J, Leisenring W, et al. Subsequent neoplasms in 5-year survivors of childhood cancer: The childhood cancer survivor study. J Natl Cancer Inst 2010;102:1083-1095. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20634481.
361. van Leeuwen FE, Klokman WJ, Stovall M, et al. Roles of radiation dose, chemotherapy, and hormonal factors in breast cancer following Hodgkin's disease. J Natl Cancer Inst 2003;95:971-980. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12837833.
362. Travis LB, Hill D, Dores GM, et al. Cumulative absolute breast cancer risk for young women treated for Hodgkin lymphoma. J Natl Cancer Inst 2005;97:1428-1437. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16204692.

363. Henderson TO, Amsterdam A, Bhatia S, et al. Systematic review: surveillance for breast cancer in women treated with chest radiation for childhood, adolescent, or young adult cancer. Ann Intern Med 2010;152:444-455; W144-454. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20368650.
364. Travis LB, Gospodarowicz M, Curtis RE, et al. Lung cancer following chemotherapy and radiotherapy for Hodgkin's disease. J Natl Cancer Inst 2002;94:182-192. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11830608.
365. Swerdlow AJ, Higgins CD, Smith P, et al. Second cancer risk after chemotherapy for Hodgkin's lymphoma: a collaborative British cohort study. J Clin Oncol 2011;29:4096-4104. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21969511.
366. Travis LB, Beard C, Allan JM, et al. Testicular cancer survivorship: research strategies and recommendations. J Natl Cancer Inst 2010;102:1114-1130. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20585105.
367. Gilligan T. Testicular cancer survivorship. Hematol Oncol Clin North Am 2011;25:627-639, x. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21570614.
368. Fossa SD, Chen J, Schonfeld SJ, et al. Risk of contralateral testicular cancer: a population-based study of 29,515 U.S. men. J Natl Cancer Inst 2005;97:1056-1066. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16030303.
369. Travis LB, Fossa SD, Schonfeld SJ, et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. J Natl Cancer Inst 2005;97:1354-1365. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16174857.
370. Wierecky J, Kollmannsberger C, Boehlke I, et al. Secondary leukemia after first-line high-dose chemotherapy for patients with advanced germ cell cancer. J Cancer Res Clin Oncol 2005;131:255-260. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15627215.
371. Howard R, Gilbert E, Lynch CF, et al. Risk of leukemia among survivors of testicular cancer: a population-based study of 42,722 patients. Ann Epidemiol 2008;18:416-421. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18433667.
372. Chaturvedi AK, Engels EA, Gilbert ES, et al. Second cancers among 104,760 survivors of cervical cancer: evaluation of long-term risk. J Natl Cancer Inst 2007;99:1634-1643. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17971527.
373. Brown LM, Chen BE, Pfeiffer RM, et al. Risk of second non-hematological malignancies among 376,825 breast cancer survivors. Breast Cancer Res Treat 2007;106:439-451. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17277968.
374. Hemminki K, Lenner P, Sundquist J, Bermejo JL. Risk of subsequent solid tumors after non-Hodgkin's lymphoma: effect of diagnostic age and time since diagnosis. J Clin Oncol 2008;26:1850-1857. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18347006.
375. Effinger KE, Migliorati CA, Hudson MM, et al. Oral and dental late effects in survivors of childhood cancer: a Children's Oncology Group report. Support Care Cancer 2014;22:2009-2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24781353.
376. Perkins SM, Dewees T, Shinohara ET, et al. Risk of subsequent malignancies in survivors of childhood leukemia. J Cancer Surviv 2013;7:544-550. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23749687.
377. Curtis RE, Freedman DM, Ron E, et al. New malignancies among cancer survivors: SEER cancer registries,1973-2000. National Cancer Institute, NIH Publ. No. 05-5302. Bethesda, MD, 2006. 2006. Available at: http://seer.cancer.gov/publications/mpmono/MPMonograph_complete.pdf.
378. Ginsberg JP, Goodman P, Leisenring W, et al. Long-term survivors of childhood Ewing sarcoma: Report from the childhood cancer survivor study. J Natl Cancer Inst 2010;102:1272-1283. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20656964.
379. Nagarajan R, Kamruzzaman A, Ness KK, et al. Twenty years of follow-up of survivors of childhood osteosarcoma: A report from the childhood cancer survivor study. Cancer 2011;117:625-634. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20922787.
380. Children's oncology group. Long-term follow-up guidelines for survivors of childhood, adolescent and young adult cancers, version 5.0.; 2018. Available at: http://www.survivorshipguidelines.org/pdf/2018/COG_LTFU_Guidelines_v5.pdf.

381. Moskowitz CS, Chou JF, Wolden SL, et al. Breast cancer after chest radiation therapy for childhood cancer. J Clin Oncol 2014;32:2217-2223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24752044.
382. Mulder RL, Hudson MM, Bhatia S, et al. Updated breast cancer surveillance recommendations for female survivors of childhood, adolescent, and young adult cancer from the international guideline harmonization group. J Clin Oncol 2020;38:4194-4207. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33078972.
383. Chen MH, Colan SD, Diller L. Cardiovascular disease: cause of morbidity and mortality in adult survivors of childhood cancers. Circ Res 2011;108:619-628. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21372293.
384. Kero AE, Jarvela LS, Arola M, et al. Cardiovascular morbidity in long-term survivors of early-onset cancer: a population-based study. Int J Cancer 2014;134:664-673. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23852751.
385. Rugbjerg K, Mellemkjaer L, Boice JD, et al. Cardiovascular disease in survivors of adolescent and young adult cancer: a Danish cohort study, 1943-2009. J Natl Cancer Inst 2014;106:dju110. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24848622.
386. van Laar M, Feltbower RG, Gale CP, et al. Cardiovascular sequelae in long-term survivors of young peoples' cancer: a linked cohort study. Br J Cancer 2014;110:1338-1341. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24504369.
387. Chao C, Xu L, Bhatia S, et al. Cardiovascular disease risk profiles in survivors of adolescent and young adult (AYA) cancer: The kaiser permanente aya cancer survivors study. J Clin Oncol 2016;34:1626-1633. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26951318.
388. Scholz-Kreisel P, Spix C, Blettner M, et al. Prevalence of cardiovascular late sequelae in long-term survivors of childhood cancer: A systematic review and meta-analysis. Pediatr Blood Cancer 2017;64. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28205419.
389. Reinders JG, Heijmen BJ, Olofsen-van Acht MJ, et al. Ischemic heart disease after mantlefield irradiation for Hodgkin's disease in long-term follow-up. Radiother Oncol 1999;51:35-42. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10386715.
390. Swerdlow AJ, Higgins CD, Smith P, et al. Myocardial infarction mortality risk after treatment for Hodgkin disease: a collaborative British cohort study. J Natl Cancer Inst 2007;99:206-214. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17284715.
391. Feijen EA, Leisenring WM, Stratton KL, et al. Equivalence ratio for daunorubicin to doxorubicin in relation to late heart failure in survivors of childhood cancer. J Clin Oncol 2015;33:3774-3780. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26304888.
392. van Dalen EC, Caron HN, Dickinson HO, Kremer LC. Cardioprotective interventions for cancer patients receiving anthracyclines. Cochrane Database Syst Rev 2011;2011:CD003917. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21678342.
393. Shaikh F, Dupuis LL, Alexander S, et al. Cardioprotection and second malignant neoplasms associated with dexrazoxane in children receiving anthracycline chemotherapy: A systematic review and meta-analysis. J Natl Cancer Inst 2016;108:djv357. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26598513.
394. Asselin BL, Devidas M, Chen L, et al. Cardioprotection and safety of dexrazoxane in patients treated for newly diagnosed t-cell acute lymphoblastic leukemia or advanced-stage lymphoblastic non-hodgkin lymphoma: A report of the children's oncology group randomized trial pediatric oncology group 9404. J Clin Oncol 2016;34:854-862. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26700126.
395. Olivieri J, Perna GP, Bocci C, et al. Modern management of anthracycline-induced cardiotoxicity in lymphoma patients: Low occurrence of cardiotoxicity with comprehensive assessment and tailored substitution by nonpegylated liposomal doxorubicin. Oncologist 2017;22:422-431. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28275118.
396. Reichardt P, Tabone MD, Mora J, et al. Risk-benefit of dexrazoxane for preventing anthracycline-related cardiotoxicity: re-evaluating the European labeling. Future Oncol 2018;14:2663-2676. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29747541.
397. van den Belt-Dusebout AW, Nuver J, de Wit R, et al. Long-term risk of cardiovascular disease in 5-year survivors of testicular cancer. J Clin Oncol 2006;24:467-475. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16421423.
398. Haugnes HS, Wethal T, Aass N, et al. Cardiovascular risk factors and morbidity in long-term survivors of testicular cancer: a 20-year

follow-up study. J Clin Oncol 2010;28:4649-4657. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20855830.
399. Abouassaly R, Fossa SD, Giwercman A, et al. Sequelae of treatment in long-term survivors of testis cancer. Eur Urol 2011;60:516-526. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21684072.
400. Mulrooney DA, Yeazel MW, Kawashima T, et al. Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: retrospective analysis of the Childhood Cancer Survivor Study cohort. BMJ 2009;339:b4606. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19996459.
401. Amini A, Murphy B, Cost CR, et al. Cardiac mortality in children and adolescents with hodgkin's lymphoma: A surveillance, epidemiology and end results analysis. J Adolesc Young Adult Oncol 2016;5:181-186. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26959398.
402. Dietz AC, Chen Y, Yasui Y, et al. Risk and impact of pulmonary complications in survivors of childhood cancer: A report from the childhood cancer survivor study. Cancer 2016;122:3687-3696. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27504874.
403. Mertens AC, Yasui Y, Liu Y, et al. Pulmonary complications in survivors of childhood and adolescent cancer. A report from the childhood cancer survivor study. Cancer 2002;95:2431-2441. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12436452.
404. Huang TT, Chen Y, Dietz AC, et al. Pulmonary outcomes in survivors of childhood central nervous system malignancies: A report from the childhood cancer survivor study. Pediatr Blood Cancer 2014;61:319-325. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24127436.
405. Fossa SD, Gilbert E, Dores GM, et al. Noncancer causes of death in survivors of testicular cancer. J Natl Cancer Inst 2007;99:533-544. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17405998.
406. O'Sullivan JM, Huddart RA, Norman AR, et al. Predicting the risk of bleomycin lung toxicity in patients with germ-cell tumours. Ann Oncol 2003;14:91-96. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12488299.
407. Haugnes HS, Aass N, Fossa SD, et al. Pulmonary function in long-term survivors of testicular cancer. J Clin Oncol 2009;27:2779-2786. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19414680.
408. Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers (ed Version 5); 2018. Available at:
409. Diller L, Chow EJ, Gurney JG, et al. Chronic disease in the childhood cancer survivor study cohort: A review of published findings. J Clin Oncol 2009;27:2339-2355. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19364955.
410. Packer RJ, Gurney JG, Punyko JA, et al. Long-term neurologic and neurosensory sequelae in adult survivors of a childhood brain tumor: childhood cancer survivor study. J Clin Oncol 2003;21:3255-3261. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12947060.
411. Bass JK, Hua CH, Huang J, et al. Hearing loss in patients who received cranial radiation therapy for childhood cancer. J Clin Oncol 2016;34:1248-1255. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26811531.
412. Brinkman TM, Krasin MJ, Liu W, et al. Long-term neurocognitive functioning and social attainment in adult survivors of pediatric CNS tumors: Results from the st jude lifetime cohort study. J Clin Oncol 2016;34:1358-1367. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26834063.
413. King AA, Seidel K, Di C, et al. Long-term neurologic health and psychosocial function of adult survivors of childhood medulloblastoma/PNET: A report from the childhood cancer survivor study. Neuro Oncol 2017;19:689-698. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28039368.
414. Annett RD, Patel SK, Phipps S. Monitoring and assessment of neuropsychological outcomes as a standard of care in pediatric oncology. Pediatr Blood Cancer 2015;62 Suppl 5:S460-513. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26700917.
415. Baum KT, Powell SK, Jacobson LA, et al. Implementing guidelines: Proposed definitions of neuropsychology services in pediatric oncology. Pediatr Blood Cancer 2017;64. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28121073.
416. Nathan PC, Patel SK, Dilley K, et al. Guidelines for identification of, advocacy for, and intervention in neurocognitive problems in survivors of childhood cancer: a report from the Children's Oncology Group. Arch Pediatr Adolesc Med 2007;161:798-806. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17679663.

417. Thornton CP, Ruble K, Jacobson LA. Beyond risk-based stratification: Impacts of processing speed and executive function on adaptive skills in adolescent and young adult cancer survivors. J Adolesc Young Adult Oncol 2021;10:288-295. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32668177.
418. Brydoy M, Oldenburg J, Klepp O, et al. Observational study of prevalence of long-term Raynaud-like phenomena and neurological side effects in testicular cancer survivors. J Natl Cancer Inst 2009;101:1682-1695. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19940282.
419. Boyette-Davis JA, Cata JP, Driver LC, et al. Persistent chemoneuropathy in patients receiving the plant alkaloids paclitaxel and vincristine. Cancer Chemother Pharmacol 2013;71:619-626. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23228992.
420. Jain P, Gulati S, Seth R, et al. Vincristine-induced neuropathy in childhood ALL (acute lymphoblastic leukemia) survivors: prevalence and electrophysiological characteristics. J Child Neurol 2014;29:932-937. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23781018.
421. Ramchandren S, Leonard M, Mody RJ, et al. Peripheral neuropathy in survivors of childhood acute lymphoblastic leukemia. J Peripher Nerv Syst 2009;14:184-189. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19909482.
422. Mustafa Ali M, Moeller M, Rybicki L, Moore HCF. Long-term peripheral neuropathy symptoms in breast cancer survivors. Breast Cancer Res Treat 2017;166:519-526. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28791499.
423. Bowers DC, McNeil DE, Liu Y, et al. Stroke as a late treatment effect of Hodgkin's Disease: A report from the childhood cancer survivor study. J Clin Oncol 2005;23:6508-6515. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16170160.
424. Bowers DC, Liu Y, Leisenring W, et al. Late-occurring stroke among long-term survivors of childhood leukemia and brain tumors: A report from the childhood cancer survivor study. J Clin Oncol 2006;24:5277-5282. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17088567.
425. Fullerton HJ, Stratton K, Mueller S, et al. Recurrent stroke in childhood cancer survivors. Neurology 2015;85:1056-1064. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26311747.
426. De Bruin ML, Dorresteijn LD, van't Veer MB, et al. Increased risk of stroke and transient ischemic attack in 5-year survivors of Hodgkin lymphoma. J Natl Cancer Inst 2009;101:928-937. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19535773.
427. Ritchey M, Ferrer F, Shearer P, Spunt SL. Late effects on the urinary bladder in patients treated for cancer in childhood: a report from the Children's Oncology Group. Pediatr Blood Cancer 2009;52:439-446. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18985721.
428. Donovan KA, Boyington AR, Judson PL, Wyman JF. Bladder and bowel symptoms in cervical and endometrial cancer survivors. Psychooncology 2014;23:672-678. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24481859.
429. Lind H, Alevronta E, Steineck G, et al. Defecation into clothing without forewarning and mean radiation dose to bowel and anal-sphincter among gynecological cancer survivors. Acta Oncol 2016;55:1285-1293. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27173757.
430. Alevronta E, Lind H, Al-Abany M, et al. Dose-response relationships for an atomized symptom of fecal incontinence after gynecological radiotherapy. Acta Oncol 2013;52:719-726. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23113592.
431. Sunesen KG, Norgaard M, Lundby L, et al. Long-term anorectal, urinary and sexual dysfunction causing distress after radiotherapy for anal cancer: a Danish multicentre cross-sectional questionnaire study. Colorectal Dis 2015;17:O230-239. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26218674.
432. Mostoufi-Moab S, Seidel K, Leisenring WM, et al. Endocrine abnormalities in aging survivors of childhood cancer: A report from the childhood cancer survivor study. J Clin Oncol 2016;34:3240-3247. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27382091.
433. Chow EJ, Friedman DL, Stovall M, et al. Risk of thyroid dysfunction and subsequent thyroid cancer among survivors of acute lymphoblastic leukemia: A report from the childhood cancer survivor study. Pediatr Blood Cancer 2009;53:432-437. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19459201.
434. Bhatti P, Veiga LH, Ronckers CM, et al. Risk of second primary thyroid cancer after radiotherapy for a childhood cancer in a large cohort study: an update from the childhood cancer survivor study. Radiat Res 2010;174:741-752. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21128798.

435. Huddart RA, Norman A, Moynihan C, et al. Fertility, gonadal and sexual function in survivors of testicular cancer. Br J Cancer 2005;93:200-207. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15999104.
436. Green DM, Liu W, Kutteh WH, et al. Cumulative alkylating agent exposure and semen parameters in adult survivors of childhood cancer: a report from the St Jude lifetime cohort study. Lancet Oncol 2014;15:1215-1223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25239573.
437. Greenberg ML. When do late effects in childhood cancer survivors cease emerging? The endocrine answer. J Clin Oncol 2016;34:3231-3232. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27480146.
438. Freyer DR. Transition of care for young adult survivors of childhood and adolescent cancer: rationale and approaches. J Clin Oncol 2010;28:4810-4818. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20351333.
439. Nathan PC, Hayes-Lattin B, Sisler JJ, Hudson MM. Critical issues in transition and survivorship for adolescents and young adults with cancers. Cancer 2011;117:2335-2341. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523755.
440. Sadak KT, Dinofia A, Reaman G. Patient-perceived facilitators in the transition of care for young adult survivors of childhood cancer. Pediatr Blood Cancer 2013;60:1365-1368. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23441065.
441. Oeffinger KC, McCabe MS. Models for delivering survivorship care. J Clin Oncol 2006;24:5117-5124. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17093273.
442. Snyder CF, Earle CC, Herbert RJ, et al. Preventive care for colorectal cancer survivors: a 5-year longitudinal study. J Clin Oncol 2008;26:1073-1079. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18309941.
443. Blaauwbroek R, Tuinier W, Meyboom-de Jong B, et al. Shared care by paediatric oncologists and family doctors for long-term follow-up of adult childhood cancer survivors: a pilot study. Lancet Oncol 2008;9:232-238. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18282804.
444. Snyder CF, Frick KD, Kantsiper ME, et al. Prevention, screening, and surveillance care for breast cancer survivors compared with controls: changes from 1998 to 2002. J Clin Oncol 2009;27:1054-1061. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19164212.
445. Wallace WH, Blacklay A, Eiser C, et al. Developing strategies for long term follow up of survivors of childhood cancer. BMJ 2001;323:271-274. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11485960.
446. Oeffinger KC. Longitudinal risk-based health care for adult survivors of childhood cancer. Curr Probl Cancer 2003;27:143-167. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12748583.
447. van der Kooi ALF, Mulder RL, Hudson MM, et al. Counseling and surveillance of obstetrical risks for female childhood, adolescent, and young adult cancer survivors: Recommendations from the international late effects of childhood cancer guideline harmonization group. Am J Obstet Gynecol 2021;224:3-15. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32502557.
448. Wein S, Pery S, Zer A. Role of palliative care in adolescent and young adult oncology. J Clin Oncol 2010;28:4819-4824. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20212259.
449. Rosenberg AR, Wolfe J. Palliative care for adolescents and young adults with cancer. Clin Oncol Adolesc Young Adults 2013;2013:41-48. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29657924.
450. Pinkerton R, Donovan L, Herbert A. Palliative care in adolescents and young adults with cancer-why do adolescents need special attention? Cancer J 2018;24:336-341. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30480579.
451. Wiener L, Weaver MS, Bell CJ, Sansom-Daly UM. Threading the cloak: palliative care education for care providers of adolescents and young adults with cancer. Clin Oncol Adolesc Young Adults 2015;5:1-18. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25750863.
452. Ferrell BR, Twaddle ML, Melnick A, Meier DE. National consensus project clinical practice guidelines for quality palliative care guidelines, 4th edition. J Palliat Med 2018;21:1684-1689. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30179523.
453. Pritchard S, Cuvelier G, Harlos M, Barr R. Palliative care in adolescents and young adults with cancer. Cancer 2011;117:2323-2328. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21523753.
454. Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American society of clinical oncology

clinical practice guideline update. J Clin Oncol 2017;35:96-112. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28034065.
455. Section On H, Palliative M, Committee On Hospital C. Pediatric palliative care and hospice care commitments, guidelines, and recommendations. Pediatrics 2013;132:966-972. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28448256.
456. Jacobs S, Perez J, Cheng YI, et al. Adolescent end of life preferences and congruence with their parents' preferences: results of a survey of adolescents with cancer. Pediatr Blood Cancer 2015;62:710-714. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25545105.
457. Pousset G, Bilsen J, De Wilde J, et al. Attitudes of adolescent cancer survivors toward end-of-life decisions for minors. Pediatrics 2009;124:e1142-1148. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19948616.
458. Weaver MS, Baker JN, Gattuso JS, et al. Adolescents' preferences for treatment decisional involvement during their cancer. Cancer 2015;121:4416-4424. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26348790.
459. Wiener L, Zadeh S, Battles H, et al. Allowing adolescents and young adults to plan their end-of-life care. Pediatrics 2012;130:897-905. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23045560.
460. Lyon ME, McCabe MA, Patel KM, D'Angelo LJ. What do adolescents want? An exploratory study regarding end-of-life decision-making. J Adolesc Health 2004;35:529 e521-526. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15581537.
461. 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. Pediatr Blood Cancer 2013;60:715-718. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23483724.
462. Johnston EE, Alvarez E, Saynina O, et al. End-of-life intensity for adolescents and young adults with cancer: A californian population-based study that shows disparities. J Oncol Pract 2017;13:e770-e781. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28829692.
463. Johnston EE, Alvarez E, Saynina O, et al. Inpatient utilization and disparities: The last year of life of adolescent and young adult oncology patients in California. Cancer 2018;124:1819-1827. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29393967.
464. Mack JW, Chen LH, Cannavale K, et al. End-of-life care intensity among adolescent and young adult patients with cancer in kaiser permanente southern california. JAMA Oncol 2015;1:592-600. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26181778.
465. Webb NM, Tucker D. Young adults' opinions about hospice and home death. J Palliat Med 2009;12:337-342. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19327070.
466. Bell CJ, Skiles J, Pradhan K, Champion VL. End-of-life experiences in adolescents dying with cancer. Support Care Cancer 2010;18:827-835. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19727847.
467. Johnston EE, Martinez I, Currie E, et al. Hospital or home? Where should children die and how do we make that a reality? J Pain Symptom Manage 2020;60:106-115. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31887402.
468. Odejide OO, Fisher L, Kushi LH, et al. Patient, family, and clinician perspectives on location of death for adolescents and young adults with cancer. JCO Oncol Pract 2022;18:e1621-e1629. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35981281.
469. Rajeshuni N, Johnston EE, Saynina O, et al. Disparities in location of death of adolescents and young adults with cancer: A longitudinal, population study in california. Cancer 2017;123:4178-4184. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28700812.
470. Mack JW, Chen K, Boscoe FP, et al. High intensity of end-of-life care among adolescent and young adult cancer patients in the new york state medicaid program. Med Care 2015;53:1018-1026. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26492211.
471. Johnston EE, Molina J, Martinez I, et al. Bereaved parents' views on end-of-life care for children with cancer: Quality marker implications. Cancer 2020;126:3352-3359. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32383817.