

Adolescent and Young Adult (AYA) Cancer

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Background

The Canadian Partnership for Cancer (CPAC) reports that approximately 7,600 Canadians aged 15 to 39 years are diagnosed with cancer every year.¹ Although the most frequent cancers in adolescent and young adults (AYAs) are thyroid cancer, breast cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, testicular cancer and melanoma, all tumour groups present in young adults.¹ While there has been an increase in the age-standardized incidence rate of cancer for the AYA population, most AYAs diagnosed with cancer in Canada will survive their disease today.¹

AYAs diagnosed with cancer face unique challenges during and after their cancer diagnosis. Ferrari et al state that, “AYA patients seem to be in a sort of no-man’s land, halfway between the two different worlds of pediatric and adult medical oncology and bearing the brunt, in terms of inclusion in clinical trials and quality of professional care, of the lack of integration between these two worlds.”² Besides differences in tumour biology, limited progress in survival, lower clinical trial participation rates, and insufficient awareness of cancer symptoms among patients and professionals, AYA cancer patients have distinct psychosocial and supportive care needs compared with pediatric and adult cancer populations.³ Late adolescence and young adulthood is a developmentally complex period of life, during which individuals are working to establish their own identity, develop a positive body image and sexual identity, detach from their parents, increase their involvement with peers, find a life partner, make decisions about higher education and careers, and possibly have their own family.⁴ A cancer diagnosis can temporarily or permanently derail these plans.

In recognition of the lack of information about AYAs diagnosed with cancer in Canada and the obligation to address their unmet needs, a Canadian framework for the care and support of AYAs with cancer was jointly published by CPAC and the Adolescent and Young Adults with Cancer National Network in 2019.⁵ The purpose of this framework was to articulate a national vision for high quality care and survivorship support of AYAs diagnosed with cancer and to provide specific individual-, service-, and system-level key actions to achieve the vision. Thus, the framework inspired the development of this provincial guideline, which endeavors to align its recommendations with the framework’s four strategic priorities to:

- Integrate an AYA-centered experience throughout care and survivorship;
- Deliver interdisciplinary, integrated and comprehensive care and survivorship support that address the unique needs of AYAs with cancer;
- Increase access to cutting-edge approaches to care and survivorship support for AYAs with cancer; and,
- Drive evidence-based improvements for AYAs with cancer.

This guideline has been developed as a supportive care guideline and not as a treatment guideline. The purpose of the guideline is to increase awareness of unique issues in AYA oncology and to recommend standards of care and interventions unique to the AYA population. Fundamentally, this guideline describes the optimal safe and high-quality care for all Albertan AYAs with cancer. Specific

treatments or clinical procedures at the patient level are the domain of the Provincial Tumour Teams and treating teams. Operationalization of these guidelines is the domain of the AYA Oncology Steering Committee and treating teams and will likely look different across healthcare facilities.

Guideline Questions

In AYAs diagnosed with cancer:

1. What specific screening and assessment are needed?
2. What considerations should be made regarding clinical trials access and participation?
3. What strategies can be used to facilitate AYA centered approaches to treatment?
4. When and how should oncofertility be addressed?
5. How can we facilitate psychosocial care?
6. How can survivorship care and planning be optimized?
7. How can palliative care be integrated and optimized?
8. How can end-of-life care be integrated in a timely manner?

Search Strategy

PubMed database was searched for relevant studies, guidelines, and consensus documents. The specific search strategies, search terms, and search results, are presented in [Appendix A](#). Evidence tables are available upon request. Online resources from oncology-based health organizations and guideline developers were also systematically searched, and relevant frameworks, care manuals, and guidelines from the following organizations were considered in the development of our recommendations: Canadian Partnership Against Cancer (CPAC), CanTeen Australia, Clinical Oncology Society of Australia (COSA), and the National Comprehensive Cancer Network (NCCN).

Target Population

This guideline's recommendations are applicable to AYAs who have been diagnosed with cancer. We defined this population as persons aged 15 to 39 years, which is in line with The Canadian Framework for the Care and Support of Adolescents and Young Adults.⁵ However, we recognize that based on their development status, persons chronologically less than 15 and older than 39 years may be best served through the recommendations of this guideline.

Target Audience

This guideline is directed at healthcare professionals who are involved in the care of AYAs who have been diagnosed with cancer, as well as for AYAs with cancer and their families and caregivers.

Recommendations

(1) AYA specific screening and assessment

- a) At the time of diagnosis or intake into the cancer care program, a comprehensive multidimensional screening and assessment for AYA specific issues should be completed and documented.⁶ This assessment can be prioritized into parts and completed by members of the healthcare team as they initially work with the AYA rather than in one encounter as appropriate. This screen should explore the AYA's cancer story, a physical symptom review, the family and home situation, education and employment status, social history and activities, relationships, habits and substance use, religious and spiritual beliefs, mental health, and current stressors. *(Level of Evidence: V, Strength of Recommendation: B)*
- b) Throughout an AYA's cancer experience, AYA specific screening and reassessment should be documented regularly and especially at times of transition (e.g., change in treatment, end of treatment, relapse or recurrence, end of surveillance, end of life). *(Level of Evidence: V, Strength of Recommendation: B)*
- c) Cancer occurring in the AYA cohort may include pediatric cancers occurring at an unexpectedly older age, a cancer of adulthood presenting at an unexpectedly young age, suggestive of an inherited cancer predisposition syndrome, or certain cancer types that are strongly predictive of an underlying germline defect. All AYAs should have a thorough family history taken at least once during their cancer experience and if appropriate be referred for genetic and familial risk assessment/counseling based on clinical/family history and/or histologic diagnosis or appropriate genetic assessments be completed based on the diagnosis.^{6,7} *(Level of Evidence: IV, Strength of Recommendation: B)*
- d) Clinicians should hold discussions that encourage AYAs to express their personal needs and preferences. Particular attention should be paid to the complex needs of individuals in low-income, Indigenous, immigrant and rural groups, among others.⁵ Attention should be paid to facilitating family-centered care approaches for the family unit as defined by the AYA. *(Level of Evidence: V, Strength of Recommendation: B)*
- e) Confidentiality is an essential component of AYA-friendly cancer care. Confidentiality and its limits should be discussed and understood at the outset to ensure clear boundaries relating to the clinical relationship with the AYA and to alleviate any concerns of family members (i.e. as defined by the patient) related to confidentiality between the AYA, family and healthcare professional.^{8,9} *(Level of Evidence: V, Strength of Recommendation: B)*
- f) Healthcare professionals working with AYAs with cancer, particularly adolescents, need to consider at each encounter the extent to which the young person is able to participate in decision-

making and provide consent or assent.^{6,10} This will depend on the patient's maturity and understanding of his/her particular situation. (*Level of Evidence: V, Strength of Recommendation: B*)

(2) Clinical Trials

- a) Healthcare professionals providing care to AYAs should make themselves aware of research opportunities for AYAs, which includes collaborating and building connections with researchers inside and outside of their institution to optimize AYA participation in clinical trials. Research should focus on generating evidence for all aspects of best-practice AYA care (e.g., biology, treatment, survivorship). (*Level of Evidence: V, Strength of Recommendation: A*)
- b) Clinical trial or tumour banking enrollment should be considered for all AYAs with a diagnosis of cancer by the healthcare team at diagnosis and reviewed throughout the cancer experience. Healthcare professionals should be aware of clinical trials in both pediatric and adult settings to increase trial prospects. (*Level of Evidence: V, Strength of Recommendation: A*)
- c) Using a shared decision-making process, healthcare professionals should inform AYAs and discuss the potential risks and benefit for AYAs and their families to participate in clinical trials, as well as enrollment on tumour banking and biologic protocols.^{5,11,12} Discussions and decisions about participation in research and clinical trials should be documented in the patient care plan.^{5,11} (*Level of Evidence: V, Strength of Recommendation: A*)
 - Refer to Alberta Clinical Trials and ClinicalTrials.gov databases for a list of current clinical studies being conducted in Alberta and around the World.

(3) Approach to Treatment

- a) AYA's should receive treatment within the tumour team best matching their case. (*Level of Evidence: V, Strength of Recommendation: B*)
- b) Developmentally-appropriate care should be delivered and/or supported by a multidisciplinary team populated with age- and disease-specific medical and psychosocial experts able to effectively communicate and provide evidence-based care.^{5,13} (*Level of Evidence: V, Strength of Recommendation: B*)
- c) When developing and updating clinical practice guidelines, all members of the provincial Tumour Teams should consider the AYA population and add specific evidence-based recommendations as needed to guidelines (e.g., dose modification, treatment-related toxicity). This is particularly important for Tumour Teams that treat cancers with high prevalence rates in the AYA population.⁵ (*Level of Evidence: V, Strength of Recommendation: B*)

- d) Dosing and schedules should consider that AYA patients may tolerate more intensive therapies that may have been associated with improved outcomes.^{6,14-17} Growth factor support may be required, and reversible toxicities may not necessarily require dose reduction as is often required in older patients. (*Level of Evidence: II, Strength of Recommendation: B*)
- e) Treatment planning should always involve consideration of late effects.¹⁶ Recognizing the majority of AYA's survive their cancer and late effects may compromise long-term function and quality of life, the monitoring of cumulative dosages and screening for treatment-related toxicities are essential.^{6,18-23} Dose reductions should be based on avoiding severe irreversible organ damage due to therapy. Screening/monitoring should be based on treatment risk assessment and may include cardiac, renal, neurologic, endocrine, ophthalmologic, dental, neurocognitive, fertility and secondary malignancy surveillance. Clinicians caring for AYAs should review current screening recommendations as required. (*Level of Evidence: IV, Strength of Recommendation: B*)
- Refer to the Children's Oncology Group (COG)²⁴ and National Comprehensive Cancer Network (NCCN)⁶ for published recommendations for late effect screening in AYA cancer survivors.
- f) Treating clinicians should work with patients to identify potential factors contributing to non-adherence with treatment regimens.⁸ It is recommended that adherence assessment and monitoring occur at every clinic visit.^{25,26} (*Level of Evidence: V, Strength of Recommendation: A*)
- g) All AYAs should be provided access to systematic and standardized symptom management for side effects related to cancer treatment.⁶ (*Level of Evidence: V, Strength of Recommendation: A*)

(4) Oncofertility

- a) All AYAs with cancer that require treatment that could compromise future fertility must be informed of the likely risk and options to protect or preserve fertility before treatment begins.²⁷ (*Level of Evidence: V, Strength of Recommendation: B*)
- Discussion can occur simultaneously with staging and the formulation of a treatment plan and should be documented in the medical record.²⁸ [Appendix B](#) provides common examples of effect of radiotherapy and systemic therapy on fertility.
 - Involving family members in these discussions may be beneficial.
 - If the clinician is unable to discuss risks and treatment options, a referral to a colleague, or an AYA oncology specialist should be initiated for further discussion, or a referral directly to the fertility clinic may be completed.
- b) Referral to a fertility clinic should be offered to AYAs as soon as possible following diagnosis²⁷ unless the risk of infertility from the cancer or treatment is 0 percent and documented. (*Level of Evidence: V, Strength of Recommendation: B*)

- c) A discussion and/or referral related to fertility should be considered when the patient returns for follow up after completion of therapy and/or if pregnancy is being considered.²⁸ (*Level of Evidence: V, Strength of Recommendation: B*)
- d) Discussions about contraceptive methods based on teratogenic and fertility risk should occur at diagnosis and be revisited at multiple points along the cancer care continuum, including during active treatment and through survivorship.^{6,29} These discussions should be documented in the medical record.²⁸ (*Level of Evidence: V, Strength of Recommendation: B*)
- e) Negative pregnancy testing for all post-pubertal AYA females should be considered prior to teratogenic treatments and based on therapy risk repeated throughout treatment. (*Level of Evidence: V, Strength of Recommendation: B*)

(5) Psychosocial

- a) All AYAs should receive psychosocial screening as part of the new patient intake process.³⁰ When indicated, a full psychosocial assessment is recommended. The goal of this process is to identify, assess, support, and intervene to address common concerns associated with having cancer during the AYA years. While there are numerous scales to assess psychosocial outcomes in cancer, few have been specifically validated for AYAs with cancer.³¹ Screening should include practical issues (housing, transport, finances), and for educational, family/social, emotional, physical, sexual, spiritual, and informational concerns.^{30,32,33}
- b) Based on results from the psychosocial screening and/or initial comprehensive assessment, healthcare professionals should: (*Level of Evidence: V, Strength of Recommendation: B*)
 - Provide AYAs and their families with information about psychosocial supports and services.^{6,8}
 - Provide information about and encourage the use of about peer support to assist AYAs establishing and maintaining relationships with their peers, as well as other AYAs with cancer through mediums such as face-to-face meetings, camp and retreat programs, online support groups, and social networking opportunities.^{5,6,8,34}
 - Address any physical/medical issues that may impact psychosocial wellbeing, including alcohol and drug use during treatment, the impact of treatment on fertility, sexuality and sexual function, physical function, and appearance.^{6,8,16,35}
 - AYAs experiencing coping, transition, mood or other mental health issues, should be referred early to a psychosocial clinician (social worker, psychologist, or spiritual care provider) and/or psychiatrist.⁶
 - Refer AYAs to a social worker and/or occupational therapist to ensure they have access to the full range of educational, vocational, and employment support services for which they are eligible.^{6,34,36}

- Refer AYAs experiencing challenges with their spirituality/faith to faith-based resources or activities, including to spiritual care providers.^{6,8}
- c) Healthcare professionals should routinely reassess the psychosocial supports of their AYA patients as they are likely to change over the patient cancer experience.^{5,37-39} (*Level of Evidence: III, Strength of Recommendation: B*)
- d) Care teams must attend to the cultural diversity (language, religious values, and diverse racial identities) within the AYA population that is required for patients and providers to work together to establish clinical care goals that address mutual concerns.⁴⁰ (*Level of Evidence: V, Strength of Recommendation: B*)

(6) Survivorship

- a) Risk stratification for late effects should be assessed for all AYA cancer survivors at the end of their treatment based on their cancer diagnosis and treatments received to help determine which member(s) of the healthcare team should be most responsible to follow-up with AYA patients.^{6,41} (*Level of Evidence: V, Strength of Recommendation: B*)
- b) Care of all AYA cancer survivors should include (*Level of Evidence: V, Strength of Recommendation: B, unless otherwise noted*):
- Evidence-based surveillance for cancer spread or recurrence, and screening for subsequent cancers.^{6,42-48} (*Level of Evidence: IV, Strength of Recommendation: B*)
 - Risk-based, exposure-related screening for late effects.^{24,49} (*Level of Evidence: I, Strength of Recommendation: A*)
 - Identifying emotional distress.^{37,39,50-52} (*Level of Evidence: III, Strength of Recommendation: B*)
 - Intervention for consequences of cancer and treatment (e.g., medical problems, symptoms, emotional distress, financial and social concerns).
 - Coordination of care between primary care providers and specialists to ensure that all the survivor's health needs are met.⁵³
 - Survivorship care planning.⁵⁴
 - A consistent primary care physician for ongoing primary healthcare, health maintenance, and treatment of intercurrent illness.^{6,51,55}
 - Assessment of sexuality and fertility related to the cancer and treatment should be considered part of routine follow up care.^{6,56,57}
 - Offer of referral to an occupational therapy or a vocational specialist who can support reentering the workforce or returning to school.^{34,36,58}
- c) Develop and provide to AYA cancer survivors and key healthcare professionals an individualized survivorship plan that includes^{6,8} (*Level of Evidence: V, Strength of Recommendation: B*):
- Summary of treatment received.
 - Information regarding follow-up care, surveillance, and screening recommendations.

- Information on post-treatment needs, including information regarding treatment-related effects and health risks when possible.
- Delineation regarding roles of oncologists, primary care physicians in survivorship care and the timing of transfer if appropriate.
- Healthy lifestyle recommendations (e.g., smoking cessation, physical activity).

(7) Palliative Care

Alberta Health Services (AHS) adopts the World Health Organization (WHO) definition of palliative care that is, “an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”⁵⁹

- a) Clinicians caring for AYAs should screen for those who may benefit from an early, integrated palliative approach to care. Early, systematic integration of palliative care into standard oncology practice is recommended.⁶⁰⁻⁶² Opportunities for screening include: symptom burden and patient concern, transitions points in care or indicators of advanced disease trajectory, requests from patient or family/caregiver for palliative care services or information, and based on clinical judgement.⁶³ (*Level of Evidence: V, Strength of Recommendation: B*)
- b) All AYAs with advanced cancer should receive palliative care services, which may include a referral to a palliative care provider. Essential components of palliative care may include:⁶⁴ (*Level of Evidence: V, Strength of Recommendation: B*)
 - Rapport and relationship building with patient and family caregiver(s).
 - Symptom, distress, and functional status management (e.g., pain, dyspnea, fatigue, sleep disturbance, mood, nausea, or constipation).
 - Exploration of understanding and education about illness and prognosis.
 - Clarification of treatment goals.
 - Assessment and support of coping needs.
 - Assistance with medical decision making.
 - Coordination with other care providers.
 - Provision of referrals to other care providers as indicated.
- c) All AYAs should be given the opportunity to participate in Advance Care Planning as a part of routine care, started early in a longitudinal relationship with a healthcare provider and revisited when the health or wishes of the AYA change.⁶⁴⁻⁶⁶ (*Level of Evidence: IV, Strength of Recommendation: B*)

- d) Goals of Care Designations should be used to establish and communicate general care directions, locations of care and transfer of the current most responsible health practitioner.⁶⁴ (*Level of Evidence: IV, Strength of Recommendation: B*)
 - e) Strategies to support an AYA must be individualized in the context of the family dynamic, including maturity of the patient and level of independence (desired and actual).^{6,67} (*Level of Evidence: IV, Strength of Recommendation: B*)
- (8) End-of-Life Care
- a) Clinicians should be comfortable discussing death and other end-of-life issues with AYAs.⁶ (*Level of Evidence: IV, Strength of Recommendation: B*)
 - b) Given that many AYAs with cancer die in hospitals,⁶ non-oncology clinicians should be knowledgeable about AYA end-of-life best practices. There should be clear communication between specialty centre clinicians initially caring for these AYA patients and the non-specialty centre clinicians that are providing end-of-life care.⁶⁸ (*Level of Evidence: IV, Strength of Recommendation: B*)
 - c) The caregiver burden associated with the provision of AYA palliative care should be recognized, prioritized, and proactively addressed. A family-centered approach to care may help to engage with family members, supporting them in the important role they play in end-of-life care.⁶⁹ (*Level of Evidence: IV, Strength of Recommendation: B*)
 - d) The burden that care delivery imposes on healthcare professionals should not be underestimated.⁷⁰ Resources should be in place to ensure adequate staff training in self-care as well as bereavement support and counselling. (*Level of Evidence: IV, Strength of Recommendation: B*)

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Appendix A. Literature Search Strategies and Results

Database	Date	Search Strategy	Limits	Results
Pubmed	Oct 22, 2019	<p>Comprehensive Assessment</p> <p>(((((neoplasms[MeSH Major Topic]) OR cancer*[Title/Abstract]) OR oncolog*[Title/Abstract])) AND (((needs assessment[MeSH Major Topic]) OR "comprehensive assessment*[Title/Abstract]) OR "needs assessment*[Title/Abstract]) OR assessment*[Title/Abstract])) AND (((AYA[Title/Abstract]) OR ("adolescent[Title/Abstract] AND young adult*[Title/Abstract])) OR "emerging adult*[Title/Abstract]) OR adolescent[MeSH Major Topic]) OR young adult[MeSH Major Topic])</p>	<p>Clinical Trial, Phase III; Clinical Trial, Phase IV; Comparative Study; Controlled Clinical Trial; Guideline; Meta-Analysis; Multicenter Study; Observational Study; Practice Guideline; Randomized Controlled Trial, Systematic Reviews; published in the last 10 years; Humans; English</p> <p>Further excluded: single institution, retrospective, avg. age ≤18</p>	10
Pubmed	Oct 23, 2019	<p>Treatment-Related Issues</p> <p>1. (((((((treatment*[Title/Abstract]) OR therap*[Title/Abstract]) OR issue*[Title/Abstract]) OR "special consideration*[Title/Abstract]) OR "toxicit*[Title/Abstract]) OR "dos*[Title/Abstract])) AND ((neoplasms[MeSH Major Topic]) OR cancer*[Title/Abstract])) AND (((("adolescent[Title/Abstract] AND young adult*[Title/Abstract])) OR AYA*[Title/Abstract]) OR adolescent[MeSH Major Topic]) OR young adult[MeSH Major Topic]) OR "emerging adult*[Title/Abstract])</p> <p>2. (((((((adolescent[MeSH Major Topic]) OR young adult[MeSH Major Topic]) OR "emerging adult*[Title/Abstract]) OR ("adolescent[Title/Abstract] AND young adult*[Title/Abstract])) OR AYA[Title/Abstract])) AND (((medication adherence[MeSH Major Topic]) OR patience compliance[MeSH Major Topic]) OR adherence[Title/Abstract])) AND ((neoplasms[MeSH Major Topic]) OR cancer*[Title/Abstract])</p>	<p>1. Clinical Trial, Phase III; Clinical Trial, Phase IV; Comparative Study; Controlled Clinical Trial; Guideline; Meta-Analysis; Multicenter Study; Observational Study; Practice Guideline; Randomized Controlled Trial, Systematic Reviews; published in the last 10 years; Humans; English</p> <p>Further excluded: single institution, retrospective, avg. age ≤18</p> <p>2. Last 10 yrs., English, human</p>	69 20
PubMed	Sep 25, 2019	<p>Fertility</p>	<p>Filters applied: Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial,</p>	327

Database	Date	Search Strategy	Limits	Results
		<p>(((((fertility preservation[MeSH Terms]) OR fertility[MeSH Terms]) OR infertility[MeSH Terms]) OR sexual behavior[MeSH Terms]) OR reproductive technique, assisted[MeSH Terms]) OR Gonadotropin-Releasing Hormone/agonists[MeSH Terms]) OR primary ovarian insufficiency[MeSH Terms]) OR "fertility preservation"[Title/Abstract]) OR fertility[Title/Abstract]) OR infertility[Title/Abstract]) OR "sexual behaviour"[Title/Abstract]) OR "gonadotropin-releasing hormone"[Title/Abstract]) OR reproduction[Title/Abstract])) AND ((neoplasms[MeSH Terms]) OR cancer*[Title/Abstract])) AND (((adolescent[MeSH Terms]) OR young adult[MeSH Terms]) OR adolescent[Title/Abstract]) OR "young adult"[Title/Abstract]) OR "emerging adult"[Title/Abstract])</p>	<p>Guideline, Meta-Analysis, Multicenter Study, Observational Study, Practice Guideline, Randomized Controlled Trial, Systematic Review, in the last 10 years, Humans, English, Young Adult: 19-24 yrs., Adult: 19-44 yrs.</p> <p>From these limitations excluded study protocols, guidelines older than 5 yrs., average age <18 yrs. and >39 yrs., retrospective, single institution, studies re survivors of childhood cancer, studies re outcomes of fertility-sparing surgery</p>	
PubMed	Dec 16, 2019	<p>Psychosocial Behavioural Considerations</p> <p>(((((work[Title/Abstract]) OR school[Title/Abstract]) OR behavior*[Title/Abstract]) OR behaviour*[Title/Abstract]) OR psycholog*[Title/Abstract]) OR relationship*[Title/Abstract]) OR emotion*[Title/Abstract]) OR social*[Title/Abstract]) OR identi*[Title/Abstract]) OR "social support"[Title/Abstract])) AND ((cancer[Title/Abstract]) OR oncology[MeSH Terms])) AND ((adolescent*[Title/Abstract]) OR "young adult"[Title/Abstract]) OR "emerging adult"[Title/Abstract])</p>	<p>Clinical Trial, Phase III; Guideline; Randomized Controlled Trial; Systematic Reviews; Multicenter Study; Meta-Analysis; Controlled Clinical Trial; Comparative Study; published in the last 10 years; Humans; English; Adult: 19-44 yrs.</p> <p>Further excluded trials if mean age ≤18 yrs., studies re survivors of childhood cancer.</p> <p>Notes: Some Rosenberg studies with “adolescent and young adults” in the title were identified, but excluded b/c they seemed to fall more in the pediatric territory (age range 12-25) (e.g., PRISM RCT, “Resilience in Adolescents and Young Adults with Cancer”)</p>	225
PubMed	Jan 22, 2020	<p>Survivorship</p> <p>(((((survivor*[Title/Abstract]) OR survivorship[Title/Abstract]) OR cancer survivor[MeSH Terms]) OR aftercare[MeSH Terms])) AND (((adolescent[MeSH Terms]) OR young adult[MeSH Terms]) OR AYA[Title/Abstract]) OR "emerging adult"[Title/Abstract]) OR ("adolescent[Title/Abstract] AND young</p>	<p>Clinical Trial, Phase III; Clinical Trial, Phase IV; Controlled Clinical Trial; Guideline; Meta-Analysis; Practice Guideline; Randomized Controlled Trial; Systematic Reviews; Observational Study; Multicenter Study; published in the last 10 years; Humans</p>	686

Database	Date	Search Strategy	Limits	Results
		adult*[Title/Abstract])) AND ((neoplasms[MeSH Terms]) OR cancer*[Title/Abstract])	Further exclude articles re. childhood cancer survivors, study populations w diagnosis at mean age <18 yrs.	
	Jul 23, 2020	((neoplasms[MeSH Terms]) OR cancer*[Title/Abstract]) AND ((((adolescent[MeSH Terms]) OR (young adult[MeSH Terms]) OR (AYA*[Title/Abstract]) OR ("emerging adult*[Title/Abstract]) OR (adolescent*[Title/Abstract]) OR ("young adult*[Title/Abstract])) AND (((((((survivor*[Title/Abstract]) OR (survivorship[Title/Abstract]) OR (aftercare[MeSH Terms]) OR ("late effect*[Title/Abstract]) OR ("secondary malignant neoplasm*[Title/Abstract]) OR ("secondary malignan*[Title/Abstract]) OR ("long-term"[Title/Abstract]))	Meta-Analysis, Randomized Controlled Trial, in the last 10 yrs., Humans, English, Adult: 19+ years, Adult: 19-44 yrs., Young Adult: 19-24 yrs.	629
PubMed	Feb 21, 2020	Palliative/End-of-Life (((((((adolescent[MeSH Terms]) OR young adult[MeSH Terms]) OR AYA[Title/Abstract]) OR "emerging adult*[Title/Abstract]) OR ("adolescent[Title/Abstract] AND young adult*[Title/Abstract])) AND (((neoplasm[MeSH Terms]) OR cancer*[Title/Abstract]) OR oncology[Title/Abstract]) AND (((((((palliative care[MeSH Terms]) OR palliative medicine[MeSH Terms]) OR terminal care[MeSH Terms]) OR "terminal care"[Title/Abstract]) OR "palliative care"[Title/Abstract]) OR "end of life"[Title/Abstract]) OR "end-of- life"[Title/Abstract]) OR "advanced care plan*[Title/Abstract])	Clinical trials, controlled clinical trials, guideline, meta-analysis, multicenter study, practice guideline, randomized controlled trial, systematic review, last 10 yrs., human., English language	171

Appendix B. Fertility Risk Classification

Providing patients with an estimate of fertility risk associated with different cancer treatments, while desirable, is challenging. Besides treatment related factors, which include modality, delivery, intensity and combinations of treatments, clinicians must also consider patient related factors such as age, baseline fertility, body mass index, smoking status, hereditary conditions, type of cancer, and previous treatments when estimating fertility risk.

In this appendix, common examples of effect of radiotherapy and systemic therapy on fertility in patients of reproductive age are provided. This is by no means a comprehensive list and should not be confused with treatments that are teratogenic.

Healthcare professionals referring to this appendix should exercise independent clinical judgment in the context of case-specific circumstances to frame discussions about fertility risk related to cancer treatment, including whether there is potential for recovery of fertility over time.

Radiation Therapy

Temporary sterilization can occur in females of reproductive age at single-fraction doses to the ovary of 1.7-6.4 Gy with permanent sterilization occurring after 3.2-10 Gy. The effect of fractionated RT on ovarian function is shown in Table 1. Ovarian damage is also associated with whole abdomen dosages of 20-30 Gy (primary or premature secondary ovarian failure), as is direct or scattered irradiation from the spinal part of craniospinal irradiation.

Table 1. Effect of fractionated irradiation on ovarian function^{i ii}

Minimum Ovarian Dosage (Gy)	Effect
0.6	No deleterious effect
1.5	No deleterious effect in most young women Age >40 yrs. some risk of sterilization
2.5-5.0	Variable Age 15-40 yrs. about 60% permanent sterilization Age >40 yrs. 100% permanent sterilization
5-8	Variable Age 15-40 yrs. about 70% permanent sterilization Age 15-40 yrs. about 30% temporary amenorrhea
>8	100% permanent sterilization

In males, multiple small fractions of radiation therapy are more toxic to spermatogenesis than a large, single fraction. Table 2 summarize the fractionated dose-related effect of spermatogenesis and Leydig cell function. In addition to testicular irradiation, the testes may be affected (transient elevation in FSH and oligospermia) by scatter from abdominal RT (>20 Gy).

Table 2. Effect of fractionated testicular irradiation on spermatogenesis and Leydig cell function^{i ii}

Testicular Dosage (Gy)	Effect on spermatogenesis and Leydig cell function
<0.1	No effect on spermatogenesis. No effect on Leydig cell function.
0.1-0.3	Temporary oligospermia with complete recovery by 12 mos. No effect on Leydig cell function.
0.3-0.5	Temporary azoospermia at 4-12 mos. after radiation with 100% recovery by 48 mos. Variable effect on Leydig cell function.
0.5-1.0	100% temporary azoospermia for 3-17 mos. after radiation with recovery beginning at 8-26 mos. Transient rise in FSH with eventual normalization.
1-2	100% azoospermia from 2 to ≥9 mos. with recovery beginning at 11-20 mos., and return of sperm counts at 30 mos. Transient rise in FSH and LH
2-3	100% azoospermia from 1-2 mos. Some patients suffer permanent azoospermia, while other patients may begin recovery at 12-14 mos. Prolonged rise in FSH with some recovery and slight increase in LH.
3-4	Reduced testicular volume. No change in testosterone. Permanent elevation in FSH and transient rise in LH. Reduced testosterone response to HCG stimulation.
12	Reduced testicular volume. Permanent azoospermia. Elevated FSH and LH. Low testosterone. Decreased or absent testosterone response to HCG stimulation. Testosterone replacement may be needed to ensure pubertal changes.
>24	Reduced testicular volume. Permanent azoospermia. Effects more severe and profound than at 12 Gy. Prepubertal testes appear more sensitive to the effects of radiation. Replacement hormone treatment probably needed in all prepubertal cases.

FSH, follicle-stimulating hormone; LH, luteinizing hormone; HCG, human chorionic gonadotropin.

Systemic Therapy

The tables below list patients as being at high risk (>70%), intermediate risk (30-70%), or low risk (<30%) of infertility based on different types of systemic therapy.ⁱⁱⁱ Very low risk can be considered <10%. This classification, while not precise, acts a critical starting point to promote uniform discussions with patients and families.^{iv}

Table 3. Known risk of effects of systemic cancer therapies on **male** fertility (adapted with permission from the Oncofertility Consortium, date unknown)^v

Risk Level	Treatment
High risk	ChIVPP, BEACOPP
	High dose alkylating chemotherapy for transplant conditioning
	Any alkylating agent (e.g., procarbazine, nitrogen mustard, cyclophosphamide) + TBI, pelvic RT, or testicular RT
	Total cyclophosphamide > 5 g/m ²
Intermediate risk	BEP x 2-4 cycles
	Cumulative cisplatin, dose >400 mg/m ²
	Cumulative carboplatin, dose >2 mg/m ²

Risk Level	Treatment
	Hormone treatments (prostate cancer)
	Oxaliplatin ^{vi}
	CHOP/CVP
Lower risk	Nonalkylating agents: ABVD, multiagent therapies for leukemia
	Anthracycline + cytarabine (acute leukemia)
	Bevacizumab
Very low / No risk	Vincristine
	Radioactive iodine
Unknown risk	Immunotherapies
	Tyrosine kinase inhibitors (e.g., erlotinib, imatinib)

ABVD, doxorubicin/bleomycin/vinblastine/dacarbazine; BEACOPP, bleomycin/etoposide/doxorubicin/cyclophosphamide/vincristine/procarbazine/prednisone; BEP, bleomycin/etoposide/cisplatin; ChIVPP, chlorambucil/vinblastine/procarbazine/prednisolone; CHOP, cyclophosphamide/hydroxydaunomycin/vincristine/prednisone; CVP, cyclophosphamide/vincristine/prednisone; RT, radiotherapy; TBI, total body irradiation

Table 4. Known risk of effects of systemic cancer therapies on **female** fertility (adapted with permission from the Oncofertility Consortium, date unknown)^{vii}

Risk Level	Treatment Type/Agent/Regimen
High risk	CMF, CEF, or CAF x 6 cycles in women >40 yrs.
	Total cyclophosphamide <ul style="list-style-type: none"> • $\geq 5 \text{ g/m}^2$ in women >40 yrs. • $>7.5 \text{ g/m}^2$ <20 yrs.
	Alkylating chemotherapy (e.g., cyclophosphamide, busulfan, melaphan) conditioning for transplant
	Any alkylating agent (e.g., cyclophosphamide, ifosfamide, busulfan, carmustine, lomustine) + TBI or pelvic RT
	ChIVPP, BEACOPP
Intermediate risk	CMF, CEF, or CAF x 6 cycles in women 30-40 yrs.
	Bevacizumab
	CHOP in women ≥ 35 yrs. ^v
	Total cyclophosphamide <ul style="list-style-type: none"> • 5 g/m^2 in women 30-40 yrs.
Lower risk	CMF, CEF or CAF x 6 cycles in women <30 yrs.
	CHOP in women < 35 yrs. ^v
	Nonalkylating chemotherapy: ABVD
	Anthracycline + cytarabine
	Oxaliplatin ^{viii}
	BEP ^v
	Radioactive iodine ^v
Very low/ no risk	MF
	Methotrexate, dactinomycin ^{ix}
	Vincristine

Risk Level	Treatment Type/Agent/Regimen
Unknown risk	Immunotherapies Tyrosine kinase inhibitors (e.g., erlotinib, imatinib)

ABVD, doxorubicin/bleomycin/vinblastine/dacarbazine; BEACOPP, bleomycin/etoposide/doxorubicin/cyclophosphamide/vincristine/procarbazine/prednisone; BEP, bleomycin/etoposide/cisplatin; CAF, cyclophosphamide/doxorubicin/fluorouracil; CEF, cyclophosphamide/epirubicin/fluorouracil; ChIVPP, chlorambucil/vinblastine/procarbazine/prednisolone; CHOP, cyclophosphamide/hydroxydaunomycin/vincristine/prednisone; CMF, cyclophosphamide/methotrexate/fluorouracil; MF, methotrexate/5-fluorouracil; RT, radiotherapy; TBI, total body irradiation

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^{vii} The Oncofertility Consortium. SaveMyFertility. Provider Pocket Guide: Fertility Preservation for Women Diagnosed with Cancer. Publish date unknown. Accessed April 10, 2023. <https://www.savemyfertility.org/pocket-guides/providers/fertility-preservation-women-diagnosed-cancer>

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Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Tumour Teams. Members include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Tumour Teams and a Knowledge Management Specialist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Resource Unit Handbook](#).

This guideline was originally developed in 2020. In 2023, the guideline was revised to include Appendix B: Fertility Risk Classification.

Levels of Evidence

I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, expert opinion

Strength of Recommendations

A	Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional
D	Moderate evidence against efficacy or for adverse outcome; generally, not recommended
E	Strong evidence against efficacy or for adverse outcome; never recommended

Maintenance

A formal review of the guideline will be conducted in 2024. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AHS, Alberta Health Services; AYA, adolescent and young adult; COG, The Children's Oncology Group; CPAC, Canadian Partnership Against Cancer; NCCN, National Comprehensive Cancer Network; WHO, World Health Organization

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Tumour Teams and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

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