Complete Summary

GUIDELINE TITLE

Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 38-91: radiation.

BIBLIOGRAPHIC SOURCE(S)

Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 38-91: radiation. Bethesda (MD): Children's Oncology Group; 2006 Mar. 74 p. [360 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 1.2. 2004 Mar.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- September 11, 2007, Rocephin (ceftriaxone sodium): Roche informed healthcare professionals about revisions made to the prescribing information for Rocephin to clarify the potential risk associated with concomitant use of Rocephin with calcium or calcium-containing solutions or products.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Late effects resulting from therapeutic exposures to radiation for treatment of pediatric malignancies

Effects include cardiovascular, dermatologic, gastrointestinal, hepatic, hormonal, immunologic, metabolic, neurologic (central, peripheral, cognitive), pulmonary, reproductive (testicular, ovarian, breast), sensory (dental, nasal, ocular, otologic), skeletal, and urologic (urinary, renal), sequelae; and secondary malignancies.

Note: These guidelines are intended for use beginning two or more years following the completion of cancer therapy, and provide a framework for ongoing late effects monitoring in childhood cancer survivors; however, these guidelines are not intended to provide guidance for follow-up of the pediatric cancer survivor's primary disease.

GUIDELINE CATEGORY

Evaluation
Management
Prevention
Screening

CLINICAL SPECIALTY

Cardiology
Dentistry
Dermatology
Endocrinology
Family Practice
Gastroenterology
Internal Medicine
Nephrology
Neurology
Obstetrics and Gynecology
Oncology
Ophthalmology
Otolaryngology
Pediatrics
Physical Medicine and Rehabilitation
Psychiatry
Pulmonary Medicine
Radiation Oncology
Urology

INTENDED USERS

Advanced Practice Nurses
Dentists
Nurses
Physical Therapists
Physician Assistants
Physicians
Speech-Language Pathologists

GUIDELINE OBJECTIVE(S)

- To provide recommendations for screening and management of late effects in survivors of pediatric malignancies
- To increase quality of life and decrease complication-related healthcare costs for pediatric cancer survivors by providing standardized and enhanced follow-up care throughout the life-span that (a) promotes healthy lifestyles, (b) provides for ongoing monitoring of health status, (c) facilitates early identification of late effects, and (d) provides timely intervention for late effects

TARGET POPULATION

Asymptomatic survivors of childhood, adolescent, or young adult cancers who were treated with radiation therapy and who present for routine exposure-related medical follow-up

INTERVENTIONS AND PRACTICES CONSIDERED

Thorough history and physical examination and targeted screening evaluations

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Pertinent information from the published medical literature over the past 20 years (updated as of October 2005) was retrieved and reviewed during the development and updating of these guidelines. For each therapeutic exposure, a complete search was performed via MEDLINE (National Library of Medicine, Bethesda, MD). Keywords included "childhood cancer therapy," "complications," and "late effects," combined with keywords for each therapeutic exposure. References from the bibliographies of selected articles were used to broaden the search.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

"High-level evidence" (recommendation category 1) was defined as evidence derived from high quality case control or cohort studies.

"Lower-level evidence" (recommendation categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series, and clinical experience.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The guidelines were scored by the multidisciplinary panel of experts using a modified version of the National Criteria: Comprehensive Cancer Network "Categories of Consensus" system. Each score reflects the expert panel's assessment of the strength of data from the literature linking a specific late effect with a therapeutic exposure, coupled with an assessment of the appropriateness of the screening recommendation based on the expert panel's collective clinical experience. "High-level evidence" (category 1) was defined as evidence derived from high quality case control or cohort studies. "Lower-level evidence" (categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series and clinical experience. Rather than submitting recommendations representing major disagreements, items scored as "Category 3" were either deleted or revised by the panel of experts to provide at least a "Category 2B" score for all recommendations included in the guidelines.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In 2002, the leadership of the Children's Oncology Group Late Effects Committee and Nursing Discipline appointed a 7-member task force, with representation from the Late Effects Committee, Nursing Discipline, and Patient Advocacy Committee. The task force was convened to review and summarize the medical literature and develop a draft of clinical practice guidelines to direct long-term follow-up care for

pediatric cancer survivors. The task force followed a modified version of the guideline development process established by the National Comprehensive Cancer Network (NCCN), integrating available literature with expert opinion using reiterative feedback loops.

The original draft went through several iterations within the task force prior to initial review. Multidisciplinary experts in the field, including nurses, physicians (pediatric oncologists and other subspecialists), patient advocates, behavioral specialists, and other healthcare professionals, were then recruited by the task force to provide an extensive, targeted review of the draft, including focused review of selected guideline sections. Revisions were made based on these recommendations. The revised draft was then sent out to additional multidisciplinary experts for further review. A total of 62 individuals participated in the review process. The guidelines subsequently underwent comprehensive review and scoring by a panel of experts in the late effects of pediatric malignancies, comprised of multidisciplinary representatives from the COG Late Effects Committee.

Revisions

In order to keep the guidelines current and clinically meaningful, the COG Late Effects Committee organized 18 multi-disciplinary task forces in March 2004. These task forces were charged with the responsibility for monitoring the medical literature in regard to specific system-related clinical topics relevant to the guidelines (e.g., cardiovascular, neurocognitive, fertility/reproductive), providing periodic reports to the Late Effects Committee, and recommending revisions to the guidelines and their associated health education materials and references (including the addition of therapeutic exposures) as new information became available. Task force members were assigned according to their respective areas of expertise and clinical interest. A list of these task forces and their membership is included in the "Contributors" section of the original guideline document. The revisions incorporated into the current release of these guidelines (Version 2.0 – March 2006) reflect the contributions and recommendations of these task forces.

All revisions proposed by the task forces were evaluated by a panel of experts, and if accepted, assigned a score (see "Rating Scheme for the Strength of the Evidence"). Proposed revisions that were rejected by the expert panel were returned with explanation to the relevant task force chair. If desired, task force chairs were given an opportunity to respond by providing additional justification and resubmitting the rejected task force recommendation(s) for further consideration by the expert panel. A total of 34 sections and 9 Health Links were added to Version 2.0 of these guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each score relates to the strength of the association of the identified late effect with the specific therapeutic exposure based on current literature, and is coupled with a recommendation for periodic health screening based on the collective clinical experience of the panel of experts. This is due to the fact that there are no randomized clinical trials (and none forthcoming in the foreseeable future) on which to base recommendations for periodic screening evaluations in this

population; therefore, the guidelines should not be misconstrued as representing conventional "evidence-based clinical practice guidelines" or "standards of care".

Each item was scored based on the level of evidence currently available to support it. Scores were assigned according to a modified version of the National Comprehensive Cancer Network "Categories of Consensus," as follows:

1 There is uniform consensus of the panel that (1) there is high-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2A There is uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2B There is non-uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

3 There is major disagreement that the recommendation is appropriate.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial version of the guidelines (Version 1.0 – Children's Oncology Group Late Effects Screening Guidelines) was released to the Children's Oncology Group (COG) membership in March 2003 for a six-month trial period. This allowed for initial feedback from the COG membership, resulting in additional review and revision of the guidelines by the Late Effects Committee prior to public release.

Revisions

All revisions proposed by the task forces were evaluated by a panel of experts, and if accepted, assigned a score (see "Rating Scheme for the Strength of the Evidence"). Proposed revisions that were rejected by the expert panel were returned with explanation to the relevant task force chair. If desired, task force chairs were given an opportunity to respond by providing additional justification and resubmitting the rejected task force recommendation(s) for further consideration by the expert panel.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Grades of recommendations (1, 2A, 2B, 3) are defined at the end of the "Major Recommendations" field.

Note from the Children's Oncology Group and the National Guideline Clearinghouse (NGC): The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* (COG LTFU) are organized according to therapeutic exposures; this guideline has been divided into individual summaries. In addition to the current summary, the following are available:

- Sections 1-2: Any Cancer Experience
- Sections 3–5: Blood/Serum Products
- Sections 6–37: Chemotherapy
- Sections 92–106: Hematopoietic Cell Transplant
- Sections 107–132: Surgery
- Sections 133–136: Other Therapeutic Modalities
- Sections 137–146: Cancer and General Health Screening

In order to accurately derive individualized screening recommendations for a specific childhood cancer survivor using this guideline, see "Using the COG LTFU Guidelines to Develop Individualized Screening Recommendations" in the original guideline document. (Note: For ease of use, a Patient-Specific Guideline Identification Tool has been developed to streamline the process and is included in Appendix I of the original guideline document.)

Guideline Organization

The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are organized according to therapeutic exposures, arranged by column as follows:

System	Body system (e.g., auditory, musculoskeletal) most relevant to each guideline section.
Score	Score assigned by expert panel representing the strength of data from the literature linking a specific late effect with a therapeutic exposure coupled with an assessment of the appropriateness of the screening recommendation based on collective clinical experience.
Section Number	Unique identifier for each guideline section corresponding with listing in Index.
Therapeutic Agent	Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.

Risk Factors	Host factors (e.g., age, sex, race, genetic predisposition), treatment factors (e.g., cumulative dose of therapeutic agent, mode of administration, combinations of agents), medical conditions (e.g., pre-morbid or co-morbid conditions), and health behaviors (e.g., diet, smoking, alcohol use) that may increase risk of developing the complication.
Highest Risk Factors	Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.
Periodic Evaluations	Recommended screening evaluations, including health history, physical examination, laboratory evaluation, imaging, and psychosocial assessment. Recommendation for minimum frequency of periodic evaluations is based on risk factors and magnitude of risk, as supported by the medical literature and/or the combined clinical experience of the reviewers and panel of experts.
Health Counseling/ Further Considerations	***Health Links***: Health education materials developed specifically to accompany these guidelines. Title(s) of Health Link(s) relevant to each guideline section are referenced in this column. Health Link documents are included in Appendix II of the original guideline document. **Counseling**: Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication. **Resources**: See the original guideline document for lists of books and web sites that may provide the clinician with additional relevant information. **Considerations for Further Testing and Intervention**: Recommendations for further diagnostic evaluations beyond minimum screening for individuals with positive screening tests, recommendations for consultation and/or referral, and recommendations for management of exacerbating or predisposing conditions.
References	References are listed immediately following each guideline section in the original guideline document. Included are medical citations that provide evidence for the association of the therapeutic intervention with the specific treatment complication and/or evaluation of predisposing risk factors. In addition, some general review articles have been included in the Reference section of the original guideline document for clinician convenience.

Note: See the end of the "Major Recommendations" field for explanations of abbreviations included in the summary.

All Fields (Except TBI)

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
38	**All Radiation Fields** (including TBI) **Info Link**: General factors influencing radiation toxicity include daily fraction size, cumulative dose, age of patient at irradiation and type of radiation used. Toxicity may not be manifest until growth is completed or patient ages.	**Secondary benign or malignant neoplasm** Occurring in or near radiation field **Info Link**: Patients with bilateral or familial retinoblastoma (implying a germline mutation) are at increased risk for developing second malignant neoplasms	**Host Factors** Cancer predisposing mutation (e.g., p53, RB1, NF1) Younger age at treatment **Treatment Factors** High cumulative radiation dose Large radiation treatment volumes Alkylating agent exposure	**Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**Physical** **Inspection and palpation of skin and soft tissues in irradiated field(s)** (Yearly) **Screening** **Other evaluations based on treatment volumes** (See recommendations for specific fields)	**Health Links** **See "Patient Resources" field** Reducing the Risk of Second Cancers **Considerations for Further Testing and Intervention** There is currently a deficiency in the literature regarding whether or not TBI is a risk factor for the development of breast cancer. Monitoring for breast cancer in females who received TBI should be determined on an individual basis. Surgical and/or oncology consultation as clinically indicated.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
39	**All Radiation Fields** (including TBI)	**Dysplastic nevi** **Skin cancer** Basal cell carcinoma Squamous cell carcinoma Melanoma	**Host Factors** Gorlin's syndrome (nevoid basal cell carcinoma syndrome)	**Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**History** **Skin lesions** **Changing moles (asymmetry, bleeding, increasing size, indistinct borders)** (Yearly) **Physical** **Dermatologic exam of irradiated fields** (Yearly)	**Health Links** **See "Patient Resources" field** Skin Health Reducing the Risk of Second Cancers **Considerations for Further Testing and Intervention** Dermatology consultation for evaluation and monitoring of atypical nevi. Oncology consultation as clinically indicated.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Dermatologic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
40	**All Radiation Fields** (including TBI)	**Dermatologic changes** Fibrosis Telangiectasias Permanent hair loss Altered skin pigmentation	**Host Factors** Younger age at treatment **Treatment Factors**	**Treatment Factors** Radiation dose $\geq$50 Gy Orthovoltage radiation (commonly used before	**Physical** **Dermatologic exam of irradiated fields** (Yearly)	**Health Links** **See "Patient Resources" field** Skin Health

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
			Total radiation dose ≥40 Gy Large dose fractions (e.g., ≥2 Gy per fraction)	1970) due to delivery of greater dose to skin and bones		

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
41	**All Radiation Fields** (including TBI)	**Bone malignancies**	**Host Factors** Adolescent at treatment Cancer-predisposing mutation (e.g., p53, RB1, NF1) **Treatment Factors** Higher radiation dose Combined with alkylating agents	**Treatment Factors** Radiation dose ≥30 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**History** **Bone pain (especially in irradiated field)** (Yearly) **Physical** **Palpation of bones in irradiated field** (Yearly)	**Counseling** Counsel patient to report symptoms promptly (e.g., bone pain, bone mass, persistent fevers) **Considerations for Further Testing and Intervention** X-ray or other diagnostic imaging in patients with clinical symptoms. Oncology consultation as clinically

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
						indicated.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Brain/Cranium

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counselin Further Considerati
42	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **TBI**	**Brain tumor** (benign or malignant)	**Host Factors** Younger age at treatment Neurofibromatosis **Treatment Factors** Higher radiation dose	**Host Factors** Age <6 years at time of treatment Ataxia telangiectasia	**History** **Headaches** **Vomiting** **Cognitive, motor, or sensory deficits** **Seizures and other neurologic symptoms** (Yearly) **Physical** **Neurologic exam** (Yearly)	**Considerati for Further Testing and Intervention** Brain MRI as clinically indicated for symptomatic patients. Consider brai MRI every oth year for patie with neurofibroma beginning 2 y after radiation therapy. Neurosurgical consultation f tissue diagnos and/or resect Neuro-oncolo consultation f medical management.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi
43	**Cranial** **Ear/Infratemporal** **TBI**	**Neurocognitive deficits** Functional deficits in: • Executive function (planning and organization) • Sustained attention • Memory (particularly visual, sequencing, temporal memory) • Processing speed • Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link**: Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher	**Host Factors** Younger age at treatment Primary CNS tumor CNS leukemia/ lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy Head/neck tumors with brain in radiation field **Treatment Factors** Radiation in combination with: • Dexamethasone • TBI • Methotrexate (IT, IO, high-dose IV) • Cytarabine (high-dose IV) Higher radiation dose Larger radiation field Greater cortical volumes Cranial radiation in combination with TBI Longer elapsed time since therapy	**Host Factors** Age <3 years at time of treatment Female sex Supratentorial tumor Premorbid or family history of learning or attention problems	**History** **Educati vocatio progres** (Yearly) **Screen** **Referra neurop evaluat** (Baselin into lon followup periodic clinically patients evidenc educatio vocation

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi
		doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. *Note: New deficits may emerge over time.*			

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
44	**Cranial**	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link**: Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g.,	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: • Dexamethasone • Methotrexate (IT,	**Treatment Factors** Radiation dose ≥24 Gy Fraction dose ≥3 Gy	**History** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologic symptoms** (Yearly)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
		leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: New deficits may emerge over time.*	IO, high-dose IV) • Cytarabine (high-dose IV) Higher radiation dose Larger radiation field Greater cortical volumes Longer elapsed time since therapy		**Physical** **Spasticity** **Ataxia** **Dysarthria** **Hemiparesis** (Yearly)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	H Cou Fu Consi
45	≥40 Gy to: **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Cerebrovascular complications** Stroke Moyamoya Occlusive cerebral vasculopathy **Info Link**:	**Host Factors** Down syndrome **Treatment Factors** Suprasellar radiation	**Treatment Factors** Radiation dose ≥55 Gy	**History** **Hemiparesis** **Hemiplegia** **Weakness** **Aphasia**	**Consi for Fu Testin Interv** Brain M diffusi weight imagin

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	H Cou Fu Consi
		Moyamoya syndrome is the complete occlusion of one or more of the three major cerebral vessels with the development of small, immature collateral vessels, which reflect an attempt to revascularize the ischemic portion of the brain.	**Medical Conditions** Sickle cell disease Neurofibromatosis		(Yearly) **Physical** **Neurologic exam** (Yearly)	angiog clinical indicat Neurol neuros consul follow- Physic occupa therap clinical indicat Revasc proced likely h moyan Aspirin prophy not ye shown benefi moyan occlusi cerebr vascul

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Coun Furthe Considerat
46	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Craniofacial abnormalities**	**Host Factors** Younger age at treatment **Treatment Factors**	**Host Factors** Age <5 years at time of treatment **Treatment Factors**	**History** **Psychosocial assessment, with attention to:** **Educational and/or vocational**	**Resources** FACES - The N Craniofacial Association www.faces-cra **Considerati Further Testi Intervention**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Coun Furthe Considerat
			Higher radiation dose	Radiation dose ≥30 Gy	**progress** **Depression** **Anxiety** **Post-traumatic stress** **Social withdrawal** (Yearly) **Physical** **Craniofacial abnormalities** (Yearly)	Reconstructive craniofacial su consultation. Consultation w psychologist in patients with adjustment dis related to facia asymmetry/de

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Immune
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseli Further Considerat
47	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Chronic sinusitis**	**Treatment Factors** Radiation dose to sinuses ≥30 Gy Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) **Medical Conditions** Atopic history Hypogammaglobulinemia		**History** **Rhinorrhea** **Postnasal discharge** (Yearly) **Physical** **Nasal exam**	**Considerat for Further Testing an Interventic** CT scan of sinuses as clinically indicated. Otolaryngolo consultation clinically indicated

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseli Further Considerat
					Sinuses (Yearly)	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
48	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Overweight** Age 2 to 20 years: BMI for age ≥85th to <95th percentile Age ≥21 years: BMI ≥25 to 29.9 **Obesity** Age 2 to 20 years: BMI for age ≥95th percentile Age ≥21 years: BMI ≥ 30 **Info Link**: BMI=wt(kg)/ht(m^2) BMI calculator available on-line at: http://nhlbisupport.com/bmi/ Growth charts for patients <21 years of age available on-line at: www.cdc.gov/growthcharts	**Host Factors** Younger at treatment **Treatment Factors** Higher cranial radiation dose Combined with corticosteroids **Medical Conditions** Familial dyslipidemia Growth hormone deficiency Hypothyroidism	**Host Factors** Age <4 years old at time of treatment Female sex **Treatment Factors** Hypothalamic radiation dose ≥20 Gy **Medical Conditions** Inability to exercise	**Physical** **Height** **Weight** **BMI** **Blood pressure** (Yearly) **Screening** **Fasting blood glucose** **Fasting serum insulin** **Fasting lipid profile** (Every 2 years in overweight or obese

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
					patients. Every 5 years in patients of normal weight. More frequently if indicated based on patient evaluation.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
49	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **TBI**	**Metabolic syndrome** **Info Link**: The metabolic syndrome is a clustering of cardiovascular risk factors that may further increase risk for cardiovascular disease. Definitions of metabolic syndrome are evolving, but generally include a combination	**Treatment Factors** Surgery in suprasellar region Prolonged corticosteroid therapy (e.g., for chronic GVHD) **Medical Conditions** Growth hormone deficiency Hypogonadism	**Host Factors** Obesity **Treatment Factors** Cranial radiation dose ≥18 Gy	**Physical** **Height** **Weight** **BMI** **Blood pressure** (Yearly) **Screening** **Fasting blood glucose** **Fasting serum insulin**	**Health Links** **See "Patient Resources" field** Diet and Physical Activity **Counseling** Counsel regarding obesity-related health risks **Considerations for Further Testing and Intervention** Consider

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
		of obesity with insulin resistance, dyslipidemia, and elevated blood pressure. *Note: Patients who received TBI may develop features of metabolic syndrome without associated obesity.*			**Fasting lipid profile** (Every 5 years. More frequently if indicated based on patient evaluation.)	endocrine consult if insulin resistance/ metabolic syndrome is suspected. Nutritional counseling. Cardiology consultation as clinically indicated.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Neuroendocrine Axis

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	F
50	**Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal** **TBI**	**Growth hormone deficiency** **Info Link**: Growth charts available on-line at: www.cdc.gov/growthcharts	**Host Factors** Younger at treatment **Treatment Factors** Higher radiation doses Surgery in suprasellar region Pretransplant	**Treatment Factors** Radiation dose ≥18 Gy Pretransplant cranial radiation TBI given in single fraction	**History** **Assessment of nutritional status** (Every six months until growth is completed, then yearly) **Physical** **Height**	H S R G D S R w C F I

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	F
			radiation TBI ≥10 Gy in single fraction TBI ≥12 Gy fractionated		**Weight** **BMI** (Every six months until growth is completed, then yearly) **Tanner staging** (Every six months until sexually mature)	C ir c c E ir c e ri g r C t a d

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counselin Further Considerat
51	**Cranial** **Orbital/Eye** **Ear/Infratemporal**	**Precocious puberty**	**Host Factors** Female sex Younger age at		**Physical** **Height** **Weight**	**Health Links** **See "Patient Resources" field** Precocious Puberty

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counselin Further Considerat
	Nasopharyngeal		treatment **Treatment Factors** Radiation doses ≥18 Gy		**Tanner stage** **Testicular volume by Prader orchidometry (males only)** (Yearly until sexually mature) **Screening** **FSH** **LH** **Testosterone** (males only) **Estradiol** (females only) (As clinically indicated in patients with signs of accelerated pubertal progression and growth)	**Resources** www.magicfoundatio **Considerations for Further Testing an Intervention** Obtain x-ray for bone in rapidly growing children. Endocrine consultation for accelerated puberty (puberty in girl <8 ye old or boy <9 years o

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Furthe
52	≥40 Gy to: **Cranial**	**Hyperprolactinemia**	**Treatment Factors** Higher	**Treatment Factors** Radiation	**History** **Galactorrhea**	**Health** **See "P Resou**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Furthe
	Orbital/Eye **Ear/Infratemporal** **Nasopharyngeal**		radiation dose Surgery or tumor in hypothalamic area	dose ≥50 Gy	**Decreased libido (males)** **Menstrual history (females)** (Yearly) **Screening** **Prolactin level** (Males with galactorrhea or decreased libido; Females with galactorrhea or amenorrhea)	Hyperp **Resou** www.m **Consid Furthe Interv** CT eva turcica adenon hyperp Endocr patient hyperp galacto ameno

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
53	≥40 Gy to: **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Central hypothyroidism** **Info Link**: Central hypothyroidism includes thyroid-releasing and thyroid-stimulating hormone deficiency	**Treatment Factors** Higher radiation dose		**History** **Fatigue** **Weight gain** **Cold intolerance** **Constipation** **Dry skin**	**Health Links** **See "Patient Resources" field** Thyroid Problems See also: Hypopituitarism **Counseling**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					Brittle hair **Depressed mood** (Yearly; Consider more frequent screening during periods of rapid growth) **Physical** **Height** **Weight** **Hair** **Skin** **Thyroid exam** (Yearly; Consider more frequent screening during periods of rapid growth) **Screening** **TSH** **Free T4** (Yearly; Consider more frequent	Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Consider TSH surge testing. Endocrine consultation for thyroid hormone replacement.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					screening during periods of rapid growth)	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Male Reproductive/Female Reproductive
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health C Fu Consid
54	≥40 Gy to: **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Gonadotropin deficiency** **Info Link**: Gonadotropin deficiency includes LH and FSH deficiency.	**Treatment Factors** Higher radiation dose		***MALES***: **History** **Pubertal (onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** (Yearly) **Physical** **Tanner stage** **Testicular volume by Prader orchidometry** (Yearly until sexually mature) **Screening** **FSH**	***MALES***: **Health L** **See "Pa Resourc** Male Hea See also: Hypopitu **Resourc** American for Repro Medicine www.asr Fertile H www.fert **Conside for Furth Testing Interve** Refer to endocrin delayed persisten abnorma levels. H

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health C Fu Consid
					LH **Testosterone** (Baseline at age 14 and as clinically indicated in patients with delayed puberty and/or clinical signs and symptoms of testosterone deficiency) **Semen analysis** (As requested by patient and for evaluation of infertility)	replacem therapy f hypogon patients. Reproduc endocrin referral f infertility and cons regardin reproduc technolo Consider density t patients gonadotr deficient.
					FEMALES: **History** **Pubertal (onset, tempo)** **Menstrual/pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** (Yearly) **Physical** **Tanner stage** (Yearly until sexually mature) **Screening** **FSH**	***FEMALE*** **Health L** **See "Pa Resourc** Female H Issues See also: Hypopitu **Resourc** American for Repro Medicine www.asr Fertile Ho www.fert **Conside for Furth Testing Interven** Refer to endocrin delayed persisten

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health C Fu Consid
					LH **Estradiol** (Baseline at age 13, and as clinically indicated in patients with delayed puberty, irregular menses, primary or secondary amenorrhea, or clinical signs and symptoms of estrogen deficiency)	abnorma levels. H replacem therapy f hypogon patients. Reproduc endocrin referral f infertility and cons regardin reproduc technolo Consider density t patients gonadotr deficient

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health C Further Co
55	≥40 Gy to: **Cranial** **Orbital/Eye** **Ear/Infratemporal** **Nasopharyngeal**	**Central adrenal insufficiency**	**Treatment Factors** Higher radiation dose Surgery or tumor in the suprasellar region	**Treatment Factors** Prior development of another hypothalamic-pituitary endocrinopathy	**History** **Failure to thrive** **Anorexia** **Dehydration** **Hypoglycemia** **Lethargy** **Unexplained hypotension** (Yearly)	**Health Lin** **See "Patie Resources** Central Adr Insufficienc See also: H **Resources** www.magic **Counseling** Counsel reg corticostero replacemen

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health C Further Co
					Screening **8:00 a.m. serum cortisol** (Yearly for at least 15 years after treatment and as clinically indicated)	stress dosin regarding M bracelet. **Considerat Further Te Interventi** Endocrine c further eval replacemen

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Eye

System = Ocular
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
56	**Cranial** **Orbital/Eye** **TBI** **Info Link**: Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose cranial radiation. However, patients with a history of an	**Cataracts**	**Treatment Factors** Radiation dose ≥10 Gy TBI ≥2 Gy in single fraction TBI ≥5 Gy fractionated Radiation combined with: • Corticosteroids • Busulfan • Longer interval since treatment	**Treatment Factors** Radiation dose ≥15 Gy Fraction dose ≥2 Gy TBI ≥5 Gy in single fraction TBI ≥10 Gy fractionated Cranial/orbital/eye radiation combined with TBI	**History** **Visual changes (decreased acuity, halos, diplopia)** (Yearly) **Physical** **Visual acuity** **Funduscopic exam to evaluate for lens opacity** (Yearly) **Screening**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
	ocular tumor (e.g., retinoblastoma) are at higher risk for late-onset ocular complications and should receive ongoing follow-up by an ophthalmologist at least annually, and more frequently if clinically indicated.				**Evaluation by ophthalmologist** (Yearly for patients with ocular tumors [regardless of radiation dose] and for those who received TBI or ≥30 Gy cranial/orbital/eye radiation. Every 3 years for patients without ocular tumors who received <30 Gy.)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Ocular
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Co F Cons
57	≥30 Gy to: **Cranial** **Orbital/Eye** **Info Link**: Radiation-related ocular complications other than cataracts are generally associated only with orbital/eye radiation or higher dose	**Ocular toxicity** Orbital hypoplasia Lacrimal duct atrophy Xerophthalmia (keratoconjunctivitis sicca) Keratitis Telangiectasias Retinopathy Optic chiasm neuropathy Enophthalmos Chronic painful eye Maculopathy Papillopathy	**Treatment Factors** Higher radiation dose Higher daily fraction dose Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) [problems related to tearing]	**Host Factors** Chronic GVHD (xerophthalmia only) **Treatment Factors** Fraction dose ≥2 Gy	**History** **Visual changes (decreased acuity, halos, diplopia)** **Dry eye** **Persistent eye irritation** **Excessive tearing** **Light sensitivity**	**Heal** **See Reso field** Eye H **Reso** FACE Natio Crani Asso webs www crani

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Co F Cons
	cranial radiation. However, patients with a history of an ocular tumor (e.g., retinoblastoma) are at higher risk for late-onset ocular complications and should receive ongoing follow-up by an ophthalmologist at least annually, and more frequently if clinically indicated.	Glaucoma **Info Link**: Reduced visual acuity may be associated with cataracts, retinal damage, and optic nerve damage.			**Poor night vision** **Painful eye** (Yearly) **Physical** **Visual acuity** **Funduscopic exam** (Yearly) **Screening** **Evaluation by ophthalmologist** (Yearly)	**Cons for F Testi Inter** Cons six m ophth evalu patie corne (usua assoc xerop or co ocula probl patie visua schoo comm cance (psyc socia schoo couns facili acqui educa resou

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Ear

System = Auditory
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi Evaluati
58	≥30 Gy to:	**Ototoxicity**	**Host**	**Treatment Factors**	**History**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi Evaluati
	Cranial **Ear/Infratemporal** **Nasopharyngeal**	Tympanosclerosis Otosclerosis Eustachian tube dysfunction Conductive hearing loss	**Factors** Younger age at treatment **Treatment Factors** Higher radiation dose **Medical Conditions** Chronic otitis Chronic cerumen impaction	Dose ≥50 Gy	**Hearing difficulties (with/with background noise)** **Tinnitus** **Vertigo** (Yearly) **Physical** **Otoscopic e** (Yearly) **Screening**
		Sensorineural hearing loss Tinnitus	**Host Factors** Younger age at treatment CNS tumor CSF shunting **Treatment Factors** Higher radiation dose Conventional (non-conformal) radiation	**Treatment Factors** Radiation administered prior to platinum chemotherapy Combined with other ototoxic agents such as: • Cisplatin • Carboplatin in myeloablative doses • Aminoglycosides	**Complete p tone audiog or brainste auditory evoked response (BAER, ABR** (Yearly after completion o therapy for 5 years [for patients <10 years old, continue yea until age 10] then every 5 years. If hea loss is detec test at least yearly or as recommende audiologist. clinical suspi of hearing lo any time, te

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi Evaluati
					clinically indicated. If audiogram is inconclusive unevaluable refer to audiologist f consideratio electrophysi testing e.g., OAEs.) **Info Link**: Complete pu tone audiogr should inclu testing of bo ears: 1. Air condu from to 80 Hz 2. Bone condu if air condu thres excee bone 15 dB any frequ 3. Spee discri tion evalu OAEs measu outer hair ce function only Because carboplatin

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi Evaluati
					selectively damages inn hair cells, patients trea with carbopl should not b evaluated w OAEs.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Oral Cavity

System = Dental
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
59	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle**	**Xerostomia** **Salivary gland dysfunction**	**Treatment Factors** Head and neck radiation involving the parotid gland Higher radiation doses Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin)	**Treatment Factors** Salivary gland dose ≥30 Gy **Medical Conditions** Chronic GVHD	**History** **Xerostomia** (Yearly) **Physical** **Oral exam** (Yearly) **Screening** **Dental exam and cleaning** (Every six months)	**Health Links** **See "Patient Resources" field** Dental Health **Considerations for Further Testing and Intervention** Supportive care with saliva substitutes, moistening agents, and sialogogues (pilocarpine); Regular dental care including fluoride applications

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Dental
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
60	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle** **TBI**	**Dental abnormalities** Tooth/root agenesis Microdontia Root thinning/ shortening Enamel dysplasia Periodontal disease Dental caries Malocclusion Temporomandibular joint dysfunction	**Host Factors** Younger age at treatment Gorlin's syndrome (nevoid basal cell carcinoma syndrome) **Treatment Factors** Higher radiation dose	**Host Factors** Age <5 years at time of treatment **Treatment Factors** Dose ≥10 Gy	**Physical** **Oral exam** (Yearly) **Screening** **Dental exam and cleaning** (Every six months)	**Health Links** **See "Patient Resources" field** Dental Health **Considerations for Further Testing and Intervention** Regular dental care including fluoride applications. Consultation with orthodontist experienced in management of irradiated childhood cancer survivors. Baseline panorex prior to dental procedures to evaluate root development.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Dental
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerati
61	≥40 Gy to: **Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle**	**Osteoradionecrosis**	**Treatment Factors** Radiation dose to bone ≥45 Gy	**Treatment Factors** Radiation dose to bone ≥50 Gy	**History** **Impaired or delayed healing following dental work** **Persistent jaw pain or swelling** **Trismus** (As clinically indicated) **Physical** **Impaired wound healing** **Jaw swelling** **Trismus** (As clinically indicated)	**Health Links** **See "Patient Resources" fi** Osteoradionecr **Considerations for Further Testing and Intervention** Imaging studie (x-ray, CT scan and/or MRI) m assist in makin diagnosis. Surg biopsy may be needed to conf diagnosis. Consider hyperbaric oxy treatments.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Neck/Thyroid

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
62	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle** **TBI**	**Thyroid nodules**	**Host Factors** Younger age at treatment Female sex **Treatment Factors** Higher radiation dose Thyroid gland directly in radiation field TBI	**Treatment Factors** Radiation dose to bone ≥25 Gy	**Physical** **Thyroid exam** (Yearly)	**Health Links** **See "Patient Resources" field** Thyroid Problems **Considerations for Further Testing and Intervention** Ultrasound and FNA for evaluation of palpable nodule(s). Endocrine and/or surgical consultation for diagnostic biopsy or thyroidectomy.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
63	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)**	**Thyroid cancer**	**Host Factors** Younger age at treatment Female sex **Treatment**		**Physical** **Thyroid exam** (Yearly)	**Health Links** **See "Patient Resources" field** Thyroid Problems

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	Supraclavicular **Mantle** **Mini-Mantle** **TBI**		**Factors** ≥5 years after irradiation Thyroid gland directly in radiation field TBI Risk increased up to 30 Gy with a downturn of risk after 30 Gy			**Considerations for Further Testing and Intervention** Ultrasound and FNA for evaluation of palpable nodule(s). Surgical consultation for resection. Nuclear medicine consultation for ablation of residual disease. Endocrine consultation for postoperative medical management.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
64	**Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)**	**Hypothyroidism**	**Host Factors** Female sex **Treatment Factors** Radiation dose ≥10	**Treatment Factors** Radiation dose ≥20 Gy	**History** **Fatigue** **Weight gain** **Cold intolerance** **Constipation**	**Health Links** **See "Patient Resources" field** Thyroid Problems **Counseling**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	Supraclavicular **Mantle** **Mini-Mantle** **TBI**		Gy Thyroid gland directly in radiation field TBI		**Dry skin** **Brittle hair** **Depressed mood** (Yearly; Consider more frequent screening during periods of rapid growth) **Physical** **Height** **Weight** **Hair** **Skin** **Thyroid exam** (Yearly; Consider more frequent screening during periods of rapid growth) **Screening** **TSH** **Free T4** (Yearly; Consider	Counsel at-risk females of childbearing potential to have their thyroid levels checked prior to attempting pregnancy and periodically throughout pregnancy. **Considerations for Further Testing and Intervention** Endocrine consultation for medical management.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					more frequent screening during periods of rapid growth)	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Endocrine/Metabolic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
65	≥40 Gy to: **Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle**	**Hypothyroidism**	**Treatment Factors** Higher radiation dose		**History** **Heat intolerance** **Tachycardia** **Palpitations** **Weight loss** **Emotional lability** **Muscular weakness** **Hyperphagia** (Yearly) **Physical** **Eyes** **Skin** **Thyroid**	**Health Links** **See "Patient Resources" field** Thyroid Problems **Considerations for Further Testing and Intervention** Endocrine consultation for medical management.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					Cardiac **Neurologic** (Yearly) **Screening** **TSH** **Free T4** (Yearly)	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Cardiovascular
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
66	≥40 Gy to: **Cranial** **Nasopharyngeal** **Oropharyngeal** **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle**	**Carotid artery disease**			**History** **Memory impairment** (Yearly) **Physical** **Diminished carotid pulses** **Carotid bruits** **Abnormal neurologic exam (compromise**	**Considerations for Further Testing and Intervention** Doppler ultrasound of carotid vessels as clinically indicated. MRI with diffusion-weighted imaging with MR angiography and cardiovascular surgery consultation as clinically indicated.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					of blood flow to brain) (Yearly)	Consider color Doppler 10 years after completion of radiation therapy to the neck as a baseline; refer to cardiologist if abnormal.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Cardiovascular
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
67	≥40 Gy to: **Spine (cervical)** **Cervical (neck)** **Supraclavicular** **Mantle** **Mini-Mantle**	**Subclavian artery disease**			**Physical** **Diminished brachial and radial pulses** **Pallor of upper extremities** **Coolness of skin** **Unequal blood pressure** (Yearly)	**Considerations for Further Testing and Intervention** Doppler ultrasound of subclavian vessels as clinically indicated. MRI with diffusion-weighted imaging with MR angiography and cardiovascular surgery consultation as clinically indicated. Consider color Doppler 10 years after

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
						completion of radiation therapy to the neck as a baseline; refer to cardiologist if abnormal.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Breast

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
68 (Female)	≥20 Gy to: **Mantle** **Mini-Mantle** **Mediastinal** **Chest (thorax)** **Axilla**	**Breast cancer**	**Host Factors** Family history of breast cancer **Treatment Factors** Higher radiation dose Longer time since radiation (≥5 years) **Info Link**: There is currently a deficiency in the literature	**Host Factors** Female gender	**Physical** **Breast exam** (Yearly beginning at puberty until age 25, then every six months) **Screening** **Mammogram** (Yearly, beginning 8 years after radiation or at age 25, whichever occurs last) **Info Link**: Mammography	**Health Links** **See "Patient Resources" field** Breast Cancer **Counseling** Teach breast self-exam and counsel to perform monthly beginning at puberty. **Considerations for Further Testing and Intervention** Surgical consultation for

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
			regarding whether or not TBI is a risk factor for the development of breast cancer. Monitoring of patients who received TBI should be determined on an individual basis.		is currently limited in its ability to evaluate the premenopausal breast. The role of MRI is evolving for screening of other populations at high risk for breast cancer (e.g., premenopausal known or likely carriers of gene mutation of known penetrance).	diagnostic procedure in patients with breast mass or suspicious radiographic finding. Decisions regarding the use of HRT should be based on current literature and should take into consideration the risk/benefit ratio for individual patients.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Female reproductive
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
69 (Female)	≥20 Gy to: **Mantle** **Mini-Mantle** **Mediastinal** **Chest (thorax)** **Whole lung** **Axilla**	**Breast tissue hypoplasia**	**Host Factors** Prepubertal at time of breast irradiation **Treatment Factors** Higher radiation dose		**Physical** **Breast exam** (Yearly)	**Considerations for Further Testing and Intervention** Surgical consultation for breast reconstruction after completion of growth.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	TBI					

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Lungs

System = Pulmonary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Considerati
70	**Mantle** **Mediastinal** **Chest (thorax)** **Whole lung** **TBI**	**Pulmonary toxicity** Pulmonary fibrosis Interstitial pneumonitis Restrictive lung disease Obstructive lung disease	**Host Factors** Younger age at irradiation **Treatment Factors** Radiation dose ≥15 Gy Chest radiation combined with TBI Radiation combined with: • Bleomycin • Busulfan • Carmustine (BCNU) • Lomustine (CCNU) • Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) **Medical Conditions** Atopic history **Health Behaviors**	**Treatment Factors** Radiation dose ≥15 Gy TBI ≥6 Gy in single fraction TBI ≥12 Gy fractionated	**History** **Cough** **SOB** **DOE** **Wheezing** (Yearly) **Physical** **Pulmonary exam** (Yearly) **Screening** **Chest x-ray** **PFTs (including DLCO and spirometry)** (Baseline at entry into long-term	**Health Links** **See "Patient Resources" f** Pulmonary He **Resources** Extensive information regarding smo cessation is available for patients on th NCI's website: www.smokefre **Counseling** Counsel regar tobacco avoidance/sm cessation. Due the potential pulmonary tox of this therapy patients who c to SCUBA dive should be adv to obtain med

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Considerati
			Smoking		follow-up. Repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction.)	clearance from diving medicin specialist. **Considerations for Further Testing and Intervention** In patients wit abnormal PFTs and/or CXR, consider repea evaluation pri general anesth Pulmonary consultation fo patients with symptomatic pulmonary dysfunction. Influenza and Pneumococcal vaccinations.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Heart

System = Cardiovascular
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	
71	**Mantle** **Mediastinal** **Chest (thorax)** **Axilla** **Spine (thoracic)**	**Cardiac toxicity** Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial	**Host Factors** Younger age at irradiation Family history of dyslipidemia Coronary artery disease **Treatment Factors** Radiation dose ≥20 Gy to chest	**Host Factors** Female sex Black/of African descent Younger than age 5 years at time of treatment	**History** **SOB** **DOE** **Orthopnea** **Chest pain** **Palpitations**	H S H D R A r

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	
	Whole abdomen **All upper abdominal fields**	infarction Arrhythmia Atherosclerotic heart disease	TBI Combined with radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Combined with other cardiotoxic chemotherapy: • Anthracyclines • Cyclophosphamide conditioning for HCT • Amsacrine **Medical Conditions** Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Febrile illness Pregnancy Premature ovarian failure (untreated) **Health Behaviors** Smoking Isometric exercise Drug use (e.g., cocaine, diet pills, ephedra)	**Treatment Factors** Anteriorly-weighted radiation fields Lack of subcarinal shielding Doses ≥30 Gy in patients who have received anthracyclines Doses ≥40 Gy in patients who have not received anthracyclines Longer time since treatment	**If under 25 years: Abdominal symptoms (nausea, vomiting)** (Yearly) **Info Link**: Exertional intolerance is uncommon in young patients (<25 years). Abdominal symptoms (nausea, emesis) may be observed more frequently than exertional dyspnea or chest pain in young patients. **Physical** **Cardiac murmur** **S3, S4** **Increased P2 sound** **Pericardial rub** **Rales** **Wheezes** **Jugular**	

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
					venous distension **Peripheral edema** (Yearly) **Screening** **Fasting glucose and lipid profile** (Every 3 to 5 years. If abnormal, refer for ongoing management.) **EKG (include evaluation of QTc interval)** (Baseline at entry into long-term followup. Repeat as clinically indicated.) **ECHO** (Baseline at entry into long-term followup, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose - *see next table*.)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Recommended Frequency of Echocardiogram

Age at Treatment*	Radiation Dose	Anthracycline Dose**	Recommended Frequency
<5 years old	Any	None	Every 2 years
		Any	Every year
≥5 years old	<30 Gy	None	Every 5 years
	≥30 Gy	None	Every 2 years
	Any	<300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
Any age with serial decrease in function			Every year

*Age at time of first cardiotoxic therapy (anthracycline or chest radiation, whichever was given first)

**Based on equivalent mg of doxorubicin/daunorubicin

Potential Impact to Spleen

System = Immune
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
72	≥40 Gy to: **Spleen (entire)** **Whole abdomen** **Left upper quadrant** **Inverted Y**	**Functional asplenia** At risk for life-threatening infection with encapsulated organisms (e.g., Haemophilus influenzae, streptococcus pneumoniae, meningococcus)	**Treatment Factors** Higher radiation dose to entire spleen		**Physical** **Physical exam at time of febrile illness to evaluate degree of illness and potential source of infection** (When febrile T ≥101 degrees F) (Yearly)	**Health Links** **See "Patient Resources" field** Splenic Precautions **Counseling** Medical alert bracelet/card noting functional asplenia; Counsel to avoid malaria and tick bites if living in or visiting endemic areas.

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					Screening **Blood culture** (When febrile T ≥101 degrees F)	**Considerations for Further Testing and Intervention** In patients with T ≥101 degrees F (38.3 degrees C) or other signs of serious illness, administer a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone), and continue close medical monitoring while awaiting blood culture results. Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever ≥104 degrees F; meningitis,

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
						pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection. Immunize with Pneumococcal, Meningococcal, and HIB vaccines. Pneumovax booster in patients ≥10 years old at ≥5 years after previous dose.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to GI/Hepatic System

System = GI/Hepatic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
73	≥30 Gy to: **Cervical (neck)** **Spine (cervical, thoracic)** **Supraclavicular** **Mantle**	**Esophageal stricture**	**Treatment Factors** Higher radiation dose Radiomimetic chemotherapy (e.g., doxorubicin, actinomycin) **Medical**	**Treatment Factors** Radiation dose ≥40 Gy	**History** **Dysphagia** **Heartburn** (Yearly)	**Health Links** **See "Patient Resources" field** Gastrointestinal Health **Considerations for Further Testing and**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	Mini-Mantle **Mediastinal** **Chest (thorax)** **Whole abdomen** **All upper abdominal fields**		**Conditions** Gastroesophageal reflux			**Intervention** Surgical and/or gastroenterology consultation for symptomatic patients.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideration
74	≥30 Gy to: **Whole abdomen** **All upper abdominal fields**	**Hepatic fibrosis** **Cirrhosis**	**Treatment Factors** Higher radiation dose **Medical Conditions** Chronic hepatitis History of VOD **Health Behaviors** Alcohol use	**Treatment Factors** Dose ≥40 Gy to at least 1/3 of liver volume Dose 20 to 30 Gy to entire liver	**Physical** **Jaundice** **Spider angiomas** **Palmar erythema** **Xanthomata** **Hepatomegaly** **Splenomegaly** (Yearly) **Screening** **ALT** **AST**	**Health Links** **See "Patient Resources" field** Liver Health **Considerations for Further Testing and Intervention** Prothrombin time for evaluation of hepatic synthetic function in patien with abnormal liver screening tests. Screen for viral hepatitis in patients with persistently abnormal liver function or any patien transfused prior to 1993. Gastroenterology/hepatolo consultation in patients wi persistent liver dysfunction

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideration
					Bilirubin (Baseline at entry into long-term follow-up. Repeat as clinically indicated.)	Hepatitis A and B immunizations in patients lacking immunity.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
75	≥30 Gy to: **Whole abdomen** **All upper abdominal fields**	**Cholelithiasis**	**Host Factors** Ileal conduit Obesity Pregnancy Family history of cholelithiasis **Treatment Factors** Abdominal surgery Abdominal radiation TPN		**History** **Colicky abdominal pain related to fatty food intake** **Excessive flatulence** (Yearly and PRN) **Physical** **RUQ or epigastric tenderness** **Positive Murphy's sign** (Yearly and	**Health Links** **See "Patient Resources" field** Gastrointestinal Health **Considerations for Further Testing and Intervention** Consider gallbladder ultrasound in patients with chronic abdominal pain

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					PRN)	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
76	≥30 Gy to: **Whole abdomen** **All upper abdominal fields** **Pelvic** **Spine (thoracic, lumbar, sacral)**	**Bowel obstruction**	**Treatment Factors** Higher radiation dose to bowel Abdominal surgery **Info Link**: Bowel obstruction is rarely seen in individuals treated with abdominal radiation who have not had abdominal surgery	**Treatment Factors** Radiation dose ≥45 Gy (Obstruction may occur in people who received lower doses of abdominal radiation during childhood)	**History** **Abdominal pain** **Emesis** **Distention** **Vomiting** **Constipation** (With clinical symptoms of obstruction) **Physical** **Tenderness** **Abdominal guarding** **Distension** (With clinical symptoms of obstruction)	**Health Links** **See "Patient Resources" field** Gastrointestinal Health **Considerations for Further Testing and Intervention** Obtain KUB in patients with clinical symptoms of obstruction. Surgical consultation in patients unresponsive to medical management.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
77	≥30 Gy to: **Whole abdomen** **All upper abdominal fields** **Pelvic** **Spine (thoracic, lumbar, sacral)**	**Chronic enterocolitis** **Fistula** **Strictures**	**Treatment Factors** Higher radiation dose to bowel Abdominal surgery	**Treatment Factors** Radiation dose ≥45 Gy	**History** **Nausea** **Vomiting** **Abdominal pain** **Diarrhea** (Yearly)	**Health Links** **See "Patient Resources" field** Gastrointestinal Health **Considerations for Further Testing and Intervention** Serum protein and albumin yearly in patients with chronic diarrhea or fistula. Surgical and/or gastroenterology consultation for symptomatic patients.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideratio
78	≥30 Gy to: **Whole abdomen** **All upper**	**Colorectal cancer** **Info Link**: Reports of colorectal cancer	**Host Factors** Current age ≥50 years **Treatment**	**Host Factors** Personal history of ulcerative colitis,	**Screening** **Colonoscopy** (Every 5 years	**Health Links** **See "Patient Resources" field**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideratio
	abdominal fields **Pelvic** **Spine (thoracic, lumbar, sacral)**	in cohorts of long-term survivors suggest that radiation likely increases risk, but the median age of onset is not as well established as that of secondary breast cancer following chest radiation. The expert panel agreed that early onset of screening is likely beneficial, and that a prudent course would be to initiate screening for colorectal cancer for those at highest risk (abdominal, pelvic, and/or spinal radiation ≥30 Gy) at age 35, or 10 years post radiation, whichever occurs last. Surveillance should be done via colonoscopy as per recommendations for populations at highest risk, with information from the first colonoscopy informing the frequency of follow-up testing.	**Factors** Higher radiation dose to bowel Higher daily dose fraction Combined with chemotherapy (especially alkylators) **Medical Conditions** Obesity **Health Behaviors** High fat/low fiber diet	gastrointestinal malignancy, adenomatous polyps, or hepatoblastoma Familial polyposis Family history of colorectal cancer or polyps in first degree relative	[minimum] beginning at 10 years after radiation or at age 35 years [whichever occurs last]; more frequently if indicated based on colonoscopy results; Per the ACS, begin screening earlier for the following high-risk groups - HNPCC: at puberty; FAP: at age 21 years; IBD: 8 years after diagnosis of IBD; Information from the first colonoscopy will inform frequency of follow-up testing)	Colorectal Cancer **Considerati for Further Testing and Intervention** Surgical and/ oncology consultation a needed.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Urinary Tract

System = Urinary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	H Cou Fu Consi
79	**Whole abdomen** **All upper abdominal fields** **TBI** **Info Link**: Includes all upper abdominal fields except Paraaortic	**Renal toxicity** Renal insufficiency Hypertension	**Host Factors** Bilateral Wilms tumor Mononephric **Treatment Factors** Radiomimetic chemotherapy (e.g., doxorubicin, dactinomycin) Radiation dose ≥10 Gy TBI combined with radiation to the kidney Combined with other nephrotoxic agents such as: • Cisplatin • Carboplatin • Ifosfamide • Aminoglycosides • Amphotericin • Immunosuppressants **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Radiation dose ≥15 Gy TBI ≥6 Gy in single fraction TBI ≥12 Gy fractionated	**Physical** **Blood pressure** (Yearly) **Screening** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** (Baseline at entry into long-term followup. If abnormal, repeat as clinically indicated.) **Urinalysis** (Yearly)	**Health** **See "R Resou field** Kidney See als Kidney **Consi for Fu Testin Interv** Nephro consult patient hypert protein progre renal insuffi

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideration
80	≥30 Gy to: **Whole abdomen** **Pelvic** **Spine (sacral)**	**Hemorrhagic cystitis**	**Treatment Factors** Higher radiation dose (≥30 Gy to entire bladder; ≥60 Gy to portion of bladder)	**Treatment Factors** Combined with cyclophosphamide and/or ifosfamide	**History** **Hematuria** **Urinary urgency/ frequency** **Urinary incontinence/ retention** **Dysuria** **Nocturia** **Abnormal urinary stream** (Yearly) **Screening** **Urinalysis** (Yearly)	**Health Links** **See "Patient Resources" fie** Bladder Health **Counseling** Counsel to promptly report dysuria or gross hematuria **Considerations for Further Testing and Intervention** Urine culture, spot urine calcium/creatini ratio, and ultrasound of kidneys and bladder for patients with microscopic hematuria (defined as ≥ 5 RBC/HPF on at least 2 occasions). Nephrology or Urology referral for patients with culture-negative microscopic hematuria AND abnormal ultrasound and/ abnormal calcium/creatini ratio. Urology referral for patients with culture negative

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideration
						macroscopic hematuria.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	He Cou Fu Consid
81	≥30 Gy to: **Whole abdomen** **Pelvic** **Spine (sacral)**	**Urinary tract toxicity** Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	**Treatment Factors** Higher cumulative radiation dose (≥45 Gy) Radiation to entire bladder Combined with: • Cyclophosphamide • Ifosfamide • Vincristine		**History** **Hematuria** **Urinary urgency/ frequency** **Urinary incontinence/ retention** **Dysuria** **Nocturia** **Abnormal urinary stream** (Yearly) **Screening** **Urinalysis** (Yearly)	**Health** **See "R Resou field** Bladde **Consid for Fu Testin Interv** Urologi consult patient inconti dysfun voiding

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
82	**Whole abdomen** **Pelvic** **Spine (sacral)** **Info Link**: Applies to sacral spine at doses ≥30 Gy only.	**Bladder malignancy**	**Treatment Factors** Radiation to pelvis Combined with: • Cyclophosphamide • Ifosfamide **Health Behaviors** Alcohol use Smoking		**History** **Hematuria** **Urinary urgency/ frequency** **Urinary incontinence/ retention** **Dysuria** **Nocturia** **Abnormal urinary stream** (Yearly) **Screening** **Urinalysis** (Yearly)	**Health Li** **See "Pat Resource** Bladder H **Counseli** Counsel t promptly dysuria o hematuria **Consider for Furth Testing a Interven** Urine cult spot urine calcium/c ratio, and ultrasoun kidneys a bladder fo patients w microscop hematuria (defined a RBC/HPF least 2 occasions Nephrolog Urology r for patien culture-ne microscop hematuria abnormal ultrasoun abnormal calcium/c ratio. Uro

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
						referral fo patients w culture ne macrosco hematuria

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Female Reproductive System

System = Female reproductive
Score = 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
83 (Female)	**Whole abdomen** **Pelvic** **Spine (lumbar, sacral)** **TBI** **Info Link**: Applies to all pelvic fields except iliac/inguinal. Applies to lumbar and sacral spine at doses ≥25 Gy.	**Uterine vascular insufficiency** (resulting in adverse pregnancy outcomes, such as spontaneous abortion, neonatal death, low-birth weight infant, fetal malposition, and premature labor) **Info Link**: 10% of girls with Wilms tumor have congenital uterine anomalies.	**Host Factors** Females with Wilms tumor and associated müllerian anomalies **Treatment Factors** Higher radiation dose to pelvis	**Host Factors** Prepubertal at treatment **Treatment Factors** Radiation dose ≥30 Gy TBI	**History** **Pregnancy** **Childbirth history** (Yearly and as clinically indicated)	**Health Links** **See "Patient Resources" field** Female Health Issues **Resources** American Society for Reproductive Medicine: www.asrm.org Fertile Hope: www.fertilehope.org **Considerations for Further Testing and Intervention** Consider high-level ultrasound evaluation of genitourinary tract after pubertal development as

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
						clinically indicated in patients contemplating pregnancy. High-risk obstetrical care during pregnancy.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Female reproductive
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Healt Further
84 (Female)	**Whole abdomen** **Pelvic** **Spine (lumbar, sacral)** **TBI** **Info Link**: Applies to lumbar and sacral spine at doses ≥25 Gy only.	**Gonadal dysfunction (ovarian)** Delayed/arrested puberty Premature menopause Infertility	**Host Factors** Older age at irradiation **Treatment Factors** Prepubertal female: Radiation dose ≥10 Gy Pubertal female: Radiation dose ≥5 Gy Combined with alkylating agent chemotherapy Longer time since treatment	**Treatment Factors** Prepubertal female: Radiation dose ≥15 Gy Pubertal female: Radiation dose ≥10 Gy Combined with cyclophosphamide conditioning for HCT	**History** **Pubertal (onset, tempo)** **Menstrual/ pregnancy history** **Sexual function (vaginal dryness, libido)** **Medication use impacting sexual function** (Yearly) **Physical** **Tanner stage** (Yearly until sexually	**Health** **See "Pa Resour** Female **Resour** America Reprodu www.as Fertile H www.fer **Counse** Counsel need for since th tremend variabili toxicity radiation fertility after the regardin benefits **Conside Further**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Heal Further
					mature) **Screening** **FSH** **LH** **Estradiol** (Baseline at age 13, and as clinically indicated in patients with delayed puberty, irregular menses or primary or secondary amenorrhea, clinical signs and symptoms of estrogen deficiency)	**Interve** Refer to for delay puberty abnorma levels. G endocrin consulta Consider conditio by hypo osteoper Reprodu endocrin consulta couples assisted technolo

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Female reproductive
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counselin Further Considerati
85 (Female)	**Pelvic**	**Vaginal fibrosis/stenosis**	**Host Factors** Vaginal tumor or pelvic tumor adjacent to vagina	**Treatment Factors** Prepubertal female: Radiation dose ≥35 Gy Postpubertal	**History** **Psychosocial assessment** **Dyspareunia** **Vulvar pain**	**Considerati for Further Testing and Interventio** Gynecologic consultation management Psychologica

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counselin Further Considerati
			Treatment Factors Prepubertal female: Radiation dose ≥25 Gy Postpubertal female: Radiation dose ≥50 Gy **Medical Conditions** Chronic GVHD	female: Radiation dose ≥55 Gy	**Post-coital bleeding** **Difficulty with tampon insertion** (Yearly)	consultation patients with emotional difficulties.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Male Reproductive System

System = Male reproductive
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Coun Further Considerat
86 (Male)	**Pelvic** **Testicular** **TBI**	**Gonadal dysfunction (testicular):** **Germ cell failure** Oligospermia Azoospermia Infertility	**Treatment Factors** Radiation dose to testes: • 1 to 3 Gy: Azoospermia may be reversible • 3 to 6 Gy:	**Treatment Factors** Radiation dose to testes ≥6 Gy: Azoospermia likely permanent	**Screening** **Semen analysis** (As requested by patient and for evaluation of infertility. Periodic evaluation over time is recommended as resumption of spermatogenesis	**Health Links** **See "Patient Resources" f** Male Health Is **Resources** American Soc for Reproducti Medicine: www.asrm.or Fertile Hope: www.fertileho

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Coun Further Considerat
			Azoospermia possibly reversible (but unlikely)		can occur up to 10 years post therapy.)	**Counseling** Counsel regar the need for contraception there is treme individual vari in gonadal tox after exposure radiation. Rec of fertility ma occur years af therapy. **Considerati for Further Testing and Intervention** Reproductive endocrinology consultation f infertile coupl interested in assisted reproductive technologies. Testing for In B can be cons in conjunction FSH as an ind of germ cell function.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Male reproductive
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
87 (Male)	≥20 Gy to: **Pelvic**	**Gonadal dysfunction (testicular):**	**Treatment Factors**	**Treatment Factors** Combined with:	**History** **Pubertal**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
	Testicular	**Leydig cell dysfunction** Delayed/arrested puberty Hypogonadism	Testicular irradiation combined with head/brain irradiation	• Alkylating agents • Cyclophosphamide conditioning for HCT	**(onset, tempo)** **Sexual function (erections, nocturnal emissions, libido)** **Medication use impacting sexual function** (Yearly) **Physical** **Tanner stage** **Testicular volume by Prader orchidometry** (Yearly until sexually mature) **Screening** **FSH, LH, testosterone** (Baseline at age 14, and as clinically indicated in patients with delayed puberty or clinical signs and symptoms of testosterone deficiency)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Potential Impact to Musculoskeletal System

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
88	**All neck fields** **All chest fields** **Whole abdomen** **All upper abdominal fields** **All extremity fields** **Pelvic** **All spinal fields** **Info Link**: Applies to spine at doses ≥12 Gy only.	**Musculoskeletal growth problems** Hypoplasia Fibrosis Reduced or uneven growth Shortened trunk height (trunk radiation) Limb length discrepancy (extremity radiation)	**Host Factors** Younger age at treatment **Treatment Factors** Higher cumulative radiation dose Larger radiation treatment field Higher radiation dose per fraction	**Host Factors** Prepubertal at treatment **Treatment Factors** Epiphysis in treatment field Dose ≥20 Gy Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**History** **Height** **Weight** (Yearly) **Sitting height** (Yearly for patients who had trunk radiation) **Limb lengths** (Yearly for patients who had extremity radiation)	**Counseling** Counsel regarding increased risk of fractures in weight-bearing irradiated bones **Considerations for Further Testing and Intervention** Orthopedic consultation for any deficit noted in growing child. Consider plastic surgery consult for reconstruction.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
89	**Mantle** **Mini-Mantle** **Mediastinal** **Whole lung** **Chest (thorax)** **Whole abdomen** **All upper abdominal fields** **Pelvic** **Spine (lumbar, sacral, thoracic)** **Info Link**: Applies to spine at doses ≥12 Gy only.	**Scoliosis**	**Host Factors** Younger age at irradiation Paraspinal malignancies **Treatment Factors** Hemithoracic or abdominal radiation Hemithoracic, abdominal or spinal surgery Radiation of only a portion of (rather than whole) vertebral body **Info Link**: With contemporary treatment approaches, scoliosis is infrequently seen as a consequence of radiation unless the patient has also undergone surgery to the hemithorax, abdomen or spine	**Treatment Factors** Radiation doses ≥20 Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**Physical** **Spine exam for scoliosis** (Yearly until growth completed. May need more frequent assessment during puberty.)	**Health Links** **See "Patient Resources" field** Scoliosis and Kyphosis **Considerations for Further Testing and Intervention** Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
90	**Mantle** **Mini-Mantle** **Mediastinal** **Whole lung** **Chest (thorax)** **Whole abdomen** **All upper abdominal fields** **Spine (thoracic)** **Info Link**: Applies to thoracic spine at doses ≥30 Gy only.	**Kyphosis**	**Host Factors** Younger age at irradiation Paraspinal malignancies Neurofibromatosis	**Treatment Factors** Radiation doses ≥20 Gy (lower doses for infants) Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**Physical** **Spine exam for kyphosis** (Yearly until growth completed. May need more frequent assessment during puberty.)	**Health Links** **See "Patient Resources" field** Scoliosis and Kyphosis **Considerations for Further Testing and Intervention** Spine films in patients with clinically apparent curve. Orthopedic consultation as indicated based on radiographic exam.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
91	≥40 Gy to: **All neck fields** **All chest fields**	**Radiation-induced fracture**	**Treatment Factors** History of surgery to cortex of bone	**Treatment Factors** Radiation doses ≥50 Gy to bone	**Physical** **Pain, swelling, deformity of bone** (As Indicated)	**Considerations for Further Testing and Intervention** Radiograph of affected bone as clinically

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	Whole abdomen **All upper abdominal fields** **Pelvic** **All spinal fields** **All extremity fields**					indicated. Orthopedic evaluation as clinically indicated.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Abbreviations

- ABR, auditory brainstem response
- ACS, American Cancer Society
- AHA, American Heart Association
- BAER, brainstem auditory evoked response
- BMI, body mass index
- BUN, blood urea nitrogen
- Ca, calcium
- CBC, complete blood count
- Cl, chloride
- CNS, central nervous system
- CO_2, carbon dioxide
- CSF, cerebrospinal fluid
- CT, computed tomography
- CXR, chest x-ray
- dB, decibel
- DLCO, diffusion capacity of carbon monoxide
- DOE, dyspnea on exertion
- ECHO, echocardiogram
- EKG, electrocardiogram
- FAP, familial adenomatous polyposis
- FM, frequency modulation
- FNA, fine needle aspiration
- FSH, follicle stimulating hormone
- GI, gastrointestinal
- GVHD, graft versus host disease
- Gy, gray

- HCT, hematopoietic cell transplant
- HIB, Haemophilus influenza b vaccine
- HNPCC, hereditary nonpolyposis colorectal cancer
- HPF, high power field
- HRT, hormone replacement therapy
- HZ, hertz
- IBD, inflammatory bowel disease
- IO, intraosseous
- IQ, intelligence quotient
- IT, intrathecal
- IV, intravenous
- K, potassium
- KUB, kidney, ureter, and bladder
- LH, luteinizing hormone
- Mg, magnesium
- MR, magnetic resonance
- MRI, magnetic resonance imaging
- Na, sodium
- NCI, National Cancer Institute
- OAE, otoacoustic emission
- PFT, pulmonary function test
- PNET, primitive neuroectodermal tumor
- PO_4, phosphate
- PRN, as needed
- RBC, red blood cell
- RUQ, right upper quadrant
- SMN, secondary malignant neoplasm
- SOB, shortness of breath
- T, temperature
- T4, thyroxine
- TBI, total body irradiation
- TPN, total parenteral nutrition
- TSH, thyroid stimulating hormone
- VOD, veno-occlusive disease

Definitions:

Explanation of Scoring for the Long-Term Follow-Up Guidelines

1 There is uniform consensus of the panel that (1) there is high-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2A There is uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2B There is non-uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the

screening recommendation is appropriate based on the collective clinical experience of panel members.

3 There is major disagreement that the recommendation is appropriate.

Rating Scheme for the Strength of the Evidence

"High-level evidence" (recommendation category 1) was defined as evidence derived from high quality case control or cohort studies.

"Lower-level evidence" (recommendation categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series, and clinical experience.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Although several well-conducted studies on large populations of childhood cancer survivors have demonstrated associations between specific exposures and late effects, the size of the survivor population and the rate of occurrence of late effects does not allow for clinical studies that would assess the impact of screening recommendations on the morbidity and mortality associated with the late effect. Therefore, scoring of each exposure reflects the expert panel's assessment of the level of literature support linking the therapeutic exposure with the late effect coupled with an assessment of the appropriateness of the recommended screening modality in identifying the potential late effect based on the panel's collective clinical experience.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Potential benefits of implementing these guidelines into clinical practice include earlier identification of and intervention for late onset therapy-related complications in this at-risk population, potentially reducing or ameliorating the impact of late complications on the health status of survivors. In addition, ongoing healthcare that promotes healthy lifestyle choices and provides ongoing monitoring of health status is important for all cancer survivors.

POTENTIAL HARMS

Potential harms of guideline implementation include increased patient anxiety related to enhanced awareness of possible complications, as well as the potential for false-positive screening evaluations, leading to unnecessary further workup. In addition, costs of long-term follow-up care may be prohibitive for some patients, particularly those lacking health insurance, or those with insurance that does not cover the recommended screening evaluations.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The information and contents of each document or series of documents made available by the Children's Oncology Group relating to late effects of cancer treatment and care or containing the title "Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers" or the title "Health Link," whether available in print or electronic format (including any digital format, e-mail transmission, or download from the website), shall be known hereinafter as "Informational Content." All Informational Content is for informational purpose only. The Informational Content is not intended to substitute for medical advice, medical care, diagnosis, or treatment obtained from a physician or healthcare provider.
- *To cancer patients (if children, their parents or legal guardians)*: Please seek the advice of a physician or other qualified healthcare provider with any questions you may have regarding a medical condition and do not rely on the Informational Content. The Children's Oncology Group is a research organization and does not provide individualized medical care or treatment.
- *To physicians and other healthcare providers*: The Informational Content is not intended to replace your independent clinical judgment, medical advice, or to exclude other legitimate criteria for screening, health counseling, or intervention for specific complications of childhood cancer treatment. Neither is the Informational Content intended to exclude other reasonable alternative follow-up procedures. The Informational Content is provided as a courtesy, but not intended as a sole source of guidance in the evaluation of childhood cancer survivors. The Children's Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.
- While the Children's Oncology Group has made every attempt to assure that the Informational Content is accurate and complete as of the date of publication, no warranty or representation, express or implied, is made as to the accuracy, reliability, completeness, relevance, or timeliness of such Informational Content.
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of action, suits, proceedings, or demands related to or arising out of use, review or access of the Informational Content.

- Ultimately, as with all clinical guidelines, decisions regarding screening and clinical management for any specific patient should be individually tailored, taking into consideration the patient's treatment history, risk factors, co-morbidities, and lifestyle. These guidelines are therefore not intended to replace clinical judgment or to exclude other reasonable alternative follow-up procedures. The Children's Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of these guidelines is intended to standardize and enhance follow-up care provided to survivors of pediatric malignancies throughout the lifespan. Considerations in this regard include the practicality and efficiency of applying these broad guidelines in individual clinical situations. Studies to address guideline implementation and refinement are a top priority of the Children's Oncology Group (COG) Late Effects Committee, and proposals to study feasibility of guideline use in limited institutions are currently underway. Issues to be addressed include description of anticipated barriers to application of the recommendations in the guidelines and development of review criteria for measuring changes in care when the guidelines are implemented. Additional concerns surround the lack of current evidence establishing the efficacy of screening for late complications in pediatric cancer survivors. While most clinicians believe that ongoing surveillance for these late complications is important in order to allow for early detection and intervention for complications that may arise, development of studies addressing the efficacy of this approach is imperative in order to determine which screening modalities are optimal for asymptomatic survivors.

In addition, the clinical utility of this lengthy document has also been a top concern of the COG Late Effects Committee. While recognizing that the length and depth of these guidelines is important in order to provide clinically-relevant, evidence-based recommendations and supporting health education materials, clinician time limitations and the effort required to identify the specific recommendations relevant to individual patients have been identified as barriers to their clinical application. Therefore, the COG Late Effects Committee is currently partnering with the Baylor School of Medicine in order to develop a web-based interface, known as "Passport for Care," that will generate individualized exposure-based recommendations from these guidelines in a clinician-focused format for ease of patient-specific application of the guidelines in the clinical setting. As additional information regarding implementation of the Passport for Care web-based interface becomes available, updates will be posted at www.survivorshipguidelines.org.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Patient Resources
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 38-91: radiation. Bethesda (MD): Children's Oncology Group; 2006 Mar. 74 p. [360 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Sep (revised 2006 Mar)

GUIDELINE DEVELOPER(S)

Children's Oncology Group - Medical Specialty Society

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All Children's Oncology Group (COG) members have complied with the COG conflict of interest policy, which requires disclosure of any potential financial or other conflicting interests.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 1.2. 2004 Mar.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Children's Oncology Group Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Instructions for use. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March. 6 p.
- Introductory material. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March. 9 p.

- Summary of cancer treatment. Appendix I: Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March.
- Patient-specific guideline identification tool. Appendix I: Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March.

Electronic copies: Available in Portable Document Format (PDF) from the Children's Oncology Group Web site.

PATIENT RESOURCES

In an effort led by the Nursing Clinical Practice Subcommittee, complementary patient education materials (*Health Links*) were developed and are available in Appendix II of the original guideline document. The following Health Links are relevant to this summary:

Sections 38, 39

- Reducing the Risk of Second Cancer

Sections 39, 40

- Skin Health

Sections 43, 58

- Educational Issues

Sections 48, 49, 71

- Diet and Physical Activity

Section 50

- Growth Hormone Deficiency

Section 51

- Precocious Puberty

Section 52

- Hyperprolactinemia

Section 53, 62, 63, 64, 65

- Thyroid Problems

Sections 53, 54, 55

- Hypopituitarism

Section 50, 54, 86, 87

- Male Health Issues

Sections 54, 83, 84

- Female Health Issues

Section 55

- Central Adrenal Insufficiency

Section 56

- Cataracts

Section 57

- Eye Health

Section 58

- Hearing Loss

Sections 59, 60

- Dental Health

Section 61

- Osteoradionecrosis

Section 68

- Breast Cancer

Section 70

- Pulmonary Health

Section 71

- Heart Health

Section 72

- Splenic Precautions

Sections 73, 75, 76, 77

- Gastrointestinal Health

Section 74

- Liver Health

Section 78

- Colorectal Cancer

Section 79

- Kidney Health
- Single Kidney Health (mononephric patients only)

Sections 80, 81, 82

- Bladder Health

Sections 89, 90

- Scoliosis and Kyphosis

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on May 10, 2007. The information was verified by the guideline developer on June 11, 2007. This summary was updated by ECRI Institute on October 3, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rocephin (ceftriaxone sodium).

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