From Surviving to Thriving:

Understanding and managing long-term effects of pediatric cancer treatment

Ashley Jean, MD

MaineHealth Maine Children's Cancer Program

1

Disclosures

- None of the planners or speakers for this event have any financial relationships to disclose

2

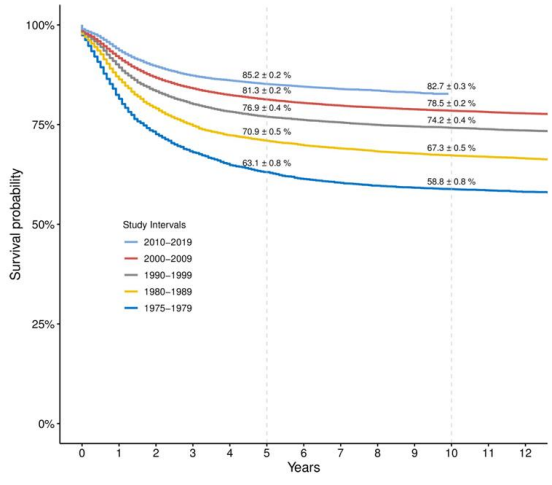
Objectives

- Review the common late effects of pediatric cancer treatments
- Discuss the importance of regular screening and surveillance
- Emphasize the crucial role of primary care providers in managing long-term follow up care

Maine Children's Cancer Program

3

Pediatric Oncology Survival



Sultan I, Alfaar AS, Sultan Y, Salman Z, Qaddoumi I. Trends in childhood cancer: Incidence and survival analysis over 45 years of SEER data. PLoS One. 2025;20(1):e0314592

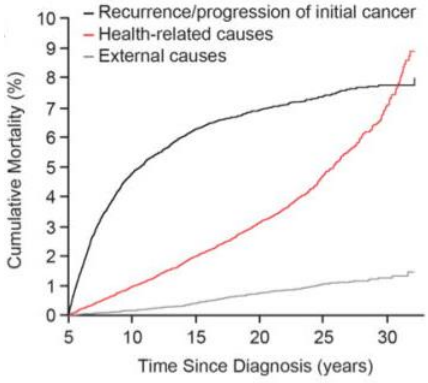
- Childhood cancer mortality rates have significantly declined over recent decades
- ~85% of children diagnosed with cancer will achieve 5-year survival
- There are currently ~500,000 childhood cancer survivors in the US

Maine Children's Cancer Program

4

Late Effects

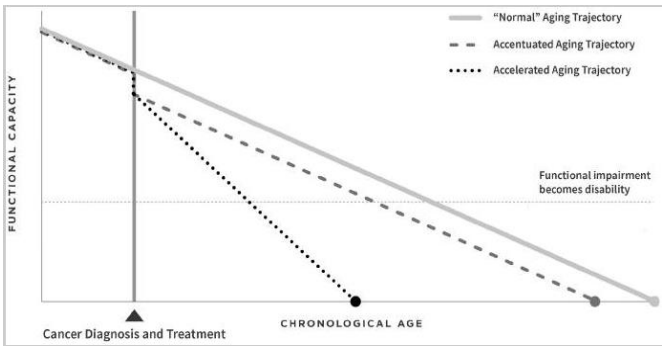
- As time from treatment increases, **risk of recurrence/progression decreases and risk for late effects increases**
- Recipients of stem cell transplant have nearly fourfold risk compared to those treated with conventional therapy



Gibson TM, Robison LL. Impact of Cancer Therapy-Related Exposures on Late Mortality in Childhood Cancer Survivors. Chem Res Toxicol. 2015;28(1):31-37

5

Accelerated Aging

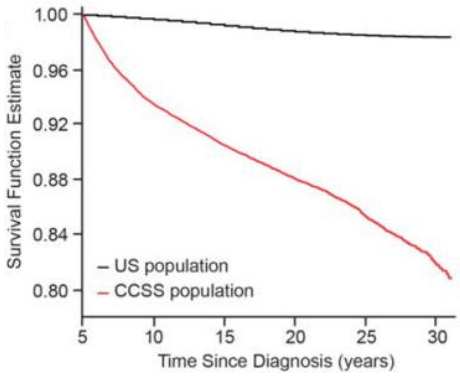


- Cancer survivors develop chronic conditions earlier and/or at a greater burden than similarly aged individuals
- Cancer and its treatments are hypothesized to create sufficient damage to accelerate or accentuate the rate of aging

Guida JL, Ahles TA, Belsky D, et al. Measuring Aging and Identifying Aging Phenotypes in Cancer Survivors. J Natl Cancer Inst. 2019;111(12):1245-1254. doi:10.1093/jnci/djz136

6

Early Mortality



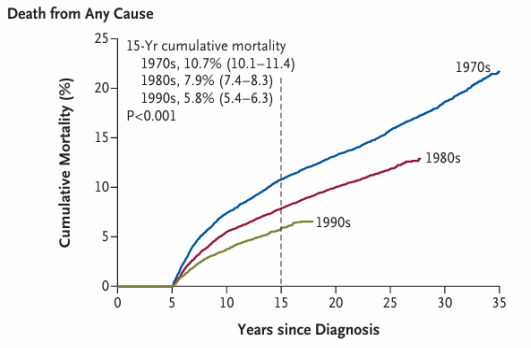
- Survivors of childhood cancer experience significantly greater mortality rates compared to those expected in the general population
- 18% of 5-year survivors had died by 30 years after their diagnosis

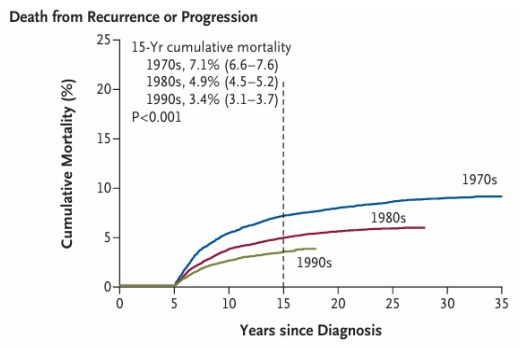
Gibson TM, Robison LL. Impact of Cancer Therapy-Related Exposures on Late Mortality in Childhood Cancer Survivors. Chem Res Toxicol. 2015;28(1):31-37

Maine Children's Cancer Program

7

Changes in Mortality





Armstrong GT, Chen Y, Yasui Y, et al. Reduction in Late Mortality among 5-Year Survivors of Childhood Cancer. N Engl J Med. 2016;374(9):833-842. doi:10.1056/NEJMoa1510795

Maine Children's Cancer Program

8

Late Effects of Cancer Treatment

Table 2. Cancer Survivors and Siblings with a Chronic Health Condition, According to the Severity Score.*

Health Condition	Survivors (N=10,397)	Siblings (N=3034)
	no. (%)	
No condition	3887 (37.4)	1917 (63.2)
Grade 1 (mild)	1931 (18.6)	610 (20.1)
Grade 2 (moderate)	1635 (15.7)	349 (11.5)
Grade 3 (severe)	2128 (20.5)	128 (4.2)
Grade 4 (life-threatening or disabling)	653 (6.3)	30 (1.0)
Grade 5 (fatal)	163 (1.6)	NA†
Any condition‡		
Grades 1–4	6482 (62.3)	1117 (36.8)
Grade 3 or 4	2858 (27.5)	158 (5.2)
Multiple health conditions		
≥2	3905 (37.6)	397 (13.1)
≥3	2470 (23.8)	163 (5.4)

Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572-1582. doi:10.1056/NEJMsa060185

As a group, cancer survivors were:

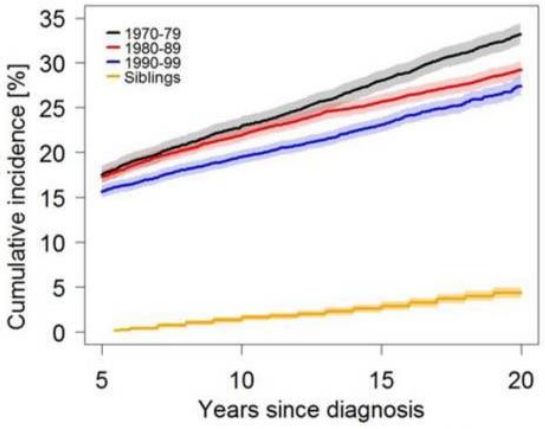
- 3.3x as likely as their siblings to have a chronic health condition of any grade
- 4.9x as likely to have two or more chronic health conditions
- 8x as likely to have severe or life-threatening chronic health conditions

Maine Children's Cancer Program

9

Changes in morbidity

Grade 3-5 Chronic Health Conditions



Gibson TM, Mostoufi-Moab S, Stratton KL, et al. Temporal patterns in the risk of chronic health conditions in survivors of childhood cancer diagnosed 1970-99: a report from the Childhood Cancer Survivor Study cohort [published correction appears in Lancet Oncol. 2019 Jan;20(1)

- Efforts to modify childhood cancer treatment regimens to maximize cure while reducing risk of late effects has led to reductions in survivor morbidity over time

Maine Children's Cancer Program

10

The Cost of Cure-Late Effects

- **Cancer-related factors**
  - Type of cancer
  - Organs/tissues involved
- **Treatment-related factors**
  - Surgery
  - Chemotherapy, immunotherapy
  - Radiation
  - Stem cell transplant
- **Patient-related factors**
  - Survivor's sex, age, pre-existing medical conditions, genetics, socioeconomic status, health habits

Maine Children's Cancer Program

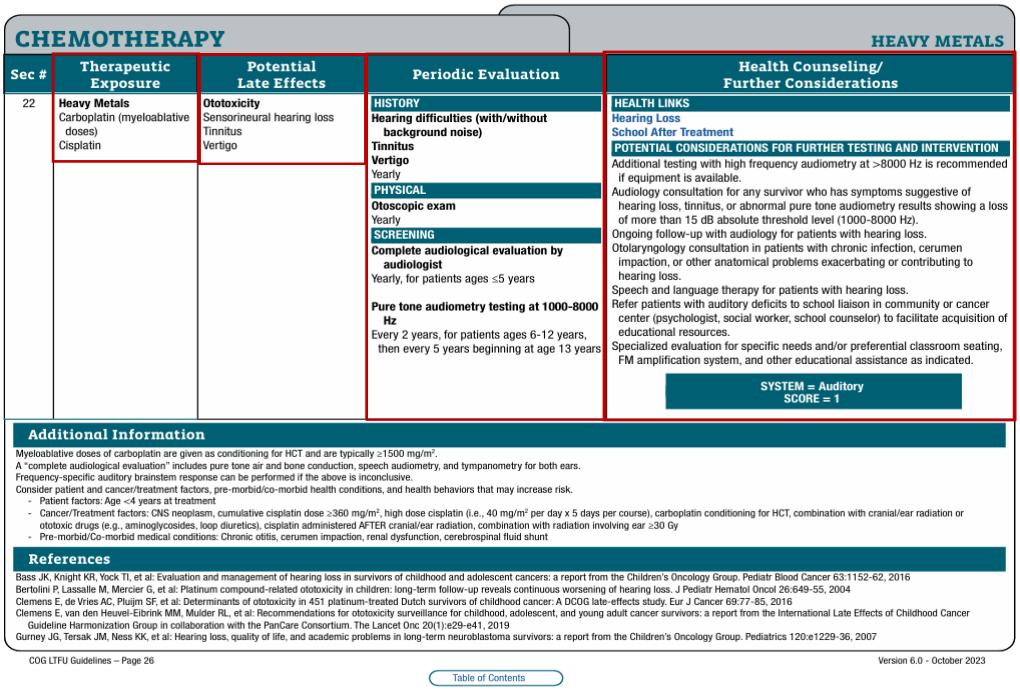
11

Children's Oncology Group Survivorship Guidelines

- www.survivorshipguidelines.org
- Updated every 5 years
- Comprehensive literature search and grading of the evidence

Maine Children's Cancer Program

12



CHEMOTHERAPY — **HEAVY METALS**

Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling/ Further Considerations
22	**Heavy Metals** Carboplatin (myeloablative doses) Cisplatin	**Ototoxicity** Sensorineural hearing loss Tinnitus Vertigo	**HISTORY** **Hearing difficulties (with/without background noise)** **Tinnitus** **Vertigo** Yearly **PHYSICAL** **Otoscopic exam** Yearly **SCREENING** **Complete audiological evaluation by audiologist** Yearly, for patients ages ≤5 years **Pure tone audiometry testing at 1000-8000 Hz** Every 2 years, for patients ages 6-12 years, then every 5 years beginning at age 13 years	**HEALTH LINKS** Hearing Loss School After Treatment **POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION** Additional testing with high frequency audiometry at >8000 Hz is recommended if equipment is available. Audiology consultation for any survivor who has symptoms suggestive of hearing loss, tinnitus, or abnormal pure tone audiometry results showing a loss of more than 15 dB absolute threshold level (1000-8000 Hz). Ongoing follow-up with audiology for patients with hearing loss. Otolaryngology consultation in patients with chronic infection, cerumen impaction, or other anatomical problems exacerbating or contributing to hearing loss. Speech and language therapy for patients with hearing loss. Refer patients with auditory deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources. Specialized evaluation for specific needs and/or preferential classroom seating, FM amplification system, and other educational assistance as indicated. **SYSTEM = Auditory** **SCORE = 1**

Additional Information

Myeloablative doses of carboplatin are given as conditioning for HCT and are typically ≥1500 mg/m^2.
A "complete audiological evaluation" includes pure tone air and bone conduction, speech audiometry, and tympanometry for both ears.
Frequency-specific auditory brainstem response can be performed if the above is inconclusive.
Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.
- Patient factors: Age <4 years at treatment
- Cancer/Treatment factors: CNS neoplasm, cumulative cisplatin dose ≥360 mg/m^2, high dose cisplatin (i.e., 40 mg/m^2 per day x 5 days per course), carboplatin conditioning for HCT, combination with cranial/ear radiation or ototoxic drugs (e.g., aminoglycosides, loop diuretics), cisplatin administered AFTER cranial/ear radiation, combination with radiation involving ear ≥30 Gy
- Pre-morbid/Co-morbid medical conditions: Chronic otitis, cerumen impaction, renal dysfunction, cerebrospinal fluid shunt

References

Bass JK, Knight KR, Yock TI, et al: Evaluation and management of hearing loss in survivors of childhood and adolescent cancers: a report from the Children's Oncology Group. Pediatr Blood Cancer 63:1152-62, 2016
Bertolini P, Lassalle M, Mercier G, et al: Platinum compound-related ototoxicity in children: long-term follow-up reveals continuous worsening of hearing loss. J Pediatr Hematol Oncol 26:649-55, 2004
Clemens E, de Vries AC, Pluijm SF, et al: Determinants of ototoxicity in 451 platinum-treated Dutch survivors of childhood cancer: A DCOG late-effects study. Eur J Cancer 69:77-85, 2016
Clemens E, van den Heuvel-Eibrink MM, Mulder RL, et al: Recommendations for ototoxicity surveillance for childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCare Consortium. The Lancet Onc 20(1):e29-e41, 2019
Gurney JG, Tersak JM, Ness KK, et al: Hearing loss, quality of life, and academic problems in long-term neuroblastoma survivors: a report from the Children's Oncology Group. Pediatrics 120:e1229-36, 2007

13

MCCP Pediatric Survivorship Visit

https://images.fineartamerica.com/images/artworkimages/mediumlarge/1/18-year-old-teenage-boy-outside-ben-gingell.jpg

Treatment Summary

Cancer Diagnosis: High-risk acute lymphoblastic leukemia
Date of Diagnosis: May 2009
End of Therapy Date: October 2011
Time off Therapy: 13 years
Treatment Protocol: AALL0232
Chemotherapy received: Doxorubicin, Methotrexate IV/PO, Cytarabine, 6MP, Prednisone, Vincristine, L-asparaginase, Cyclophosphamide, Dexamethasone, Thioguanine
Intrathecal chemotherapy received: MTX, Cytarabine
Cumulative anthracycline dose: 175mg/m2
Cumulative Cyclophosphamide Dose: 1 gm/m2
Radiation: None
Surgery: Central line placement and removal
Blood products: yes

Maine Children's Cancer Program

14

Psychosocial

Late Effects

- Increased risk of mental health disorders
- Educational problems
- Underemployment/unemployment
- Relationship problems
- Dependent living
- Risky behaviors
- Limitations in healthcare and insurance access

Exposure

- Any chemotherapy

Evaluation/Screening

- Psychosocial assessment with attention to:
  - Educational/vocational progress
  - Healthcare/insurance access
  - Depression/anxiety/PTSD/SI
  - Social withdrawal
- Social work involvement
- Psychiatry/psychology

Maine Children's Cancer Program

15

Neurocognitive

Late Effects

- Functional deficits in:
  - Executive function (planning and organizing)
  - Sustained attention
  - Memory (particularly visual, sequencing, temporal memory)
  - Processing speed
  - Visual-motor integration
  - Fine motor dexterity
- Diminished IQ
- Behavioral change

Exposures

- CNS disease, IV/IT MTX, HD cytarabine, cranial and total body radiation

Evaluation/Screening

- Educational/vocational progress yearly
- Formal Neuropsychological Testing
- School liaison

Maine Children's Cancer Program

16

Cardiac Toxicity

Late Effects

- Cardiomyopathy
- Subclinical left ventricular dysfunction
- Congestive heart failure
- Arrhythmia

Exposure

- Anthracyclines, radiation

Evaluation/Screening

- History-SOB, dyspnea on exertion, orthopnea, chest pain, palpitations
- Blood pressure
- Cardiac exam
- Echo/EKG

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM

Anthracycline Dose*	Radiation Dose**	Recommended Frequency
None to <100mg/m^2	None to <15Gy	No screening
None to <100mg/m^2 ≥100 to <250mg/m^2	15Gy to <30Gy None to <15Gy	Every 5 years
≥100 to <250mg/m^2 None to Any ≥ 250mg/m^2	≥15Gy ≥30Gy None to Any	Every 2 years

*Based on doxorubicin isotonic equivalent dose.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 77.

17

Bone Toxicity

Late Effects

- Reduced bone mineral density
- Osteonecrosis

Exposure:

- Dexamethasone, prednisone
- HD MTX
- Radiation

Evaluation/Screening

- History-joint pain/swelling, immobility, limited ROM, fractures, smoking, exercise
- MSK exam
- Vitamin D level
- DEXA scan*
- MRI
- Endocrine referral

18

Dental abnormalities

Late Effects

- Dental abnormalities
  - Tooth/root agenesis
  - Root thinning/shortening
  - Enamel dysplasia
  - Microdontia
  - Ectopic molar eruption
  - Dental caries

Exposure

- Any chemotherapy

Evaluation/Screening

- Oral exam
- Education to families and dental providers
- Regular dental care including fluoride application

Maine Children's Cancer Program

19

Subsequent Malignancy

Late Effects

- AML/MDS
  - Alkylating agents (cyclophos, ifosfamide, busulfan)
  - Etoposide
  - Radiation
- Skin Cancer-Radiation, HSCT
- Solid tumors-Radiation, HSCT
  - Breast, thyroid, brain, bone and soft tissue, lung, stomach, liver, colorectal, oral, kidney, bladder
- Consideration for cancer predisposition

Evaluation

- Yearly physical exam
- Routine cancer screenings*
- Addressing health behaviors: tobacco use, physical activity, diet, smoking, alcohol, sun exposure, tanning, sleep hygiene
- HPV vaccine
- Detailed family history
- MaineHealth Cancer Risk and Prevention Clinic

Maine Children's Cancer Program

20

MCCP Pediatric Survivorship Visit

https://images.fineartamerica.com/images/artworkimages/mediumlarge/1/18-year-old-teenage-boy-outside-ben-gingell.jpg

Summary

- Health education was provided and cancer prevention strategies were discussed and adapted based on recent Children's Oncology Group Long Term Follow-up guidelines (2023)
- Echocardiograms every 5 years due to the increased risk of cardiomyopathy secondary to anthracycline agents
- CBCD if new symptoms of pallor, bleeding, bruising, fatigue
- Continue routine follow up with dentistry
- Follow up blood pressure with PCP
- Consider neuropsychological evaluation if any concerns with memory or executive function due to the risk of chemotherapy-associated cognitive impairment
- Immunizations: Yearly influenza, third HPV

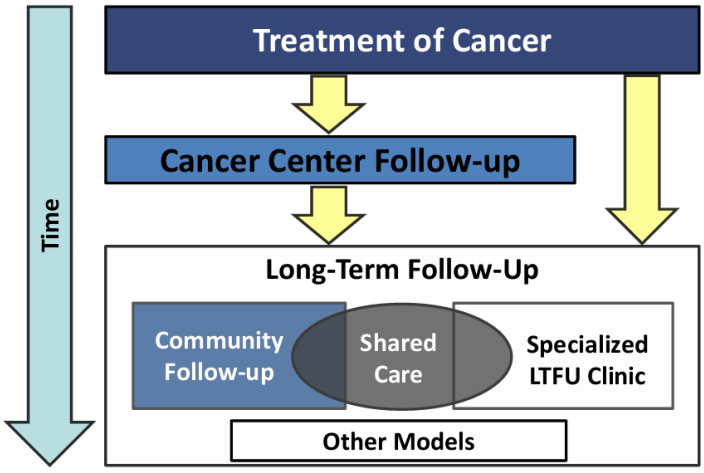
Follow-up Information:

- Cancer Survivorship Follow up: 1 year
- Labs/Studies/referrals ordered: Vitamin D level, lipid panel, echocardiogram

Maine Children's Cancer Program

21

Models of Survivorship Care



Singer S, Gianinazzi ME, Hohn A, Kuehni CE, Michel G. General practitioner involvement in follow-up of childhood cancer survivors: a systematic review. Pediatr Blood Cancer. 2013;60(10):1565-1573. doi:10.1002/pbc.24586

Maine Children's Cancer Program

22

Models of Survivorship Care

Specialized LTFU Program

- Backbone of care for pediatric survivors
  - Limited number see adults
- Based at hospital or cancer center
  - Original treatment center may loose contact with survivor
- Multidisciplinary care team
  - Medical
  - Psychosocial
- Delivery of risk-based care
- Venue for research & training

Community LTFU Care

- Geographically and financially more accessible
- Integrates survivorship care and primary care
  - Focus on primary care health education
  - Less focus on cancer-related health education
- Risk-based survivor-focused care dependent on provider/survivor knowledge
- Supports independence of young adult survivors
- Poses challenge to outcome research

Singer S, Gianinazzi ME, Hohn A, Kuehni CE, Michel G. General practitioner involvement in follow-up of childhood cancer survivors: a systematic review. Pediatr Blood Cancer. 2013;60(10):1565-1573. doi:10.1002/pbc.24586

Maine Children's Cancer Program

23

MCCP Pediatric Survivorship Clinic

Cheri Lozoraitis
Medical Secretary

Amanda McGeachey, RN
Clinical Manager

Sunita Nijhawan, PsyD, LP

Dee-Dee Hogan, LCSW

Elizabeth Murray, LCSW

Emily Smolin, LCSW

Ashley Jean, MD

"Cure is not enough"
-Dr. Giulio D'Angio

Susan A Speckhart, MD
MH Cancer Care and IV Therapy
South Portland

Maine Children's Cancer Program

24

Consortium for New England Childhood Cancer Survivors

Mission is to advance the quality of health care services provided to survivors of pediatric cancer in New England through regional collaboration by enhancing clinical practice, education, and program development, and to advance the science of pediatric survivorship services through collaborative research and funding

Current study: Household material hardship among childhood cancer survivors in New England

Maine Children's Cancer Program

25

Summary

- Childhood cancer survivors are at increased risk for chronic health conditions compared to the general population
- Risk-based guidelines provide recommendations regarding care delivery for this medically complex population-screening and surveillance are key
- Management of long-term effects takes teamwork. Primary care physicians have an important role to play!

Maine Children's Cancer Program

26

Questions?

"Ring this bell, three times well, it's toll to clearly say, my treatment's done, it's course is run, and I am on my way. A great victory was won today!"

27

Sources

- Armstrong GT, Chen Y, Yasui Y, et al. Reduction in Late Mortality among 5-Year Survivors of Childhood Cancer. N Engl J Med. 2016;374(9):833-842. doi:10.1056/NEJMoa1510795
- Gibson TM, Robison LL. Impact of Cancer Therapy-Related Exposures on Late Mortality in Childhood Cancer Survivors. Chem Res Toxicol. 2015;28(1):31-37
- Guida JL, Ahles TA, Belsky D, et al. Measuring Aging and Identifying Aging Phenotypes in Cancer Survivors. J Natl Cancer Inst. 2019;111(12):1245-1254. doi:10.1093/jnci/djz136
- Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572-1582. doi:10.1056/NEJMsa060185
- Singer S, Gianinazzi ME, Hohn A, Kuehni CE, Michel G. General practitioner involvement in follow-up of childhood cancer survivors: a systematic review. Pediatr Blood Cancer. 2013;60(10):1565-1573. doi:10.1002/pbc.24586
- Sultan I, Alfaar AS, Sultan Y, Salman Z, Qaddoumi I. Trends in childhood cancer: Incidence and survival analysis over 45 years of SEER data. PLoS One. 2025;20(1):e0314592. Published 2025 Jan 3. doi:10.1371/journal.pone.0314592

28