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LATE EFFECTS IN SURVIVORS OF AYA CANCERS

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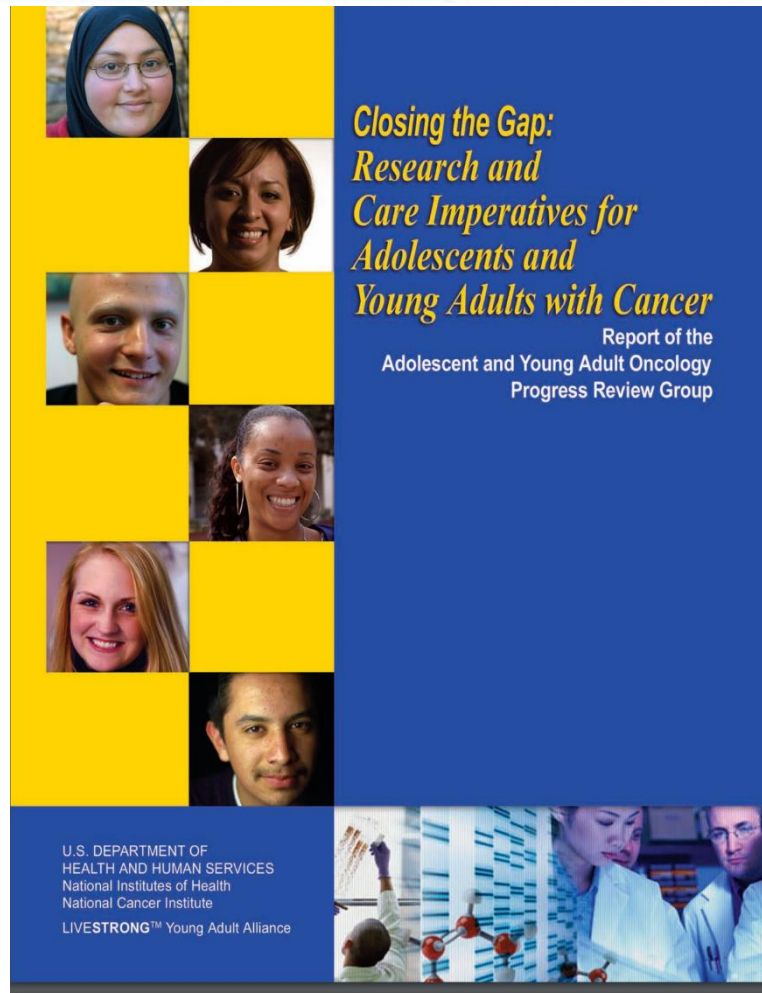
Conflicts

Nothing to declare

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National Cancer Institute & LiveStrong 2006 Progress Review Group Call to Action

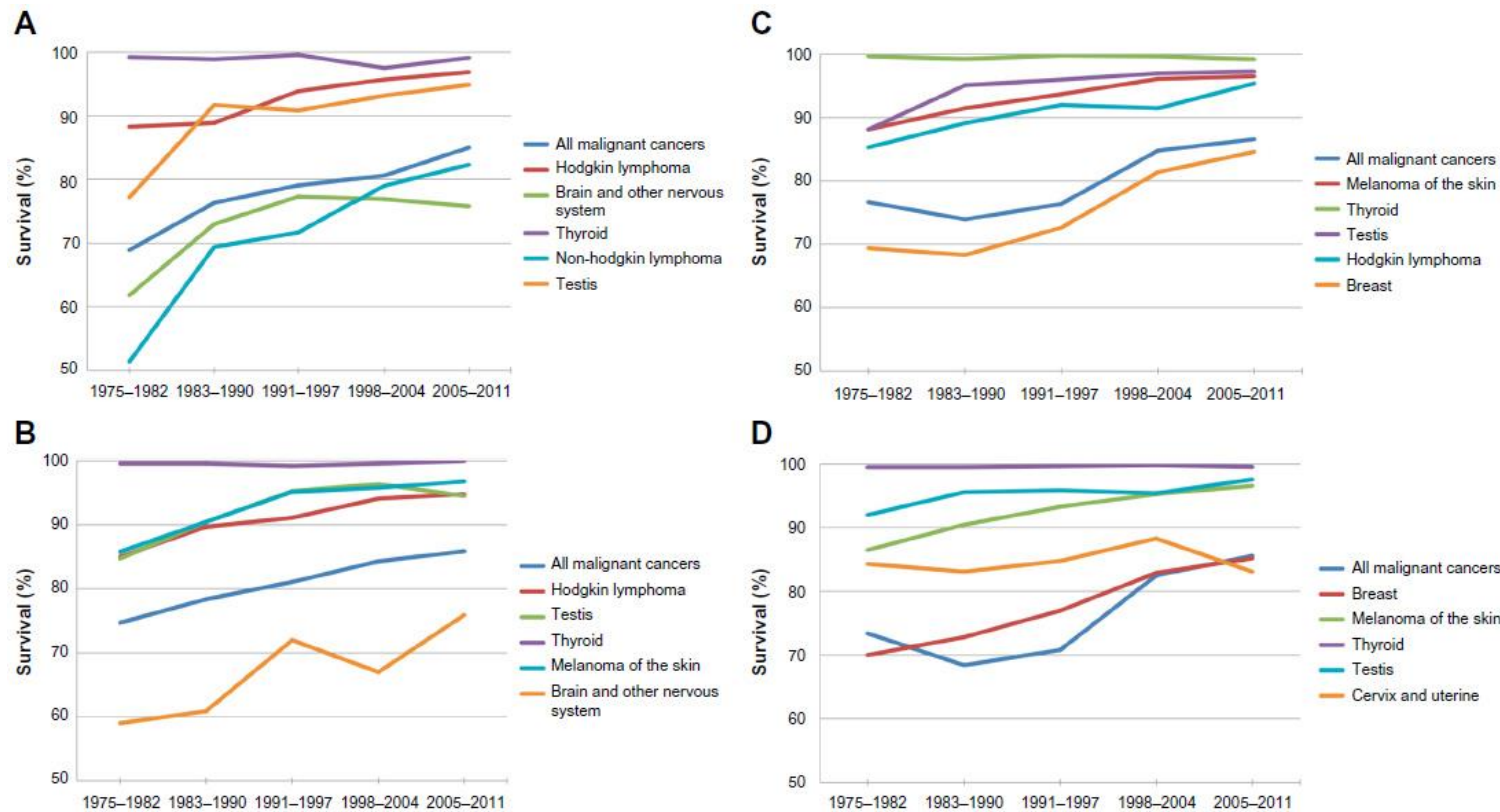


1. Identify the characteristics that distinguish the unique cancer burden in the AYA patient.
2. Provide education, training and communication to improve awareness, prevention, access and quality cancer care.
3. Create tools to study the AYA cancer problem.
4. Ensure excellence in service delivery across the cancer care continuum.
5. Strengthen and promote advocacy and support of the AYA

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The AYA cancer success story...yes, there is one



A. 15-19 y.o.
B. 20-24 y.o.
C. 25-29 y.o.
D. 30-34 y.o.



But, AYA survivorship care lags...

Our understanding and approach to AYA cancer survivorship is informed (mostly) by survivors of childhood and adolescent cancer diagnosed prior to age 21 years

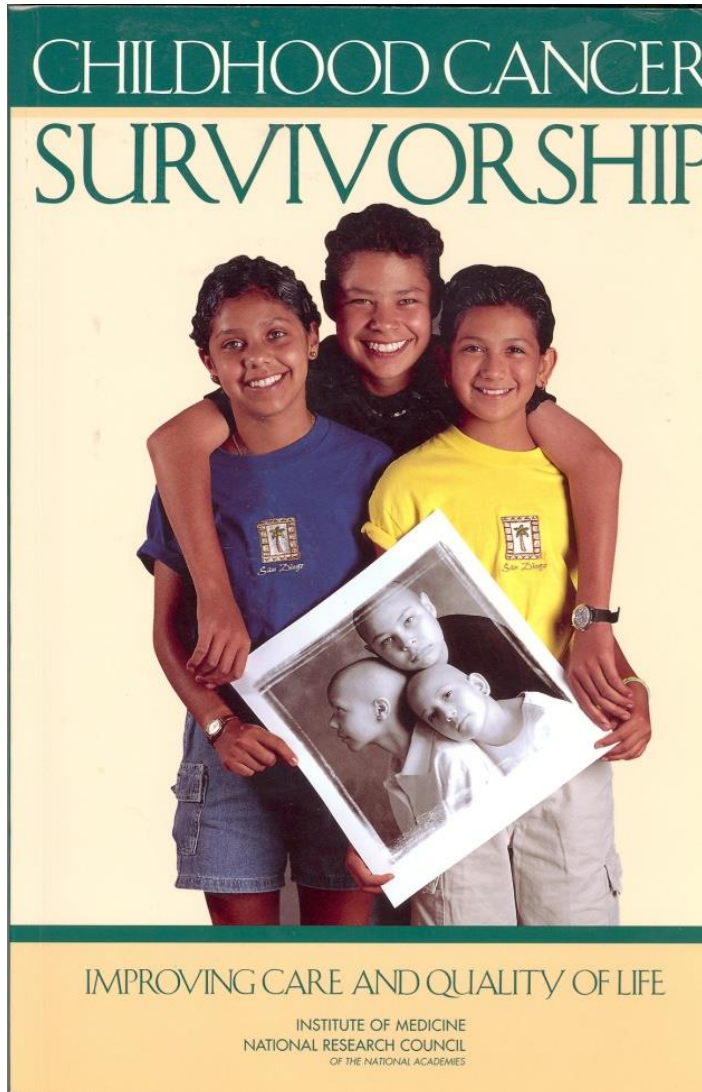
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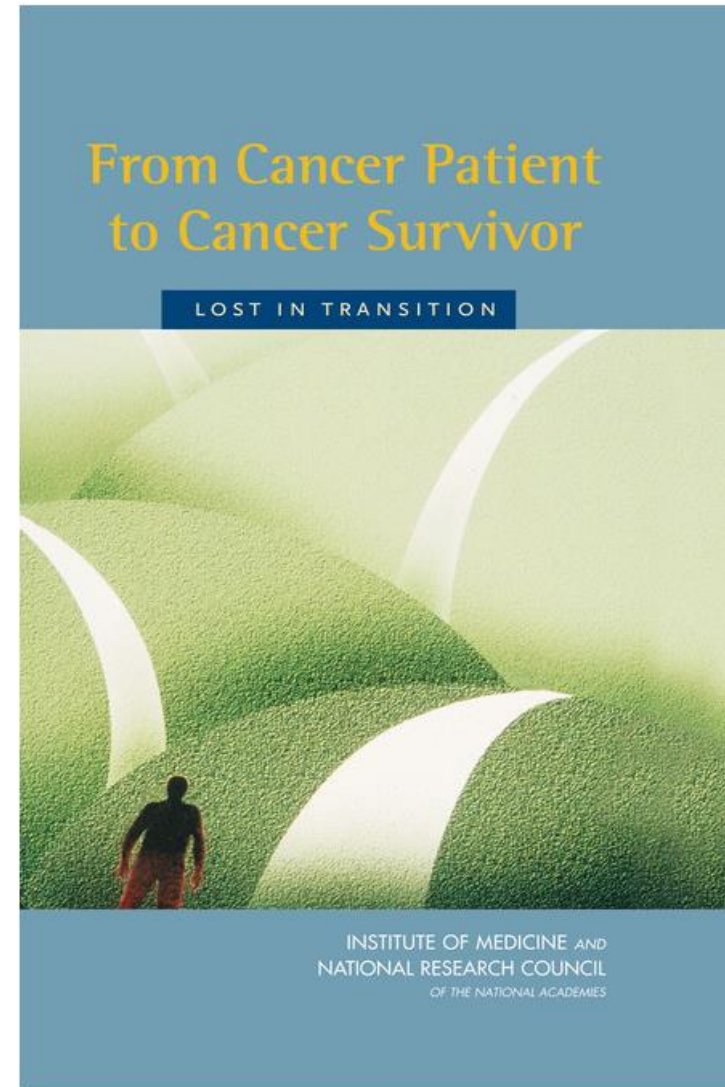
TABLE 1 International survivor cohorts that include survivors of AYA cancer

Cohort name or registry	Geographical location	Age at diagnosis (years)	Study design	Calendar years of diagnosis	No. of survivors overall; No. of AYA ^a	Survival interval at entry
Teenage and Young Adult Cancer Survivor Study (TYACSS)	England and Wales, United Kingdom	15-39	Population based	1971-2006	200 945 AYA ^{13,14,26,39}	5-year survivors
Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP)	Yorkshire and Humber region, England, United Kingdom	0-29	Population based	1990-2012	5902; 3644 AYA 4580; 2857 AYA	No survivorship restriction 5-year survivors
Finnish Cancer Registry	Finland	0-34	Population based	1971-2012	13 960; 10 770 AYA ³⁶	5-year survivors
Danish Cancer Registry	Denmark	15-39	Population based	1943-2009 1943-2004	43 153 AYA ³⁷ 33 555 AYA ³⁸	1-year survivors 5-year survivors
Scottish Cancer Registry	Scotland	0-24	Population based	1981-2003	5229; 3053 AYA ¹⁰	5-year survivors
Swiss Childhood Cancer Survivor Study (SCCSS)	Switzerland	0-20	Population based	1976-2010	7600; 1,886 AYA ¹¹⁸	5-year survivors
Adult Life after Childhood Cancer in Scandinavia (ALiCCS)	Denmark, Finland, Iceland, Norway, Sweden	0-19	Population based	1943-2008	33 160; 10,687 AYA ¹¹⁸	1-year survivors
Dutch Childhood Oncology Group LATER (DCOG LATER)	The Netherlands	0-17	Nationwide hospital based	1963-2002	6165; 401 AYA ¹¹⁹	5-year survivors
Initiative to Maximize Progress in Adolescent and Young Adult Cancer Therapy (IMPACT)	Ontario, Canada	15-21	Population based	1992-2012	2931 AYA	No survivorship time restriction, selected diagnoses ^b
Childhood, Adolescent, and Young Adult Cancer Survivors Research Program (CAYACS)	British Columbia, Canada	20-24	Population based	1970-2010	4776 AYA	No survivorship time restriction
Surveillance, Epidemiology, and End Results (SEER)	Connecticut, Detroit, Atlanta, San Francisco-Oakland, Hawaii, Iowa, New Mexico, Seattle-Puget Sound, Utah	15-39	Population based	1973-2011	148 558 AYA ²⁷	5-year survivors
Childhood Cancer Survivor Study (CCSS)	United States	0-20	Hospital-based	1970-1999	35 937; 5600 AYA ^{118,120}	5-year survivors, selected diagnoses ^c
St Jude Lifetime Cohort Study (SJLIFE)	St. Jude Children's Hospital, Tennessee	0-24	Hospital-based	1962-2009	5122; 793 AYA	5-year survivors

Institute of Medicine Call To Action



2003



2005

How many AYA cancer survivors are there?

New diagnoses



Number of AYA survivors



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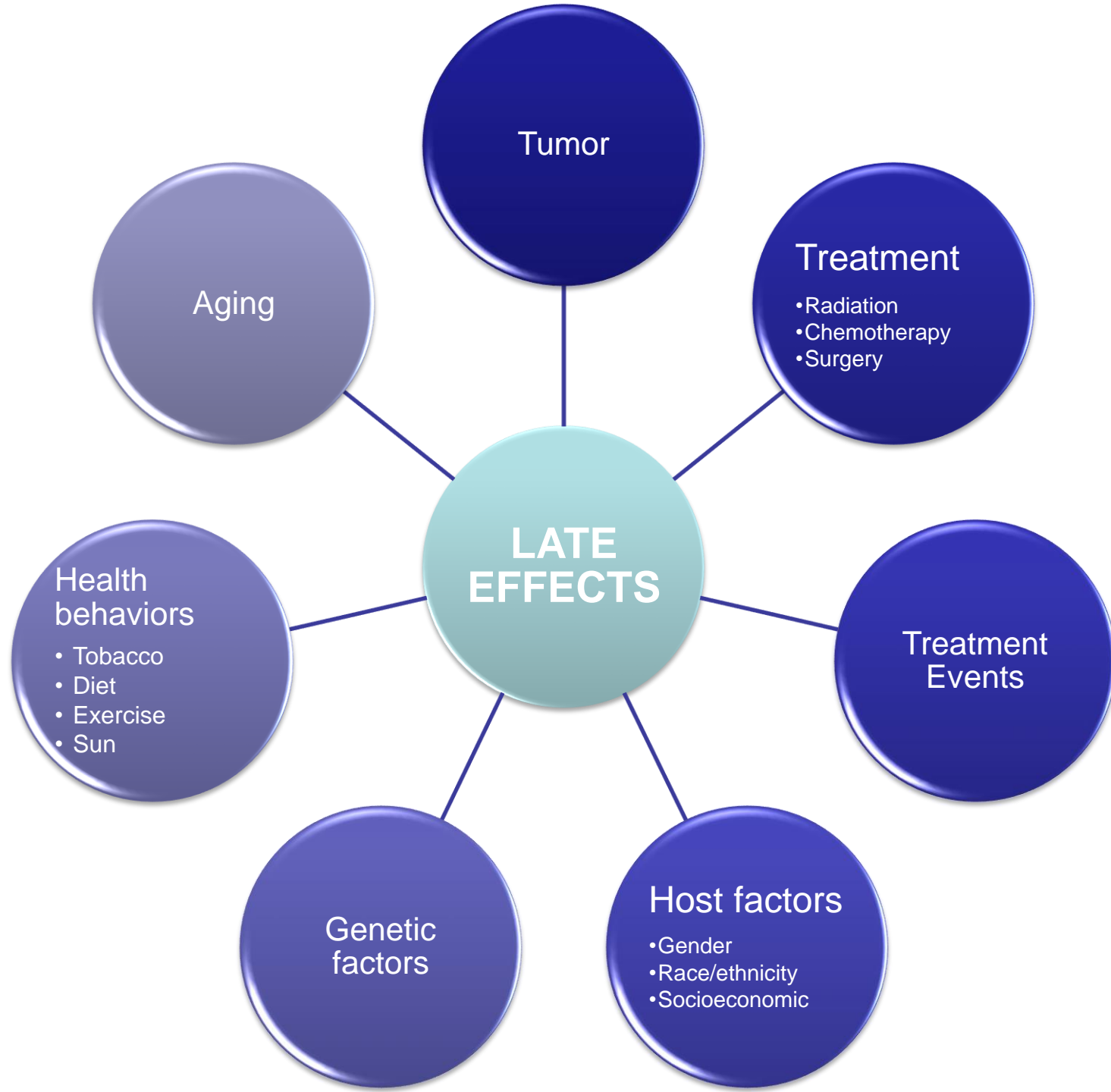


Long-term challenges faced by survivors

1. Cancer recurrence
 2. Chronic physical health conditions
 3. Premature mortality
 4. Mental health problems
 5. Reduced health-related QOL
 6. Financial toxicity
- Late effects

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Late Effects: Physical

Growth and Development <ul style="list-style-type: none">• Linear growth• Skeletal maturation• Emotional/social maturation• Sexual development	Organ Function <ul style="list-style-type: none">• Cardiac• Pulmonary• Endocrine• GI/Hepatic• Genitourinary• Musculoskeletal• Neurocognitive• Neurologic• Neurosensory
Fertility and Reproduction <ul style="list-style-type: none">• Sexual functioning• Fertility• Health of offspring	Cancer <ul style="list-style-type: none">• Recurrent (primary)• Subsequent cancers

Late Effects: Psychosocial

Mental Health <ul style="list-style-type: none">• Depression/mood disorders• Cancer-related anxiety• Post-traumatic stress Physical/Body image <ul style="list-style-type: none">• Weight loss/gain• Loss of organs/tissues	Education/Vocation <ul style="list-style-type: none">• Academic underachievement• Vocational limitations• Under/unemployment• Loss of job/benefits Insurance discrimination <ul style="list-style-type: none">• Access to health care
Chronic Symptoms <ul style="list-style-type: none">• Fatigue/ low energy• Disrupted sleep• Poor memory/concentration• Chronic pain Self-care <ul style="list-style-type: none">• Independent living	Financial/economic <ul style="list-style-type: none">• Debt (medical/other) Social Interaction <ul style="list-style-type: none">• Family/peer relationships• Social withdrawal/isolation• Intimacy/marriage/family• Cancer-related stigma

Premature mortality

Risk elevated, but lower than childhood survivors:

- Scottish (SMR 4.7 vs 11) and Finnish data
- Cancer-related death primary cause: relapse, SMN
- Infection, cardiovascular follow
- Lower cause-specific mortality (respiratory, cardiac)

Brewster DH et al. EJC, 2013

Kero AE et al. Int J Cancer, 2015

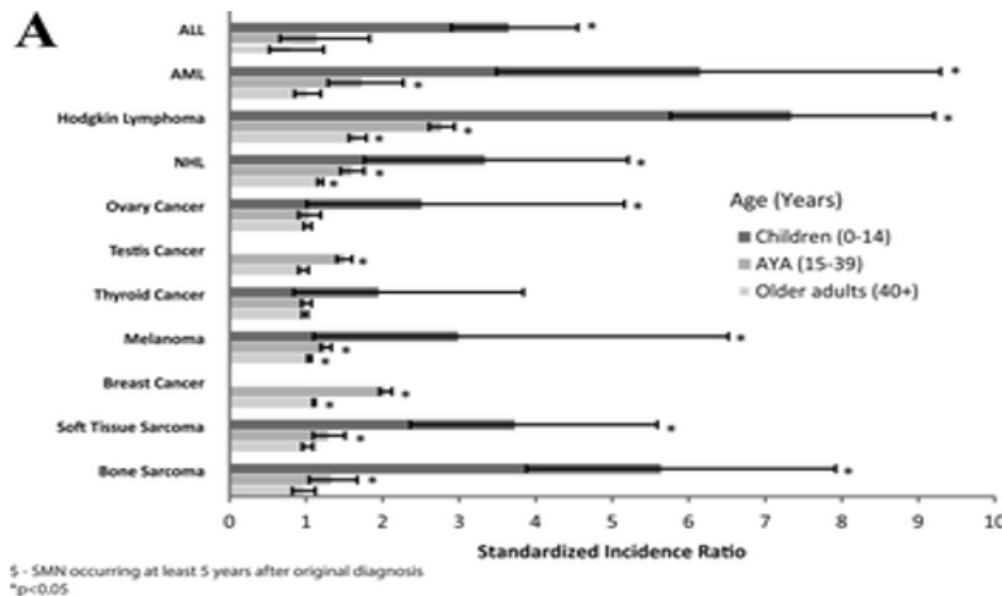
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Subsequent Neoplasms

Risk elevated, but less than observed in childhood cancer survivors

- SIR 1.6 in AYA; 4.3 in children (SEER)
- Breast cancer risk in Hodgkin lymphoma survivors (UK):
 - 15-19 y.o. 3x more likely than 25-29 y.o. to develop breast cancer



Lee JS et al. Cancer, 2016

Bright CR et al. Lancet Oncol, 2018

Reulen et al. JAMA, 2011

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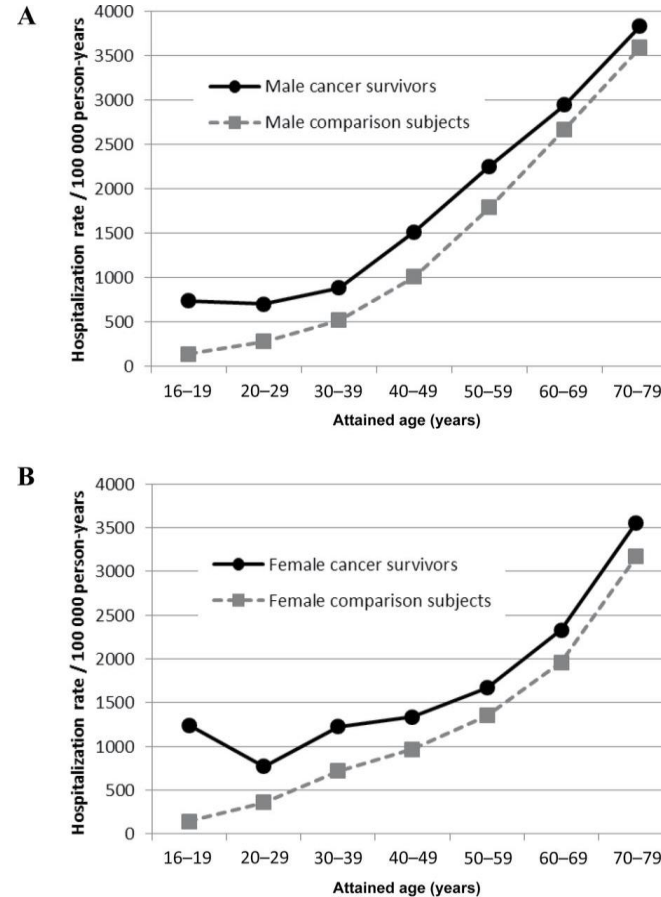
Chronic Health Conditions

Most research has focused on hospitalizations:

- 1.4 x risk of general population
- Infections and cancers drive admissions
- Also, elevated risk for cardiac disease

But, risk not as high as in childhood cancer survivors

Rugbjerg K et al. JNCI, 2014



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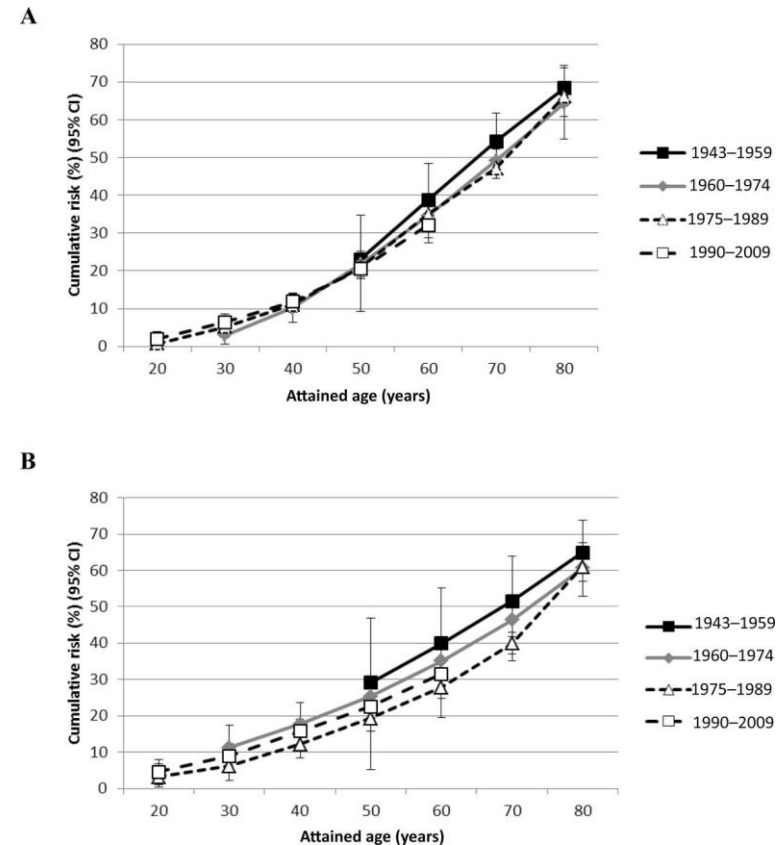
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Late Mortality and Chronic Health Conditions in Long-term Survivors of Adolescent and Early Young Adult Cancers

- 5804 early AYA cancer survivors (15-20.9): median age 42
- 5804 childhood cancer survivors (0-14.9): median age 34

	AYA	Childhood
Standardized mortality ratio (SMR)*	5.9	6.2
Non-recurrent SMR*	4.8	6.8
Grade 3-5 health conditions (HR)**	4.2	5.6
Grade 3-5 cardiac (HR)**	4.3	5.6
Grade 3-5 endocrine(HR)**	3.9	6.4
Grade 3-5 MSK (HR)**	6.5	8.0

*compared to general population

** compared to siblings

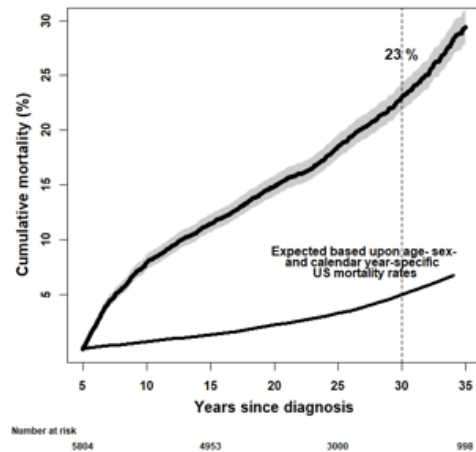
Su et al. Under review

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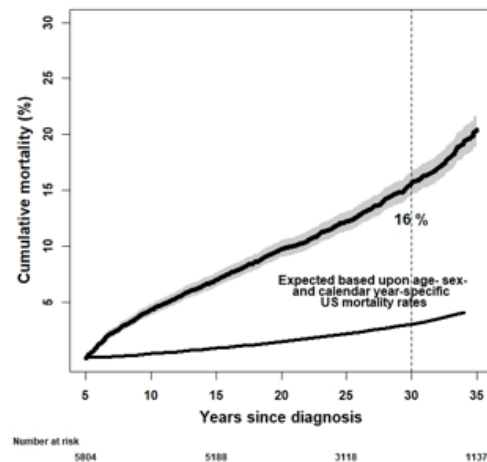


All-cause cumulative mortality >5 years from cancer diagnosis

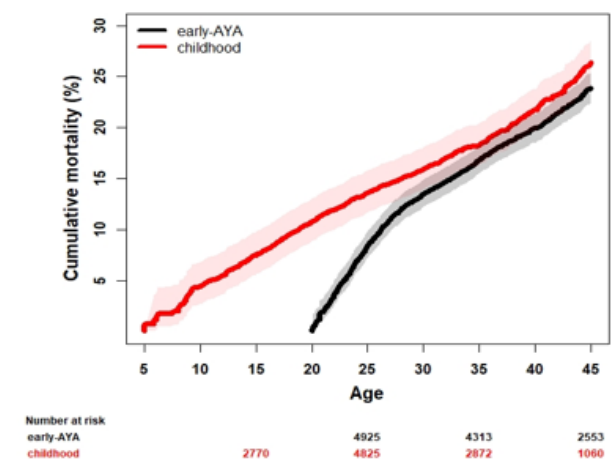
A. Early-AYA survivors by time since diagnosis



B. Childhood cancer survivors by time since diagnosis



C. Early-AYA and childhood survivors by attained age



Psychosocial outcomes

- Mental health, HRQL, social functioning, fatigue
 - Cancer-related distress (fear of recurrence, late effects, death)
 - Altered relationships
 - Body/sexual image
 - Interrupted future plans
 - Forced dependence
- Elevated risk for depression, suicidal ideation, anxiety, PTSD
- Screening critical (e.g. ESAS)

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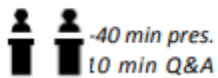
Fertility and interpersonal issues

- AYA report lack of awareness of gonadotoxic treatments and reproductive impact
- Fertility information is one of the most cited needs by AYA
- Sexuality, intimacy, relationship formation
- Body image

WS C – SEXUAL HEALTH MATTERS: WHY AND HOW TO TALK ABOUT IT WITH PATIENTS

Sylvie Aubin (Psychologist, Louise Granofsky Psychosocial Oncology Program (POP), AYA Team, Jewish General Hospital); **Chanah Korenblum** (Physician, SickKids/ Princess Margaret Cancer Centre); **Laura Mitchell** (Clinical Nurse Specialist, AYA Oncology Program, Princess Margaret Cancer Centre)

3:45 pm – 4:30 pm



-40 min pres.
10 min Q&A

NEW ADVANCES IN MALE AND FEMALE FERTILITY PRESERVATION

Claire Jones (Reproductive Endocrinology and Infertility Specialist, Mount Sinai Hospital)
Keith Jarvi, (Urologist, Mount Sinai Hospital)

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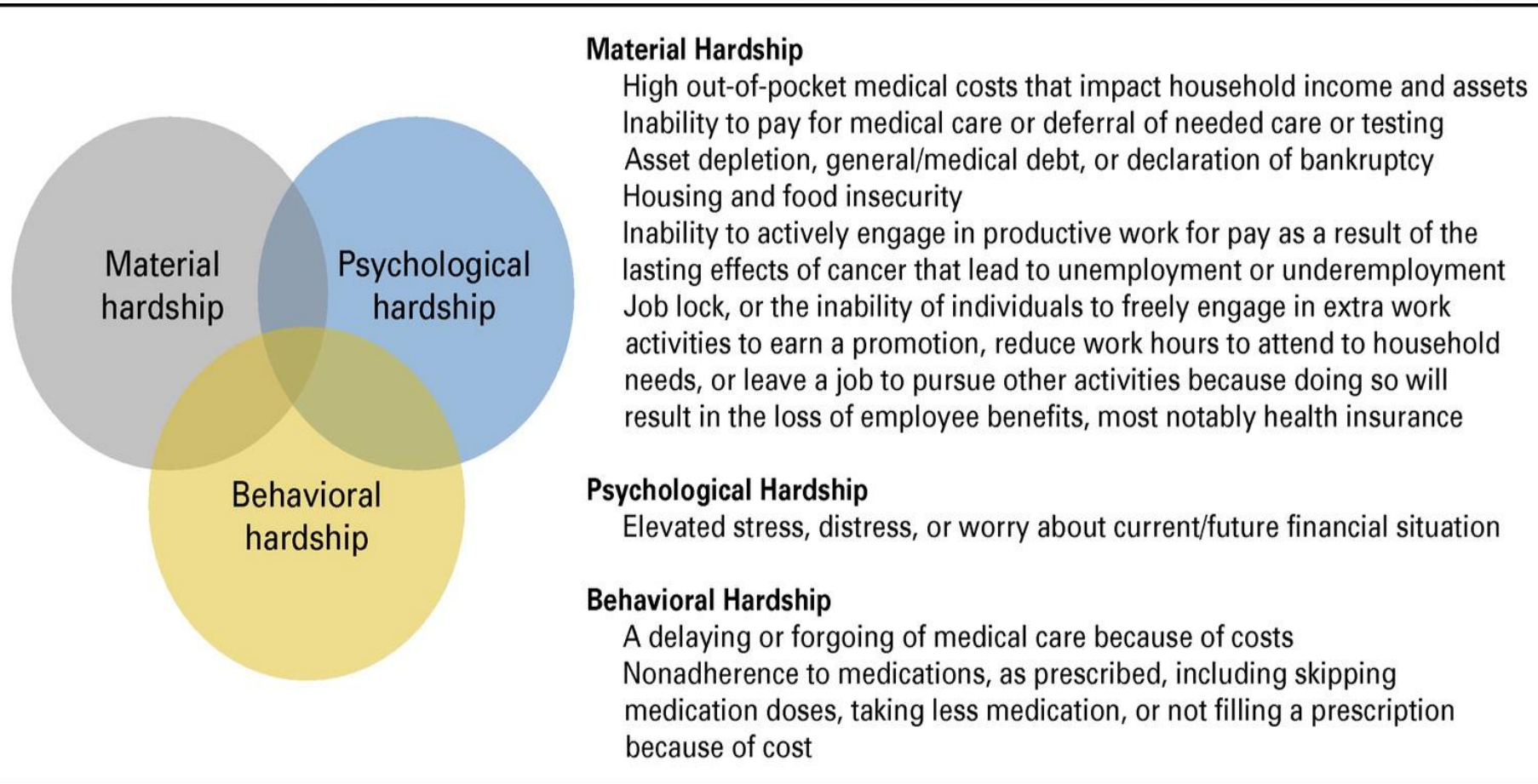
Financial hardship (FH)

- Also called financial *toxicity* or *burden*
- FH → physical/psychological harm
- Physical, psychological or neurocognitive late effects → FH
- Multidimensional construct

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Dimensions of financial toxicity





National Health Interview Survey

- Nationally representative, annual cross-sectional USA survey
- Age at survey: ≥ 18 years
- 2010-2018
- AYA: age at cancer diagnosis 15-29 years
- Comparison group: no history of cancer



Sample Characteristics

		AYA Cancer Survivors (n = 996)	Adults Without a History of Cancer (n = 256,964)	p
Age at time of survey	18-39	22%	23%	<.001
	40-49	28%	18%	
	50-64	15%	18%	
	65-80	23%	25%	
	81+	9%	12%	
Sex	Male	38%	49%	<.001
	Female	62%	51%	
Cancer diagnosis	Lymphoma	10%		-
	Melanoma	12%		
	Testicular	7%		
	Thyroid	9%		
	Ovarian	10%	-	
	Uterine	9%		
	Brain	3%		
	Leukemia/Blood	4%		
	Breast	8%		
Time since diagnosis	< 2 years	8%	-	-
	≥ 2 years	92%		

Median time from cancer dx: 15.4 years

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Sample Characteristics

		AYA Cancer Survivors (n = 996)	Adults Without a History of Cancer (n = 256,964)	p
Education	< High school or missing	11%	14%	.01
	High school graduate	22%	25%	
	≥ Some college	67%	61%	
Family income as % of federal poverty level (FPL)	< 200%	29%	29%	.009
	≥ 200% and < 400%	25%	27%	
	≥ 400%	40%	36%	
	Missing	6%	8%	
Health insurance at time of survey; age < 65	Any private	54%	56%	<.001
	Public only	19%	14%	
	Uninsured	15%	15%	
Health insurance at time of survey; age ≥ 65	Medicare and private	6%	7%	<.001
	Medicare & public	2%	2%	
	Medicare only	3%	6%	
	Uninsured	0%	0%	
Number of comorbid conditions	0	48%	59%	<.001
	1	29%	27%	
	2	14%	9%	
	≥3	9%	5%	





Material Hardship

	Survivors	No cancer history	P
Problems paying off medical bills	21%	16%	.001
Paying off medical bills now	32%	23%	<.001

Survivors: $n = 897$
Comparison: $n = 231,221$

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Psychological Hardship

	Survivors	No cancer history	P
Worried about medical costs of illness/accident	42%	42%	NS
Worried about medical costs of healthcare	32%	29%	NS

Survivors: $n = 649$
Comparison: $n = 169,880$

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Behavioral Hardship

	Survivors	No cancer history	P
Delayed medical care due to worry about cost	15%	10%	<.001
Forgone medical care due to worry about cost	10%	7%	.005
Couldn't afford prescription medicine	11%	7%	.001
Couldn't afford mental health care/counselling	4%	2%	.04
Couldn't afford dental care	16%	12%	.004
Couldn't afford eyeglasses	9%	7%	.01
Couldn't afford to see a specialist	9%	5%	<.001
Couldn't afford follow-up care	9%	4%	<.001

Survivors: $n = 994$; 824 (S, F/U)
Comparison: $n = 255,967$; 208,822 (S, F/U)

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Summary Measures of Hardship



Any material hardship

38%

28%

<.001



Any psychological hardship

44%

45%

NS



Any behavioral hardship

31%

22%

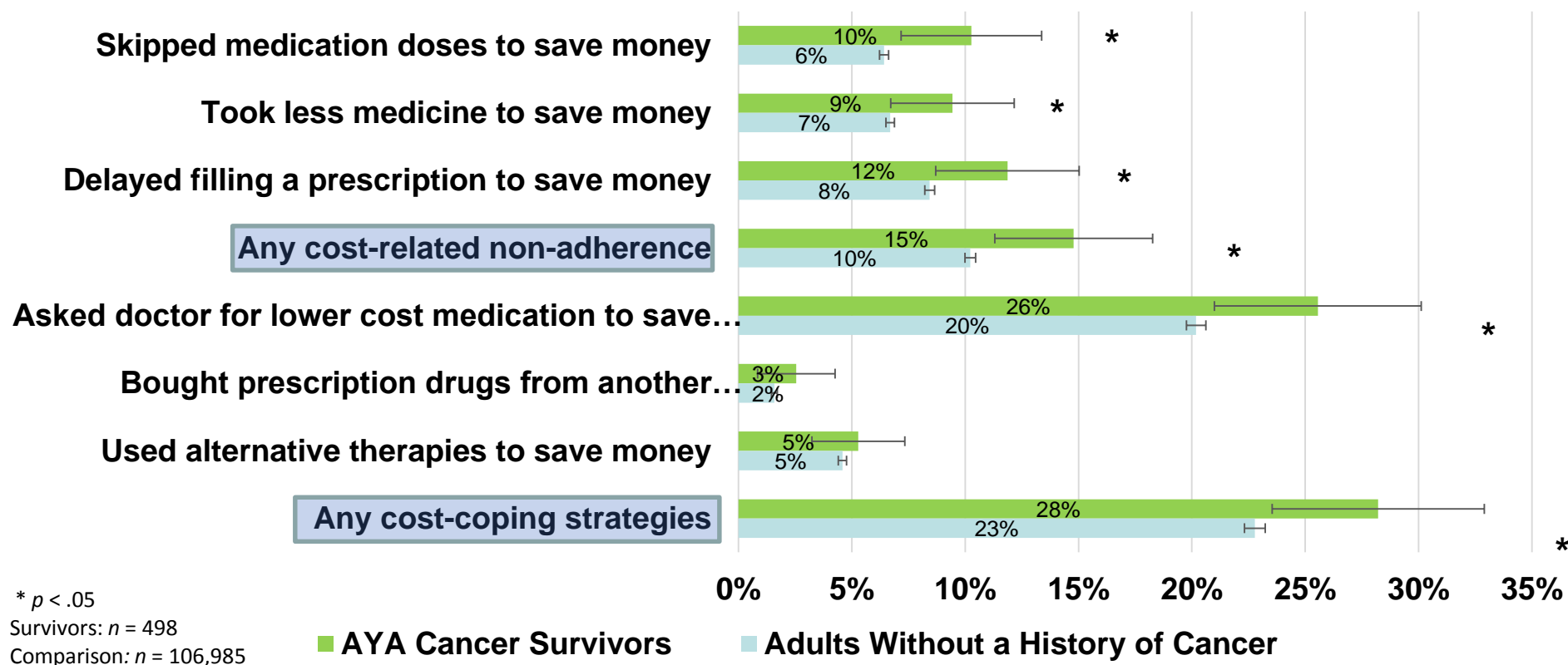
<.001

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Prescription Medication Adherence



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Models of AYA survivor care

- No single location or provider
 - Acute oncology clinics
 - Specialized survivor clinics
 - Shared care
 - PCP
- Guidelines generally written for children but extend into young AYA
- Survivor care plans

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Survivorship guidelines that include AYA

Publisher	Age range at cancer diagnosis	Web link
International Guidelines Harmonization Group (IGHG)	Childhood, adolescence and young adulthood	www.ighg.org
Children's Oncology Group (COG)	Childhood, adolescence and young adulthood	http://survivorshipguidelines.org/
Scottish Intercollegiate Guidelines Network (SIGN)	<24 years	http://www.sign.ac.uk/assets/sign132.pdf
Children's Cancer and Leukaemia Group (CCLG)	Childhood	https://www.cclg.org.uk/write/MediaUploads/Member%20area/Treatment%20guidelines/LTFU-full.pdf
National Comprehensive Cancer Network (NCCN)	15-39 years	https://www.nccn.org/professionals/physician_gls/pdf/aya.pdf
Dutch Childhood Oncology Group (DCOG-LATER)	Pediatric	https://www.skion.nl/workspace/uploads/vertaling-richtlijn-LATER-versie-final-okt-2014_2.pdf
German Society for Paediatric Oncology and Haematology (GPOH; German)	Childhood, adolescence and young adulthood	https://www.awmf.org/leitlinien/detail/II/025-003.html
Swedish Working Group for Long-term Follow-up after Childhood Cancer (SALUB)	Childhood	http://www.blf.net/onko/page6/page14/files/Salub_5_2010_Eng.pdf



IGHG

Breast cancer	+
Cardiomyopathy	+
Premature ovarian insufficiency	+
Male gonadotoxicity	+
Thyroid cancer	+
Ototoxicity	+
Obstetric care	
Central nervous system neoplasms	
Coronary artery disease	
Hypothalamic-pituitary dysfunction	
Fatigue, mental health and psychosocial problems	
Metabolic syndrome	
Pulmonary dysfunction	
Bone toxicity	
Nephrotoxicity surveillance	
Thyroid dysfunction	
Neurocognitive problems	

Who needs breast cancer surveillance?

Providers and female childhood, adolescent and young adult cancer survivors treated with chest radiation should be aware of breast cancer risk.

Breast cancer surveillance is recommended for female childhood, adolescent and young adult cancer survivors treated with ≥ 20 Gy chest radiation.

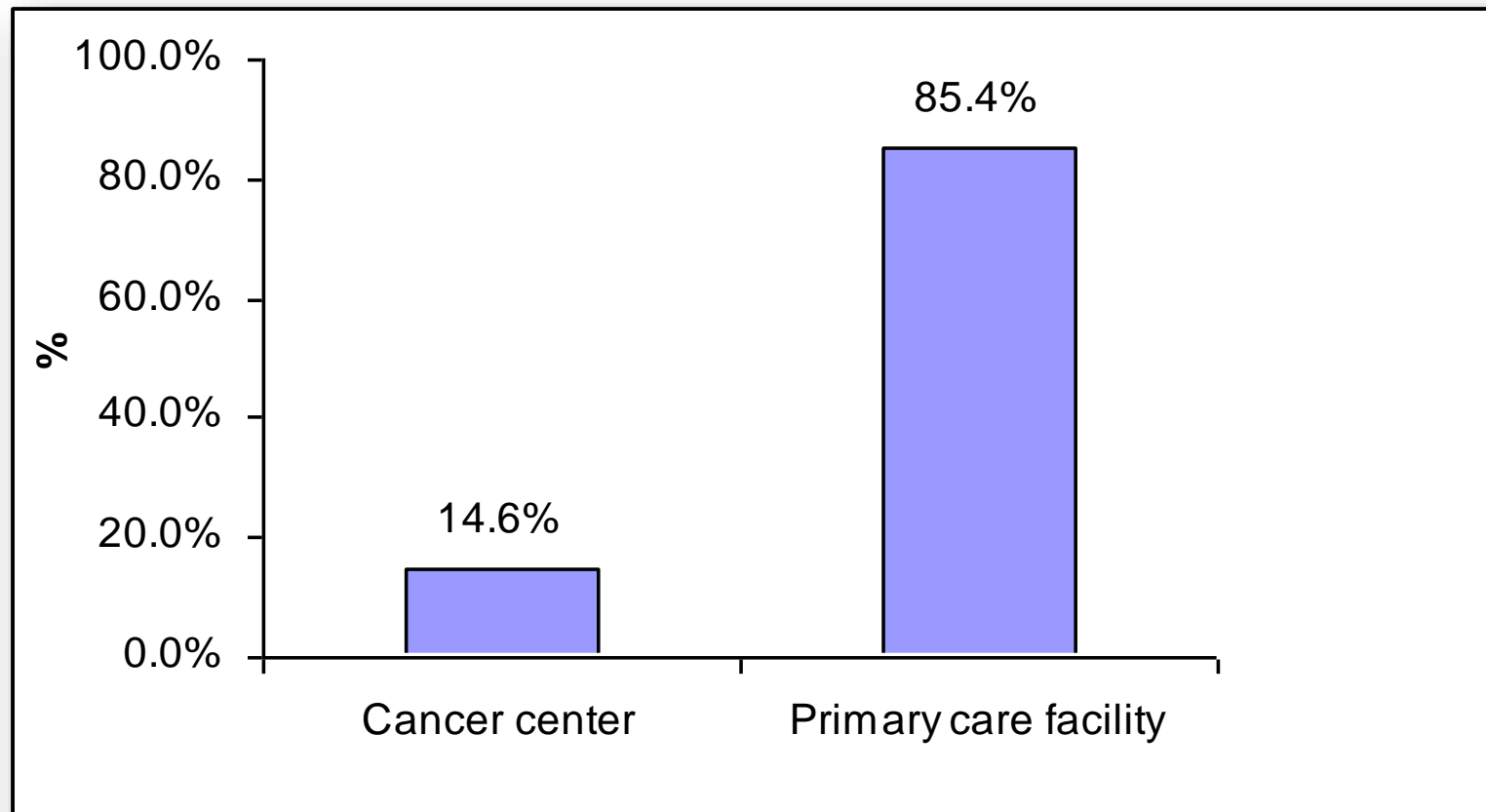
Breast cancer surveillance is reasonable for female childhood, adolescent and young adult cancer survivors treated with 10-19 Gy chest radiation based on clinical judgment and considering additional risk factors.

Breast cancer surveillance may be reasonable for female childhood, adolescent and young adult cancer survivors treated with 1-9 Gy chest radiation based on clinical judgment and considering additional risk factors.

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Where do adult survivors of childhood and AYA cancer getting their care?



Are physicians aware of long-term follow up guidelines for childhood and AYA cancer survivors?

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C.L. is a 29 year old female patient treated for *Hodgkin lymphoma* when she was 16 years old.

She received combination chemotherapy (including *Adriamycin 150 mg/m²* and *Cyclophosphamide 15 g/m²*) and *mantle radiation (25 Gy)*.

Questions regarding:

- Cardiomyopathy screening
- Thyroid function screening
- Breast cancer screening

Significant Gaps in Provider Knowledge

AYA Hodgkin Lymphoma Survivor Vignette			
Responses Concordant with COG Guidelines	General Internists (N=1110)	Family Physicians (N=1124)	Pediatric Oncologists (N=665)
Breast cancer screening	27%	16%	66%
Thyroid screening	76%	74%	76%
Cardiac screening	15%	10%	57%
Total	5%	2%	33%

Gaps in AYA survivor research

- Creation of cohorts that include the complete range of AYA ages (15-39 years)
- Creation of cohorts that capture the full spectrum of cancers most common in AYA
- Characterization and comparison of morbidity and mortality across the AYA age spectrum
- Factors affecting AYA' decisions to undergo fertility preservation
- Factors affecting transition of care after treatment
- Factors affecting, and health outcomes related to, locus and provider of survivor care
- The impact of survivor care plans on outcomes
- Interventions to improve adherence to recommended surveillance for late effects
- Study of barriers to completing school/obtaining employment after therapy
- Characterization of the psychosocial support needed by survivors
- Characterization of the rehabilitation services needed by survivors
- Characterization of financial toxicity and its risk factors
- Factors affecting research investment in AYA

Conclusions

- AYA at risk for range of physical, mental health and psychosocial late effects
- Risks lower than childhood cancer survivors, but still elevated
- Lack of systematic approach to care for survivors
- Ample opportunity for research to inform policy

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Questions



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