Cancer & Survivorship in the AYA (Adolescent & Young Adult) Population

Wilmot Cancer Institute
Survivorship Symposium

Jeffrey Andolina, MD, MS
Pediatric Hematology, Oncology,
and Stem Cell Transplantation

January 23rd, 2016

Disclosures

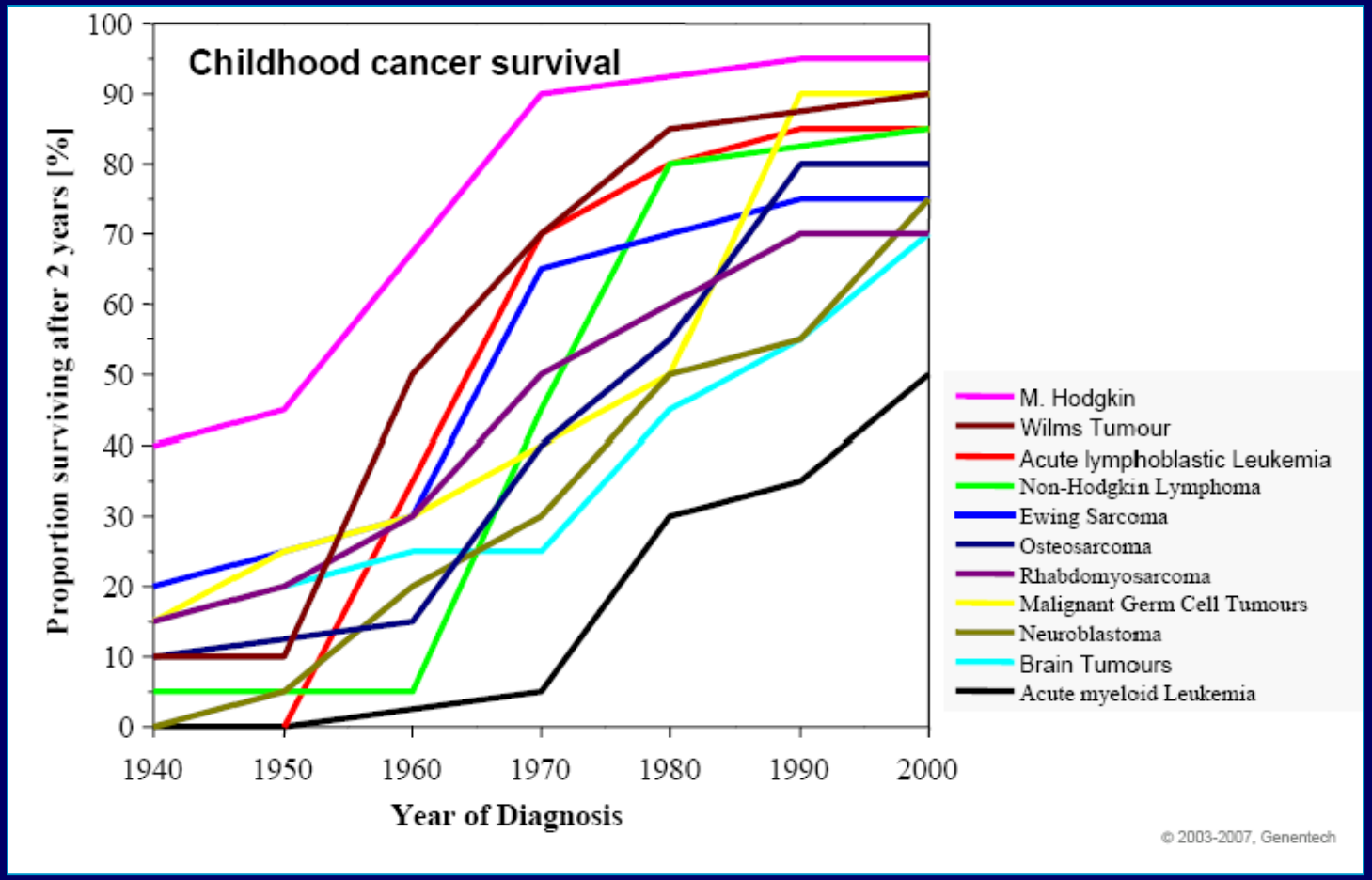
- I have nothing to disclose

Objectives

- 1. AYA oncology defined
- 2. Current survival gaps for this population
- 3. Challenges for AYA survivors
- 4. Recommendations: Late effects management
- 5. Recommendations: Supportive care and psychosocial

Large increase in cure rates for pediatric cancers

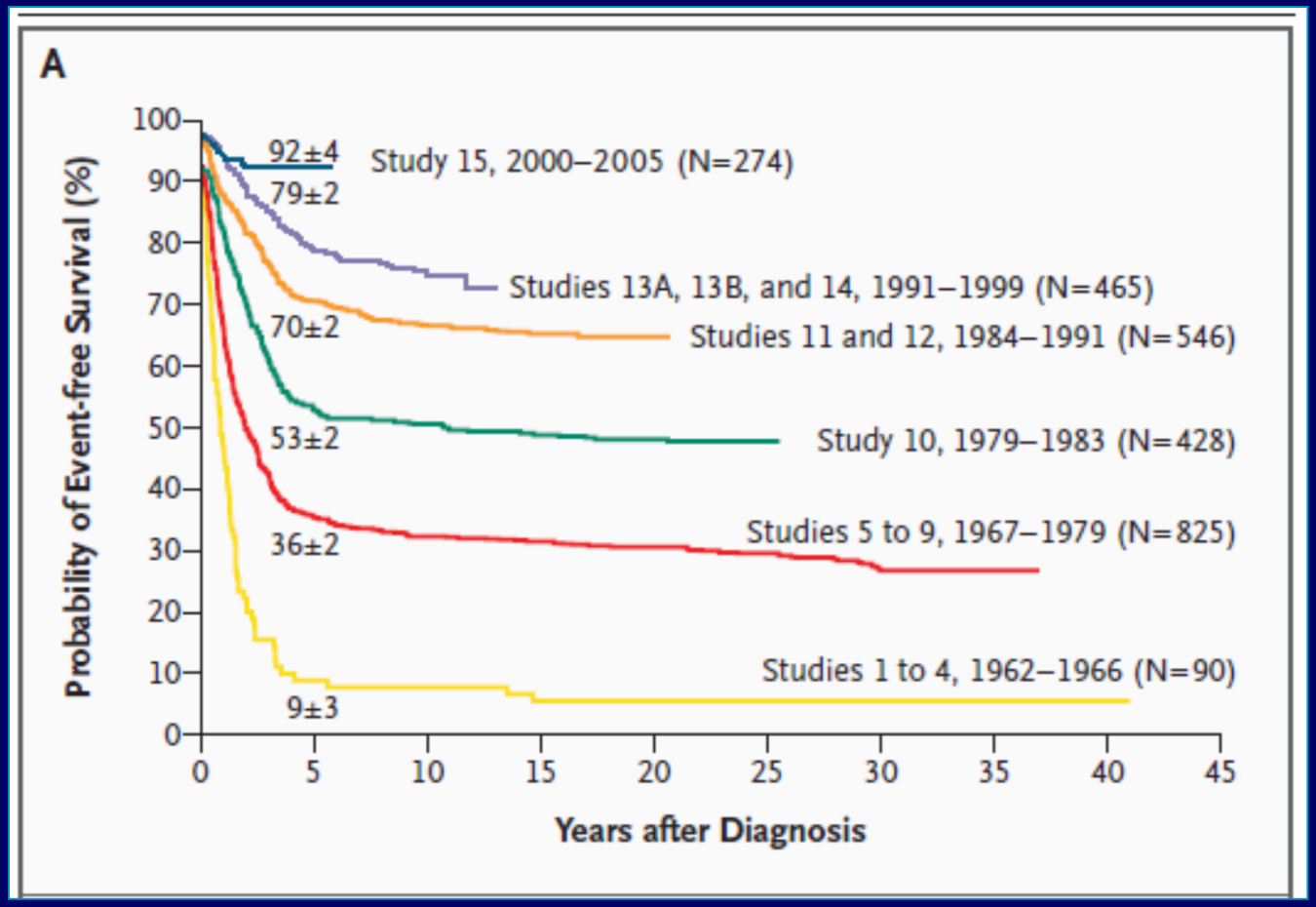
*Overall cure rates for children have now reached 80%



- This is largely due to basic science and clinical research!

Large increase in cure rates for ALL (acute lymphoblastic leukemia)

- This is due to enrolling patients on open clinical trials



Research in Pediatric Oncology

- National cooperative groups have paved the way for successful clinical trials
  - COG- Children's Oncology Group
  - PBMTC- Pediatric Blood and Marrow Tissue Consortium
- Our institution opens numerous trials from each of these institutions
- This allows optimal care at many institutions across the US

Children's Oncology Group (COG)

- National cooperative group including approximately 250 children's hospitals in the US, Canada, Australia, and some European countries
- Includes every major children's hospital in the US

Children's Oncology Group (COG)

- Benefits of one centralized group writing clinical trials that can then be opened at all centers across the US
- This allows for standardized care and collaboration among all pediatric oncologists
- This allows our patients in Rochester to have access to the best clinical trials
- In most cases, the treatment will therefore be identical regardless of the city you are treated
- This is allowed in that only tertiary care centers generally treat pediatric cancer (in comparison to adults)

Pediatric Enrollment on COG Trials

- Amazingly, 60-70% of children with cancer will enroll on a treatment clinical trial at our institution and in the US in general
  - This likely underlies the improving cure rates in pediatric cancers
- The cure rate for children diagnosed with cancer today is now 80%
  - And this number is rising

AYA Defined

- AYA= Adolescent and Young Adult
- Ages 15-39 (or ages 15-29)

- This is a distinct population
- Distinct diseases
- Distinct outcomes
- Distinct challenges

AYA Defined

- There is growing consensus that this population needs more resources and more support from the medical community
- NCCN (National Comprehensive Cancer Network) has developed specific guidelines for this population

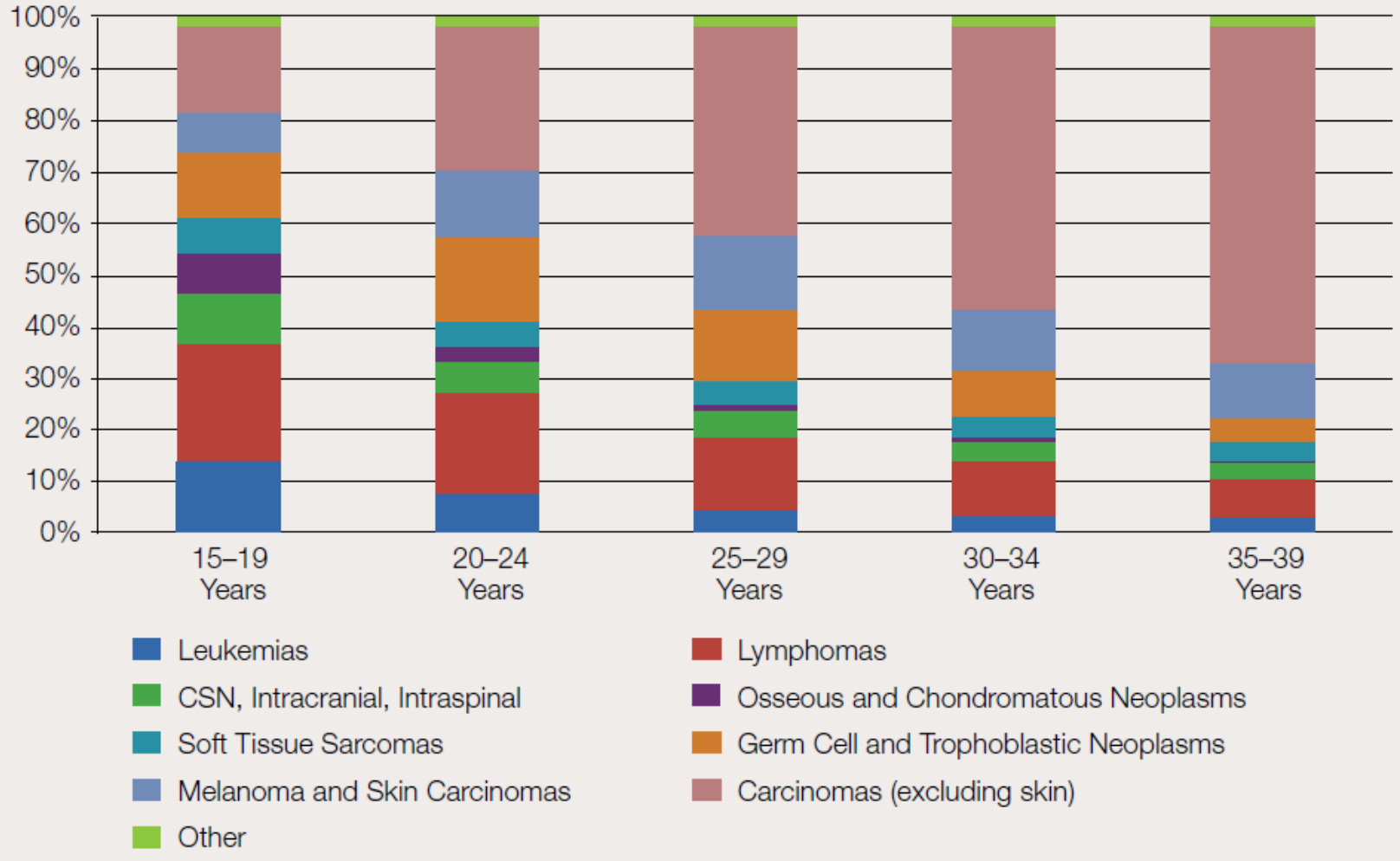
AYA Cancers

- Adolescents and young adults have a distinct group of cancers:

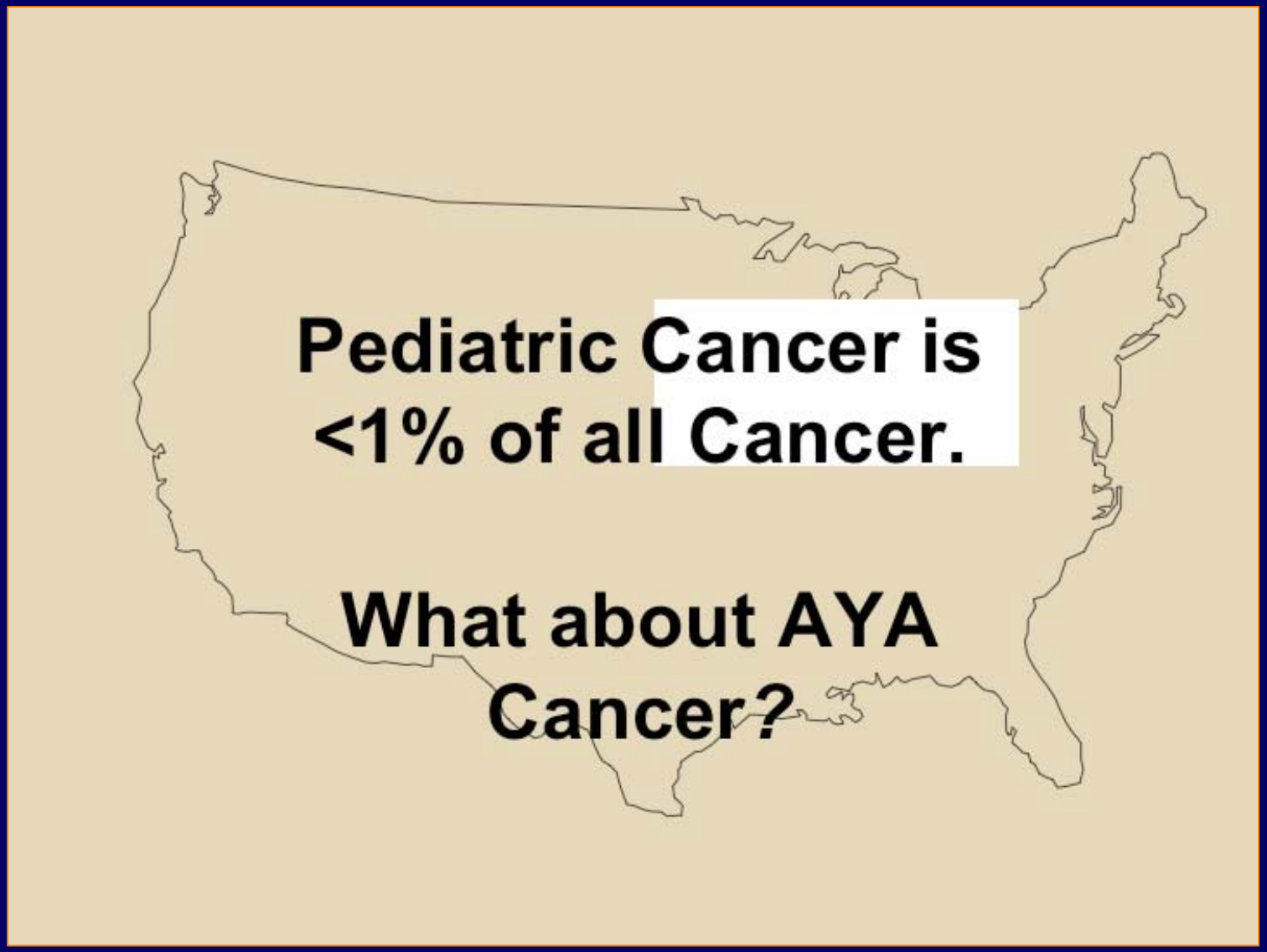
- Leukemia
- Lymphoma
- Sarcomas (osteosarcoma, Ewing's sarcoma)
- Testicular/ovarian cancers
- Brain tumors
- Breast cancer
- Other carcinomas

AYA Cancers

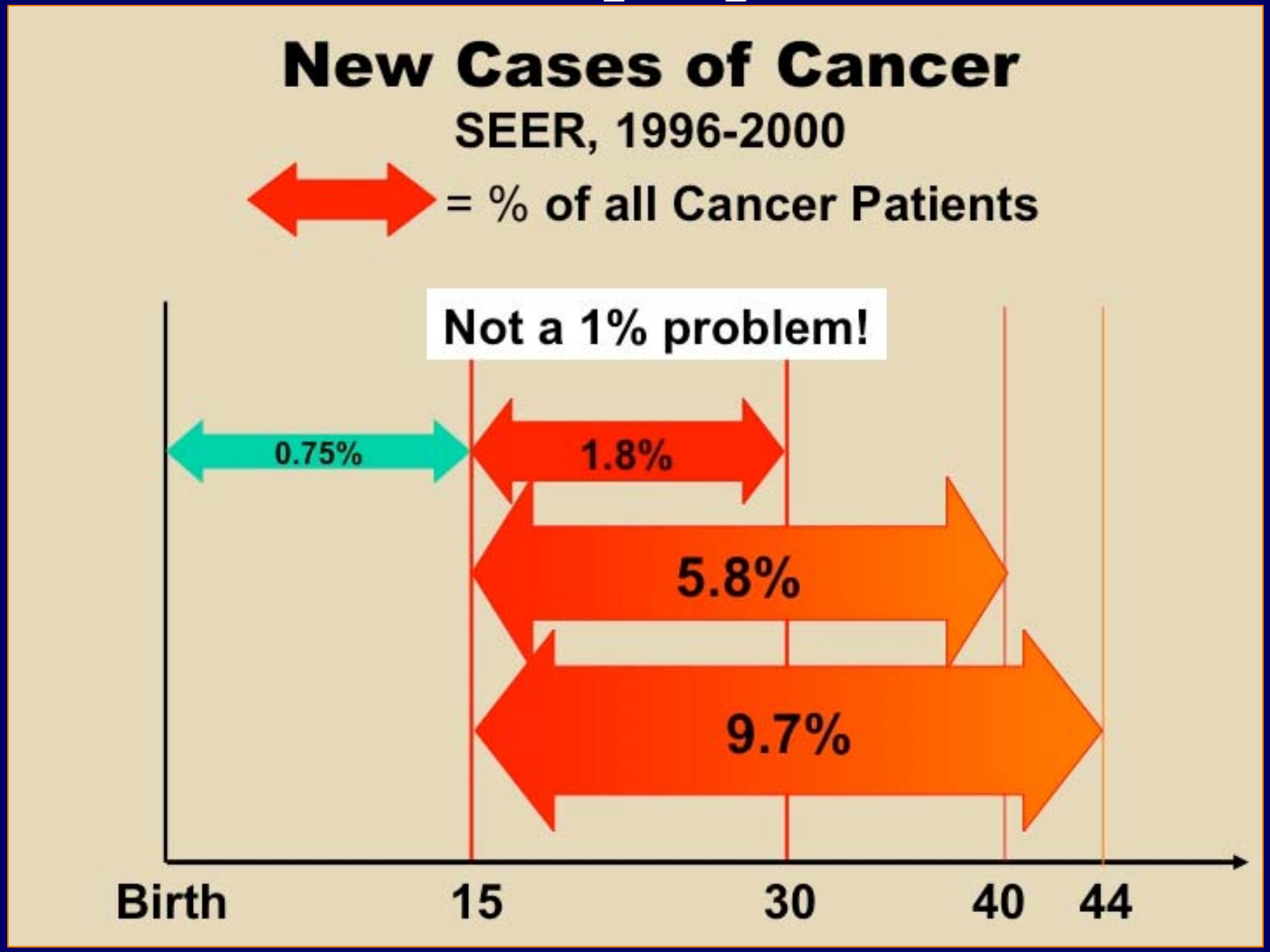
Figure 1. Age-Specific SEER Incidence by Adapted Classification Scheme for Tumors of Adolescents and Young Adults



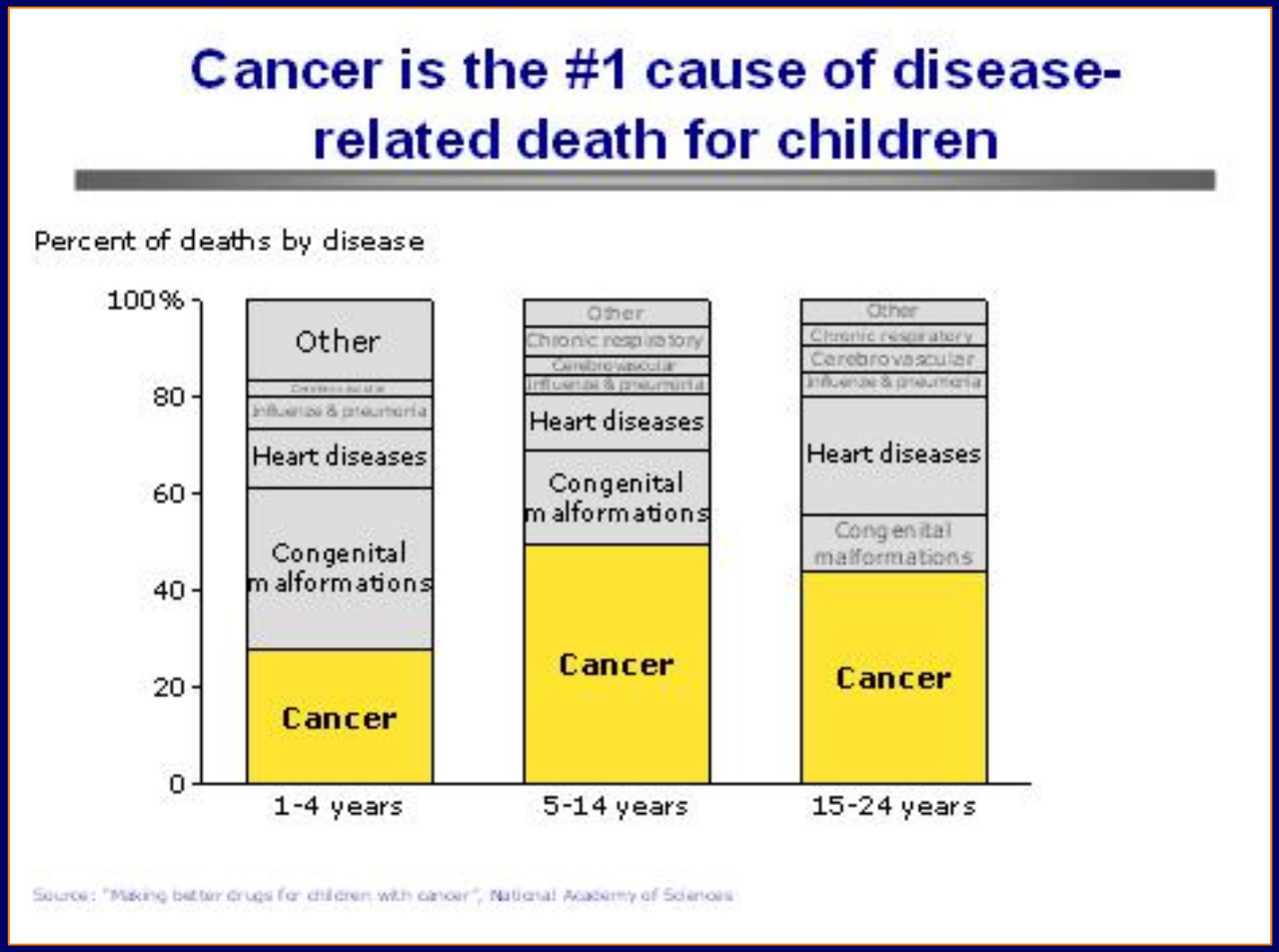
How common is AYA cancer?



AYA cancer is much more common than most people think!



Cancer remains a major cause of death for children and AYAs



- Childhood cancer kills more children than any other disease- more than AIDS, asthma, diabetes, cystic fibrosis, and congenital anomalies combined

AYA patient outcome

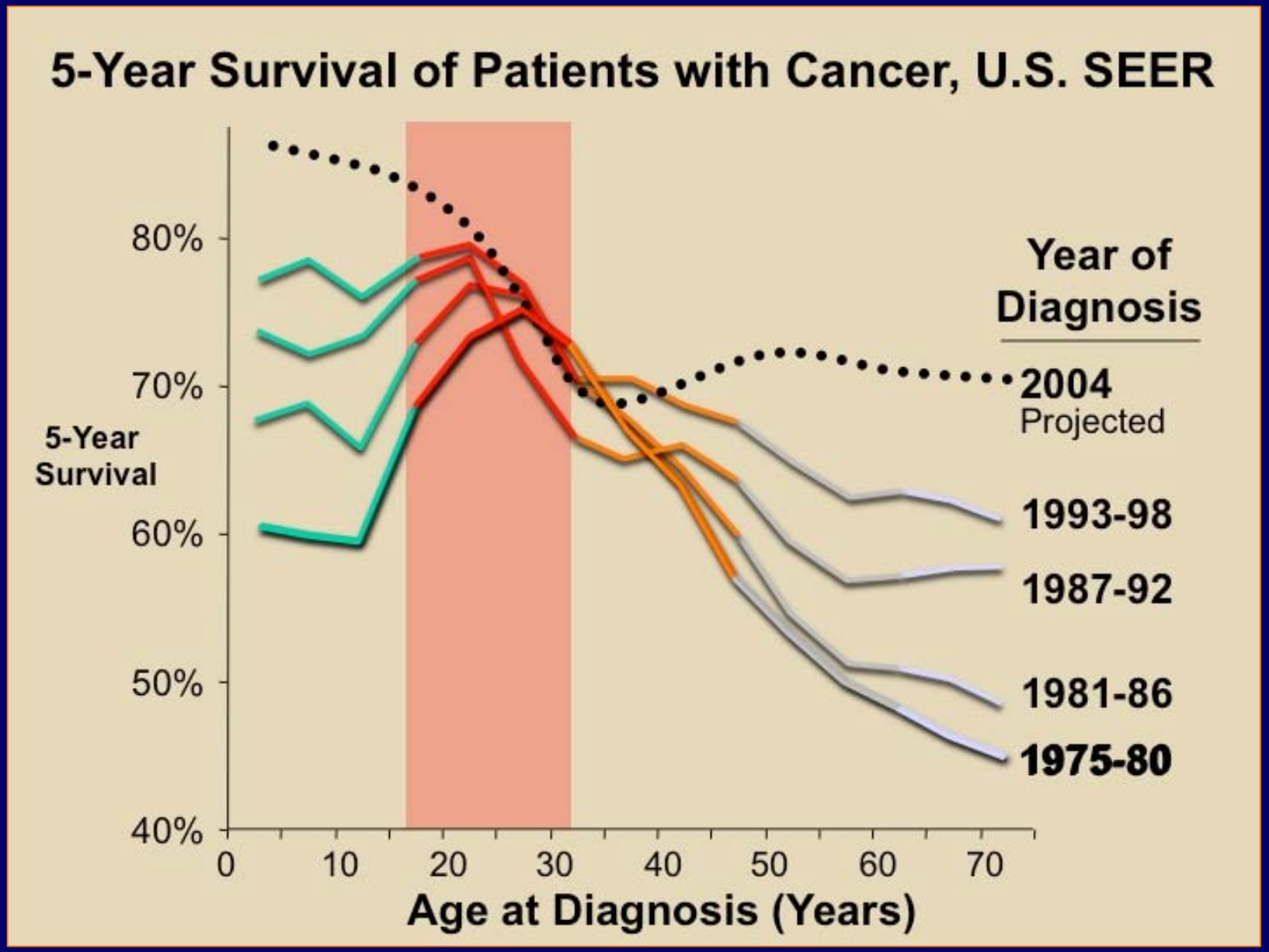
- **Unfortunately, the AYA population has NOT enjoyed any significant survival gains over the past few decades!**

AYA patient outcome

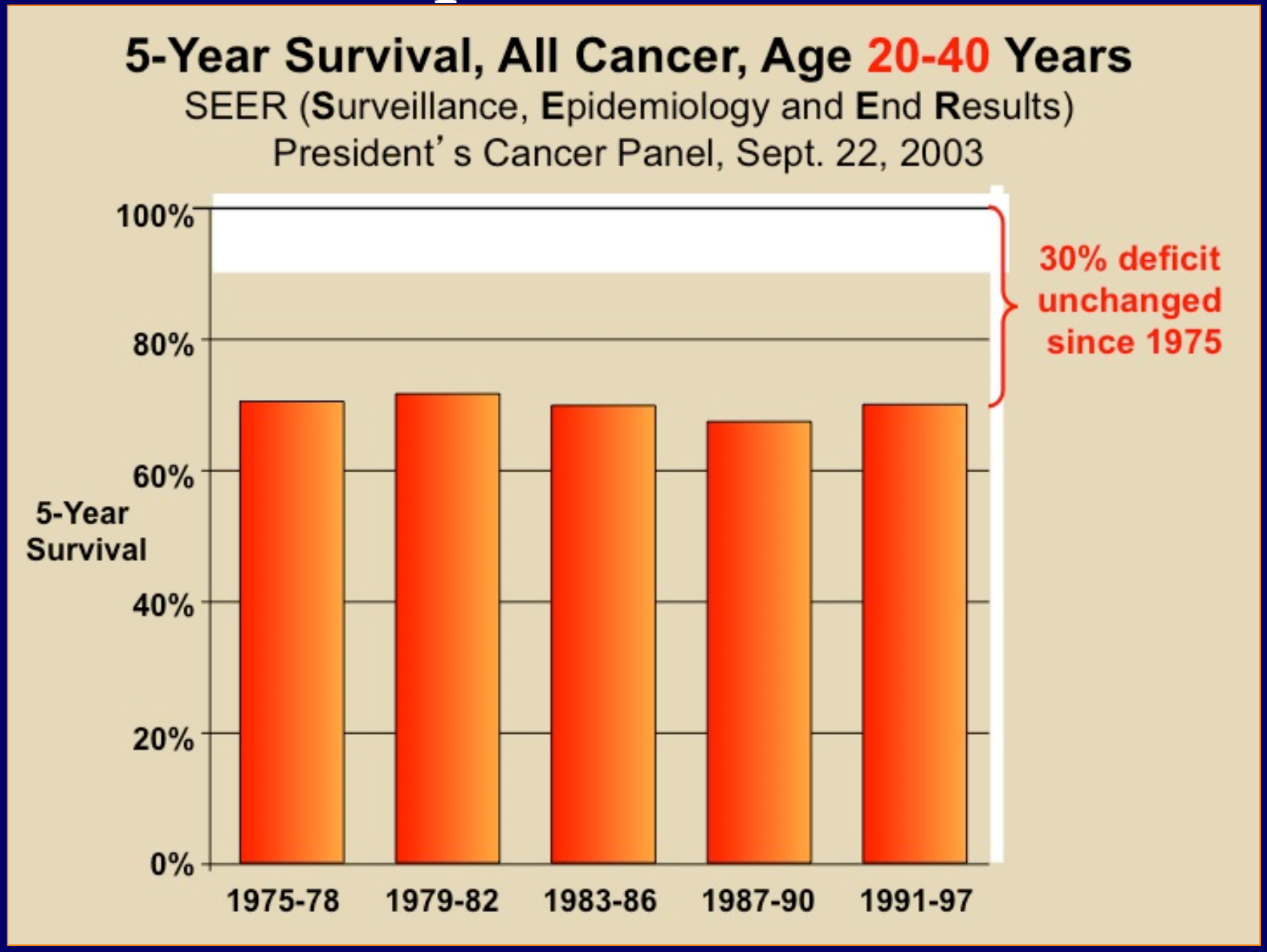
- **Unfortunately, the AYA population has NOT enjoyed any significant survival gains over the past few decades!**

- Pediatric (age <20) overall has seen tremendous improvements in outcome with >80% long term cure rate today
- These gains have been limited to patients ages 0-15 years

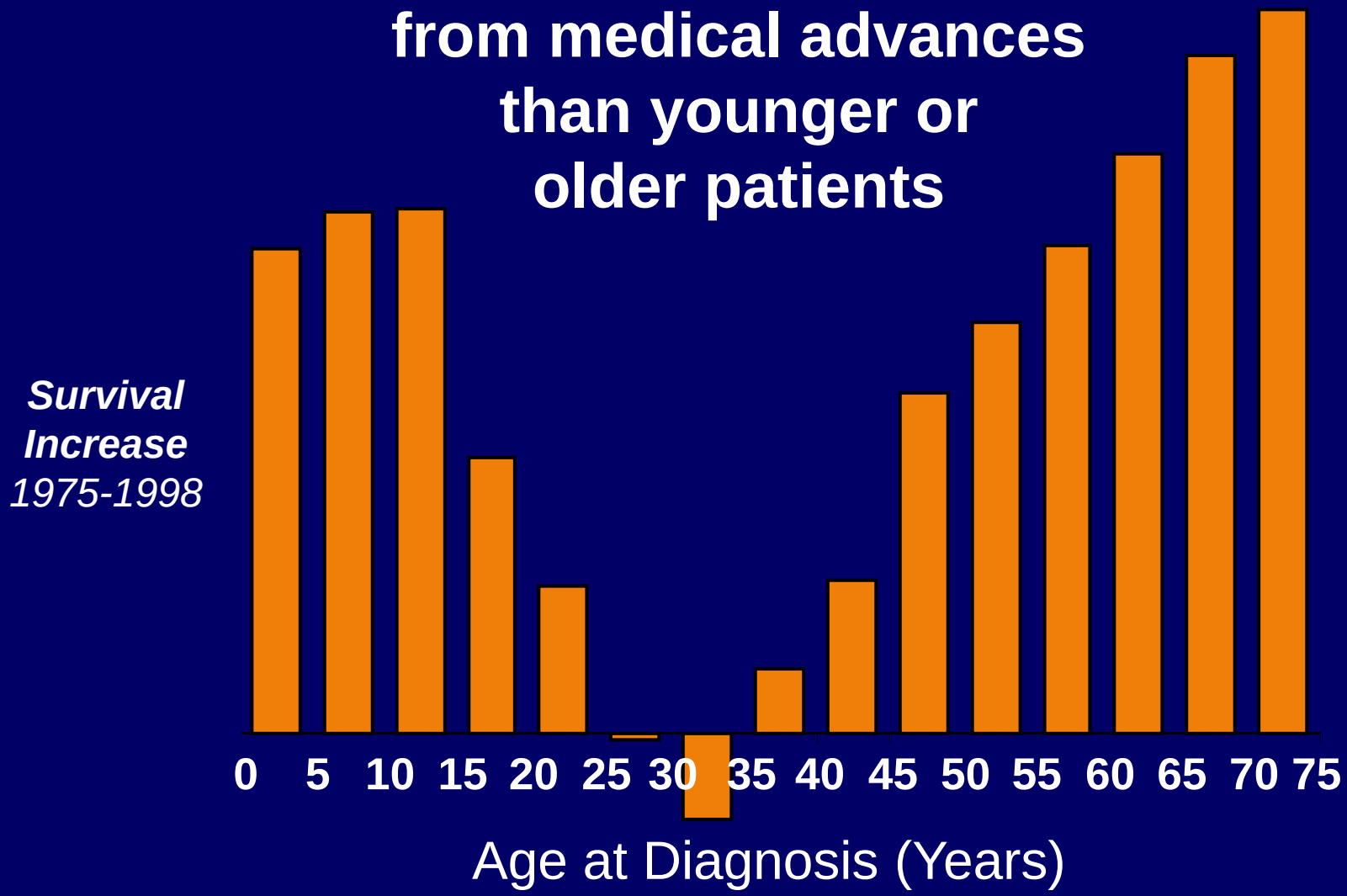
AYA patient outcome



AYA patient outcome

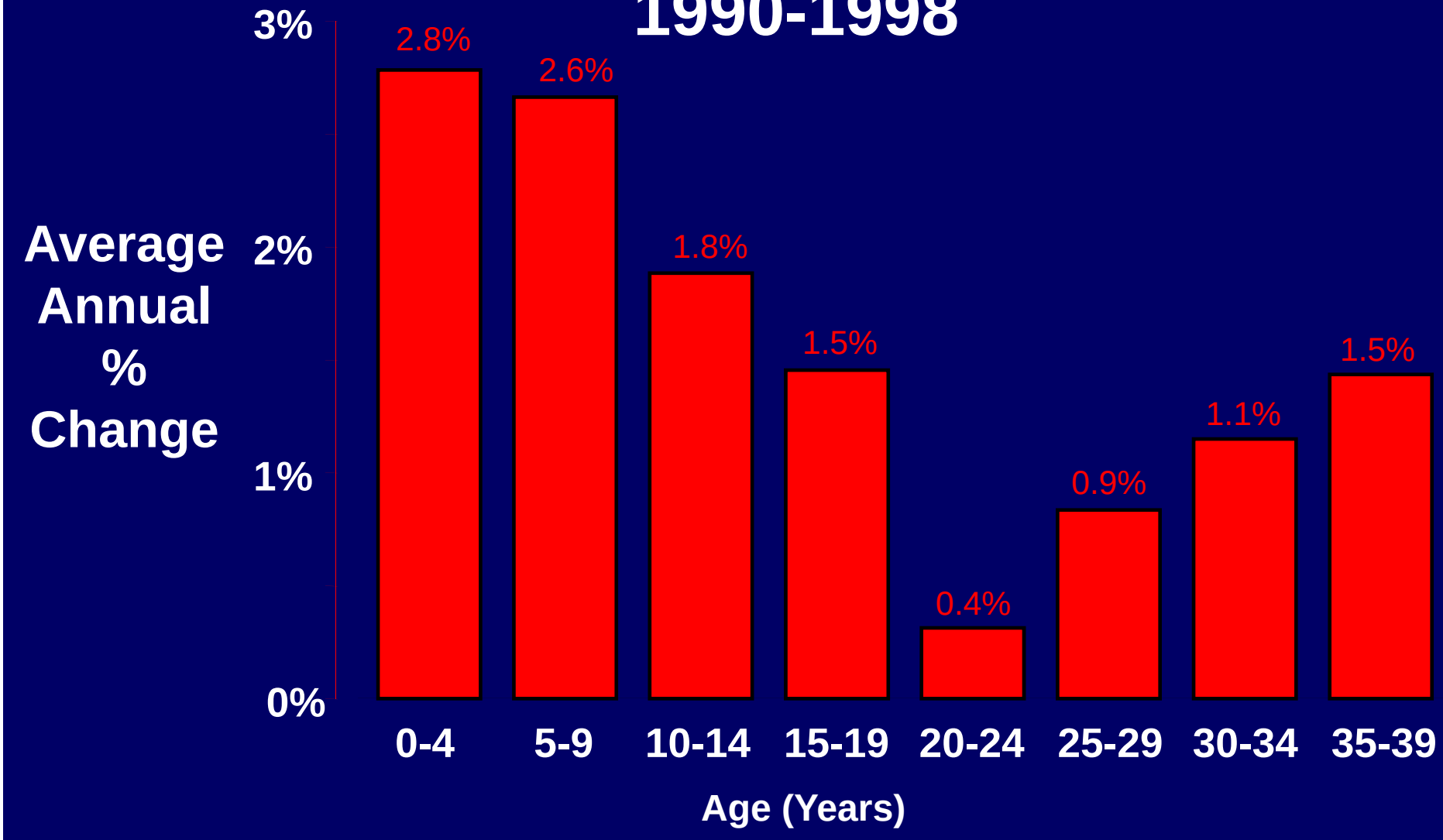


Older adolescents & young adults with cancer have had less benefit from medical advances than younger or older patients



Mortality

National Cancer Mortality Reduction 1990-1998



AYA Survival Summary

- Patients in this AYA age group have worse survival rates and have had no improvement in survival rates in comparison to younger and older patients.

WHY are cancer outcomes so poor for the AYA population?

WHY are cancer outcomes so poor for the AYA population?

- 1. Low rates of clinical trial participation
- 2. Referral patterns/ treatment facility
- 3. Medical treatment protocols used
- 4. Compliance
- 5. Lack of insurance
- 6. Delay in diagnosis
- 7. Low index of suspicion for cancer in AYA population
- 8. Poor understanding of biology of AYA malignancies

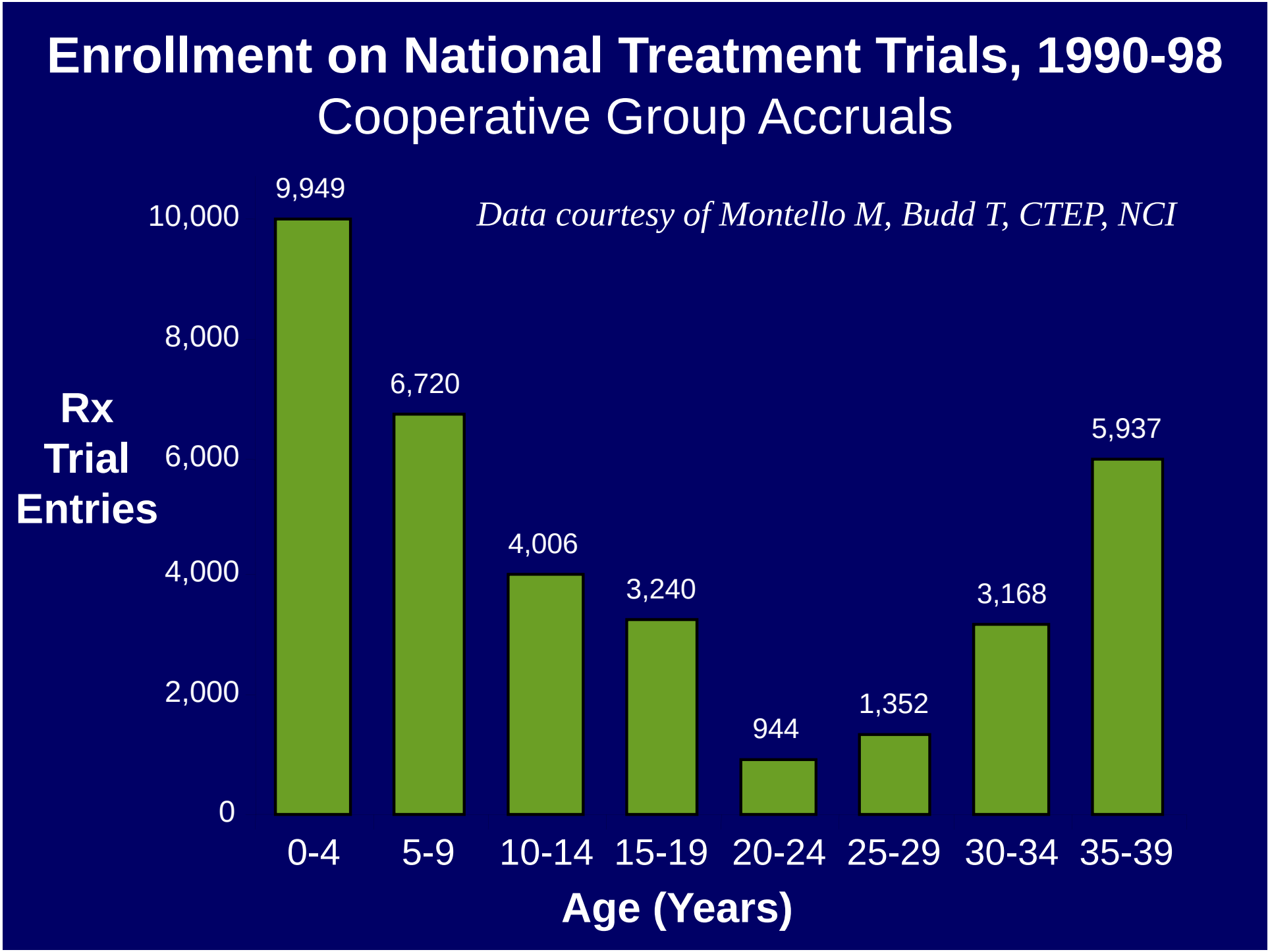
Low rates of clinical trial participation

- The majority (60-70%) of children (ages 0-15) are formally enrolled on a national clinical trial
- In adults, the number drops to 2-3%
- In the AYA population (15-29), the number is even lower at approximately 1-2%

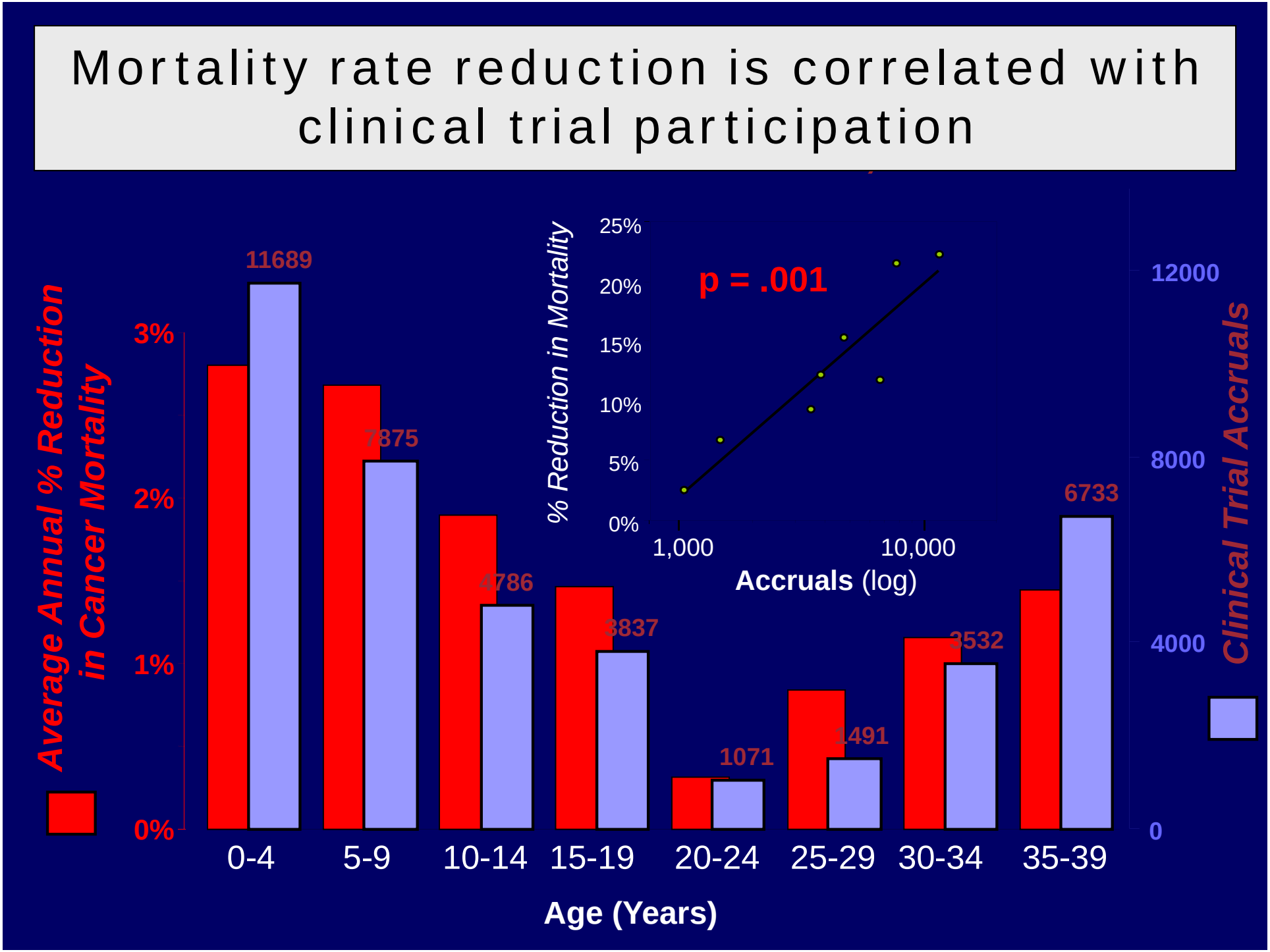
- AYA patients are disproportionately under-represented in clinical trials!

Enrollment on National Treatment Trials, 1990-98

Cooperative Group Accruals



Mortality rate reduction is correlated with clinical trial participation



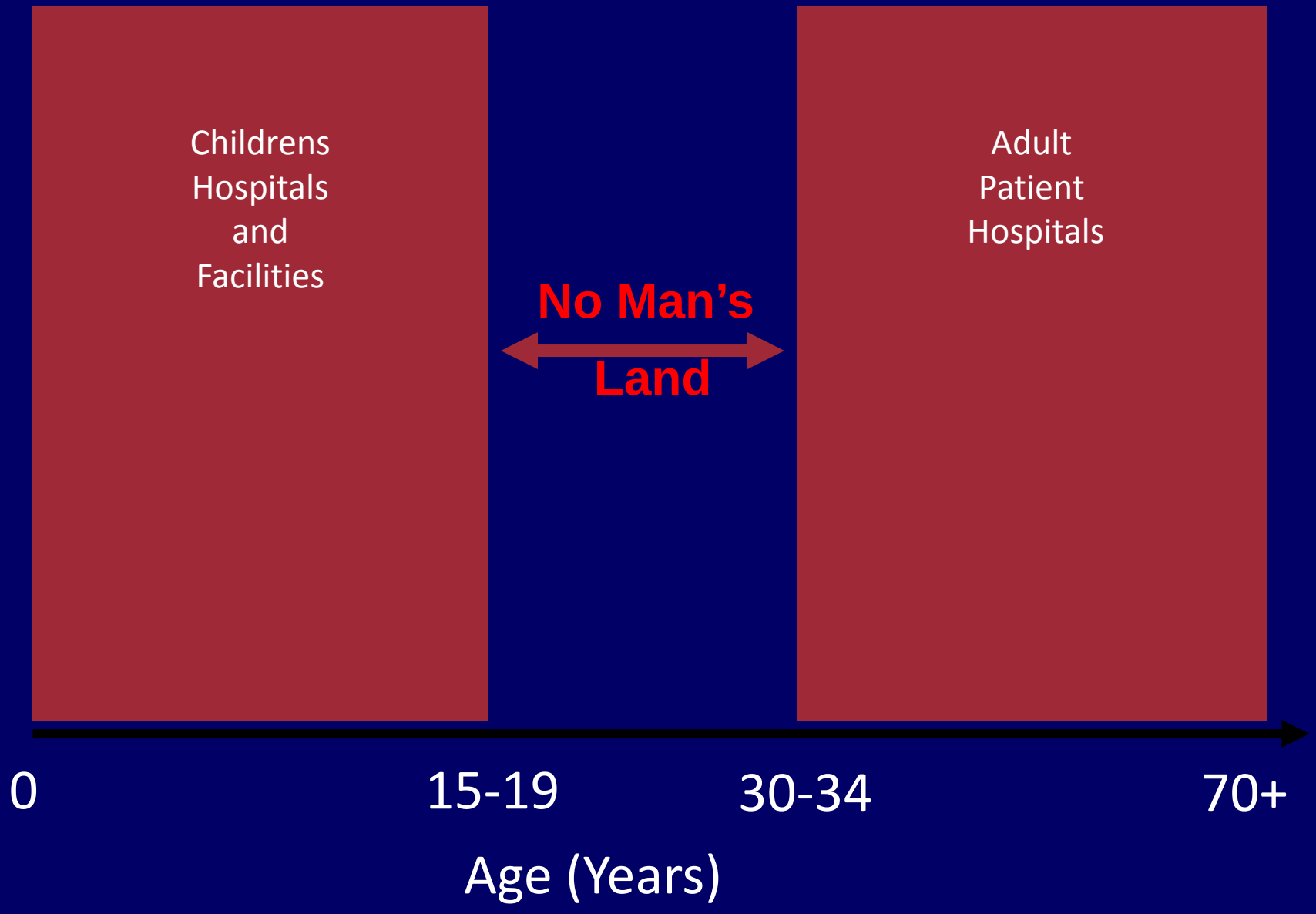
WHY is clinical trial participation in AYAs so low?

- Multiple reasons…
- Referral patterns and location of treatment are large factors

WHY is clinical trial participation in AYAs so low?

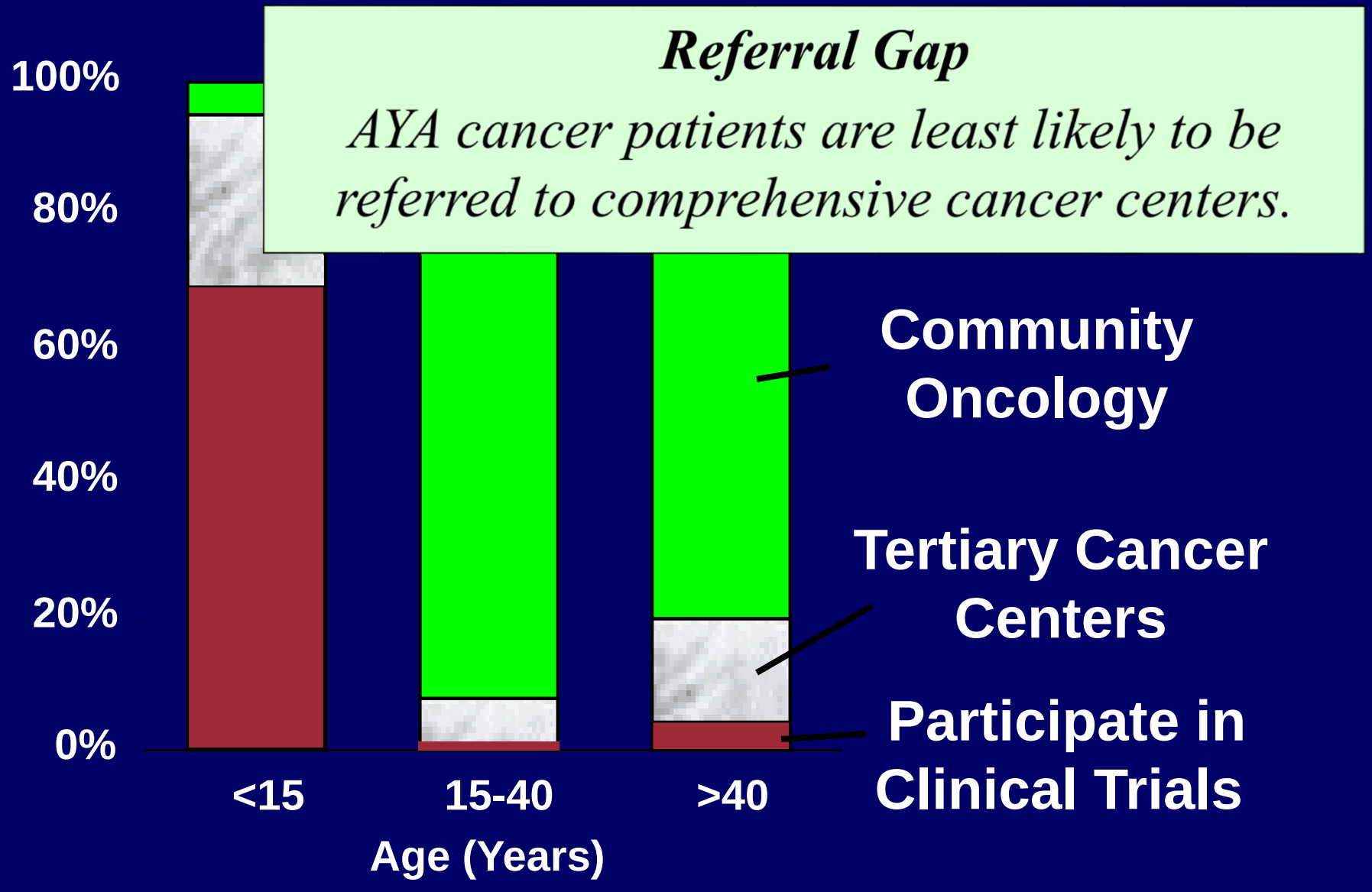
- Clinical trial infrastructure typically requires a tertiary care center, or at least significant hospital-wide or cancer center-wide resources to commit to opening and enrolling patients on trials
- Consequently, patients are MUCH more likely to be enrolled at an academic center vs private practice
- Cost, time, ancillary support (research assistants, etc)

Facilities & Services Gap



Management Sites of Cancer Patients, U.S.

in part from Lui L, et al, Cancer 97, 1339, 2003



WHY is clinical trial participation in AYAs so low?

- Many AYAs are treated at an institution that does not have clinical trials available
- Further, there have generally been fewer open national clinical trials for this population

AYAs and the medical gap

- AYAs are often caught between pediatric and adult oncologists, as well as pediatric and adult institutions, supportive care teams, etc.
- Thus, many AYAs are treated by providers with less than optimal expertise in their cancer

AYAs and the medical gap

- Many examples abound:
- 1. A 22 year old young adult with ALL is treated at an adult institution and is treated by adult protocols and best practices
  - This is not optimal, as certainly a 22 year old would be better served by a protocol for her own age group (or for children) versus for an older adult
- 2. A 14 year old teenager with ovarian carcinoma (adult type) is treated by a pediatric oncologist rather than by gyn-oncologist
  - This is not optimal, as pediatric oncologists have little to no expertise with ovarian carcinoma treatments and supportive care

AYAs and the medical gap

- AYAs should be ideally treated in a setting dedicated to this patient population
- Dr Sandy Constine has been working very hard to develop a dedicated AYA clinic with dedicated space, providers, and protocols

Are there data regarding how AYAs should be best treated?

- Yes, there are.
- Multiple comparisons between pediatric vs adult centers, and pediatric vs adult protocols

- In general, outcomes are better if the treating oncologist/institution is more familiar with the disease
  - Acute lymphoblastic leukemia → pediatric-inspired protocol
  - Ovarian carcinoma → adult-inspired protocol

On to survivorship

- The majority of AYA patients will survive their cancer
- (Hopefully with more awareness cure rates will continue to increase)

AYA Survivors: Medical Late Effect Concerns

- AYA patients treated for cancer typically undergo very intensive therapies (on par with children)
- Intensive chemotherapy
- Radiation
- Surgeries, including major resections and/or amputations

AYA Survivors:
Medical Late Effect Concerns

- 1. Second malignancies
- 2. Cardiac toxicity
- 3. Orthopedic issues
- 4. Infertility

AYA Survivors: Medical Late Effect Concerns

- 1. Second malignancies
- Most often contributing factors include certain chemotherapy agents (etoposide) as well as radiation
- Sarcoma and Hodgkin lymphoma patients are at particular risk
- Some screening guidelines exist for some malignancies:
  - Ex. Breast MRI screening for breast cancer starting at age 25 for young women who have received radiation

AYA Survivors: Medical Late Effect Concerns

- 2. Cardiac toxicity
- Exposure to anthracycline chemotherapy induces a dose-dependent risk
- Echocardiogram screening is recommended indefinitely for survivors

Chemotherapy: Screening

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM OR MUGA SCAN

Age at Treatment*	Radiation with Potential Impact to the Heart§	Anthracycline Dose†	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	<200 mg/m²	Every 2 years
		≥200 mg/m²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m²	Every 5 years
		≥100 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
≥5 years old	Yes	<300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
	No	<200 mg/m²	Every 5 years
		≥200 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
Any age with decrease in serial function			Every year

*Age at time of first cardiotoxic therapy (anthracycline or radiation [see fields below], whichever was given first)
§See Section 71
†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]

COG LTFU Guidelines: 2008

AYA Survivors:
Medical Late Effect Concerns

- 3. Orthopedic issues
- AYA survivors may have undergone amputation or limb-sparing surgery for bone or muscle tumors
- Many of these patients will need consistent orthopedic and/or physical therapy follow up

AYA Survivors: Medical Late Effect Concerns

- 4. Infertility
- Having children is probably the biggest issue for most AYA patients
- We are lucky to have Dr Vitek here to meet with our patients before and after therapy
- Infertility needs to be discussed early and often with this population
  - Males- sperm banking
  - Females- embryo cryopreservation, oocyte or ovarian tissue cryopreservation (experimental)
- For some patients, even a delay in therapy or undergoing a surgical procedure prior to therapy may be in the patient's best interest

AYA Survivors:
Supportive Care & Psychosocial Concerns

Additional Challenges in the AYA population

- Compliance & lack of social support
- This is a huge issue
- Many in this age group do not show up for visits and do not take their medications

- For patients ≥18 years of age, the medical system often does not track them down
  - Younger patients will be tracked down by the police!

Additional Challenges in the AYA population

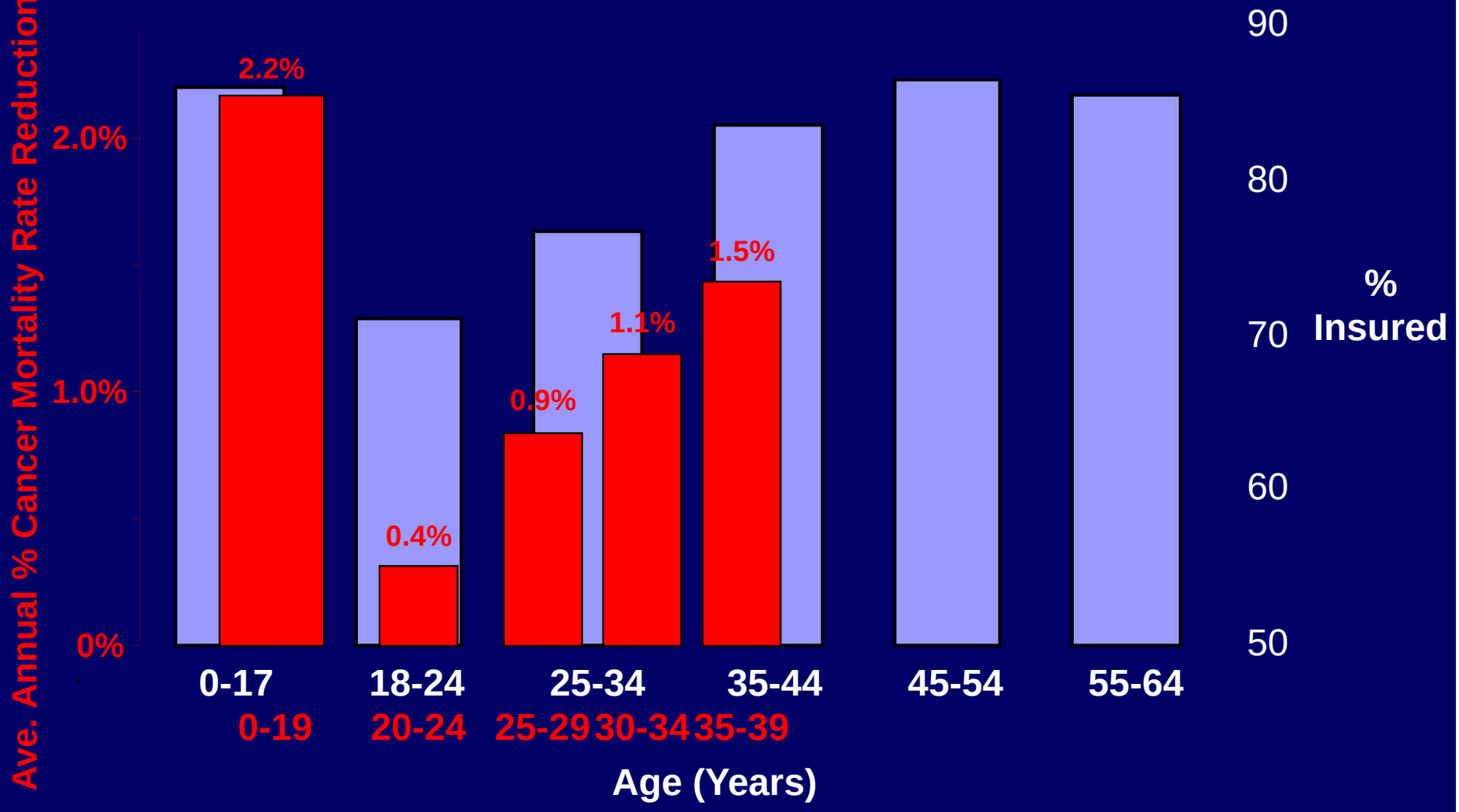
- Many of this age group are without strong social supports
- Parents are excellent if involved, though many are living on their own

Additional Challenges in the AYA population

- Lack of a medical provider, lack of insurance, and delay in diagnosis
- Many AYAs have no primary care physician
- Many lack insurance (expanded access should theoretically help this issue)

Percentage of the U.S. Population < 65 Years of Age who are Insured, according to Age

General Accounting Office. Analyses of the March|2000 Current Population Survey of Nonelderly (<65) and of Young Adults (18-24-Year-Olds). Wash., D.C.



Managing the AYA patient

- Is clearly difficult!!

- While they typically don't lie, adolescents will just not be forthcoming with any information…
- These patients are very hesitant to ask for help
- They prefer communicating through technology and/or social media
  - Ex. Facebook, MyChart, texting
- Support groups are critical for these patients
- They need to be able to see other patients undergoing similar struggles

AYA challenges

Table 2. Challenges that Face Adolescent and Young Adult Cancer Patients

Health

- Second primary malignancies
- Cardiotoxicity
- Infertility
- Amputation
- Increased risk-taking behavior, including alcohol, tobacco, and illicit drug use and abuse

Psychosocial

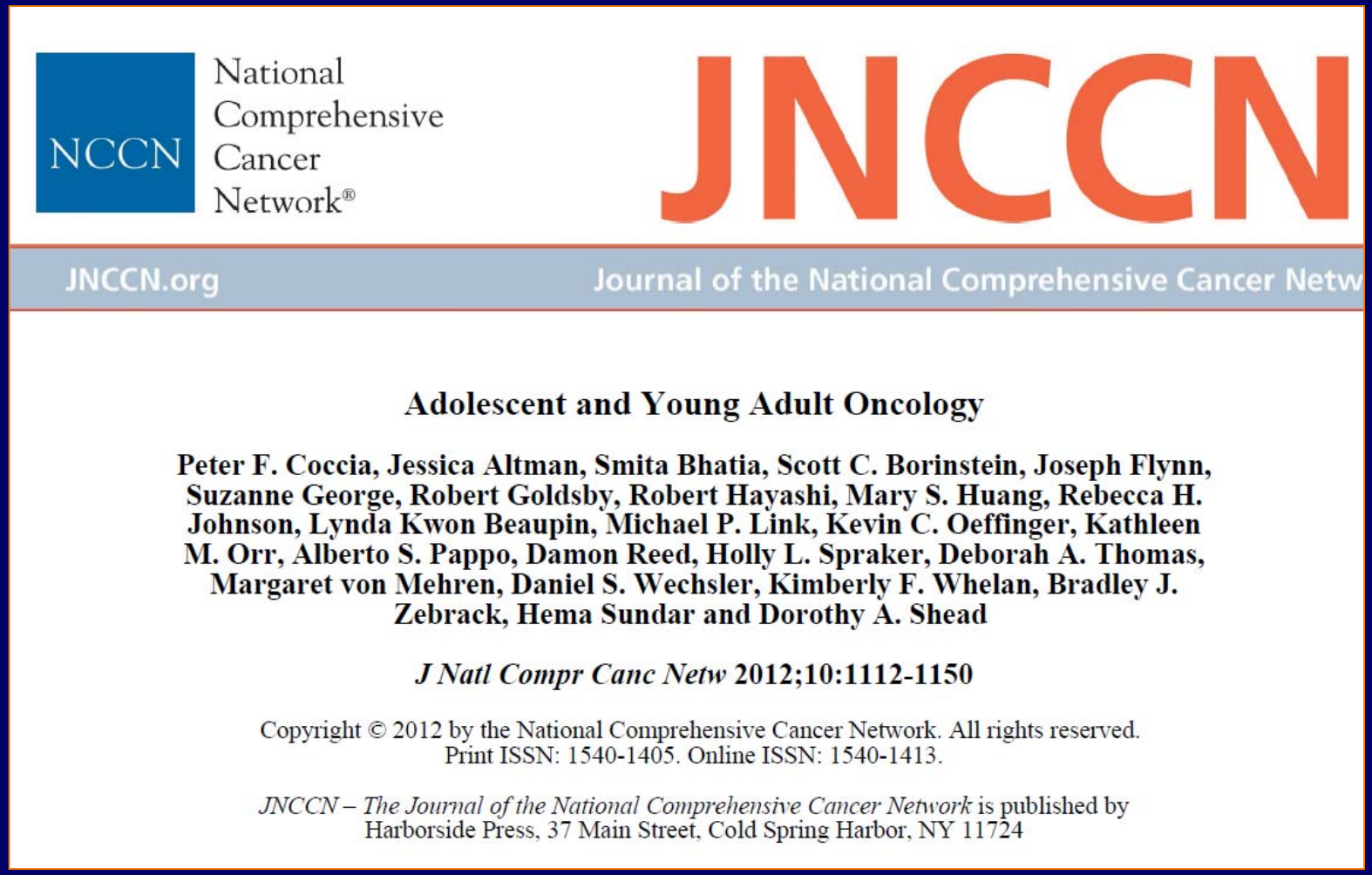
- Depression and anxiety
- Post-traumatic stress disorder
- Setbacks in education (due to time and/or poor academic achievement)
- Behavioral adjustment problems
- Poor self-image with regard to body
- Psychological distress
- Less likely to marry

Socioeconomic

- Health insurance
- Employment opportunities

Sources: Soliman H, Agresta SV. Current issues in adolescent and young adult cancer survivorship. *Cancer Control.* 2008 Jan;15(1):55-62. Bleyer A. Young adult oncology: the patients and their survival challenges. *CA Cancer J Clin.* 2007 Jul-Aug;57(4):242-55.

Published Recommendations



National Comprehensive Cancer Network®

JNCCN

JNCCN.org Journal of the National Comprehensive Cancer Netw

Adolescent and Young Adult Oncology

Peter F. Coccia, Jessica Altman, Smita Bhatia, Scott C. Borinstein, Joseph Flynn, Suzanne George, Robert Goldsby, Robert Hayashi, Mary S. Huang, Rebecca H. Johnson, Lynda Kwon Beaupin, Michael P. Link, Kevin C. Oeffinger, Kathleen M. Orr, Alberto S. Pappo, Damon Reed, Holly L. Spraker, Deborah A. Thomas, Margaret von Mehren, Daniel S. Wechsler, Kimberly F. Whelan, Bradley J. Zebrack, Hema Sundar and Dorothy A. Shead

***J Natl Compr Canc Netw* 2012;10:1112-1150**

Print ISSN: 1540-1405. Online ISSN: 1540-1413.

JNCCN – The Journal of the National Comprehensive Cancer Network is published by Harborside Press, 37 Main Street, Cold Spring Harbor, NY 11724

NCCN AYA recommendations

Dose schedules →

- AYA patients are usually tolerant of intensive therapies compared to older patients
  - Dose intensity and dose density are associated with improved outcomes[i]
  - See NCCN Guidelines for Myeloid Growth Factors* for growth factor support
- Dose reductions are often based on avoiding severe, irreversible organ damage
  - Assume that the patient population has a significant long-term survival and that significant end-organ damage may compromise long-term function and quality of life
- Monitoring of cumulative dosing for certain medications associated with irreversible organ damage may be essential when certain life time exposure is encountered
  - Anthracycline-based chemotherapy (cardiac dysfunction)
  - Epipodophyllotoxins (secondary acute myeloid leukemia [AML])
  - Cisplatin (hearing impairment)
  - Ifosfamide (renal dysfunction)
- Maximum cumulative dosing parameters are often established for a patient to reduce the risk of significant irreversible damage

Toxicities →

- Reversible toxicities do not necessarily warrant dose reductions
  See NCCN Guidelines for Supportive Care* for the management of treatment-related toxicities, including:
  - See NCCN Guidelines for Adult Cancer Pain*
  - See NCCN Guidelines for Antiemesis*
  - See NCCN Guidelines for Cancer- and Chemotherapy-Induced Anemia*
  - See NCCN Guidelines for Cancer-Related Fatigue*
  - See NCCN Guidelines for Palliative Care*
  - See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections*
- Intensive screening is recommended for the following treatment-related toxicities:
  - Cardiac toxicity: regular echocardiograms (EKG) to monitor cardiac toxicity associated with anthracycline-based chemotherapy
  - Renal toxicity: regular glomerular filtration rate (GFR) calculations to monitor renal toxicity associated with cisplatin- and ifosfamide-based chemotherapy
  - Neurotoxicity: regular audiogram to monitor hearing loss associated with cisplatin- or carboplatin-based chemotherapy

Recommendations: Supportive Care & Psychosocial

- 1. Discuss living arrangement, family structure, high risk behaviors, peer groups

- Peer groups especially important for this age group
- Strongly consider support groups if available
  - Ex. Teens Living with Cancer
  - Ex. LIVESTRONG young adult alliance

Recommendations: Supportive Care & Psychosocial

- 2. Discuss socio-economic issues, insurance coverage, payment problems

- Many AYA patients will need financial assistance

Recommendations: Supportive Care & Psychosocial

- 3. Discuss mental health issues and risk factors: anxiety and depression are especially common

- Consider counseling as needed
- Consider SSRIs or other medical therapies
- Provide good continuity of care and form close relationships

- We should provide multidisciplinary and team-based care for these patients

Conclusions (1)

- 1. AYA population includes patients 15-39
- 2. AYA cancer patients have relatively poor survival rates and have seen no gains in survival in the last few decades
- 3. The reasons for these issues are vast and include biologic differences, medical expertise, social issues, and the lack of enrollment on clinical trials
- 4. Data generally show that patients should be treated by AYA specialists and/or the group (pediatric vs adult) with the most expertise in the tumor type

Conclusions (2)

- 5. AYA survivors are at risk for specific late effects, which include second malignancies, cardiac toxicity, orthopedic conditions, and infertility.
- 6. AYA survivors also have numerous other challenges, which include lack of social support, lack of insurance, financial issues, and anxiety and depression.
- 7. We should strive to have AYA patients treated as a separate group; they should be treated differently with their own issues and challenges addressed.
- 8. AYA patients need a team-based approach, ensuring a trusting relationship where they will feel willing to discuss their cancer care and survivorship issues.

The End.

- Thank you!
- Please contact me with any questions.
- Jeffrey_andolina@urmc.rochester.edu