

Collaborating to Conquer Cancer

Lessons From Our Children

Presidential Address

Michael Link, MD



Thank You



My Kids



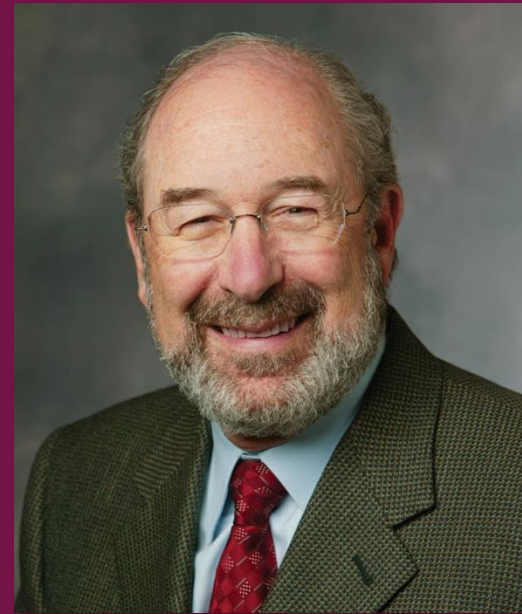
My Brother



2012 Annual Meeting Chairs



Harold Burstein, MD, PhD
Education Committee Chair



Ronald Levy, MD
Scientific Program Chair



The ASCO Staff



To My Patients and Their Families



**Collaborators in
advancing the field**



**Partners in a wonderful
profession**



2011 Membership Highlights

- Total Membership:
31,276
 - From 122 countries
- New Members:
2,953
 - Record number
- Retention:
96.7%



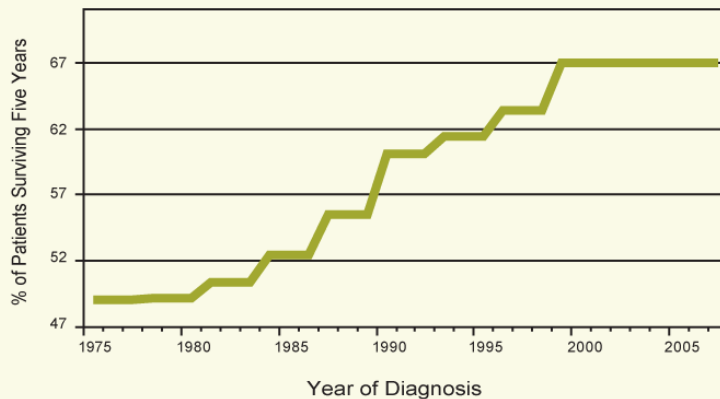
The National Cancer Act: Forty Years of Progress



1971:
The National
Cancer Act
is signed
into law

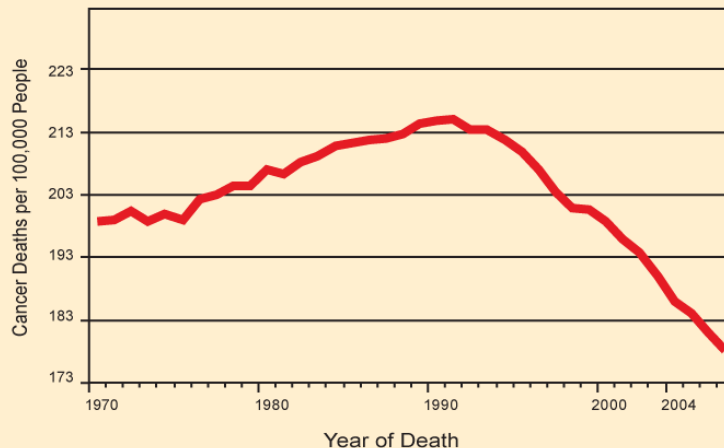
40 Years: What We've Achieved

Five-Year Survival

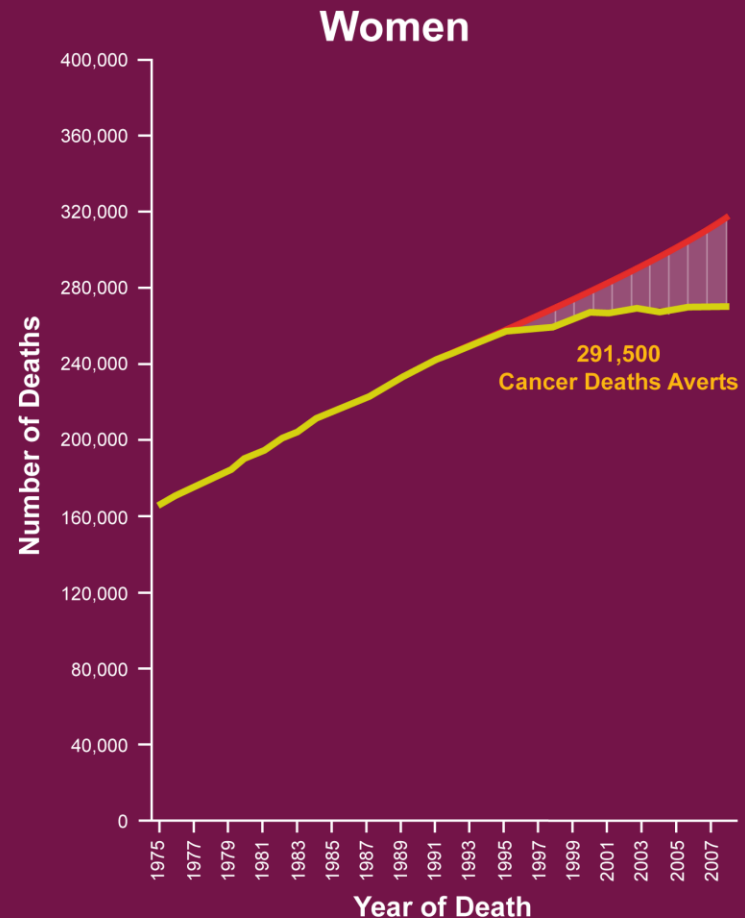
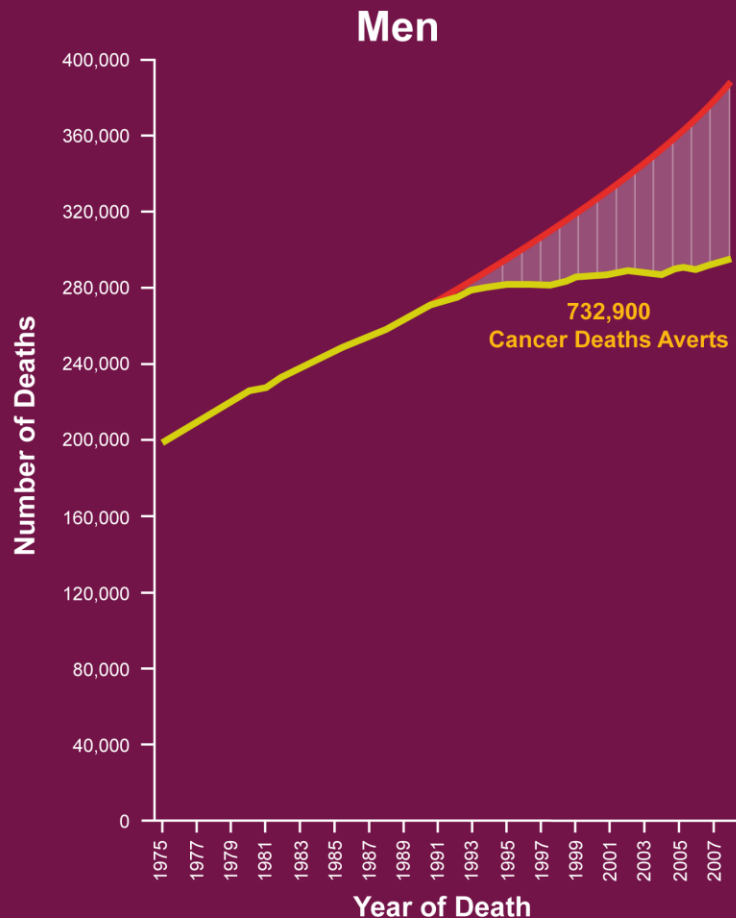


- Nation's cancer death rate has dropped 18 percent since early 1990s
- 12 million cancer survivors alive today—up from just 3 million in the 1970s
- Patients are living longer—and *with greater quality of life*

Cancer Mortality

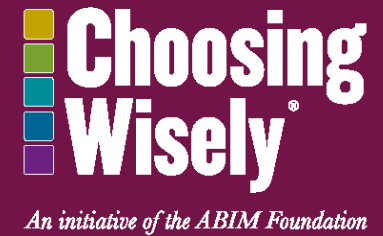


Cancer Deaths Averted



“The reduction in overall cancer death rates since 1990 in men and 1991 in women translates to the avoidance of about 1,024,400 deaths from cancer.”

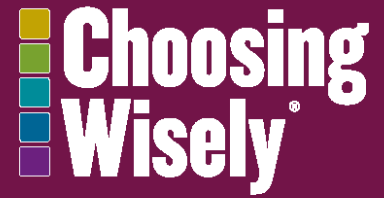
The “Choosing Wisely Campaign”



- Proposed by Howard Brody, MD, PhD
 - “Medicine's Ethical Responsibility for Health Care Reform — The Top Five List”
N Engl J Med 2010; 362:283-285
- Challenged medical specialties to identify five costly practices that are:
 - Commonly performed
 - Lacking evidence of efficacy



ASCO Participation



An initiative of the ABIM Foundation

- Led by ASCO Cost of Cancer Care Task Force
 - Multidisciplinary group of oncologists
- Chose treatments based on comprehensive review of published studies, guidelines from ASCO and other organizations
- Input from more than 200 oncologists
 - Practicing oncologists
 - State leaders
 - Patient advocates



“Top 5” List for Oncology

Question these things before doing them:

1. Use of chemotherapy for patients with advanced cancers who are unlikely to benefit, and who would gain more from a focus on palliative care and symptom management.
2. For early breast cancer, use of advanced imaging technologies (i.e., CT, PET and radionuclide bone scans) in cancer staging.
3. For early prostate cancer, use of advanced imaging technologies (i.e., CT, PET and radionuclide bone scans) in cancer staging.
4. Routine use of advanced imaging and blood biomarker tests for women treated with curative therapy for breast cancer and who have no symptoms of recurrence.
5. Use of white cell stimulating factors for patients who are at low risk for febrile neutropenia.



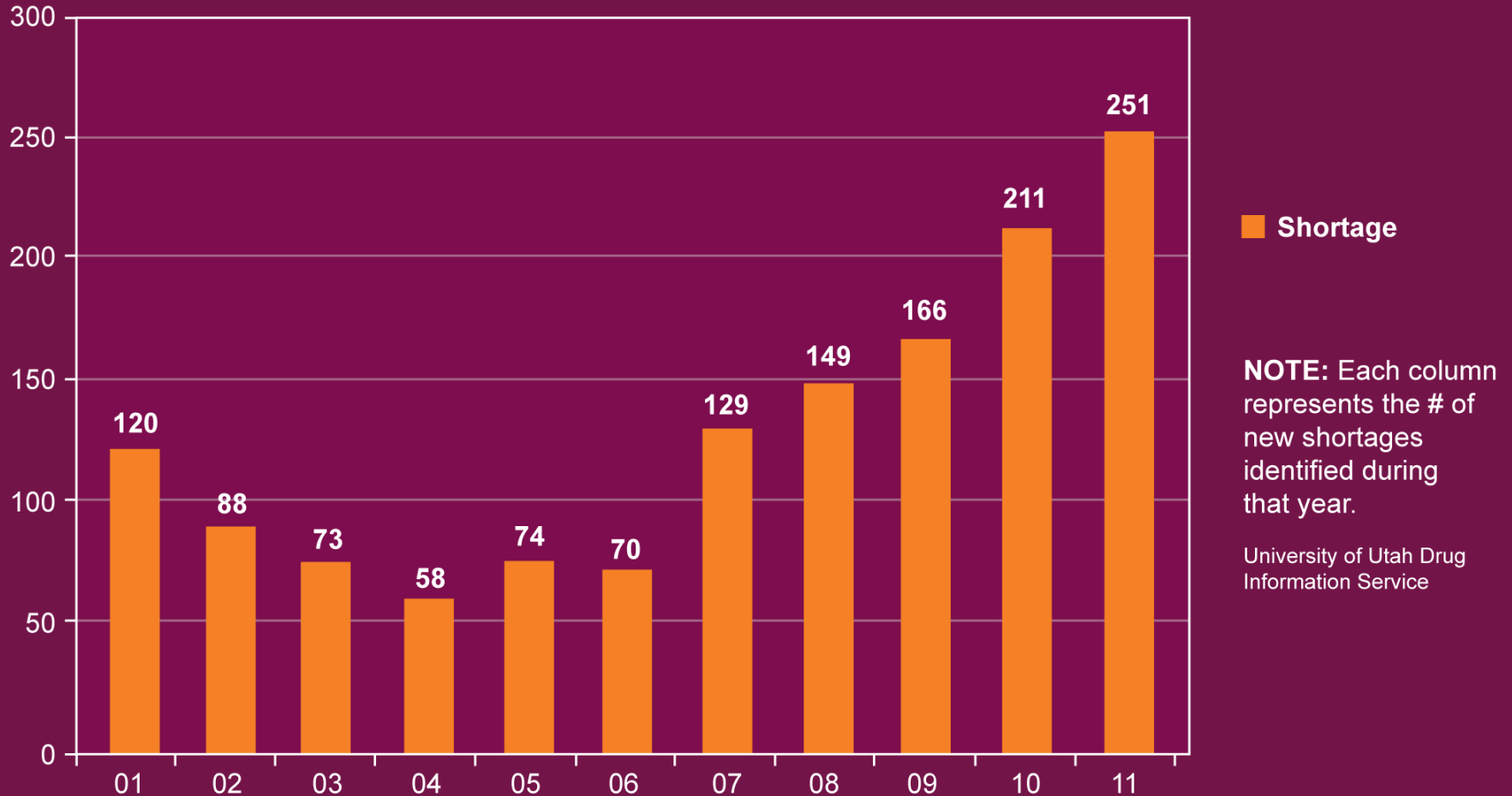
Drug Shortages

- Growing crisis
- Generic injectables
- Multiple cancers
- Many causes
- No quick solution

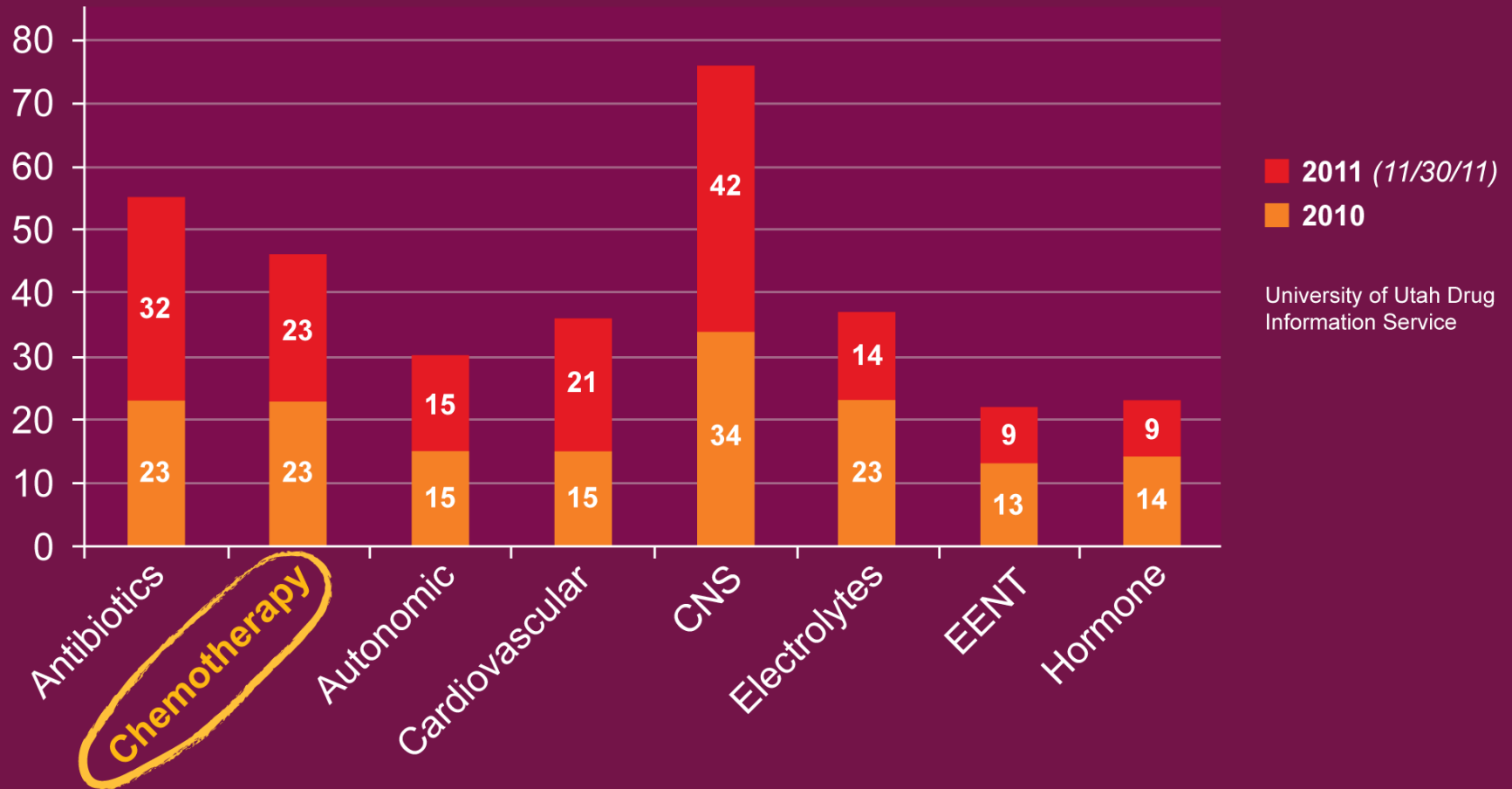


National Drug Shortages

January 2001 to November 30, 2011



Shortages by Drug Class



Raising Awareness



Dr. Charles Penley testifies at House Energy and Commerce hearing.

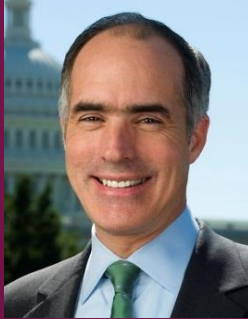
- Briefed Congressional Staff
- Congressional testimony
- Testimony at FDA workshop
- Met with HHS secretary
- Outreach to companies



Briefing Congressional staff on drug shortages.



Legislation



112TH CONGRESS
1ST SESSION

S. 296

To amend the Federal Food, Drug, and Cosmetic Act to provide the Food and Drug Administration with improved capacity to prevent drug shortages.

IN THE SENATE OF THE UNITED STATES

FEBRUARY 7, 2011

Ms. KLOBUCHAR (for herself and Mr. CASEY) introduced the following bill, which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to provide the Food and Drug Administration with improved capacity to prevent drug shortages.

112TH CONGRESS
1ST SESSION

H. R. 2245

To amend the Federal Food, Drug, and Cosmetic Act to provide the Food and Drug Administration with improved capacity to prevent drug shortages.

IN THE HOUSE OF REPRESENTATIVES

JUNE 21, 2011

Ms. DeGETTE (for herself and Mr. ROONEY) introduced the following bill, which was referred to the Committee on Energy and Commerce

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to provide the Food and Drug Administration with improved capacity to prevent drug shortages.

February 2011

Sen. Klobuchar (D-MN)

Sen. Casey (D-PA)

June 2011

Rep. DeGette (D-CO)

Rep. Rooney (R-FL)



Collaborating to Conquer Cancer

Lessons From Our Children



Lessons from our Children

- Importance of collaboration
- Importance of laboratory investigations of tumor tissue
- Cancers are heterogeneous collections of diseases
- Focus on survivors



Causes of Death in Children and Young Adults

Ages 1-14

1. Accidents
- 2. Cancer**
3. Birth Defects
4. Infections

Ages 15-34

Males

1. Accidents
2. Homicide
3. Suicide
- 4. Cancer**

Females

1. Accidents
- 2. Cancer**
3. Homicide
4. Suicide

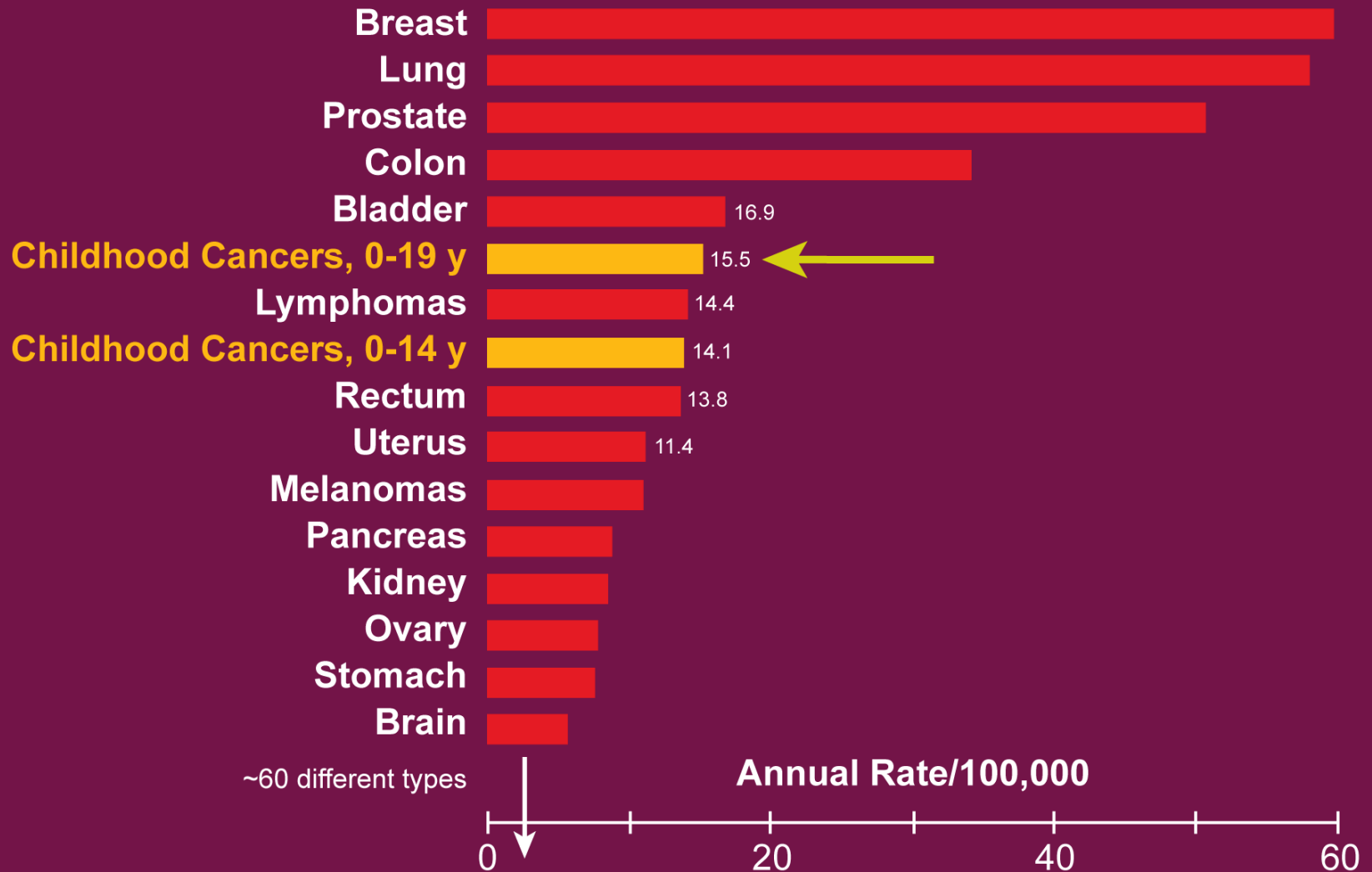


Cancer in Children

- 1/300 children diagnosed before age 20
- 12,500 new cases in children and adolescents younger than 20 years each year in the USA
- 2,225 children and adolescents died of cancer in 2004

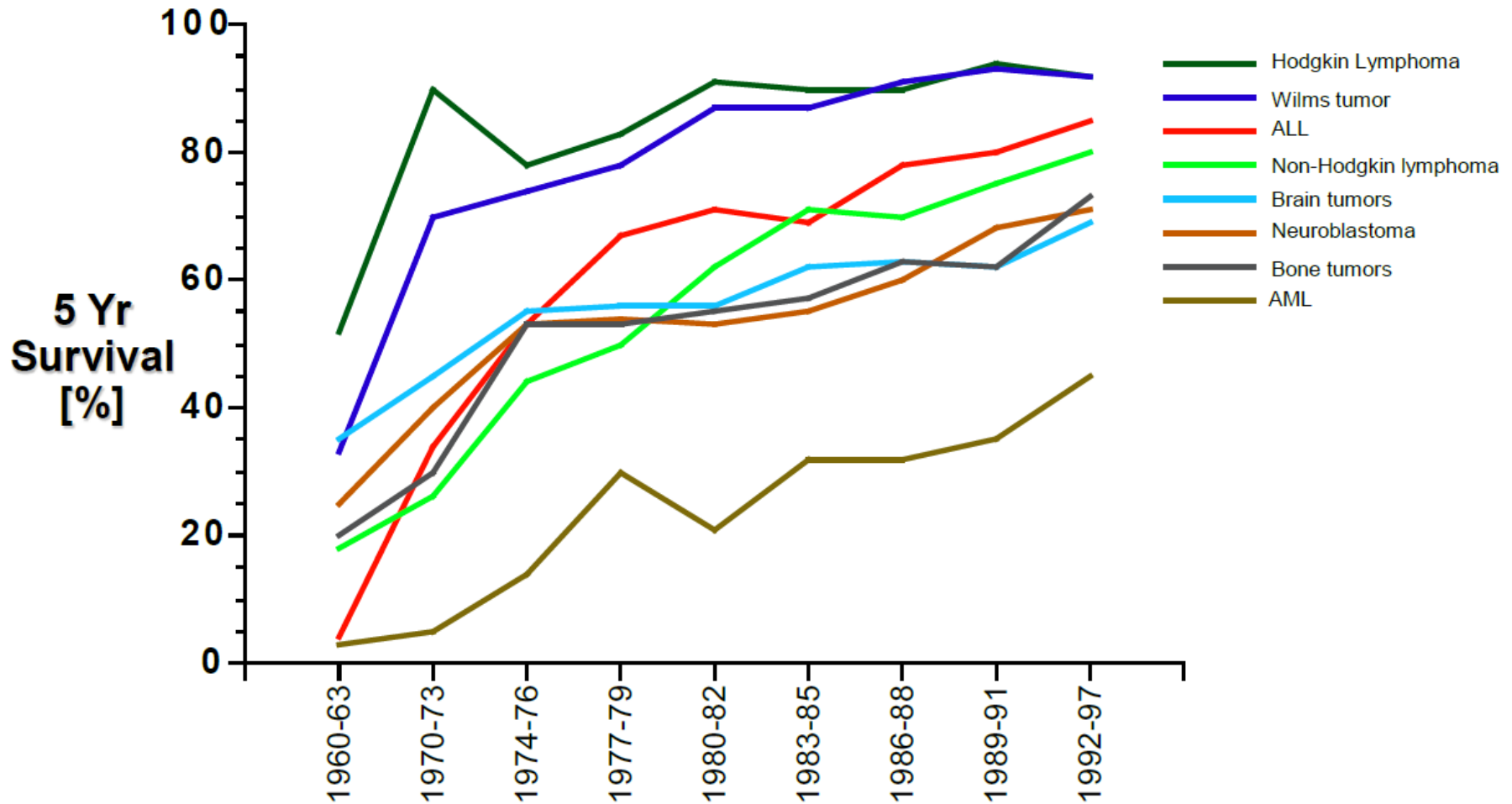


Most Frequent Cancers in the U.S.A. 1986-1991



Data from SEER Cancer Statistics Review, 1973-1991. NCI 1994.

Survival Trends in Common Pediatric Cancers



Keys to Success of Pediatric Oncology

- **Luck**
 - Tumors responsive to radiotherapy
 - Remarkable responsiveness to early drugs
 - Durable remissions and cures
- **Relatively few mutations** (“stupid cancers”)



Stupid and Smart Cancers

Stupid Cancers

- Single dominant mutation
- Small mutational load
- Monotherapy effective
- Resistance rare, late, same pathway

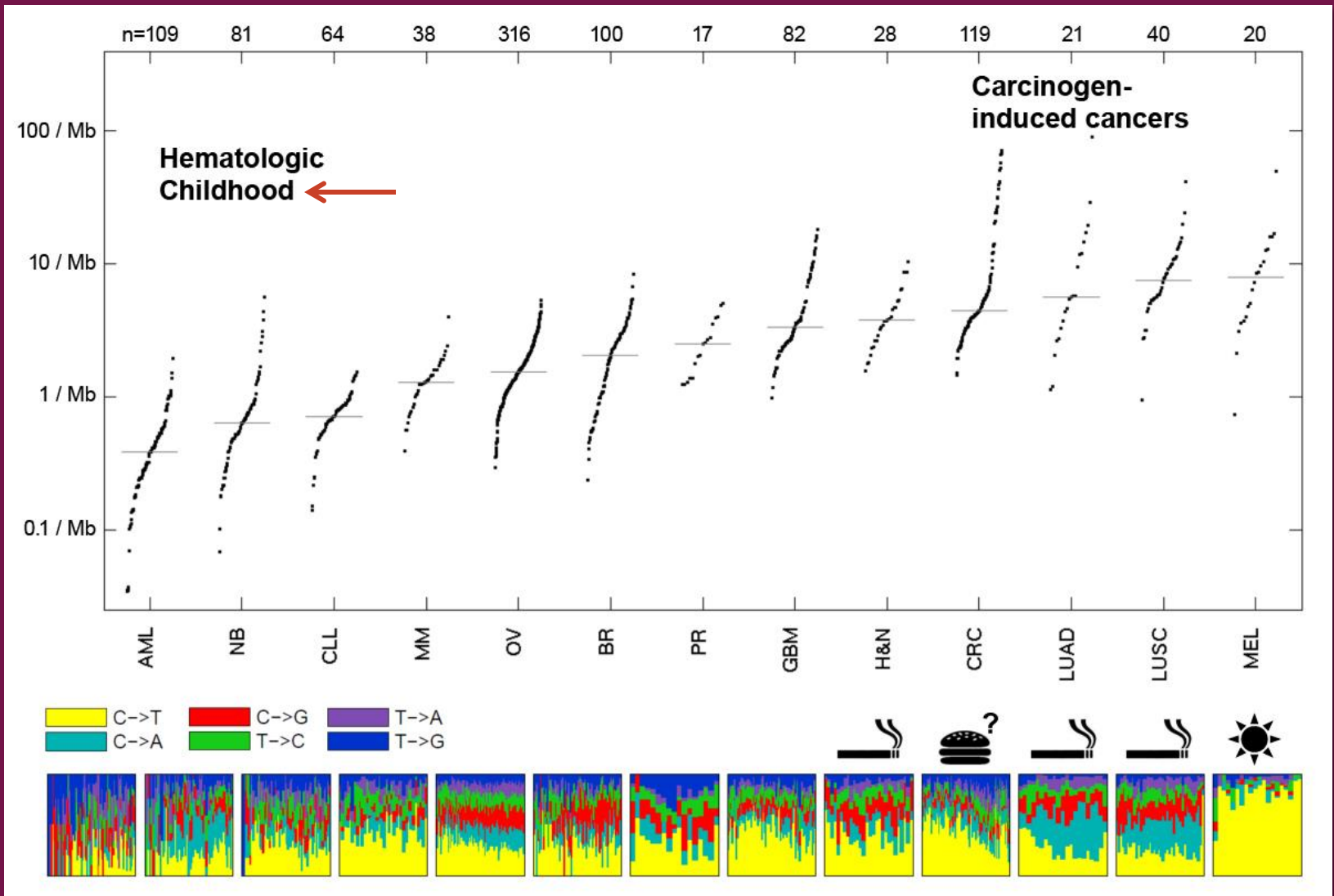
Smart Cancers

- Multiple mutational drivers
- Large mutational load
- Multi-targeted therapy required
- Resistance common, early

Sledge, G. ASCO Presidential Address, 2011



Mutation Rates Across Cancer



Keys to Success of Pediatric Oncology

- Host with few co-morbidities in otherwise excellent health
- Lenient regulatory environment
- Optimism that emerges from success



“Shortly after St. Jude Children’s Research Hospital opened in 1962, it was decided to attempt cure of ALL by combining all known effective agents in a strategy called **Total Therapy**. This was based on information available from laboratory investigations and clinical experience regarding leukemia therapy...”

Ninth Annual Karnofsky Lecture
Cancer 43:1128, 1979

Total Therapy for Childhood ALL



Donald Pinkel, MD.

First Director of the
St Jude Children's
Research Hospital



Joseph Simone, MD.

Third Director of the
St Jude Children's
Research Hospital

Lessons from our Children

- **Importance of collaboration**
- Importance of laboratory investigations of tumor tissue
- Cancers are heterogeneous collections of diseases
- Focus on survivors

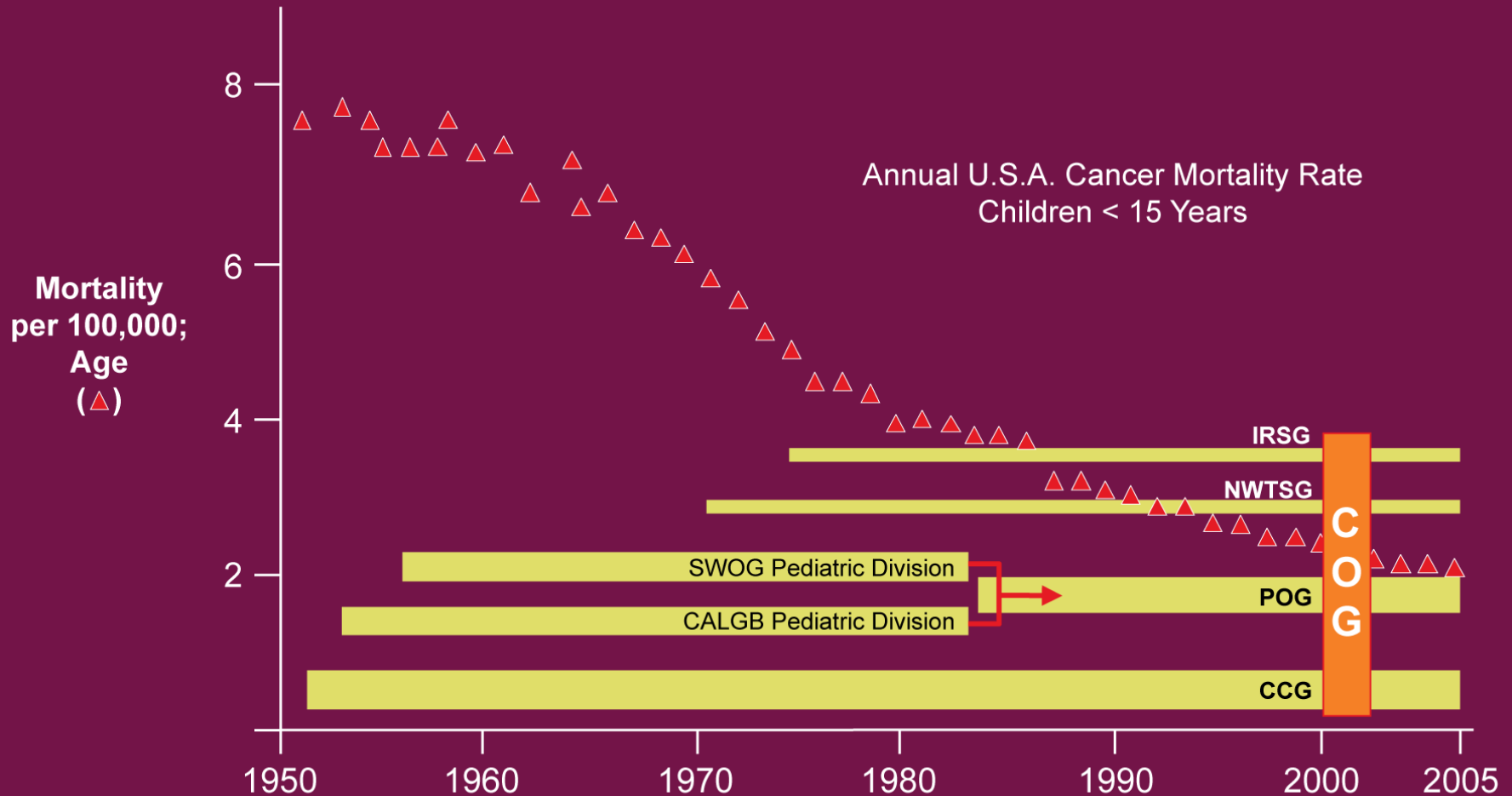


Collaborations in Pediatric Oncology: It Takes a Village

- Multi-disciplinary approach
- Multi-institutional trials
 - Rarity of patients to support single institution trials
- Pediatric Cooperative Groups as infrastructure
- Clinical trial as “standard of care”
 - Majority of children with cancer participate
- Results of trials rapidly incorporated into practice



The National Childhood Cancer Mortality Rate and the Pediatric Cooperative Groups



Contribution of Cooperative Group

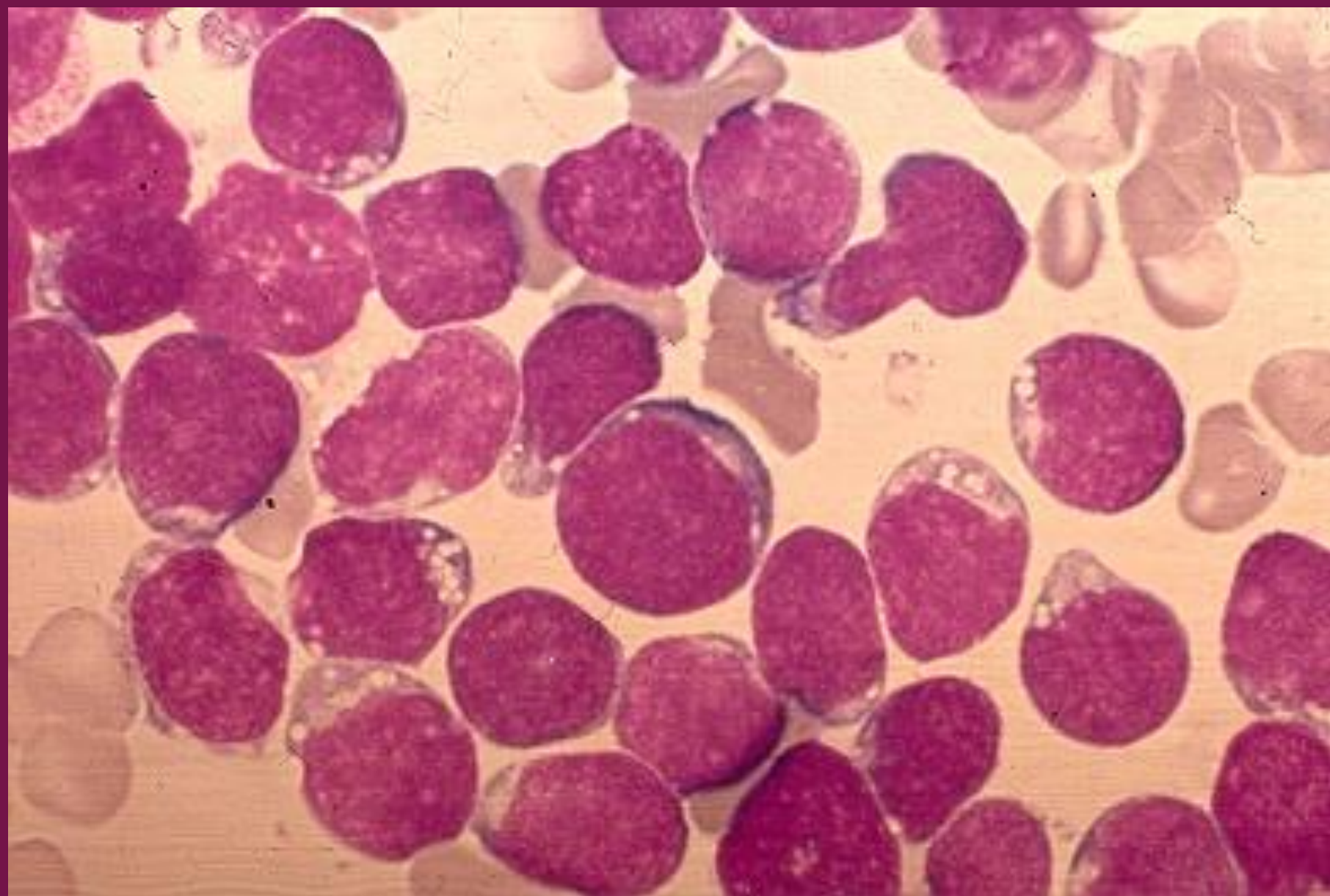
- Protocols written by acknowledged experts
- Clinical trials infrastructure
 - Enabling even small practices to participate in clinical trials
- Expert central pathology review
- Reference laboratories for immunodiagnosis and novel diagnostics
- Radiotherapy on-treatment review by experts



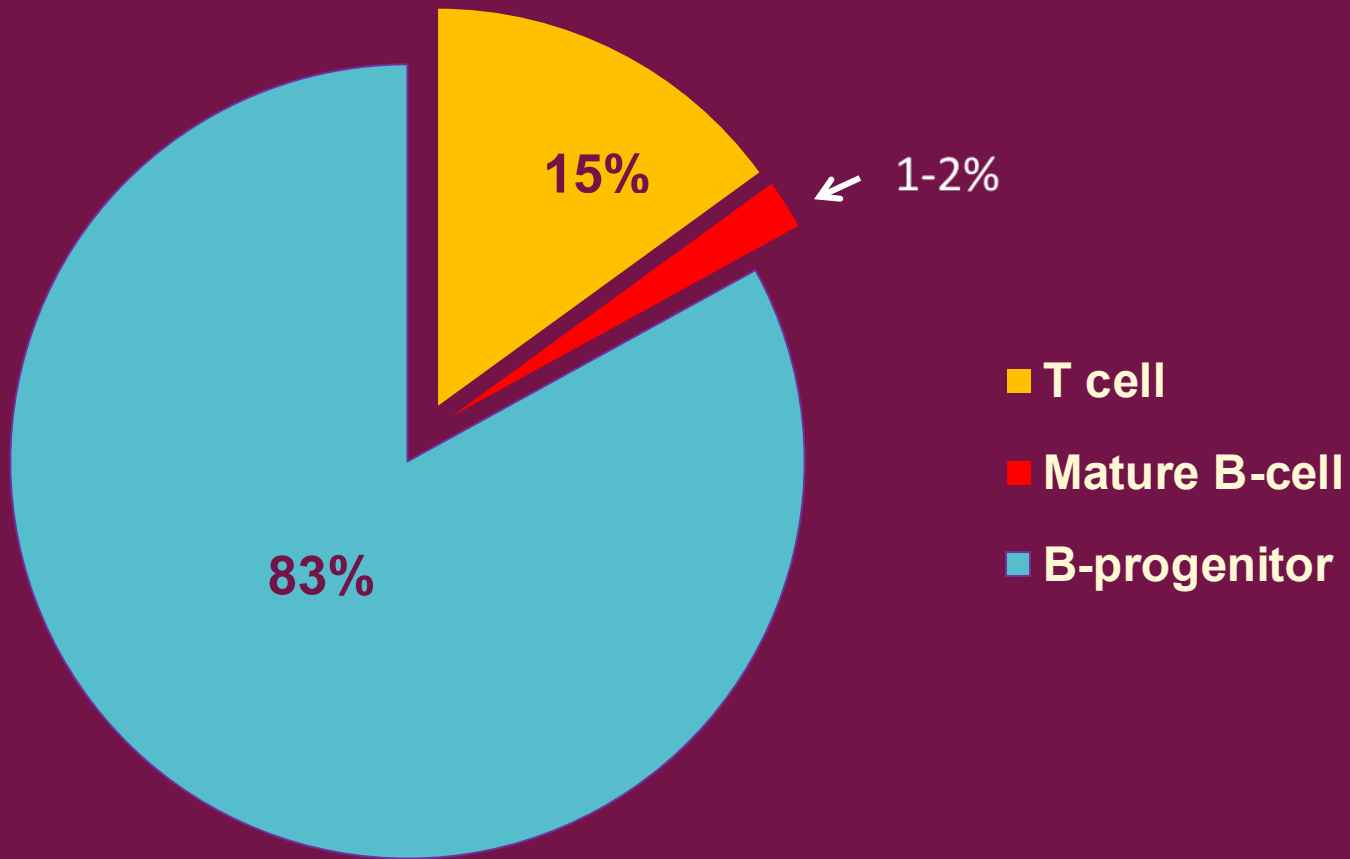
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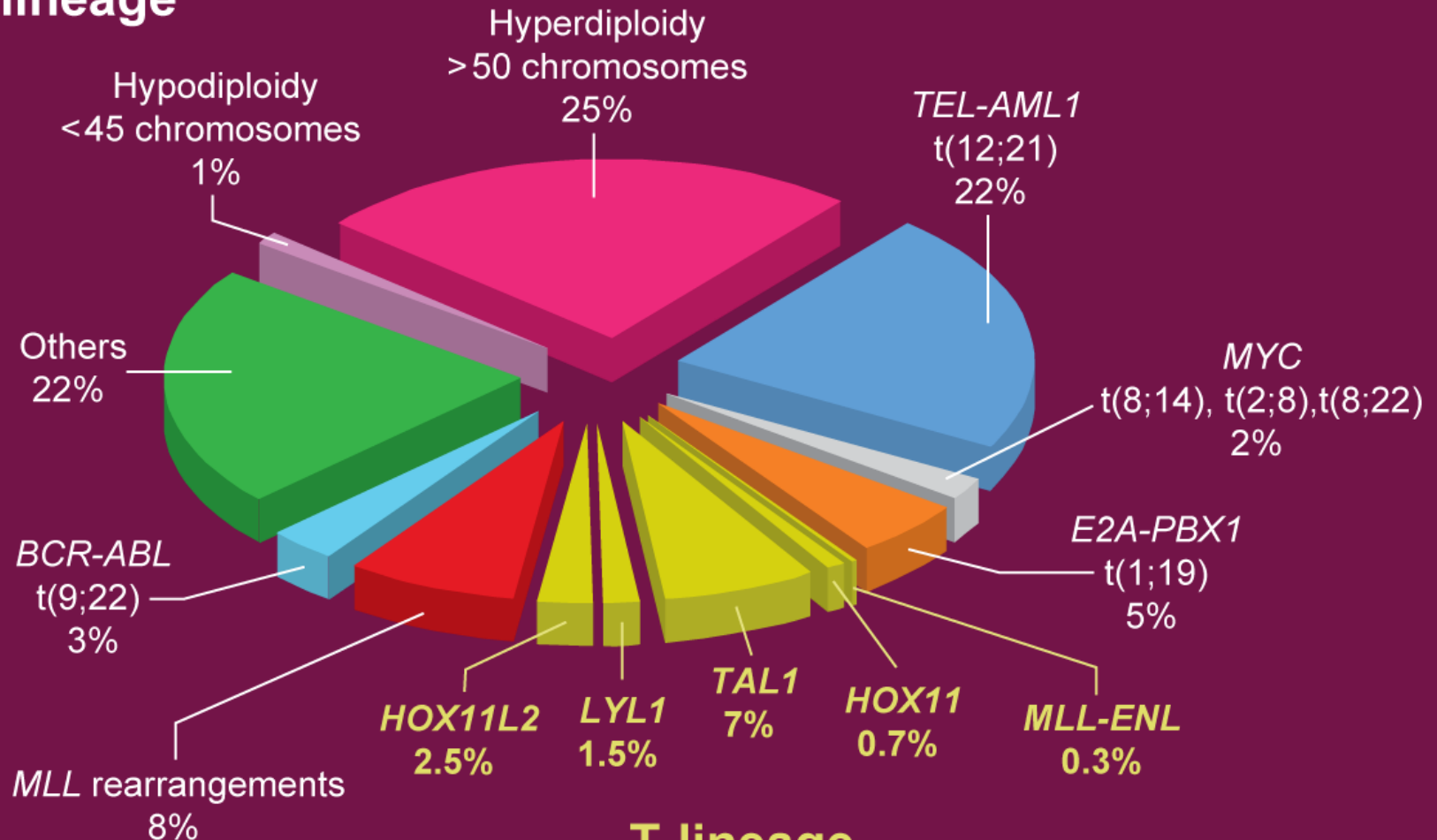


Immunophenotypes of Childhood Acute Lymphoblastic Leukemia



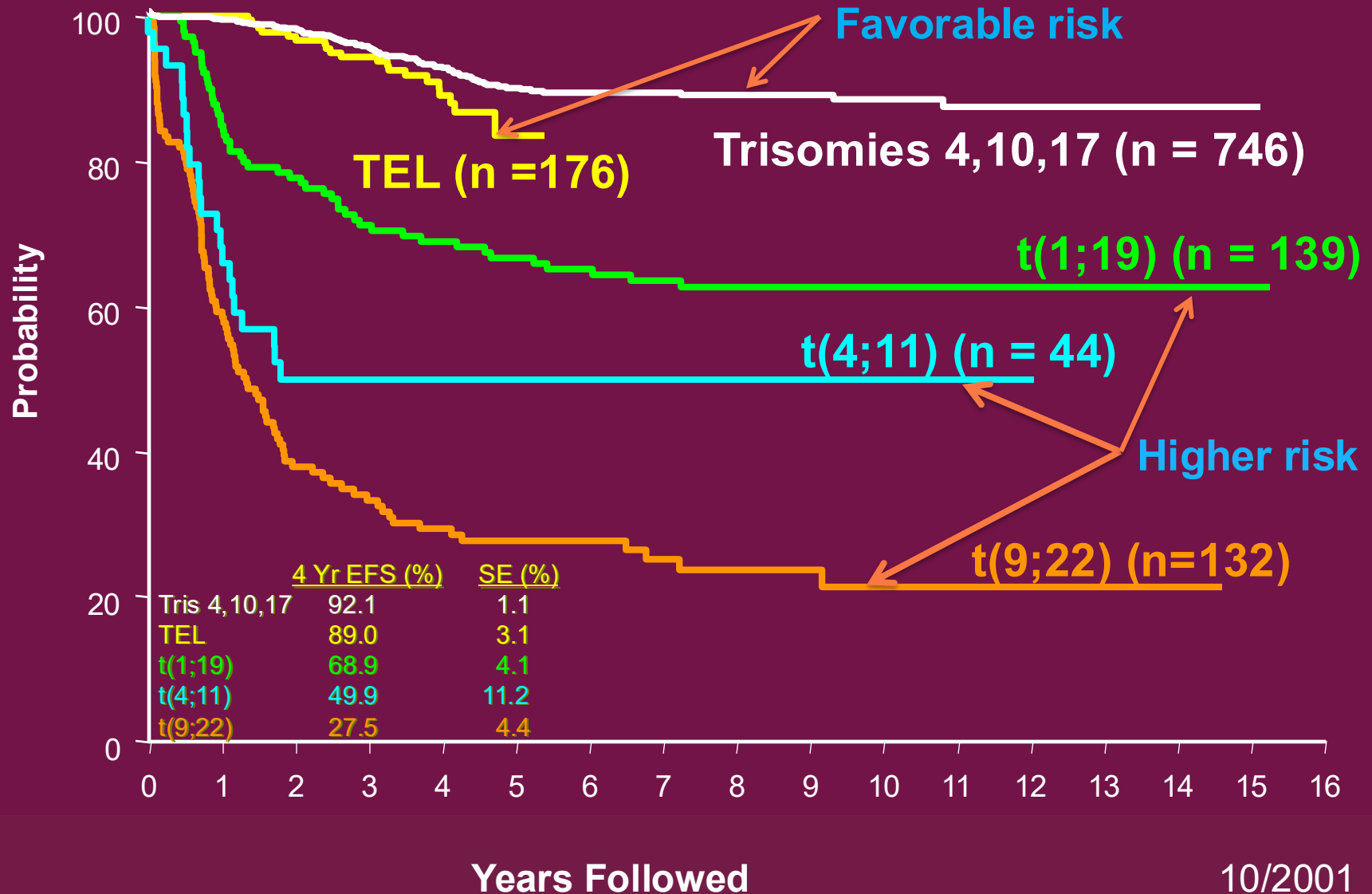
Specific Genetic Abnormalities of Childhood ALL

B-lineage

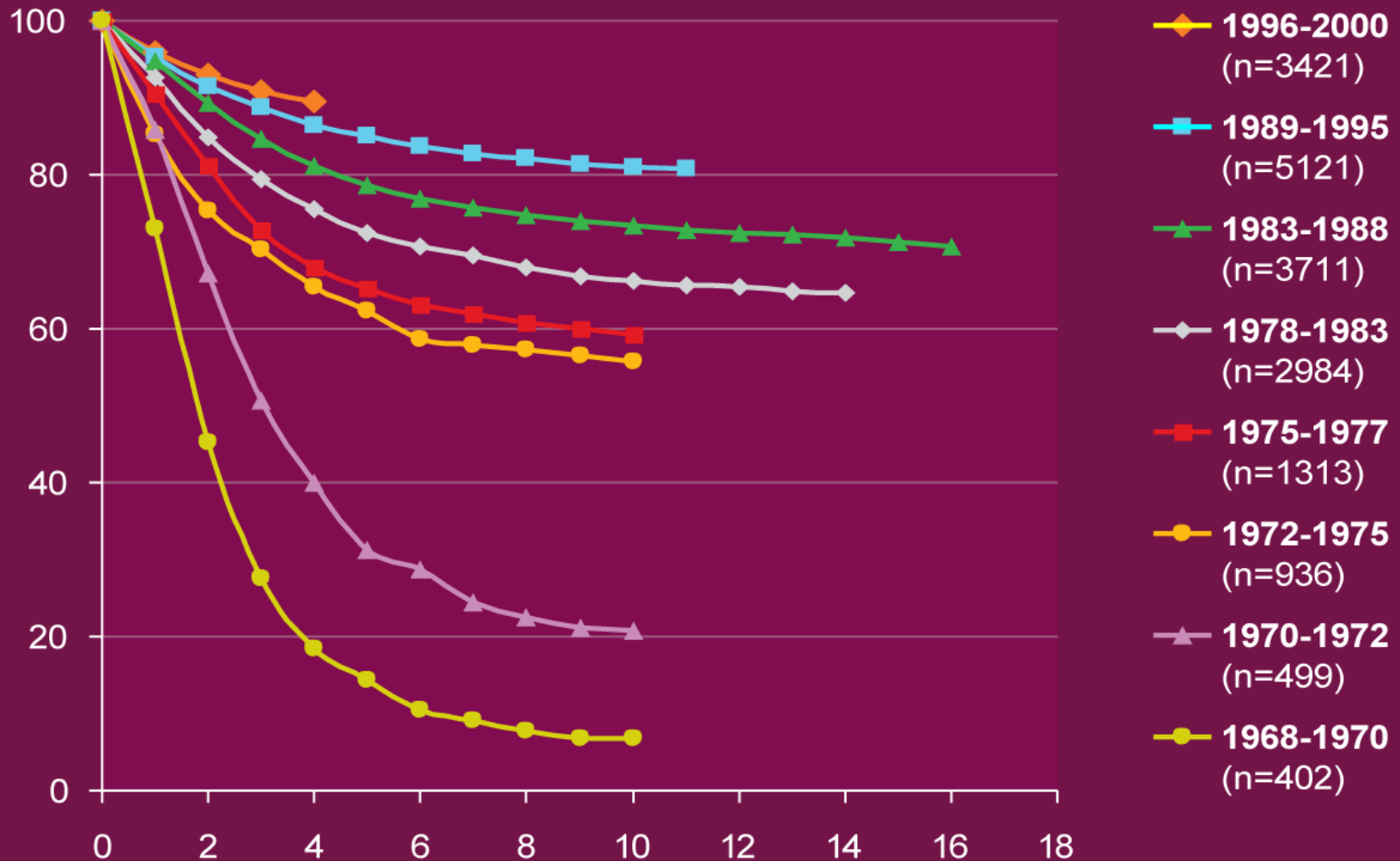


T-lineage

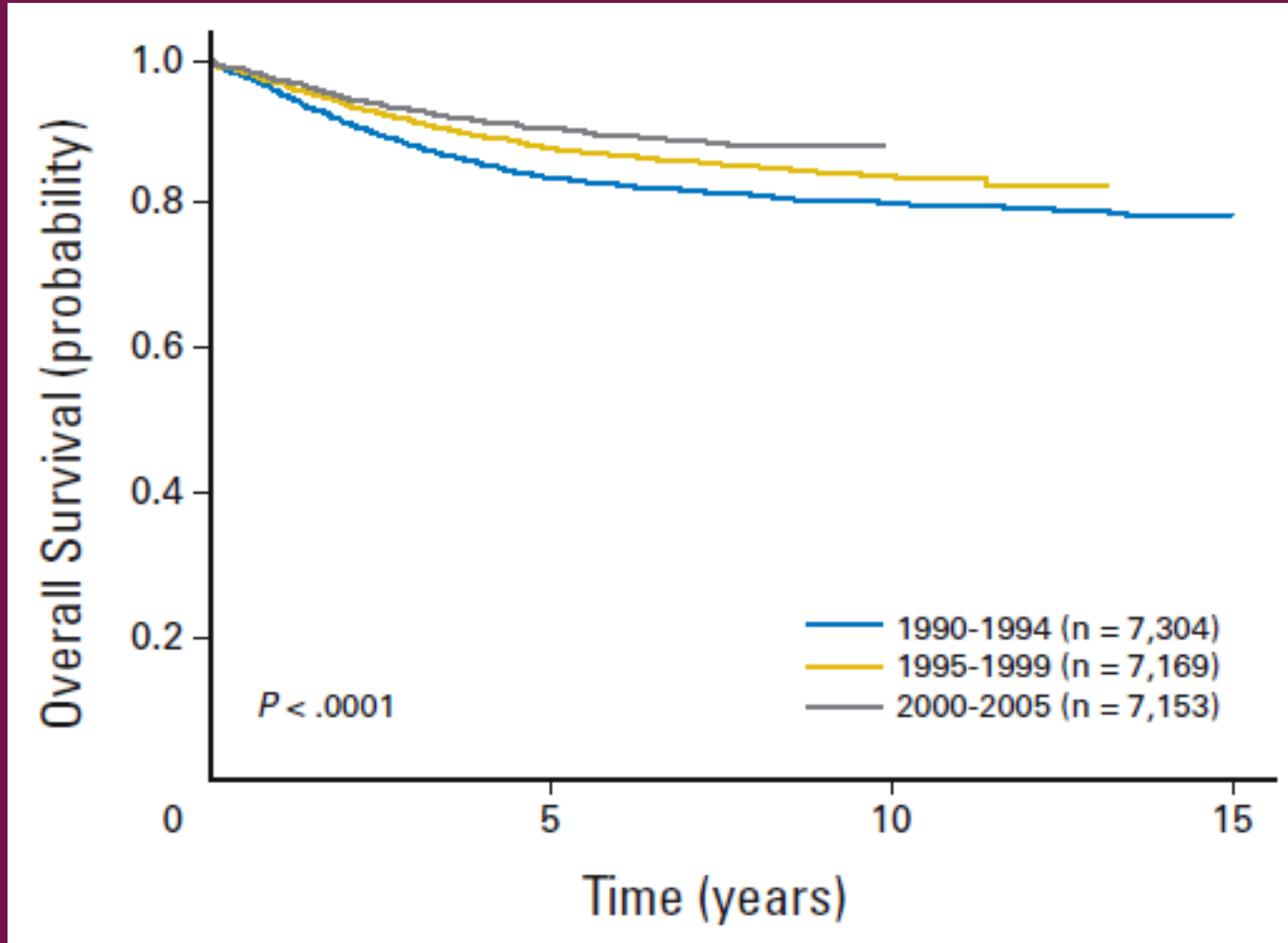
Correlation of Genotype and Outcome in Childhood B-Progenitor ALL



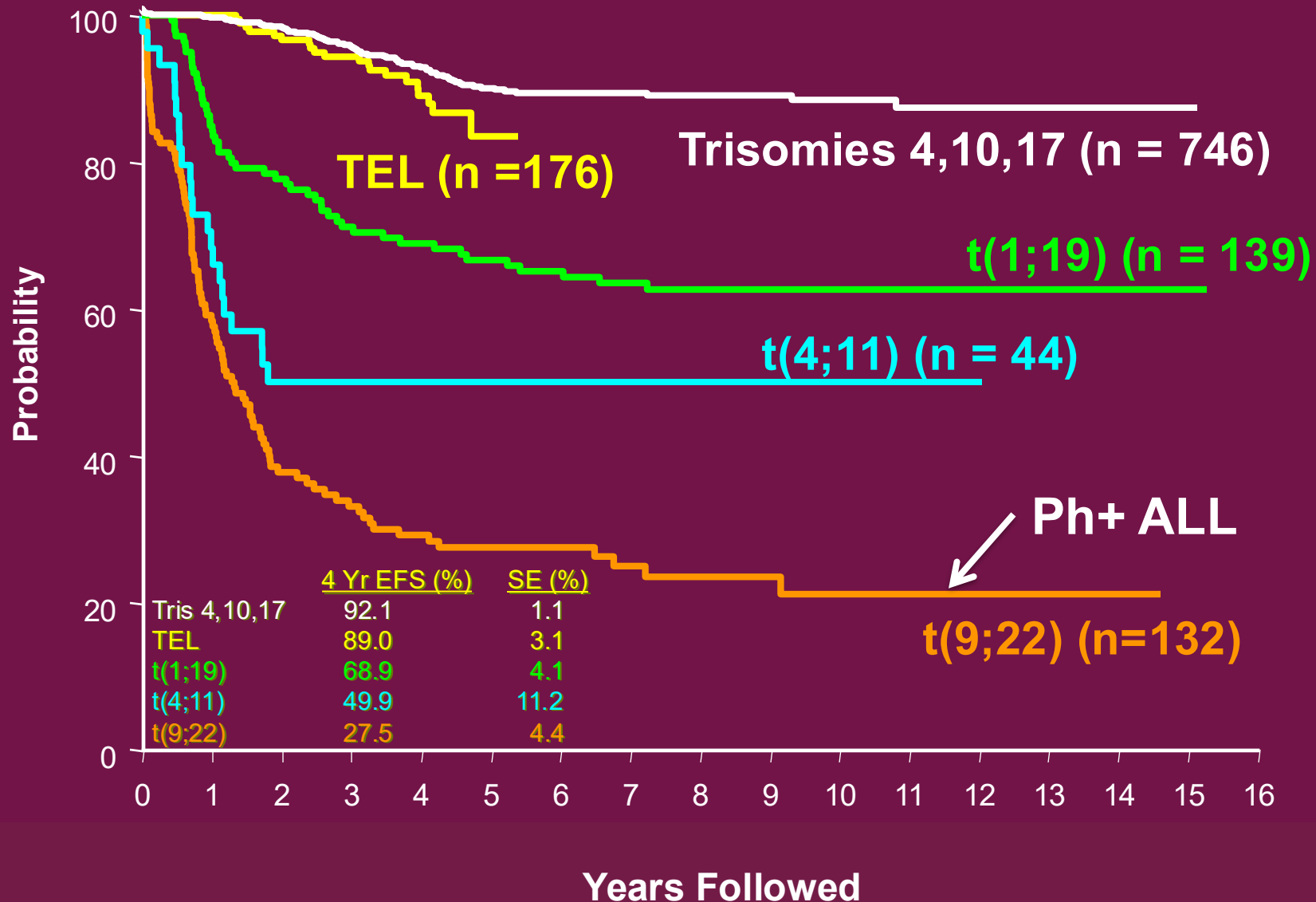
Improvement in Outcome Over Time: Results of COG Studies of ALL



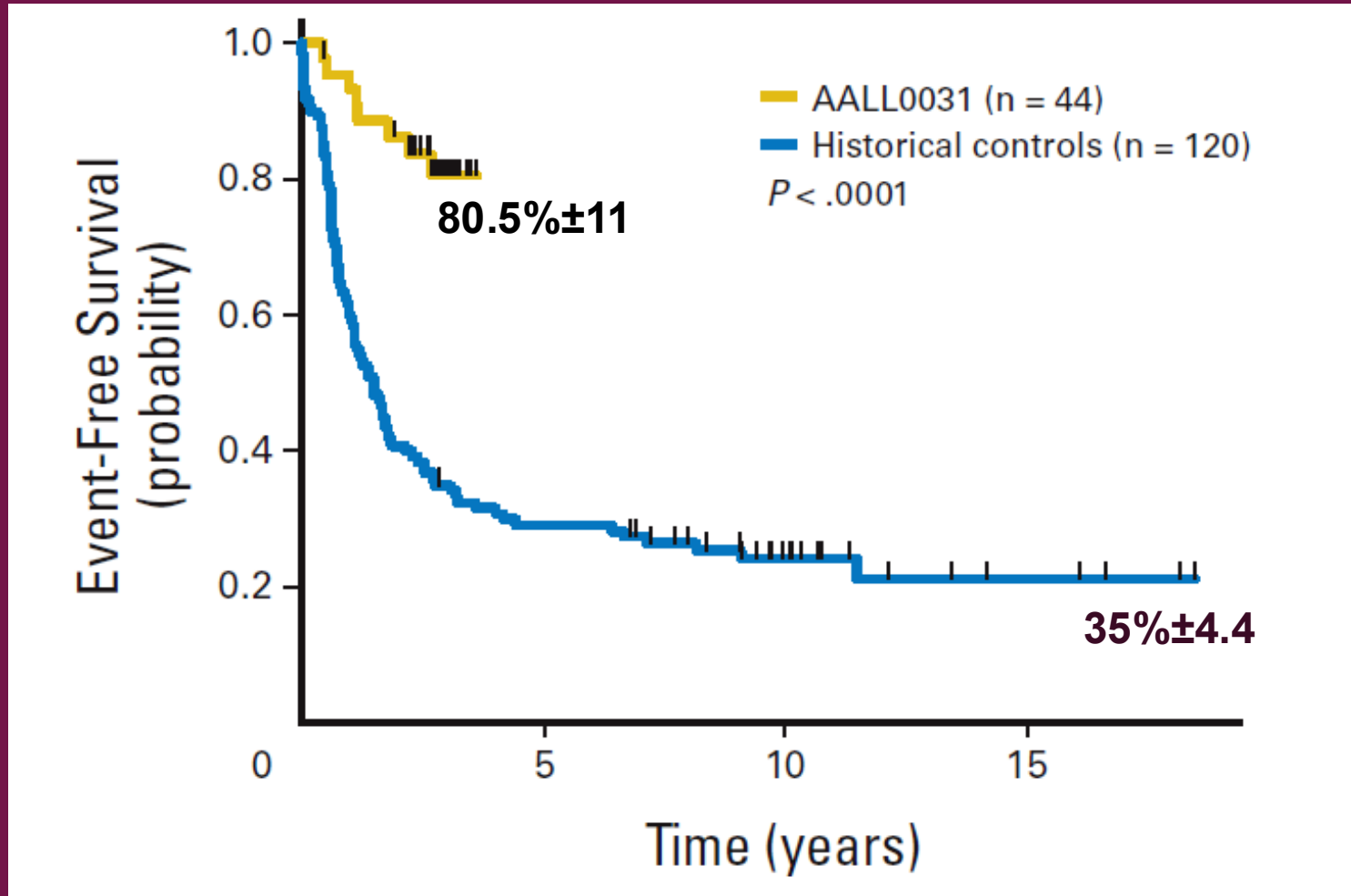
Improved Survival for Children and Adolescents with ALL: 1990-2005



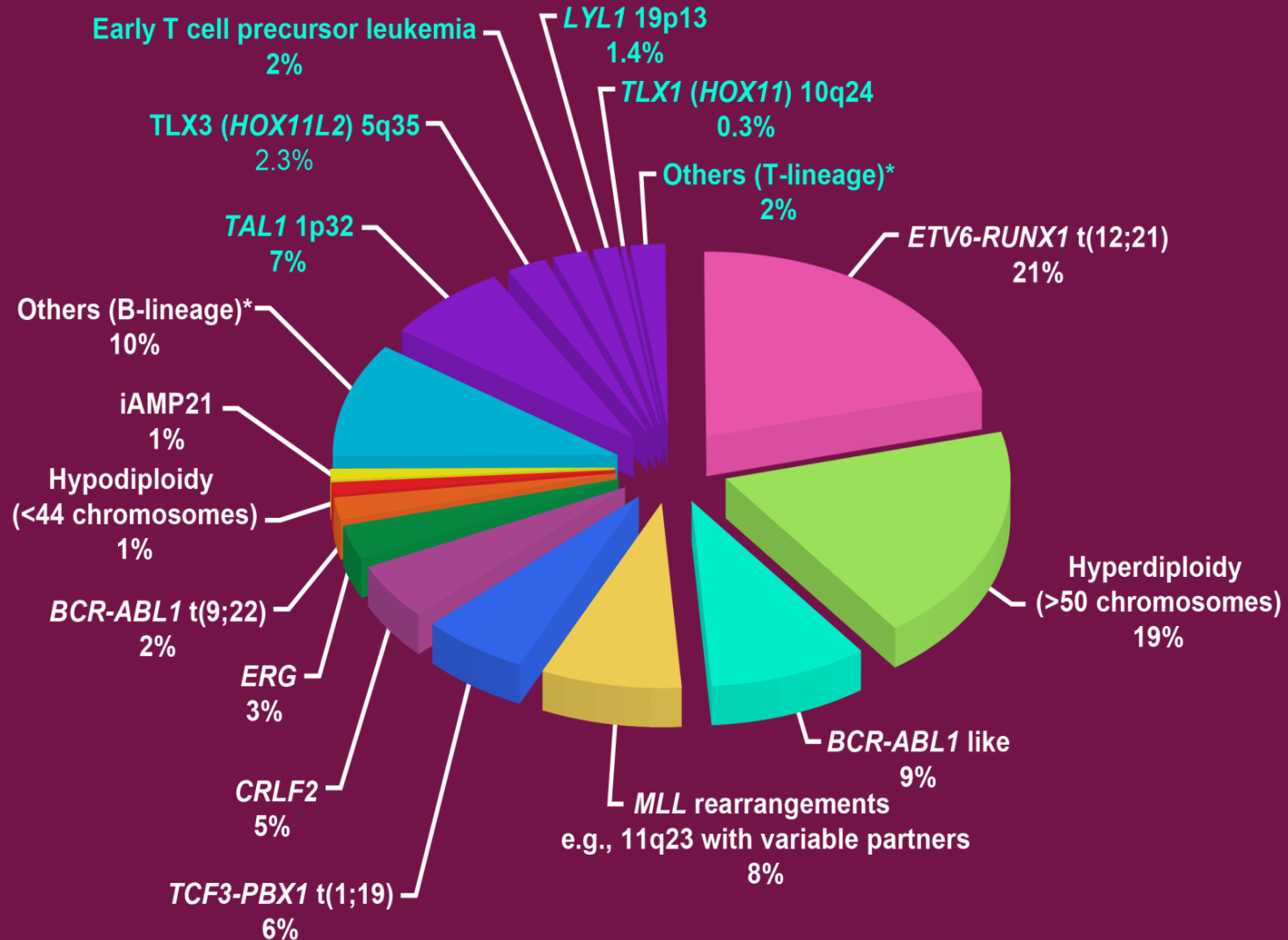
Correlation of Genotype and Outcome in Childhood B-Progenitor ALL



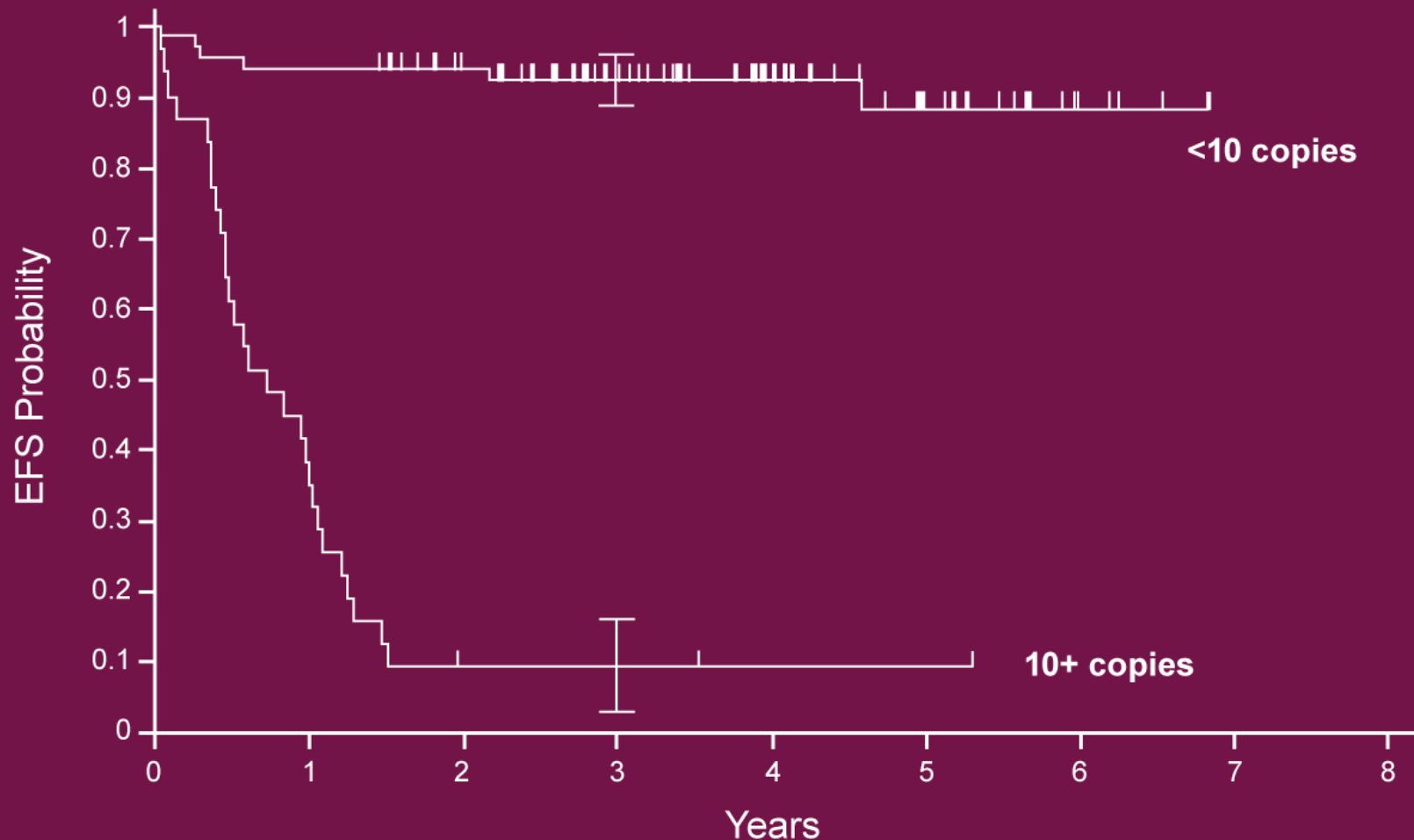
Addition of Imatinib for Ph+ ALL: Comparison to Historical Controls



All Childhood ALL Cases Have Specific Genetic Abnormality



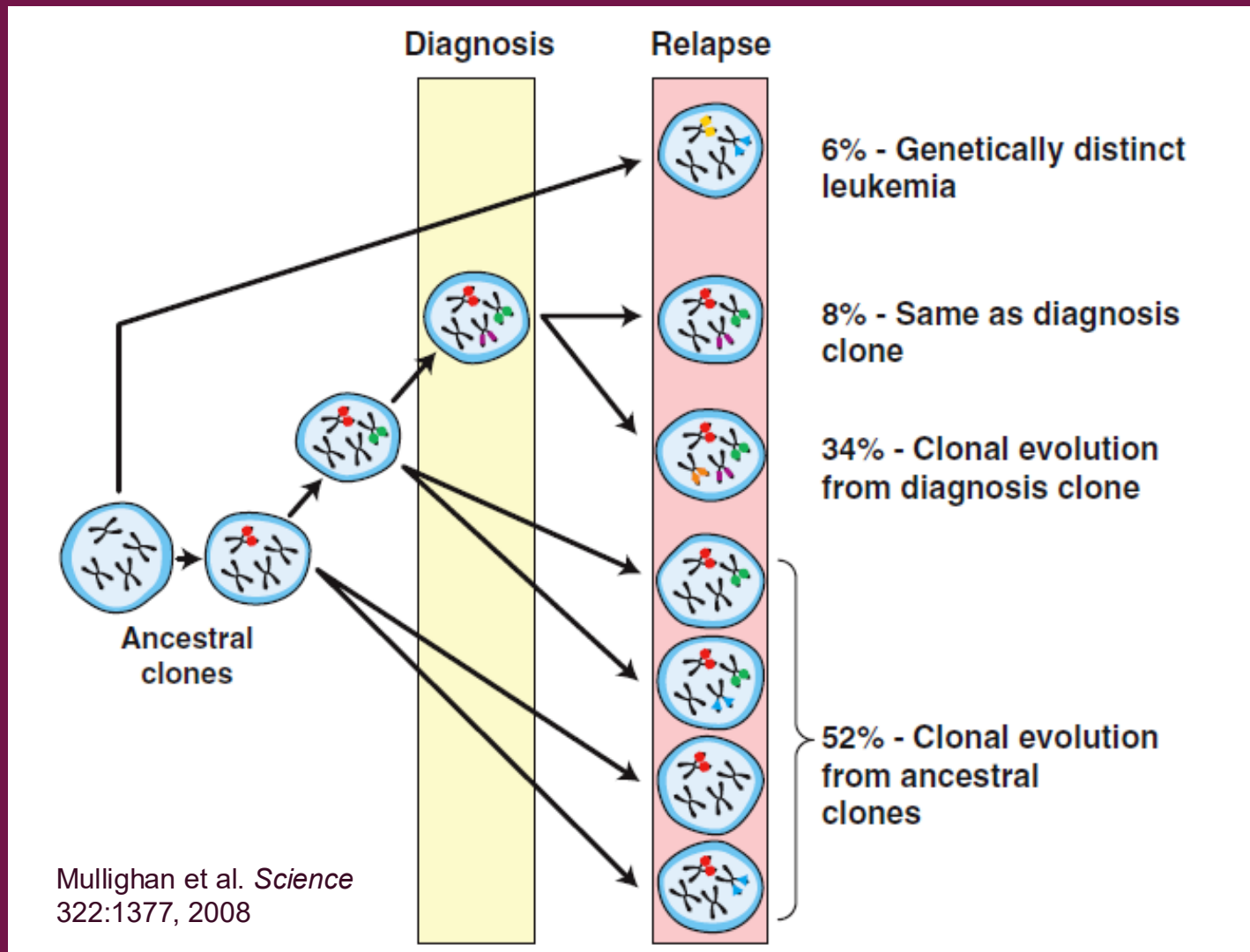
Neuroblastoma: Impact of NMYC Amplification on Outcome of Infants with Stage IV



International Neuroblastoma Risk Group (INRG) Pretreatment Classification

INRG Stage	Age (months)	Histologic Category	Grade of Tumor Differentiation	MYCN	11q Aberration	Ploidy	Pretreatment Risk Group
L1/L2		GN maturing; GNB intermixed					A Very low
L1		Any, except GN maturing or GNB intermixed		NA			B Very low
				Amp			K High
L2	< 18	Any, except GN maturing or GNB intermixed		NA	No		D Low
					Yes		G Intermediate
	≥ 18	GNB nodular; neuroblastoma	Differentiating	NA	No		E Low
			Poorly differentiated or undifferentiated	NA	Yes		H Intermediate
				Amp			N High
M	< 18			NA		Hyperdiploid	F Low
	< 12			NA		Diploid	I Intermediate
	12 to < 18			NA		Diploid	J Intermediate
	< 18			Amp			O High
	≥ 18						P High
MS	< 18			NA	No		C Very low
					Yes		Q High
				Amp			R High

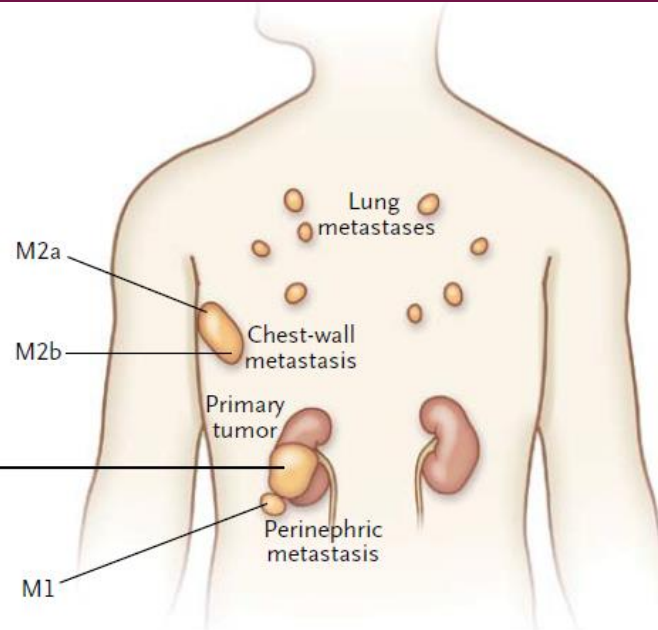
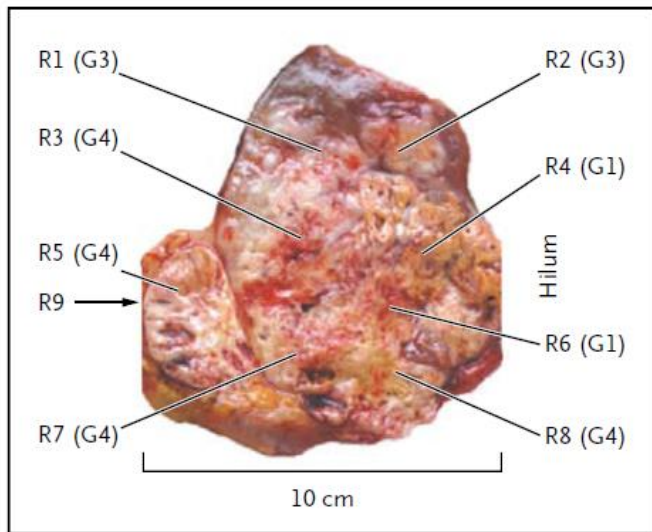
The Molecular Biology of Relapse in Acute Lymphoblastic Leukemia



Intratumor Heterogeneity:

Gene-Expression Signatures of Good and Poor Prognosis in Different Regions of the Same Tumor

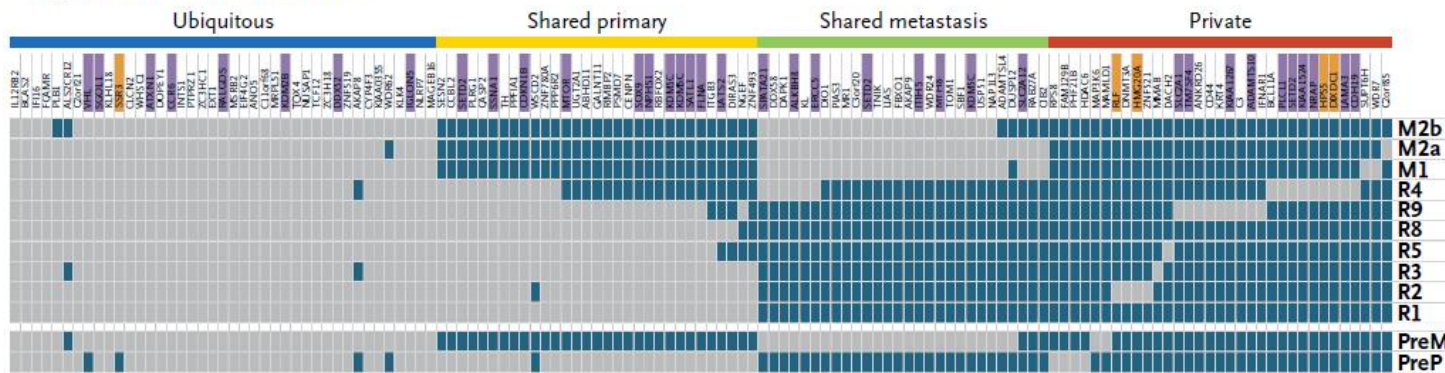
A Biopsy Sites



■ Mutation

■ No Mutation

B Regional Distribution of Mutations



Gerlinger et al. *N Engl J Med* 366:883, 2012

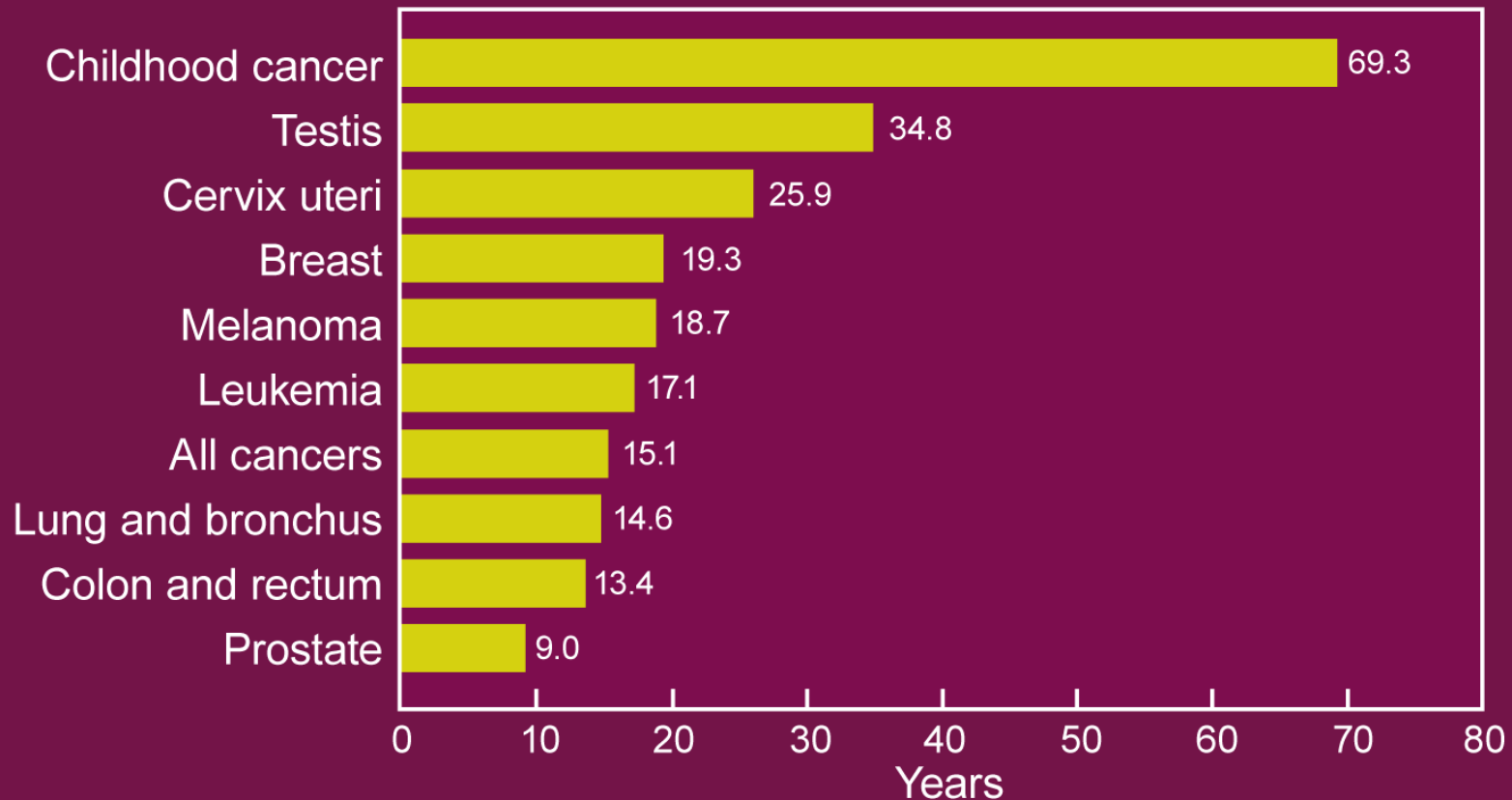
Lessons from our Children

- Importance of collaboration
- Importance of laboratory investigations of tumor tissue
- Cancers are heterogeneous collections of diseases
- **Focus on survivors**



Average Years of Life Lost to Cancer

Average years of life lost per person dying of cancer*:



*Data are for all races and both sexes, and the estimates were made using 1996 life tables from the National Center for Health Statistics.

Source: *SEER Cancer Statistics Review, 1973-1997* (NCI 2000); access at <http://seer.cancer.gov/>

Nearly 2/3 of long term survivors of childhood cancer have at least one chronic condition and more than 1/4 of them have a severe or life-threatening condition.

Oeffinger et al. *N Engl J Med*
355:1572, 2006

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Chronic Health Conditions in Adult Survivors of Childhood Cancer

Kevin C. Oeffinger, M.D., Ann C. Mertens, Ph.D., Charles A. Sklar, M.D., Toana Kawashima, M.S., Melissa M. Hudson, M.D., Anna T. Meadows, M.D., Debra L. Friedman, M.D., Neyssa Marina, M.D., Wendy Hobbie, C.P.N.P., Nina S. Kadan-Lottick, M.D., Cindy L. Schwartz, M.D., Wendy Leisenring, Sc.D., and Leslie L. Robison, Ph.D., for the Childhood Cancer Survivor Study*

ABSTRACT

BACKGROUND

Only a few small studies have assessed the long-term morbidity that follows the treatment of childhood cancer. We determined the incidence and severity of chronic health conditions in adult survivors.

METHODS

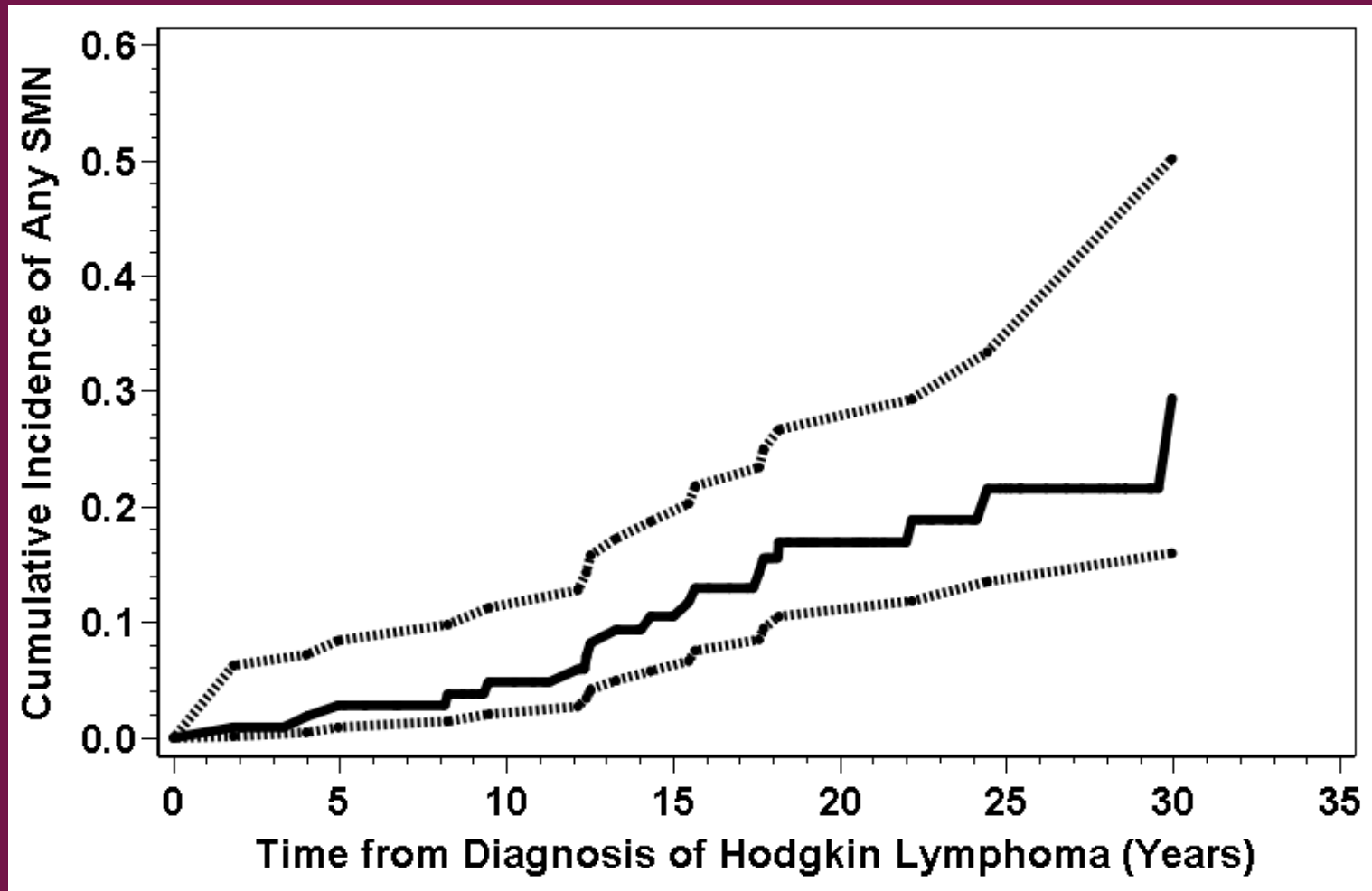
The Childhood Cancer Survivor Study is a retrospective cohort study that tracks the health status of adults who received a diagnosis of childhood cancer between 1970 and 1986 and compares the results with those of siblings. We calculated the frequencies of chronic conditions in 10,397 survivors and 3034 siblings. A severity score



Effect of Irradiation on Skeletal Growth: 25 years after Irradiation for Hodgkin Disease



20-year Cumulative Incidence of Second Cancer

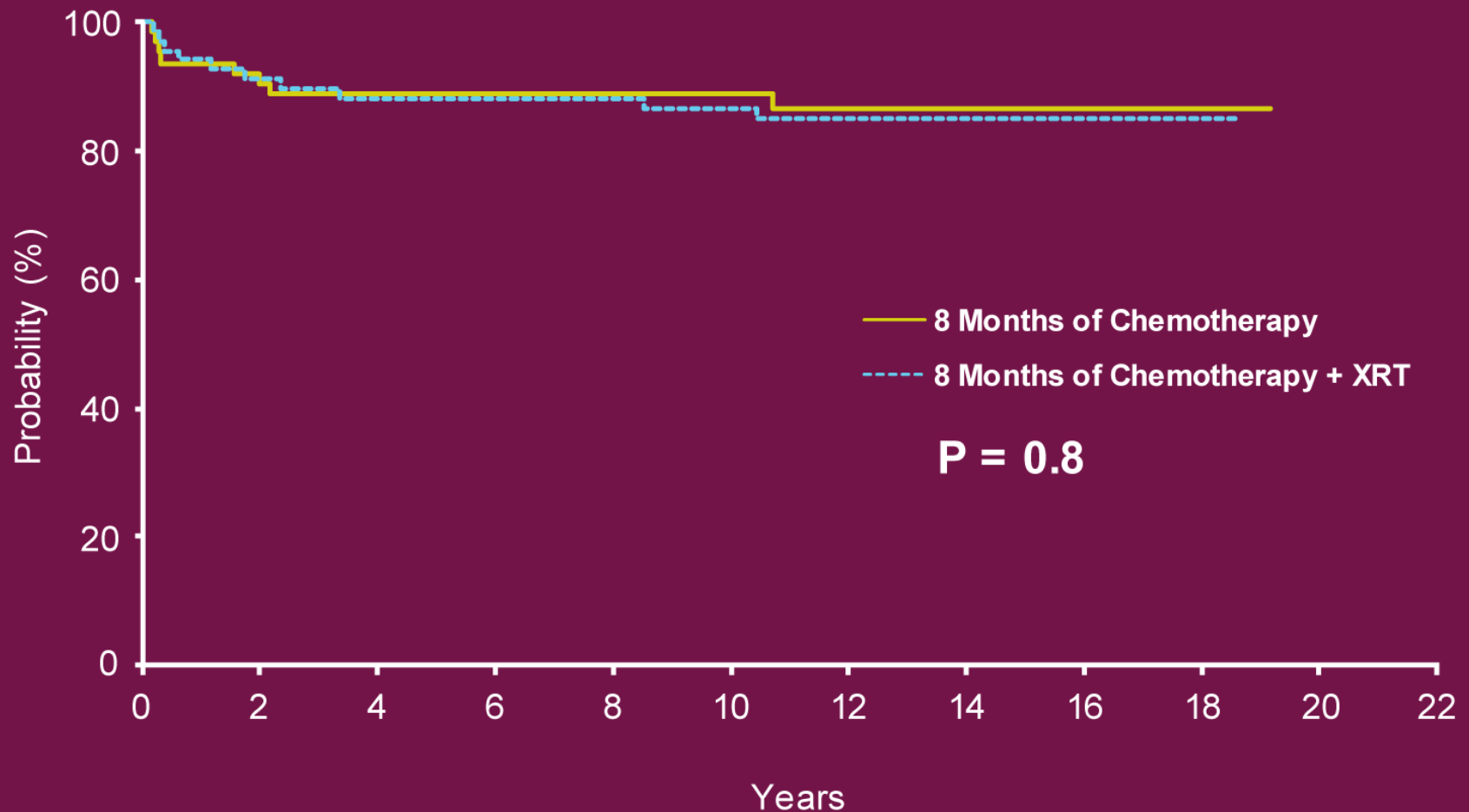


**“Cure is not
enough.”**

Giulio D'Angio, MD



Early Stage Non-Hodgkin Lymphoma: Outcome According to Treatment [\pm XRT]

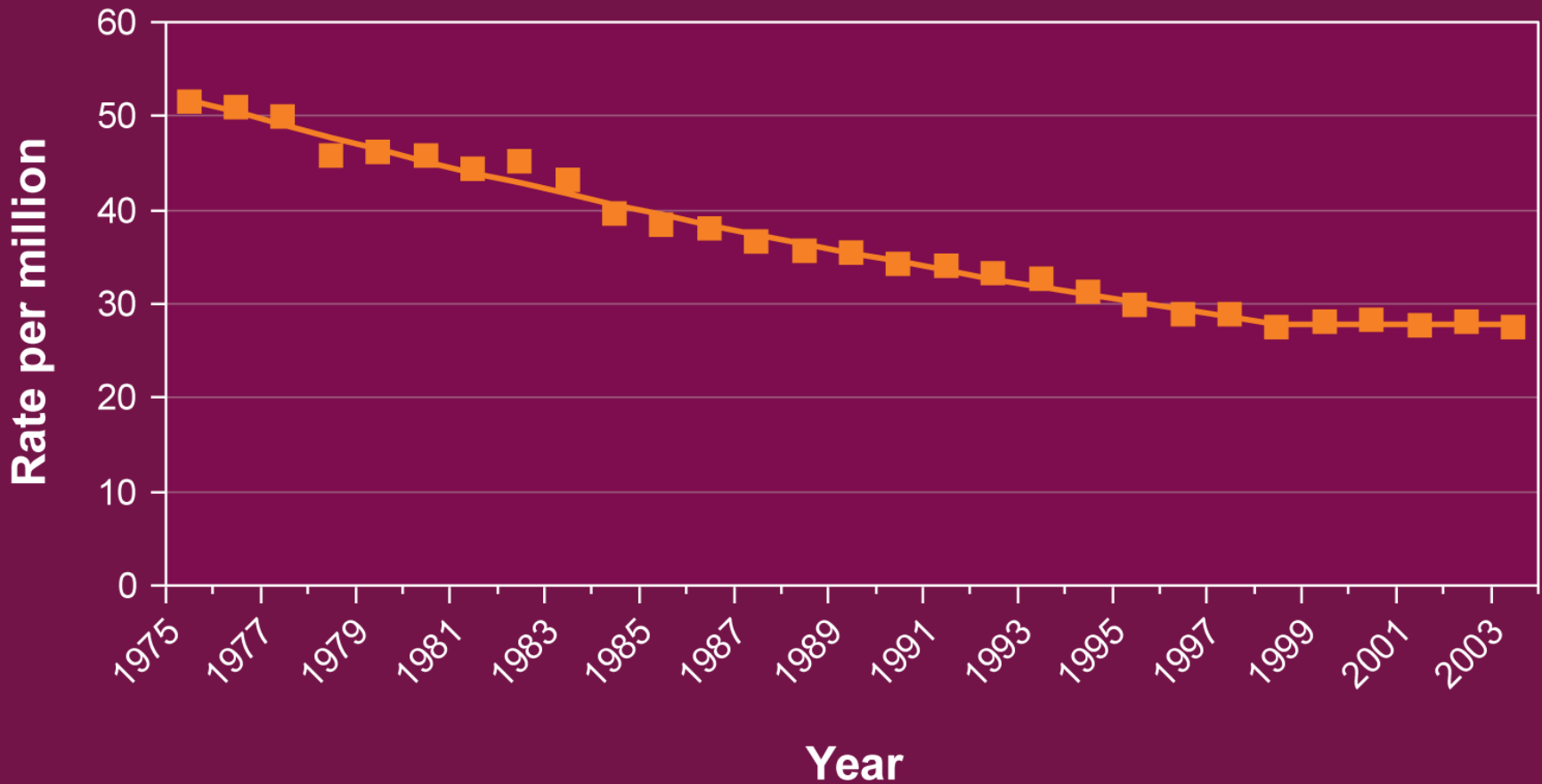


Selecting Therapy With a Consideration of Late Effects

- Elimination of irradiation in non-Hodgkin lymphoma
- Elimination of irradiation for most children with Wilms tumor
- Elimination of cranial irradiation for almost all children with acute lymphoblastic leukemia
- Reduced exposure to alkylating agents
- Reduced exposure to anthracyclines and introduction of cardioprotective agents



Childhood Cancer Mortality 1975-2003



The New Paradigm: Pathways Rather Than Tumors

- Pathways driving cancers are promiscuous
 - The number of pathways is finite
 - Drivers of disparate cancers
- Agents that target a specific pathway should be active against several tumors
 - Imatinib and relatives in CML and GIST
 - Targeting ALK in lung cancer, anaplastic large cell lymphoma, neuroblastoma and others [crizotinib]
- Collaborations across specialties and across tumor types



Lessons From Our Children

- It takes a village
- Importance of tumor tissue
- Cancers are heterogeneous collections of diseases
- Cancers are collections of rare (orphan) diseases



Lessons From Our Children

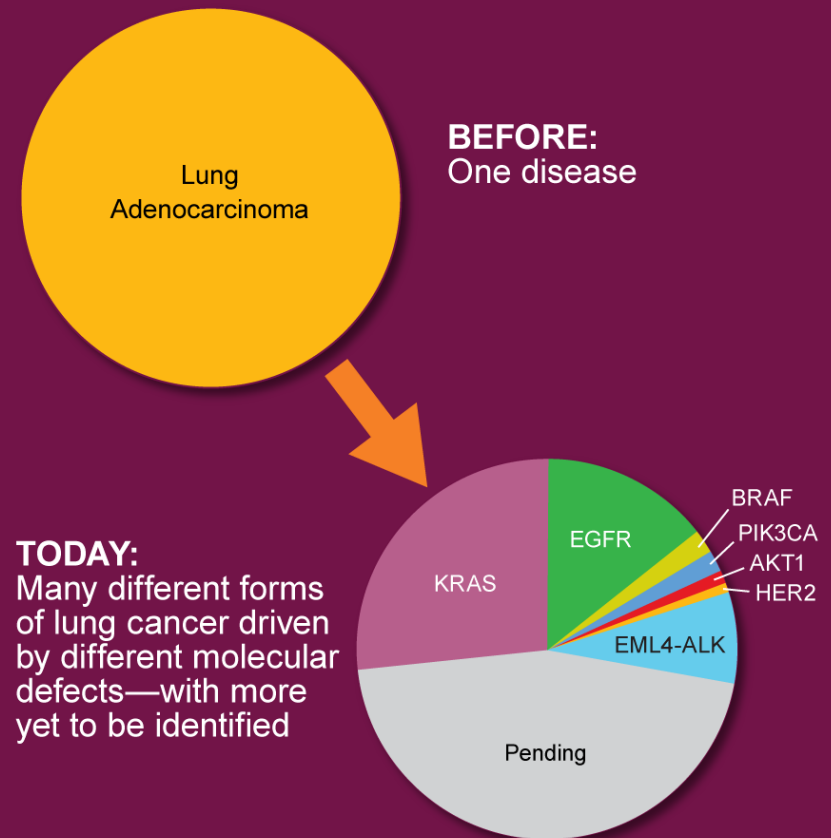
- Cancers as rare (orphan) diseases
 - Implications for clinical trials
 - Implications for drug development
- Must leverage information from the laboratory
- Must combine care delivery and clinical research



Challenges We Face

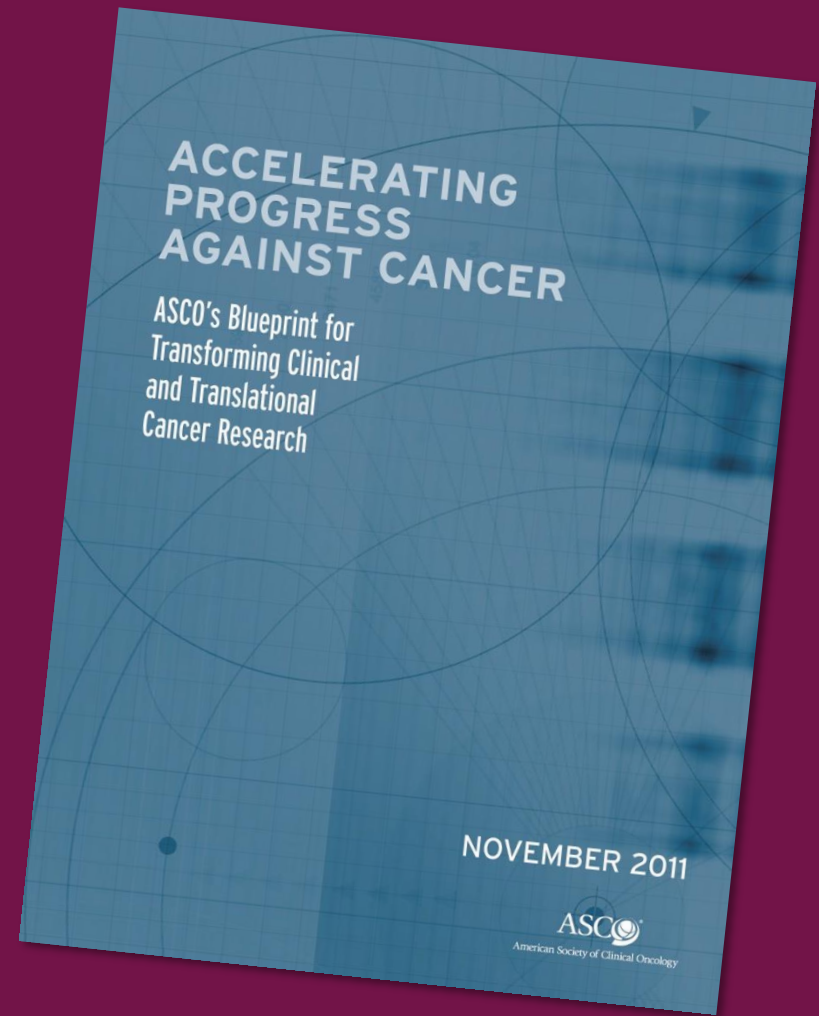
- Limited understanding of which molecular pathways are most important to target
- Clinical trial designs haven't kept pace with personalized cancer medicine
- Promise of health information technology is only beginning to be realized

Cancer in the Molecular Era: Identifying the Drivers of Lung Cancer



A Vision for the Future

- A New Approach to Therapeutic Development
- Faster, Smarter Clinical Trials
- Harnessing Health Information through Technology



More Lessons from our Children

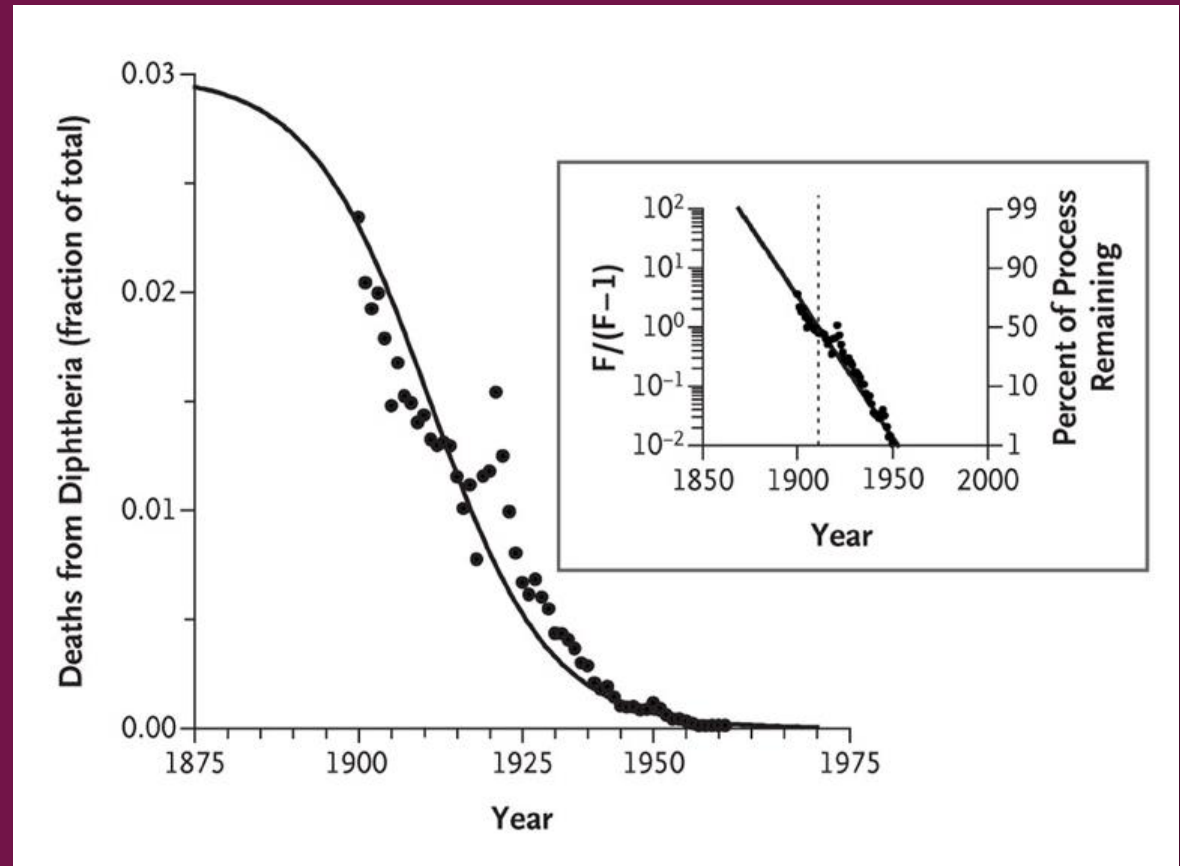
- Survivorship
 - “Cure is not enough”
 - Impact on longevity and on quality of life for survivors
 - Must modify current treatments in light of late effects
- Host genome may predict short and long term toxicities
 - Cardiac toxicity of anthracyclines
 - Risk of radiation-induced second cancer
 - Taxane-induced neuropathy



“An ounce of prevention is worth a pound of cure.”

Diphtheria as a Fraction of All Deaths in the United States, 1900–1956

Hostetter MK. *N Engl J Med* 2012;366:1328-1334



The Paradigm of Prevention

“Diagnose and treat” → **“Predict and prevent”**

- Immunization
 - Hepatitis B—Hepatocellular Carcinoma
 - HPV—Cervical Cancer, Head & Neck Cancer
 - ??EBV
 - ??Hepatitis C
 - ??H. Pylori
- Healthy life style counseling
 - Smoking
 - Diet
 - Sun exposure



Pediatric Oncology: Secrets to Success

- A culture of collaboration and learning
- Research embedded in medical practice
 - Well annotated tissues for study
 - Commitment to clinical trials

Research cures cancer



The Lesson From Our Children

Looking beyond Translation — Integrating Clinical Research with Medical Practice

Annetine C. Gelijns, Ph.D., and Sherine E. Gabriel, M.D.

N Eng J Med 366:1659, 2012

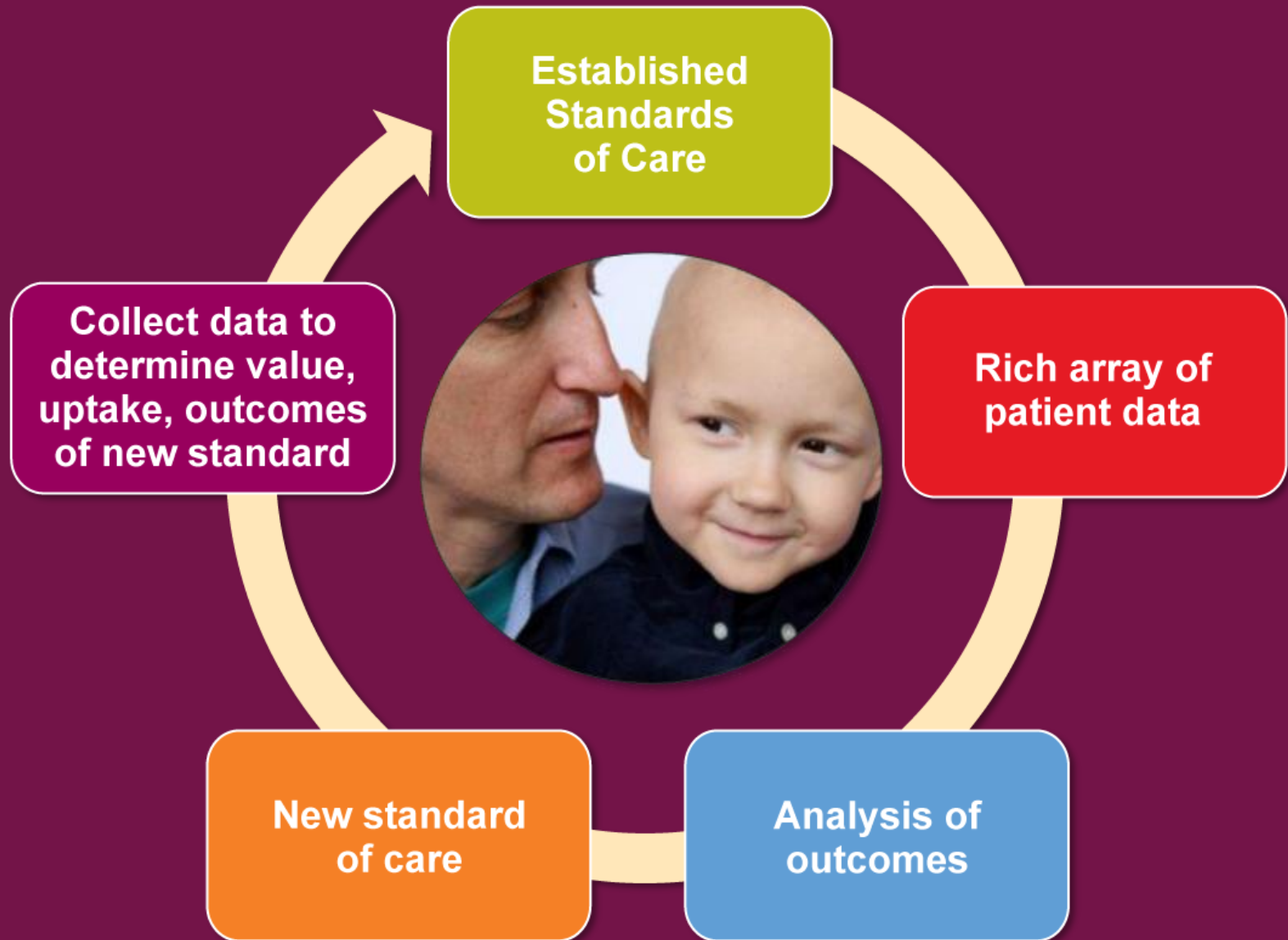


Pediatric Oncology: Secrets to Success

- A culture of collaboration and learning
- Research embedded in medical practice
- **Learning from every patient**
 - Engagement of patients and families in continuous improvement of outcome
 - Recruitment of patients and families as collaborators and advocates for the cause



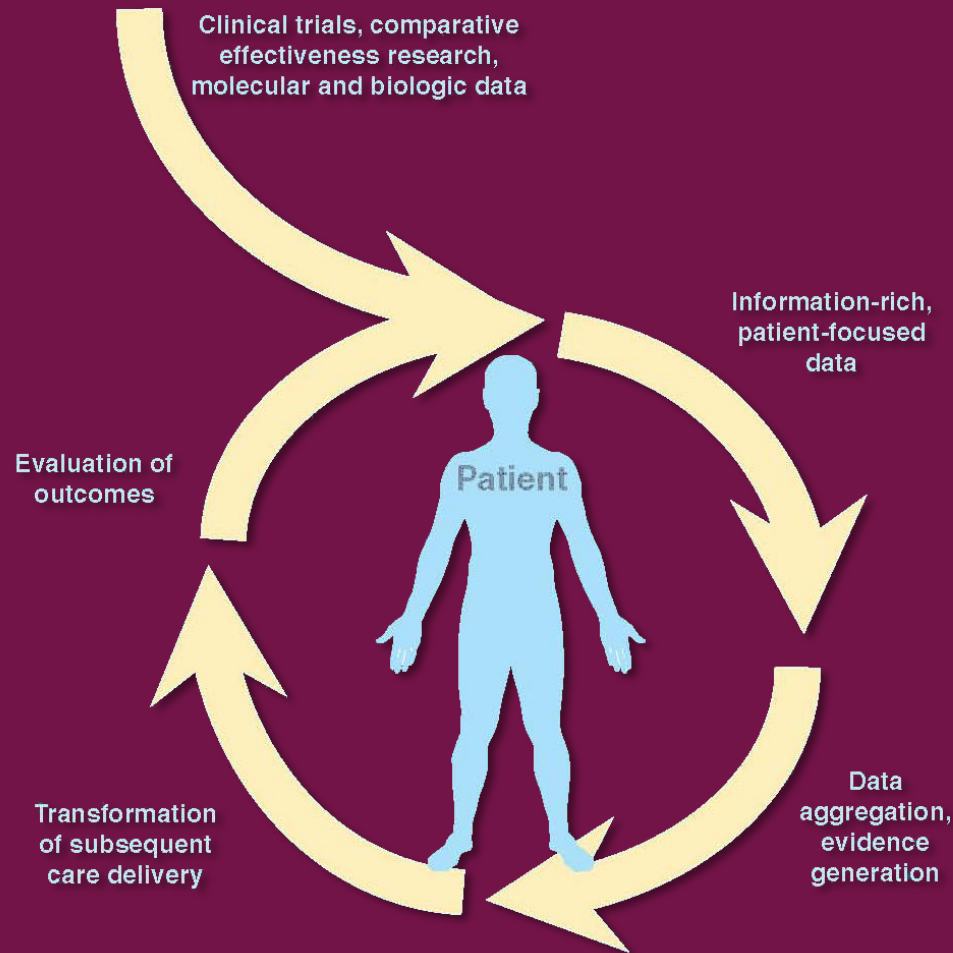
Pediatric Oncology: RLS Prototype



Vast Information—Untapped



A Rapid Learning System for Cancer Care





ASCO's Rapid Learning Oncology System

Drug Shortages

Emblematic of the
precarious path between
discovery and delivery



THE LANCET

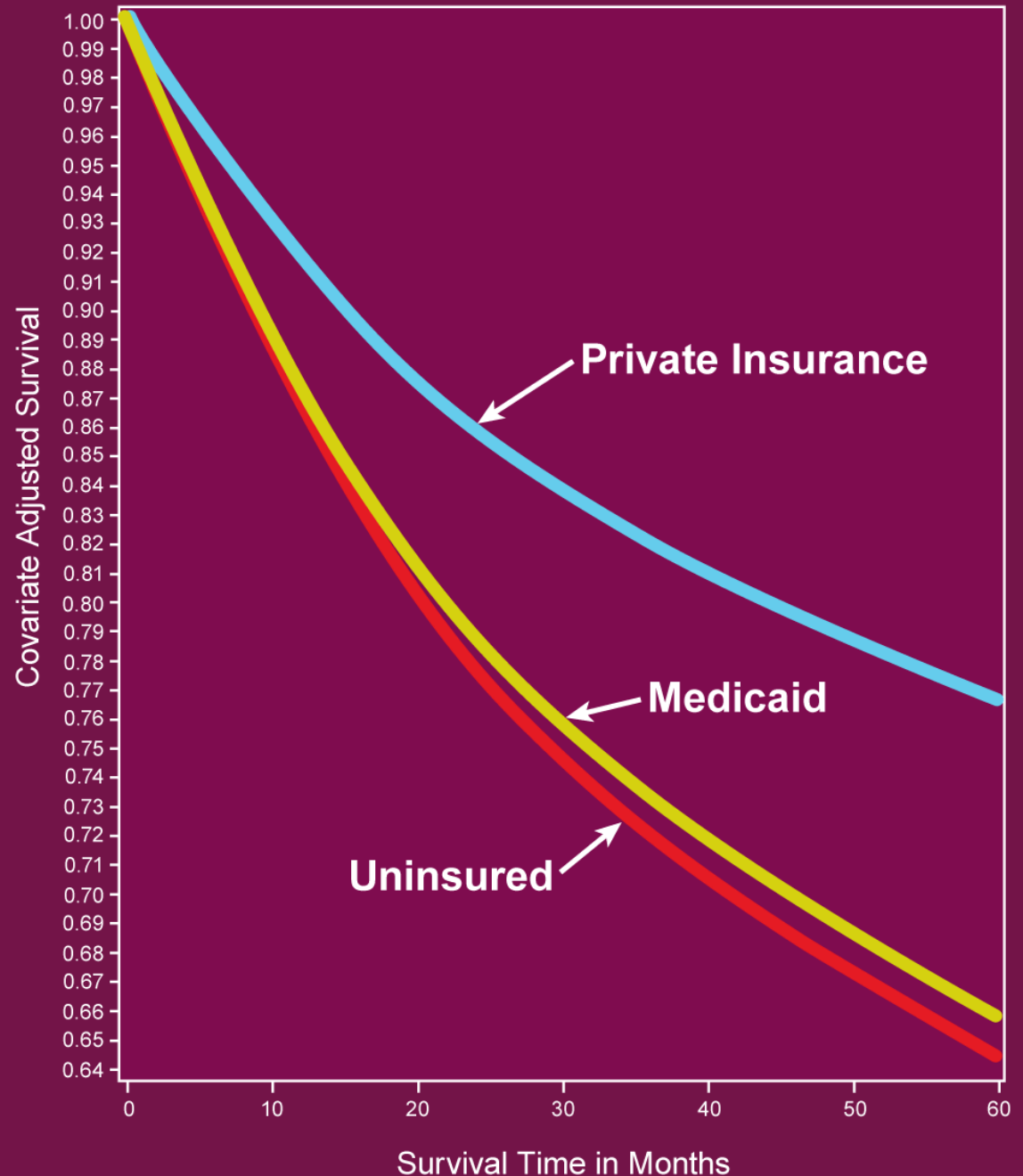
Volume 379 · Number 9823 · Pages 1273-1364 · April 7-13, 2012

www.thelancet.com

"More than 60% of personal bankruptcies in the USA arise from inability to pay the costs of essential health care for serious illness.... Right now, 50 million Americans do not have health insurance."

See World Report page 1288

Effect of Insurance Status On Outcomes for Patients with Cancer



Conquering Cancer: A Global Goal

- 85% of world's population lives in low and middle income countries
- In resource-rich countries, 80% of children with cancer are cured
- In resource-poor countries, 80% of children with cancer die



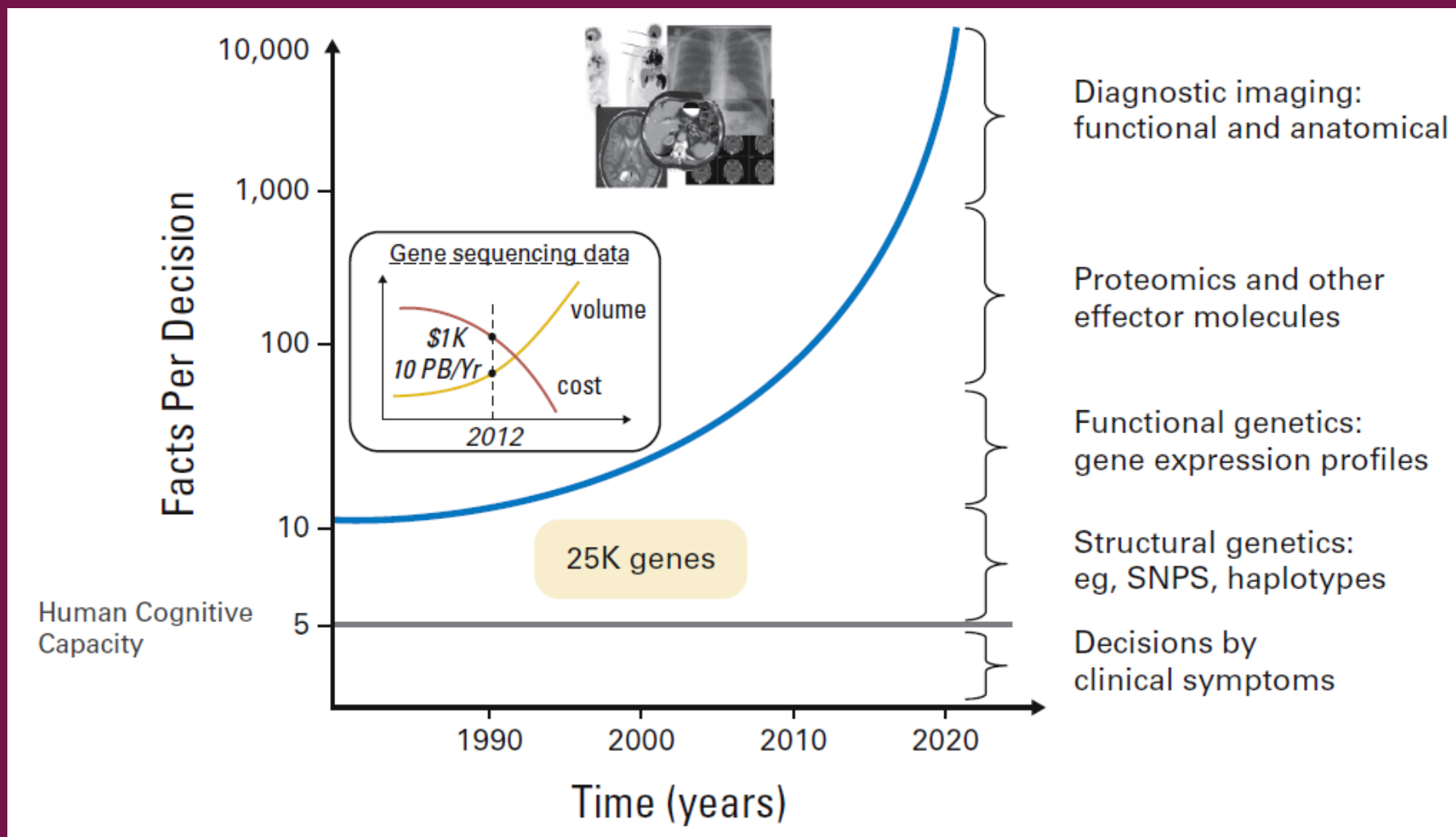
ASCO Board member Dr. Eduardo Cazap presents the World Cancer Declaration to Madam Margaret Chan, Director of the World Health Organization



The Most Important
Collaboration...
...With Our Patients



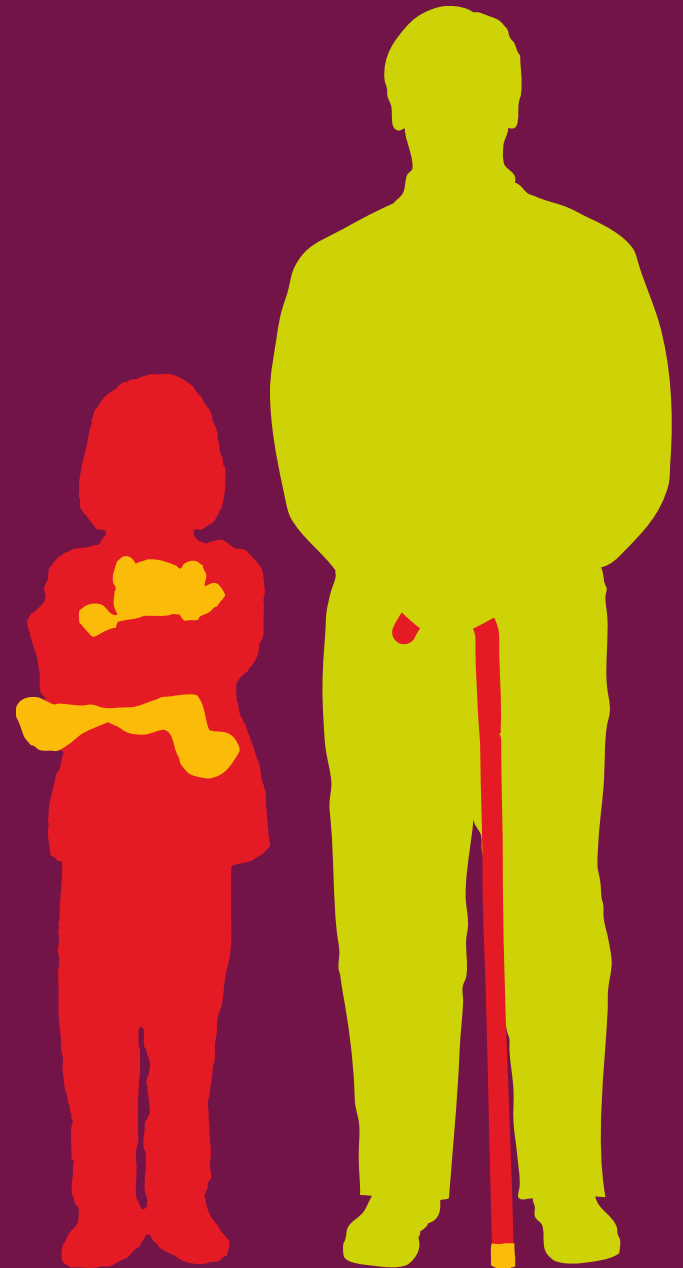
Data Needed for Medical Decision Making Exceeds Human Cognitive Capacity



Tumor Sequence on a Thumb Drive



The Most Important
Collaboration...
...With Our Patients









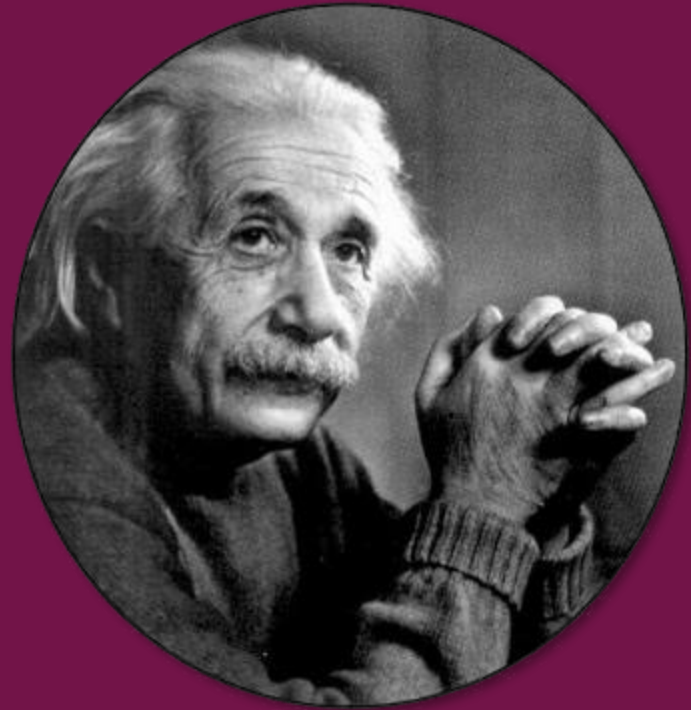






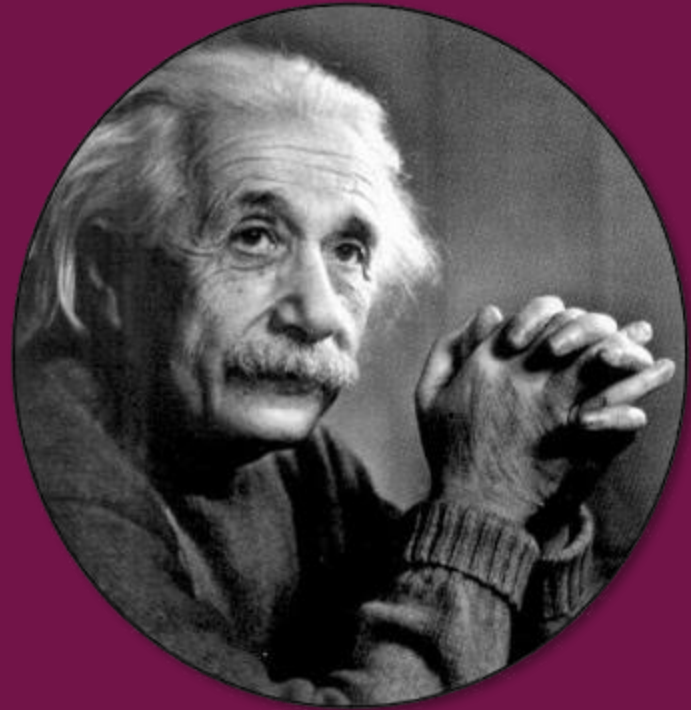
**“Not everything
that can be
counted
counts...”**

Albert Einstein



“...and not everything that counts can be counted.”

Albert Einstein



The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 88, No. 12

CHICAGO, ILLINOIS

MARCH 19, 1927

THE CARE OF THE PATIENT*

FRANCIS W. PEABODY, M.D.

BOSTON

science to the diagnosis and treatment of disease is only one limited aspect of medical practice. The practice of medicine in its broadest sense includes the whole relationship of the physician with his patient. It is an art, based to an increasing extent on the medical

“...they are too scientific and do not know how to take care of patients...”

The good physician knows his patients through and through... Time, sympathy and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, **for the secret of the care of the patient is in caring for the patient.**”

**“The secret of care
of the patient is in
caring for the
patient.”**

Francis Peabody
March, 1927

