Cancer in Young Adults (18-35)

Epidemiology, risk factors, genetics and molecular biology

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No disclosures

Since 1997: Long-term survivorship after Cancer

Limitations: Clinician (urological oncology / long-term effects after cancer)
Molecular biology: restricted to Clinical Relevance

Sources: Literature
SEER data (28% of the US population)
NORDCAN data (>90% of the Nordic pop.)

EPIDEMIOLOGY
(ALL sites)

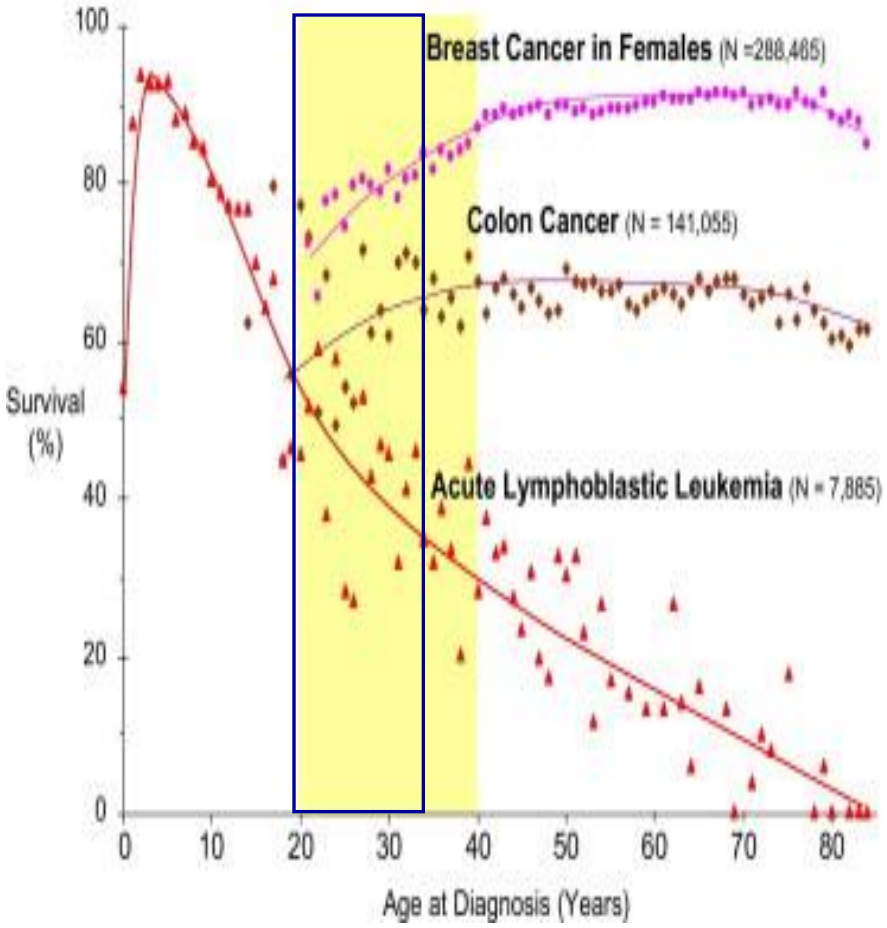
Adolescents and Young Adults AYAs

Variable definitions in the literature:

- 13 – 29 years (1)
- 20 – 39 years (2)
- 18 – 35 years (3)
- 15 – 34 years (4)

1. Epelman, Curr.Oncol.Rep.2013
2. Bleyer, Sem.Oncol.2009
3. ESMO 2014 (expected)
4. ESMO 2014 (Fosså, NORDSCAN)

AYAs – A unique entity?
Epidemiological challenges



Survival

ALL: Reduced

versus childhood ALL

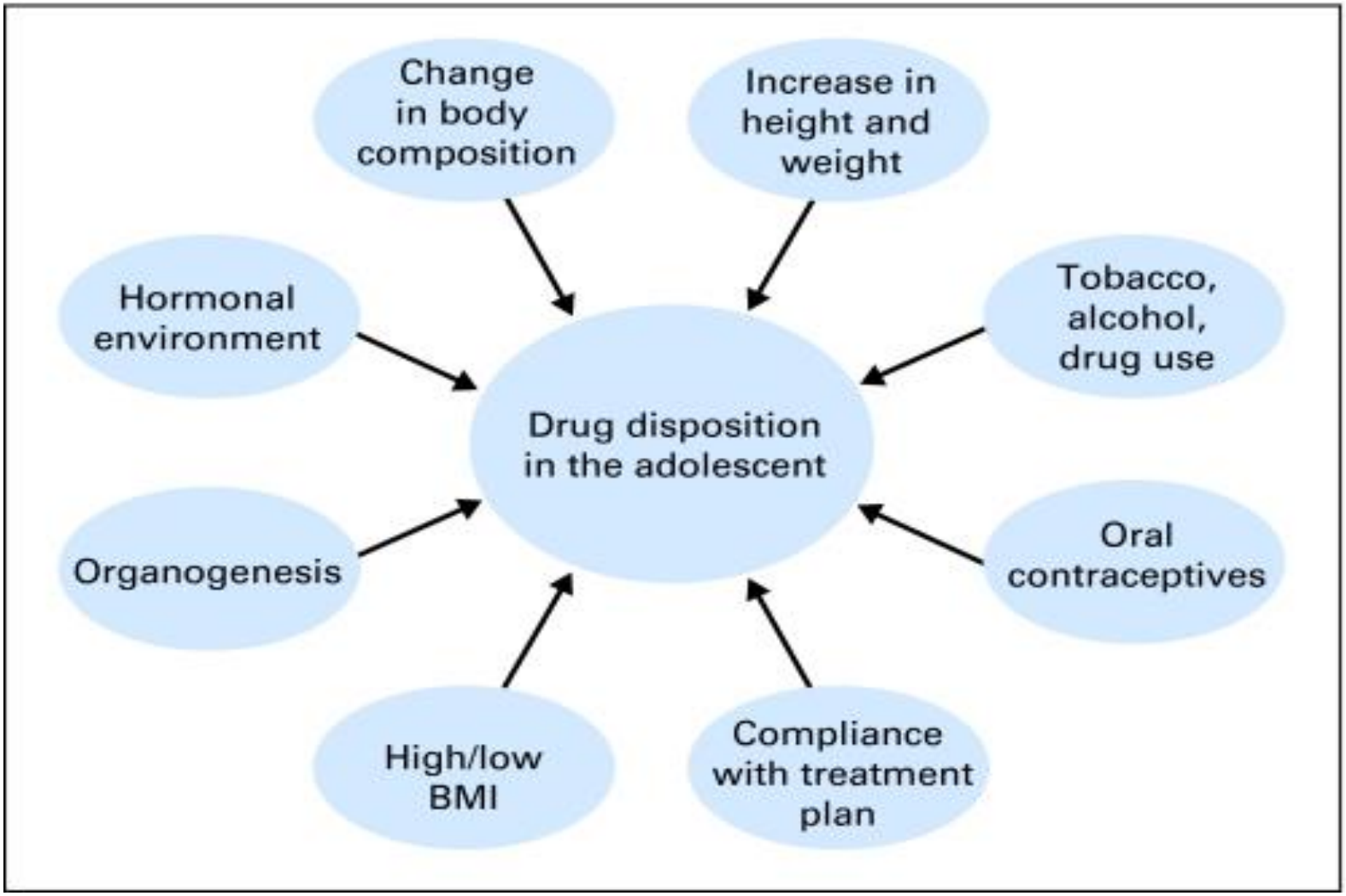
Colon Ca / Breast Ca:

Reduced
versus adult cancers

Bleyer, 2009

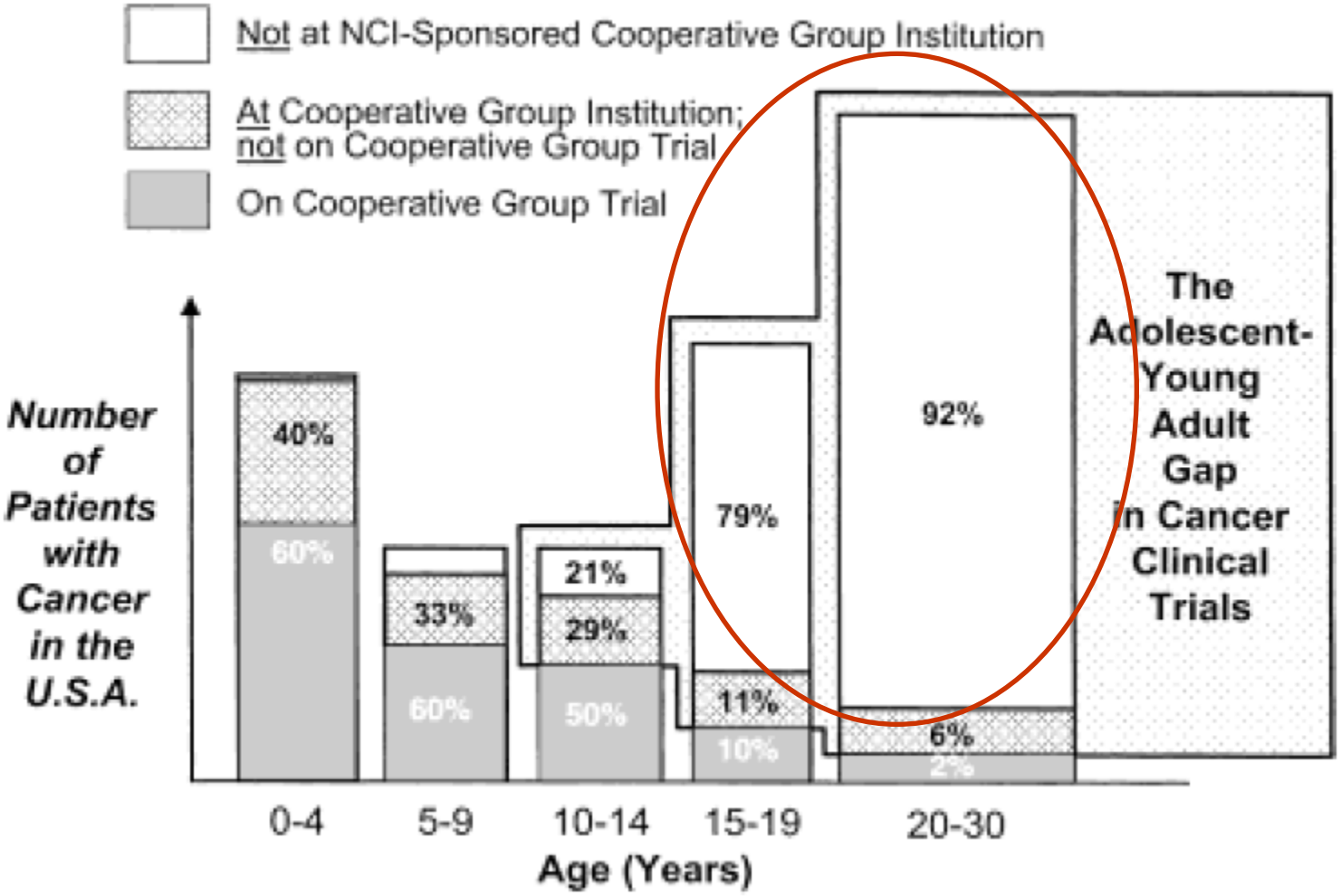
AYAs – A unique entity?

Therapeutic challenges are different from adult oncology



Veal JCO(2010);10:4790

The "adolescent and young adult gap" in cancer clinical trials in USA



Med Pediatr Oncol 2002;38:1-10

Age and Incidence 2000-2005

A: Rates B: Numbers

SEER

Incidence of all invasive cancers by 5-year intervals

20-40 years: **2%**

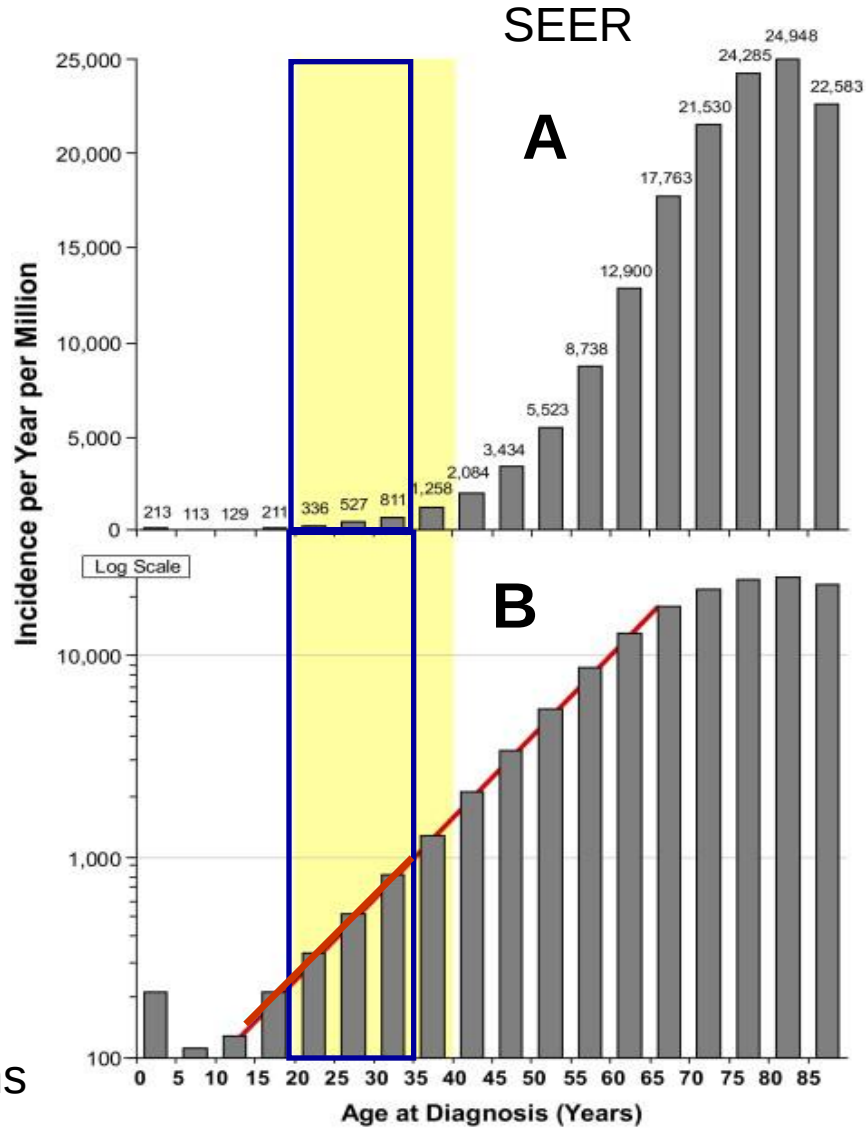
NORDCAN

20-39 years: 3,7%

N: 27703

15-34 years: **2,4%**

N: 17616



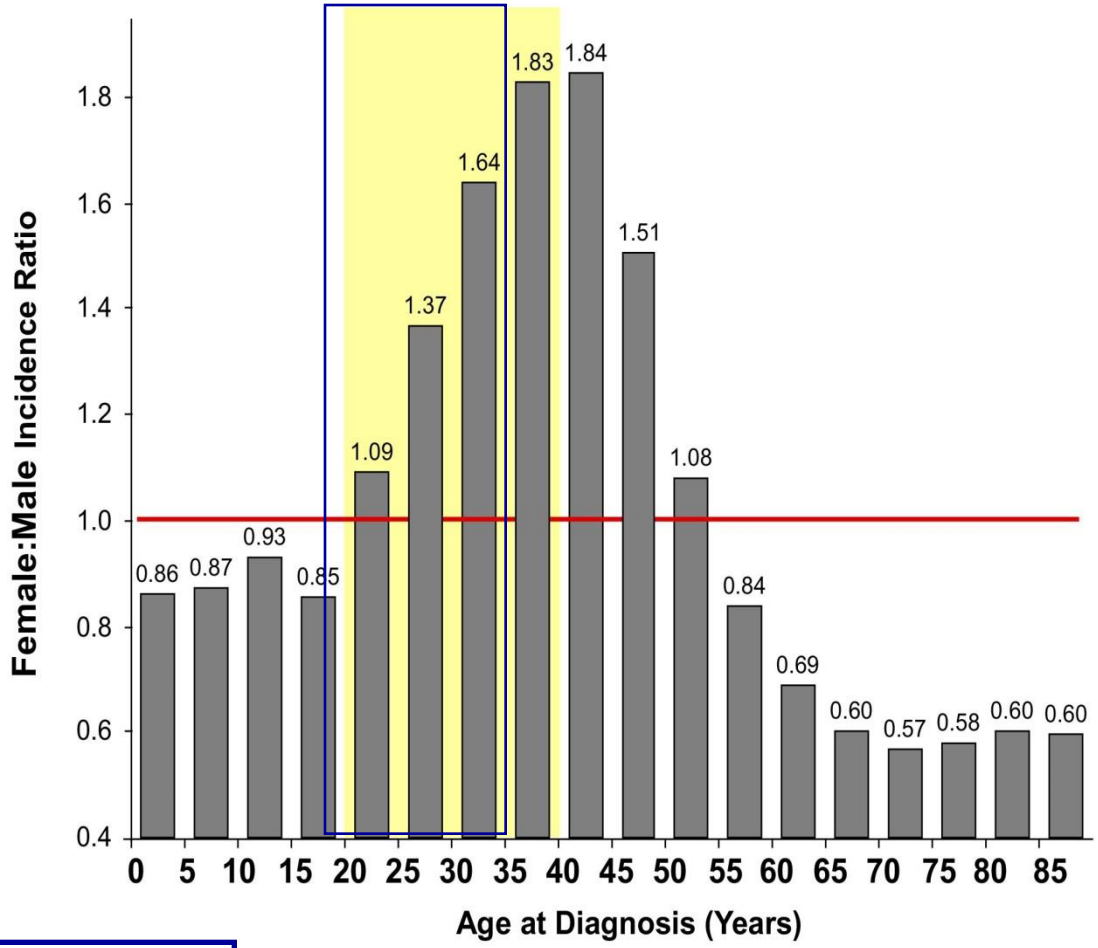
Only 5 % of cancers in AYAs are heritable with known germline alterations

Bleyer, Sem.Oncol.2009;36,194

Female / Male ratio: 2000-2005 SEER

NORDCAN

Age	F/M ratio
15-19	0,9
20-24	0,9
25-29	1,1
30-34	1,5
35-40	1,9

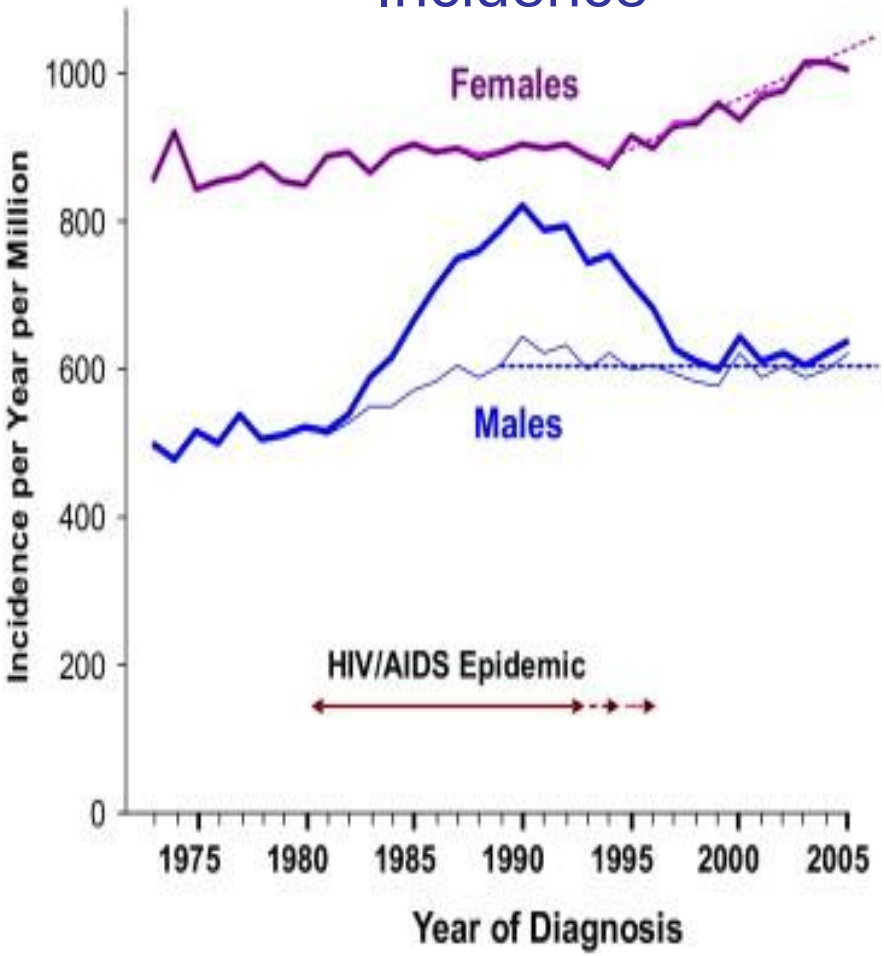


→ **More females than males**

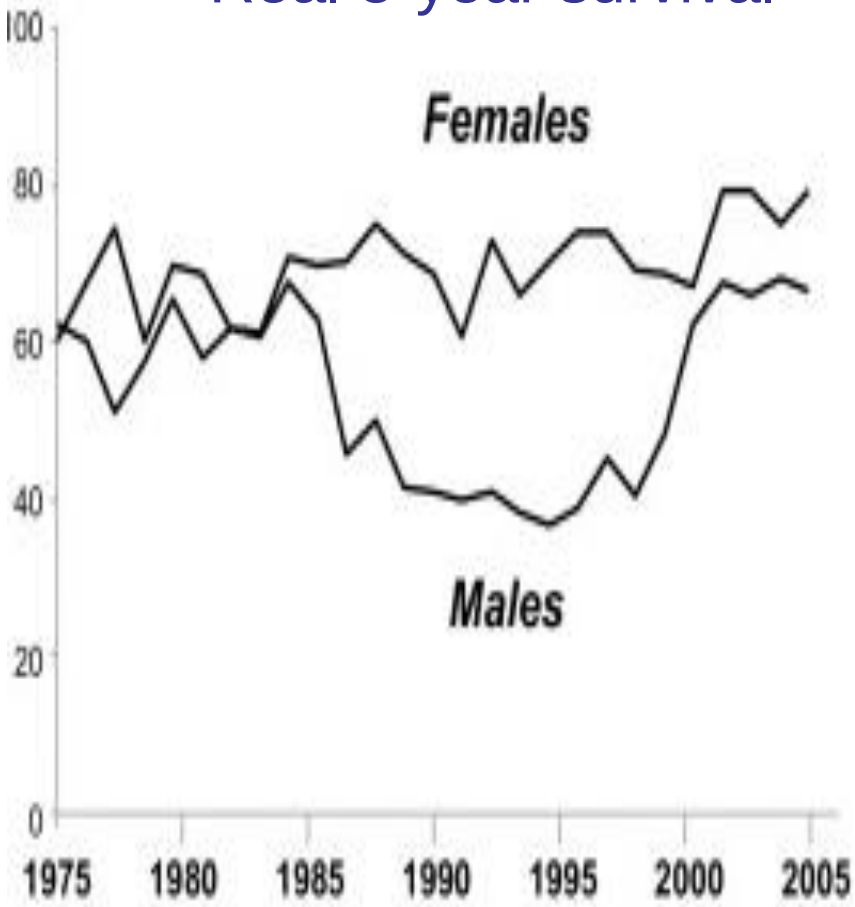
Bleyer& Barr, 2009

SEER: Increasing Incidence and slightly improved 5-year relative survival

Incidence



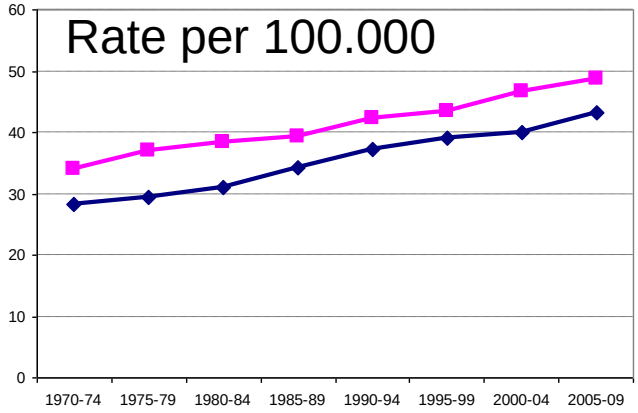
Real 5-year survival

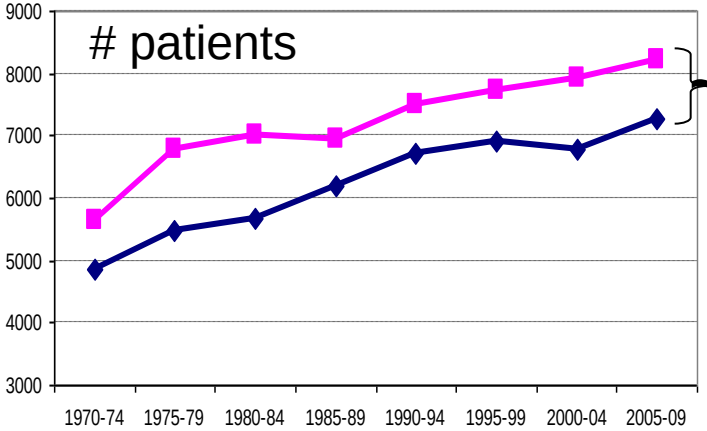


Bleyer & Barr, 2009
Albritton & Bleyer, 2009

NORDCAN 1970-2009: Cancer (all sites) in AYAs
(age 15-34 years)

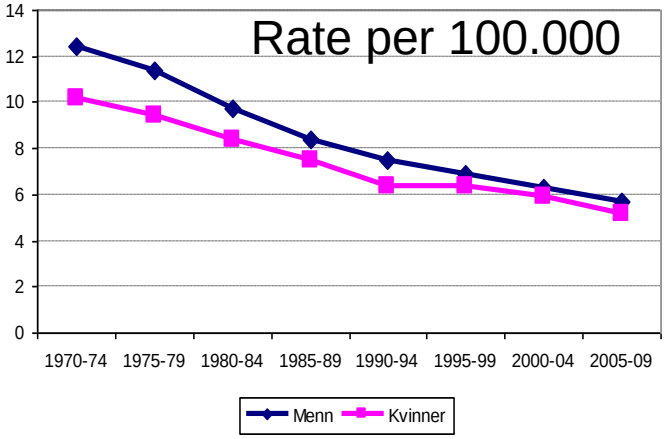
Incidence

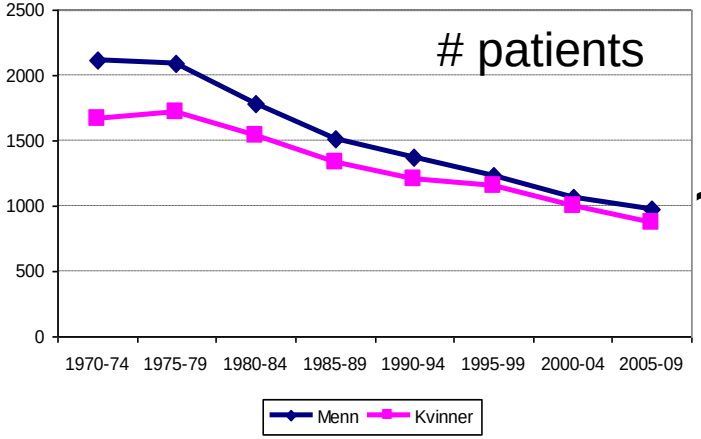




~15000

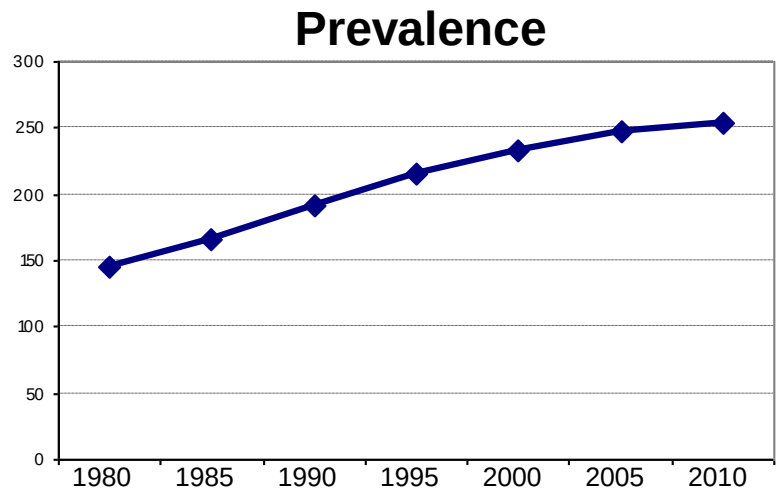
Mortality

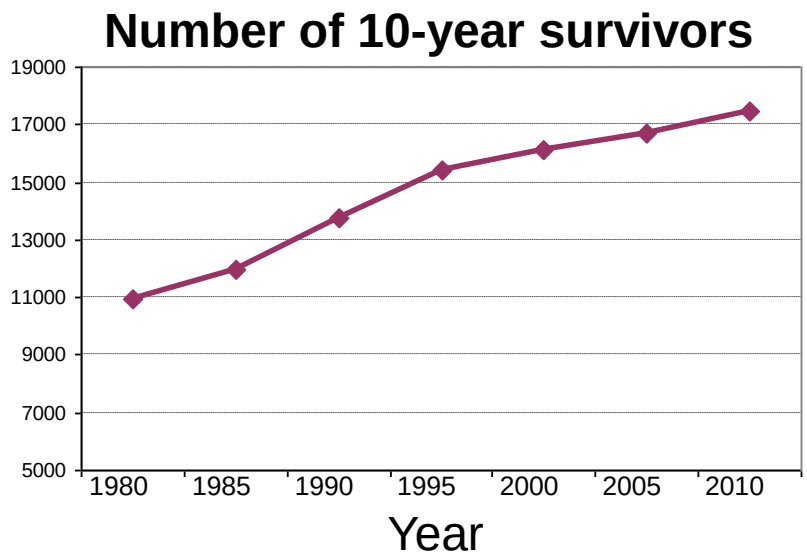




~2000

NORDCAN: Prevalence of 10-year survivors after AYA cancer (all sites) (per 100,000)

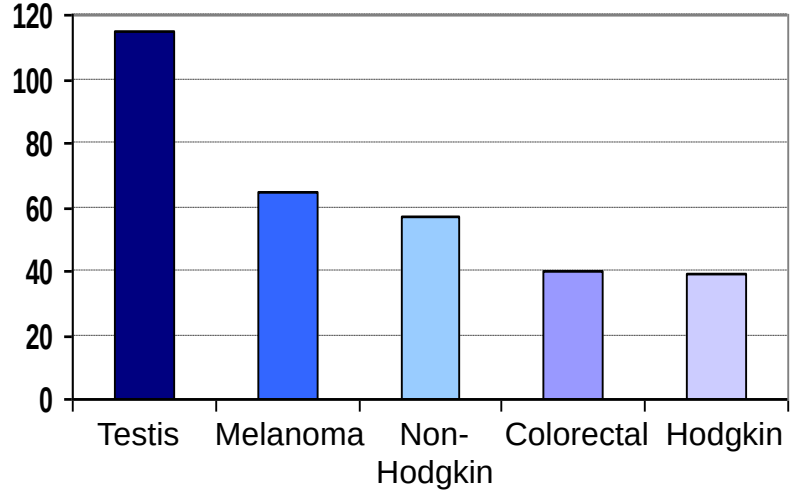




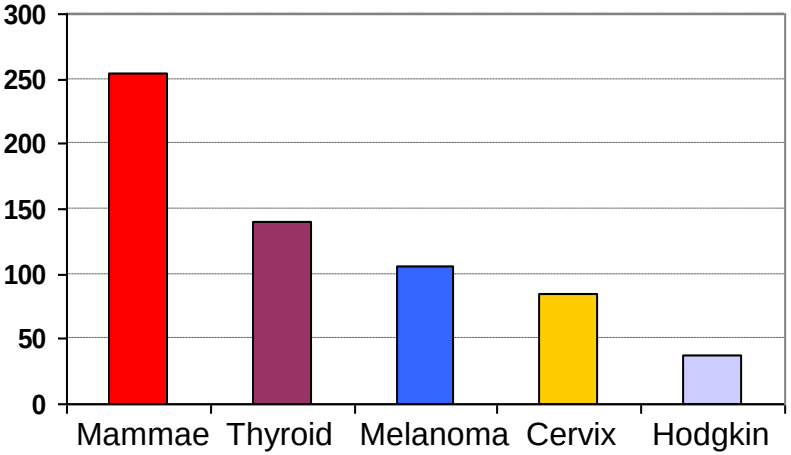
The most frequent Cancer Types

SEER 2000-2005 (20-40 years)

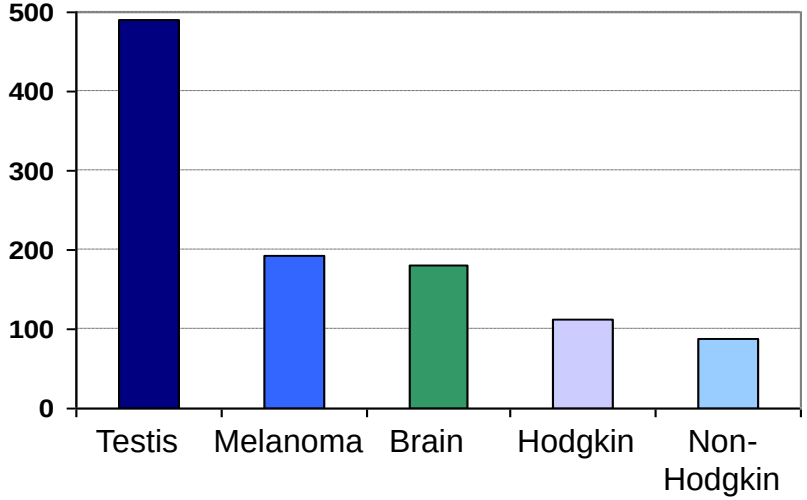
MALES

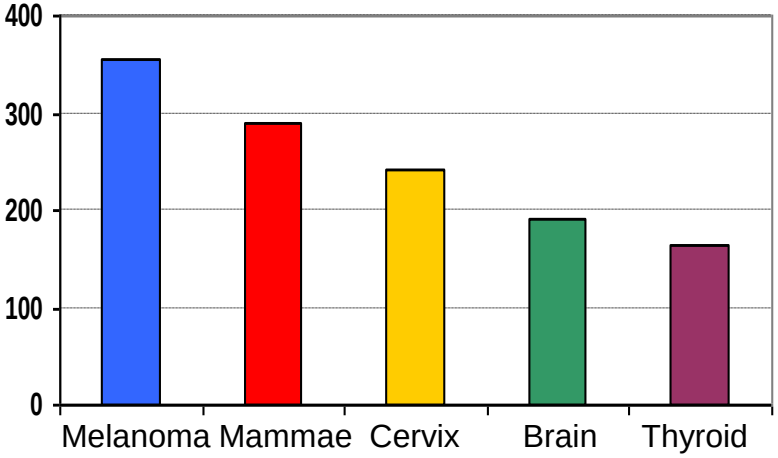


FEMALES



NORDCAN 2011 (15-34 years)



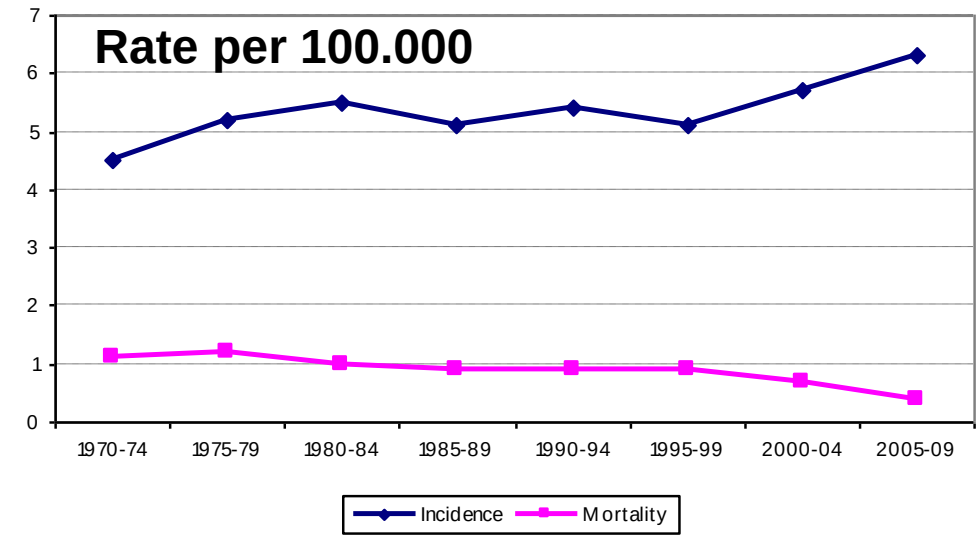


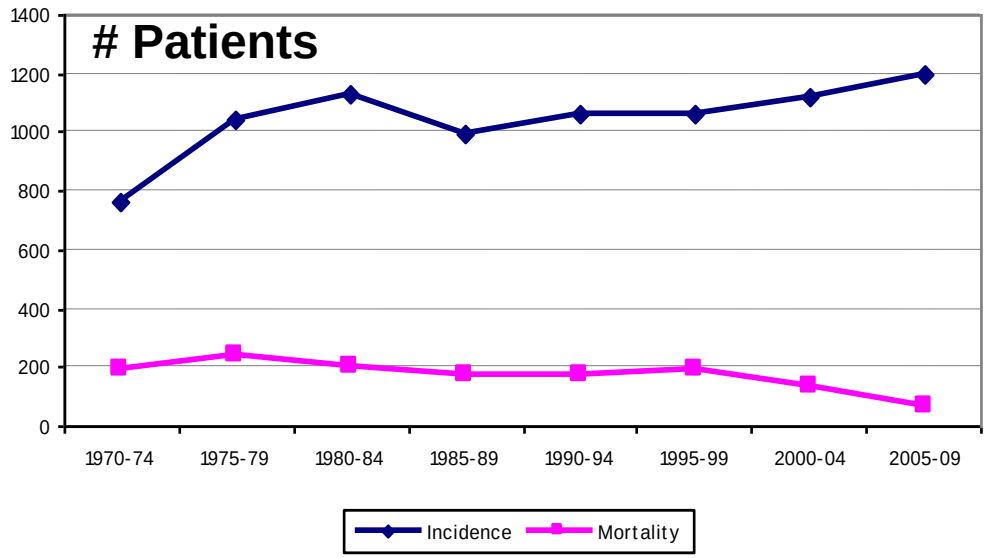
Selected cancer sites

*most common among AYAs

*of special interest among AYAs

NORDCAN: Cancer mammae (15-34)
Incidence (–) Mortality (–)





~1200

<100

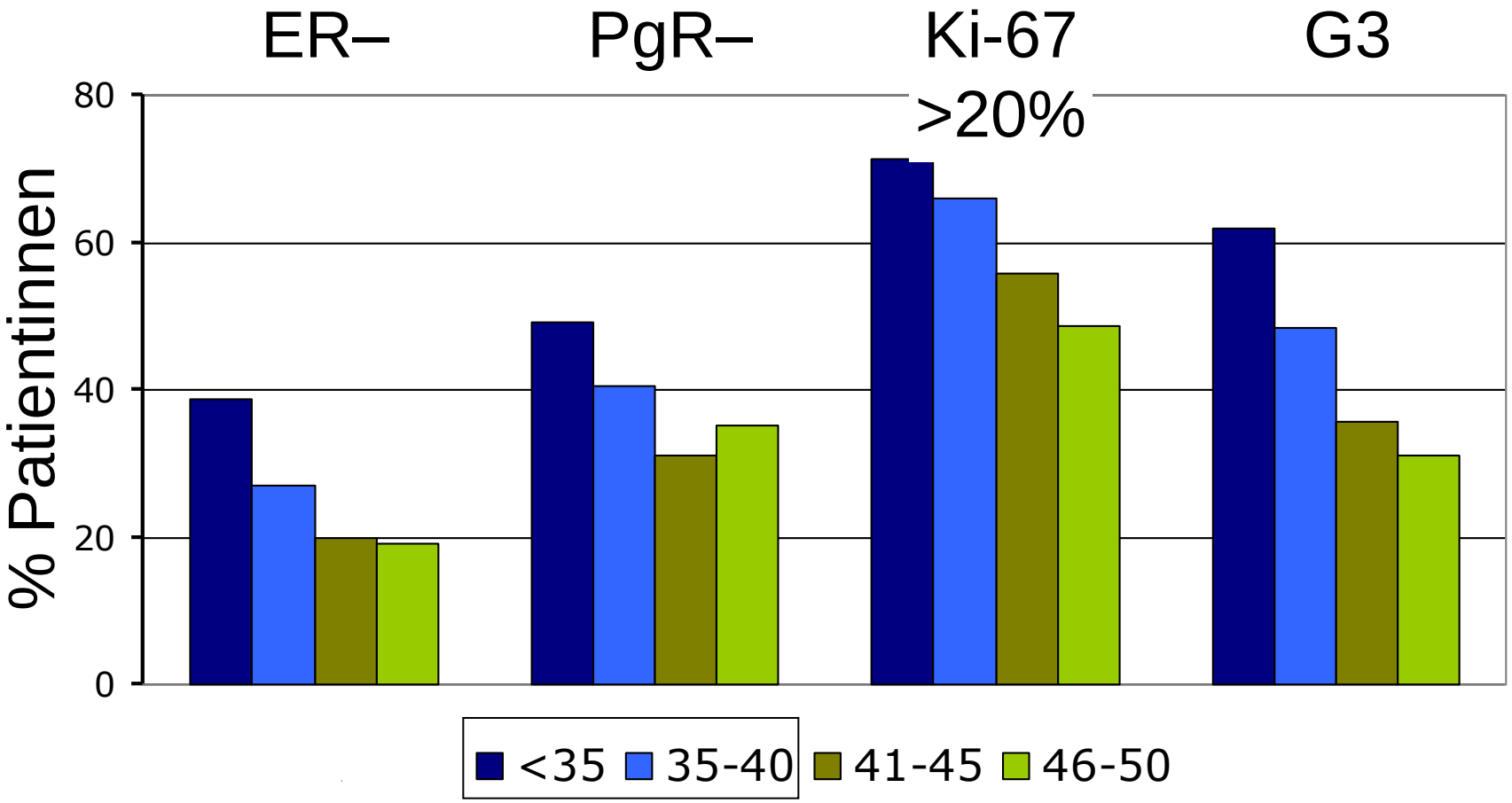
AYAs: Breast Cancer
(Age 15-39 years)

	Risk factors		
Presentation	**Clinical**	**Germ line genetics**	**Molecular biology**
Stage II ↑ Triple negatives ↑ Higher grade ↑ HER+ ↑	Family history Prior thoracic radiotherapy	BRCA 1 BRCA 2 (Polygenetics)	Early results to be confirmed (Myc pathway,mRNA expression) HER2+: Trastuzumab

→ Known risk factors more frequent in AYAs, but not specific for AYAs, occur also in older women

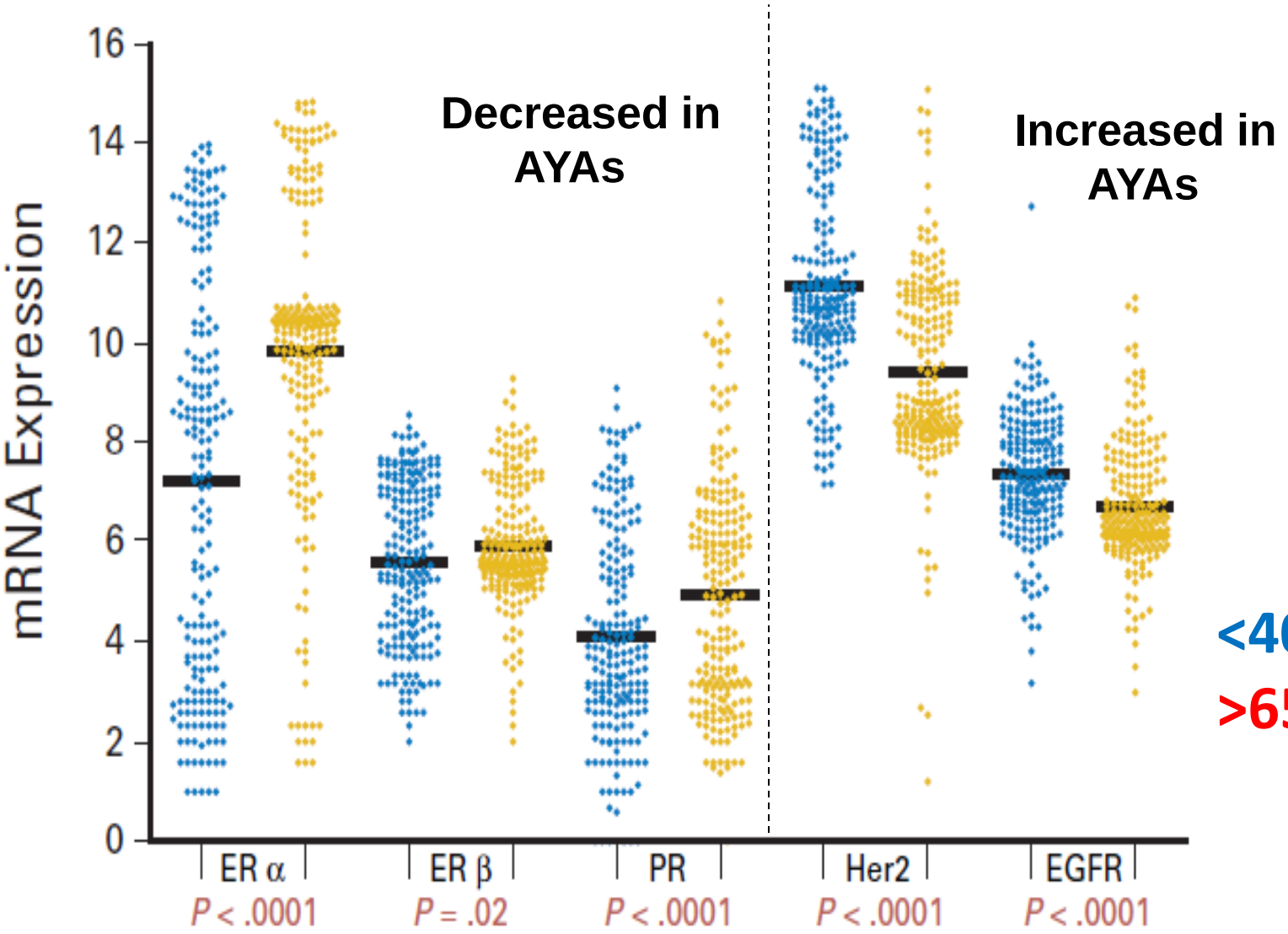
Tichy, JNCCN,2013;11,1060
Tricoli, JNCI,2011;103,628

Ca. mammae: Immunohistochemistry and age



Colleoni Ann Oncol 2002 13 273

Ca. mammae: Gene expression and age



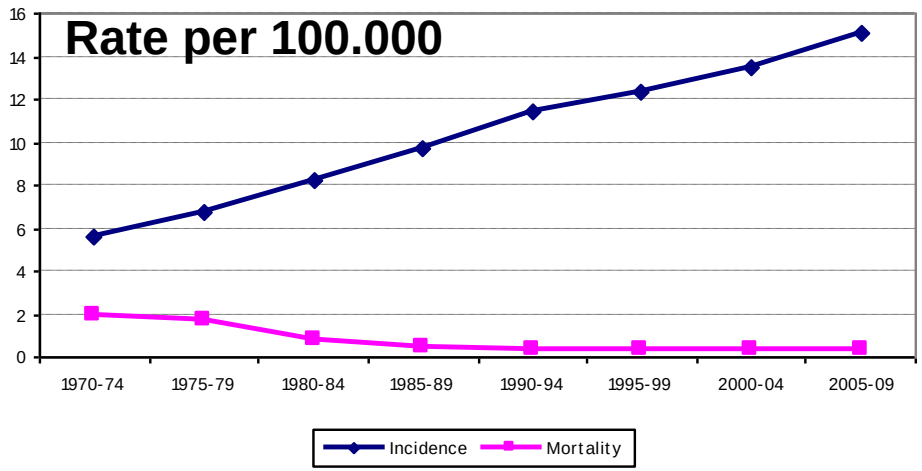
Age:

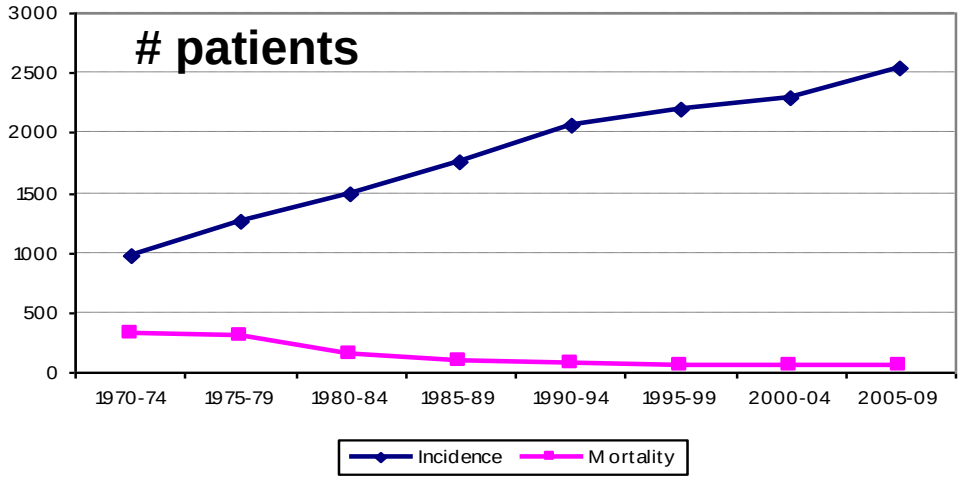
<40 (N:200)

>65 (N:211)

Anders JCO 2008 26 3324

NORDCAN: Cancer testis (15-34)
Incidence (—) Mortality (—)





~2500

~100

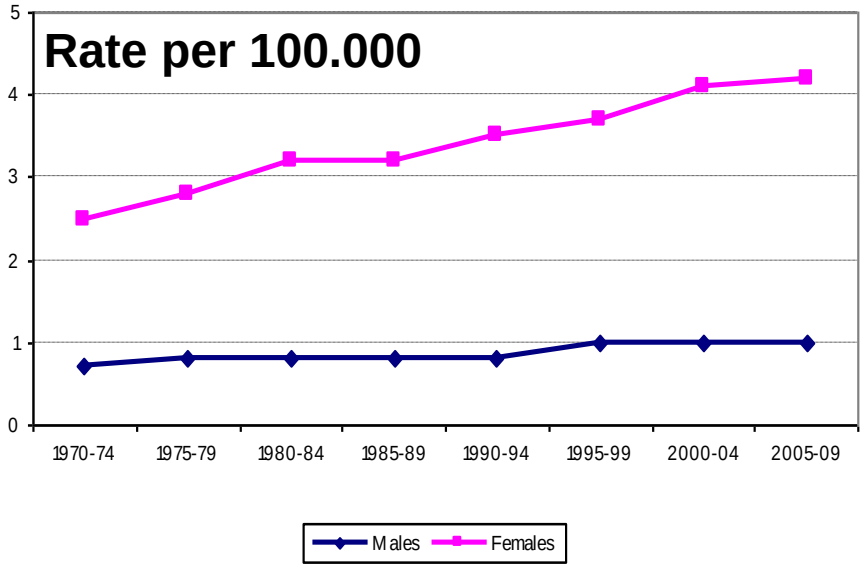
AYAs: Testicular Cancer

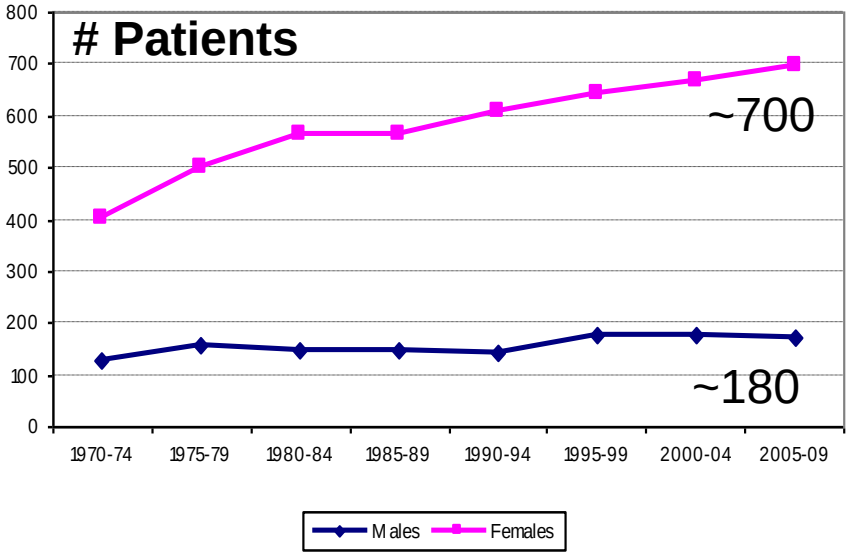
	Risk Factors		
Presentation	**Clinical**	**Germ line genetics**	**Molecular biology**
- Non-seminoma more frequent than seminoma - Metastases ↑	- Family history - Infertility - Cryptorchidism - Testicular atrophy - Inguinal hernia - Prior extra-gonadal germ cell tumor - Prior unilateral testis cancer -Microlithiasis	Not recognized	KIT ligand (no therapeutic consequence) Isochromosome p12 (i12p) → Diagnostic Importance

Hayes-Lattin B, Sem.Oncol.2009;36,432

NORDCAN: Ca. thyroideae (15-34)

Incidence





Mortality

Rate: Unchanged from 0.0 in 1970/74 to 2005/2009

 # Deaths: 1970/74: Males: 5 Females: 6
2005/09: Males: 1 Females: 3

AYAs: Thyroid Cancer*

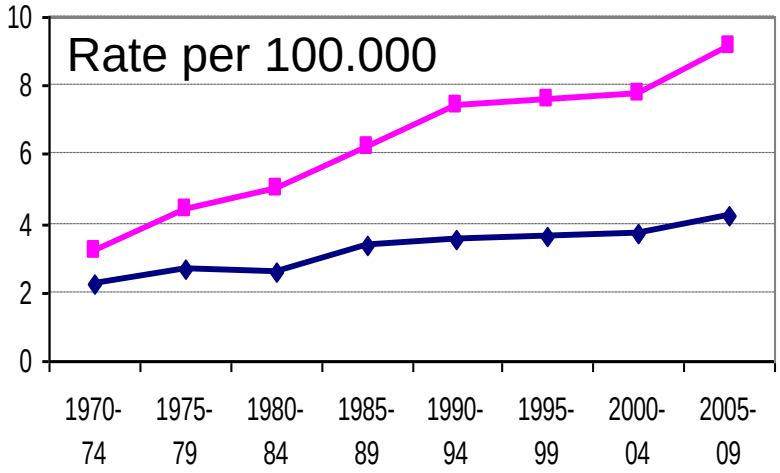
	RISK Factors		
Presentation	**Clinical**	**Germ line genetics****	**Molecular biology**
Males/Females 1:6.6 (USA) Medullary Differentiated (DTC): 95% - Papillary (PTC) - Follicular (FTC) - Thyroglobulin(TG)-producing	-Radiation exposure (therapeutic, diagnostic, A-bomb)	- Familial medullary cancer (MEN2a/2B) -Familial non-medullary thyroid carcinoma (FNMTC) - Gardner syndrome (APC) - Cowden syndrome (PTEN) - Werner syndrome (RECQL2) - Carney Complex (PRKAR1a)	RET mutations RAS/BRAF mutations RET/PTC rearrangements EGFR → So far without therapeutic consequence

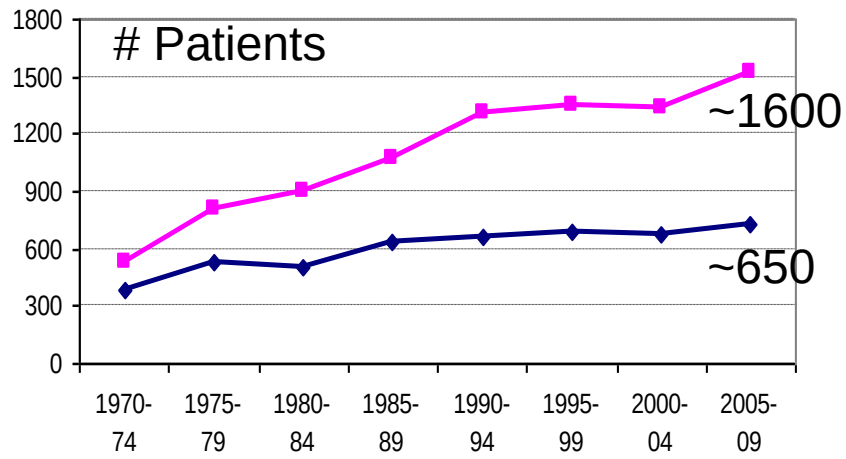
*USA: 28% of all thyroid malignancies are AYA tumors,**prophyl. thyroidect.

www.co-otolaryngology.com 2013;King, Sem.Oncol.2009;36,258

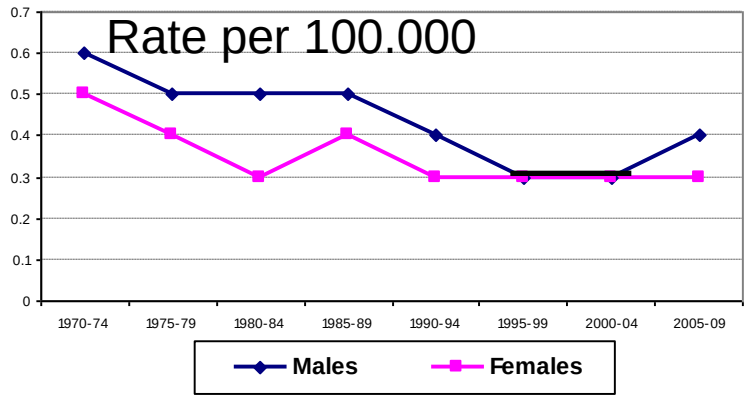
NORDCAN: Malignant melanoma (15-34)

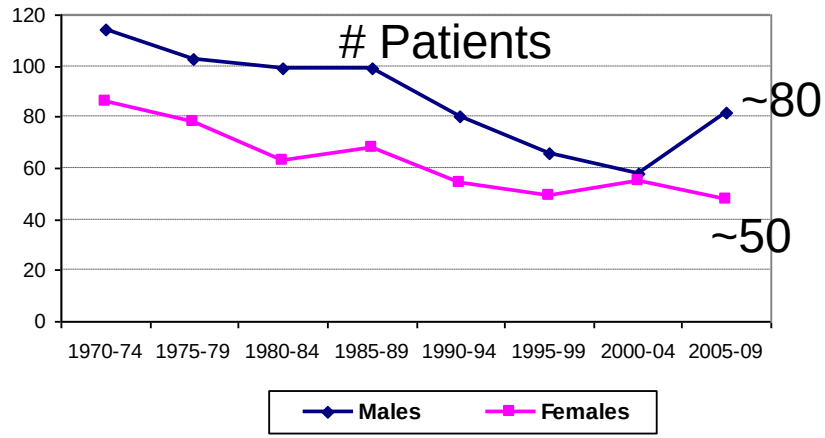
Incidence





Mortality





AYAs Malignant melanoma (15-34)*

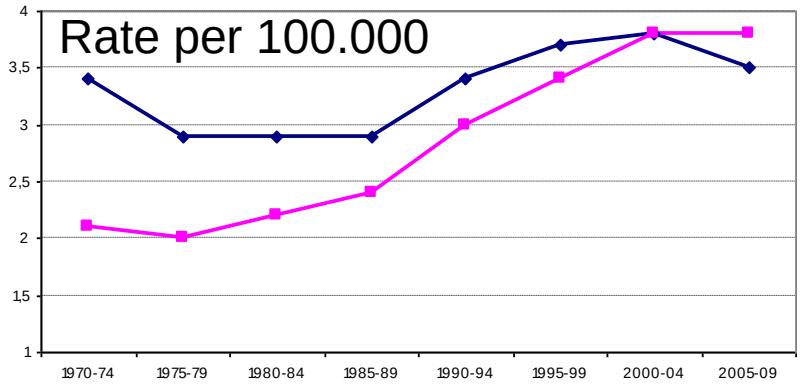
	Risk Factors		
Presentation	**Clinical**	**Germ line genetics**	**Molecular biology**
Delayed diagnosis Trunk localization	- Intermittent sun exposure -Immunocompetence↓ -Organtransplantation - Post-chemotherapy - Multiple melanocytic nævi >2 mm - Fair complexion - Facial frekling - Family history - Inability to tan	- Melanocytic neurocutaneous melanosis - Xeroderma pigmentosum -Werner's syndrome - Retinoblastoma survivors -Survivors after ca.testis	RAS/RAF/MAPK signaling pathway ↓ Targeted therapy

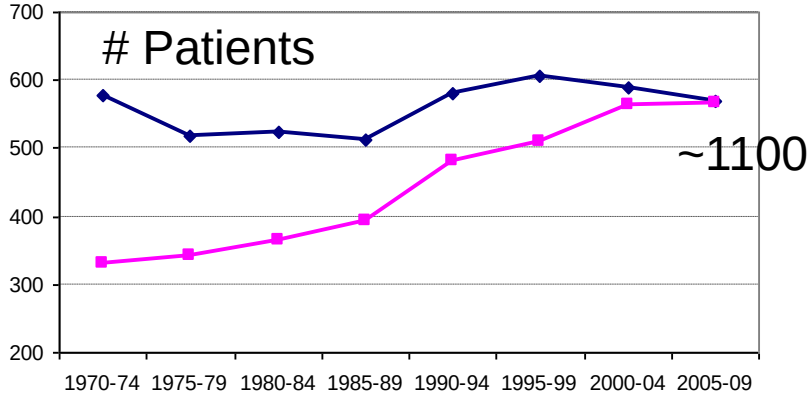
*~15% of all AYA tumors

Ferreira, Curr.Oncol.Rep.2013;15,287

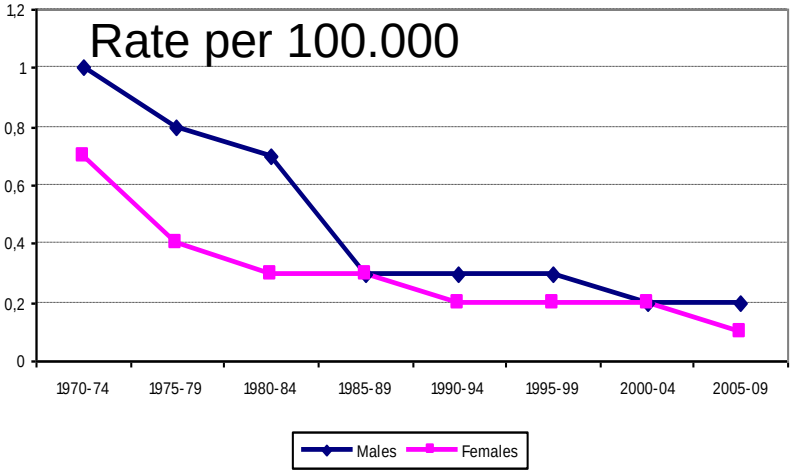
NORDCAN: Hodgkin lymphoma (15-34)

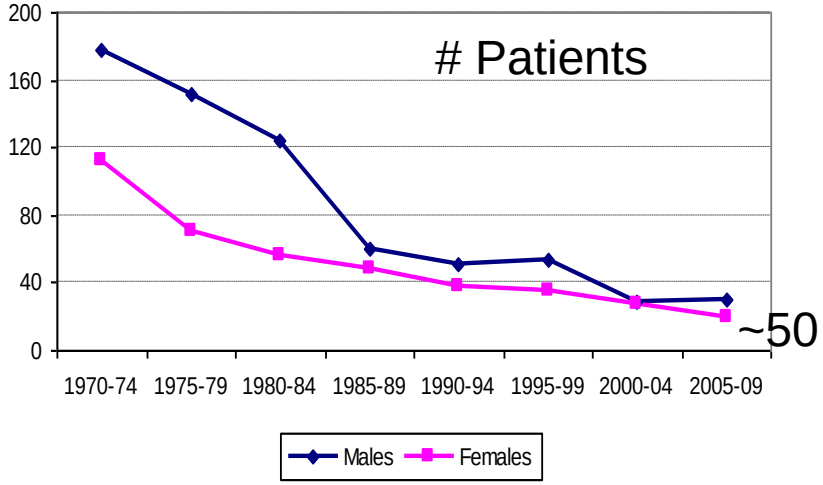
Incidence





Mortality





AYAs: Hodgkin lymphoma (15-34)

	Risk Factors		
Presentation	**Clinical**	**Germ line genetics**	**Molecular biology**
Histological subtypes: Dominant: Nodular sclerosis	- High socioeconomic development - EBV infections -Mononucleosis -HIV infection -Cigarette smoking?	-Monocygotic twin studies -Ethnic differences -HLA alleles (class I, II and III) -Rare familial mutations (NPAT)	No specific findings in AYAs

AYA: Acute lymphoblastic leukemia (ALL)

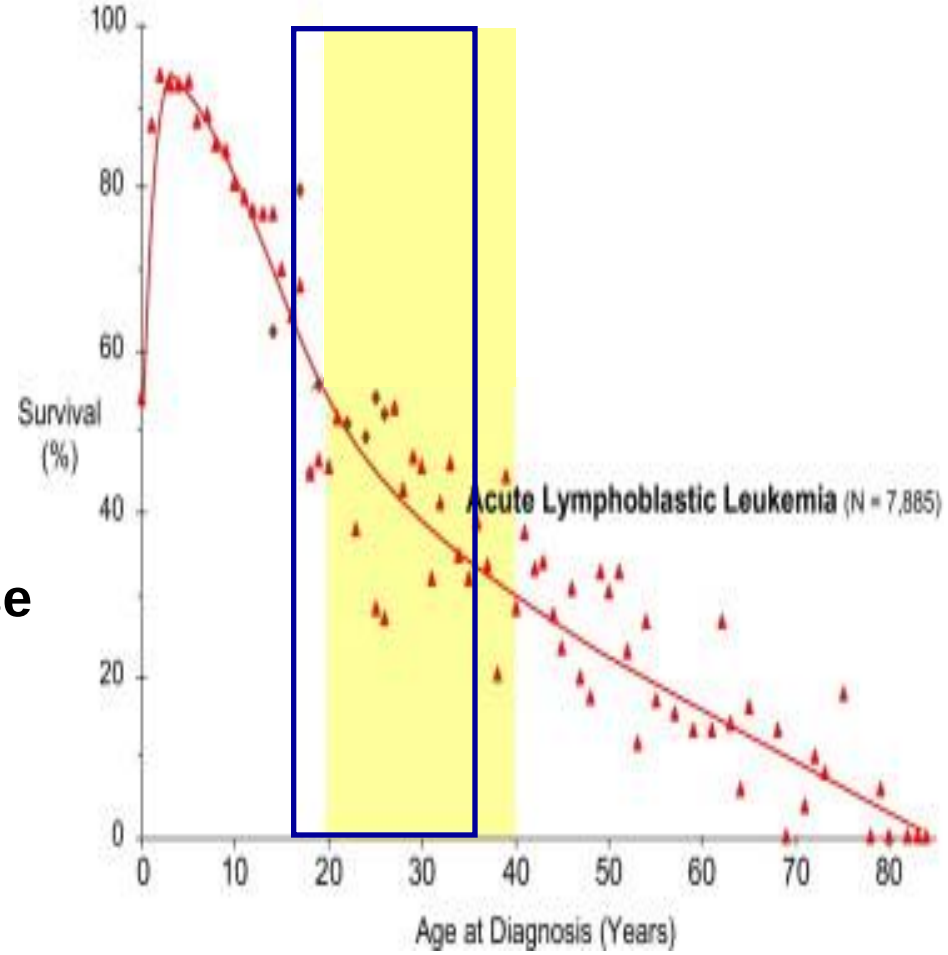
AYA compared to children

- Higher incidence of poor prognosis cytogenetic features

- Lower incidence of favorable cytogenetic features

- **Poor tolerance of asparginase**

- **Adult vs Pediatric treatment protocols**



Tricoli, JNCI.2011;103,628
Bleyer, Sem.Oncol.2009;36,380
Rusell ,JCO 2014 : 32 ,1453

Conclusion (1a)

International consensus for future reports

Pediatric
Adolescent
Young Adult
} Malignancies

if age classification is retained

Conclusion (1b)

No indications that AYAs display any age-specific clinical or molecular-biological risk factors or disease parameters

BUT

Unfavorable risk factors , also observed in older or younger patients, are more often present in AYAs

(Should age persist as an important risk factor?)

However, treatment of AYAs may be particularly challenging as they have reached an extremely vulnerable and unstable phase of their lives

Conclusion (2)

Improved national and international co-operation and protocols for experts treating these patients

ENTYAC European Course

- To create a European Multidisciplinary Framework and network for TYA Cancer
- To promote and develop TYA multi professional education
- To improve the access to clinical trials for TYA
- To develop a European TYA research initiative
- To promote healthy lifestyles in TYA population and cancer survivors
- To establish links to patient and support organisations

Conclusion (3)

Comprehensive cancer centers in Europe:

Intensified

epidemiological, clinical and translational research

needed in AYAs,

including life-time medical and psychosocial outcome

THANK YOU!