Epidemiology of AYA tumours

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Summary

- Why we should study the epidemiology of AYA tumours
- What is already known
- What is not already known and is important
- Where to go from here

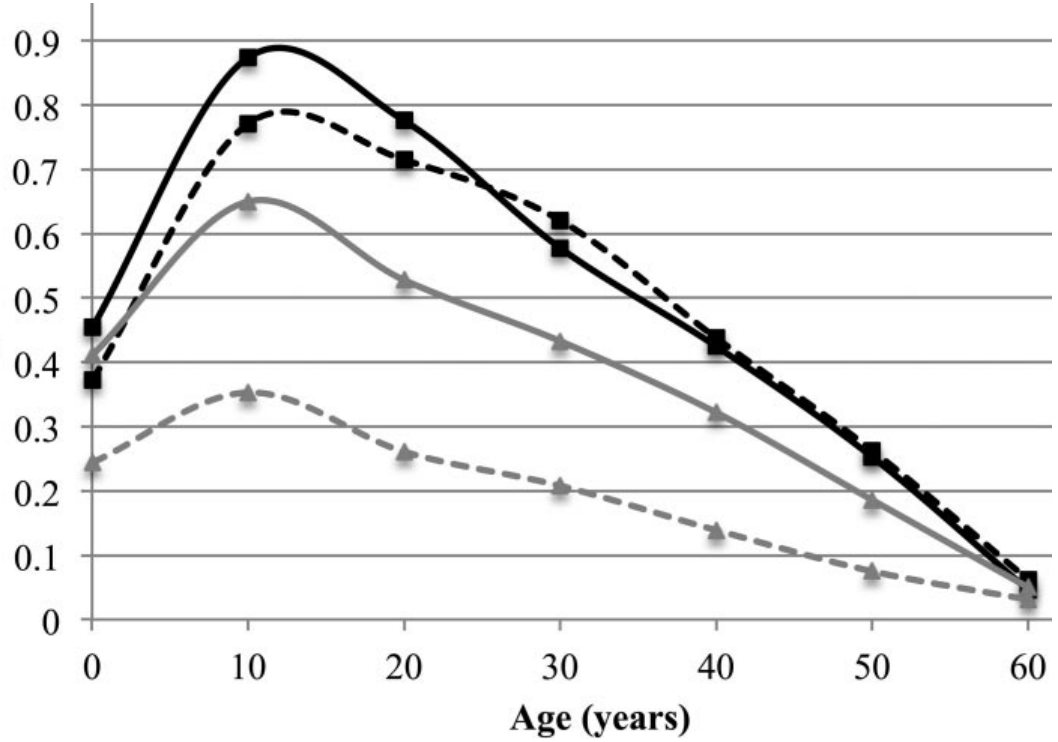
Why to study this

We need to understand epidemiology

1. To design services that meet public health needs
    - Volumes of patients to treat
    - Skill-mix required to treat them
    - Structure of services
2. To identify patterns that might tell us the causes, outcomes and remaining unmet healthcare needs in AYA with (or after) cancer

Huge privilege to treat TYA with cancer

- Not only my view
- Asked range of choice scenarios and interviews with US public, forcing them to make choices between people of different ages
  - Healthcare – e.g. blood, organ
  - Adverse event – e.g. accidental injury
- 'Tease out' relative value by age, and why these were the decisions



Hard line = positive and dotted = negative framing
Dark line = people's societal value, pale line = people's rights

Goodwin and Landy. **Valuing Different Human Lives** J.Exp Psychol 2013

Why?

1. TYA's social relationships are numerous and meaningful – illness is such a sad event.

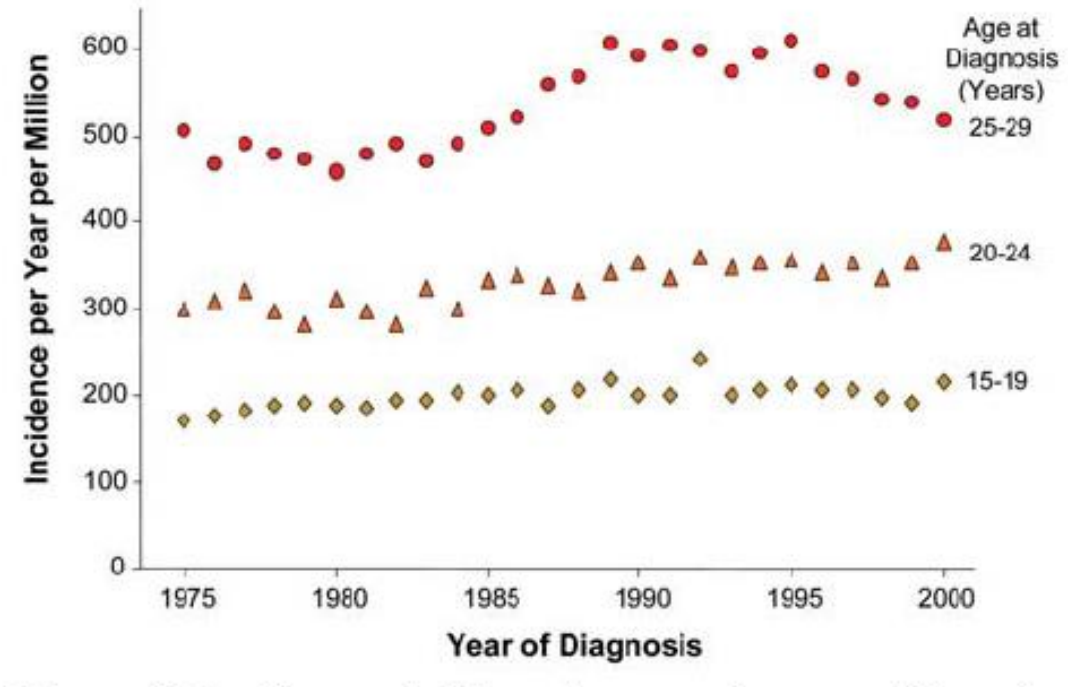
Other reasons much less important, but were

2. Societal investment in TYA
3. TYA understand and may fear death, while having limited experience
4. Years of quality life lived/left

Table 1. Distribution of people aged 15–39 years in Europe in 2014

Age group, years	Number	Percentage (/total population)
15–19	27,162,572	5.4
20–24	30,229,721	6.0
25–29	32,166,058	6.3
30–34	34,014,208	6.7
35–39	35,086,745	6.9
15–39	158,659,304	31.3

Epidemiology
Absolute numbers of cases



50% higher annual incidence comparing adolescents to younger children, and 50% higher again comparing adolescents to young adults.

Incidence

- Rare
  - Annual rate: 66,000 cases annually in Europe
  - c.25,000 deaths.[1]

But

- Among 15– 24 years aged AYAs, cancer is the leading disease related cause of death and ranks third as the most significant cause of mortality in young people in Europe (10% of deaths, about 2,000 deaths annually)
  - behind
    - road traffic injuries (46%, 10,500 deaths annually)
    - suicides (24% of deaths)
- Among those of 25–39 years, cancer is the second leading cause of disease-related cause of death (13% of deaths)
  - behind cardiovascular disease (15% of deaths)

Which cancer types?

Classification

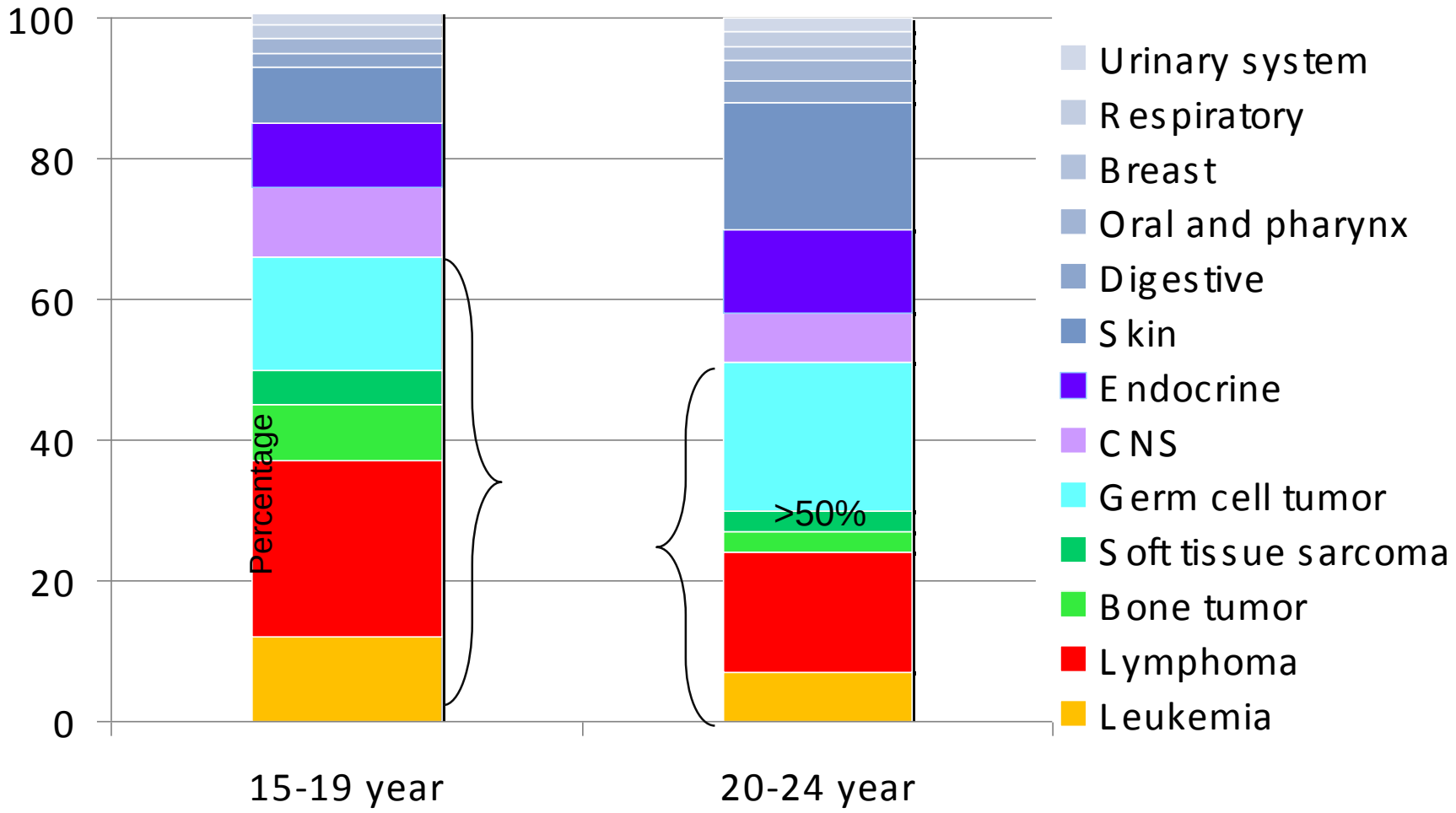
AYA tumours are not best classified using an adult cancer classification system which is tumour primary-site specific.

In contrast, they may be classified by a pathology-driven approach.

Tumour group	Definition
Group 1	Leukaemias
Group 2	Lymphomas
Group 3	CNS tumours
Group 4	Bone tumours
Group 5	Soft tissue sarcomas
Group 6	Germ cell tumours
Group 7	Melanoma and skin carcinoma
Group 8	Carcinomas (except of skin)
Group 9	Miscellaneous specified neoplasms (including embryonal paediatric tumours)
Group 10	Unspecified malignant neoplasms

Birch JM *et al*. Br J Cancer 2002;87(11):1267-74

Distribution of cancer types in AYA



Pritchard-Jones K *et al*. Lancet Oncol 2013;14(3):e95-103

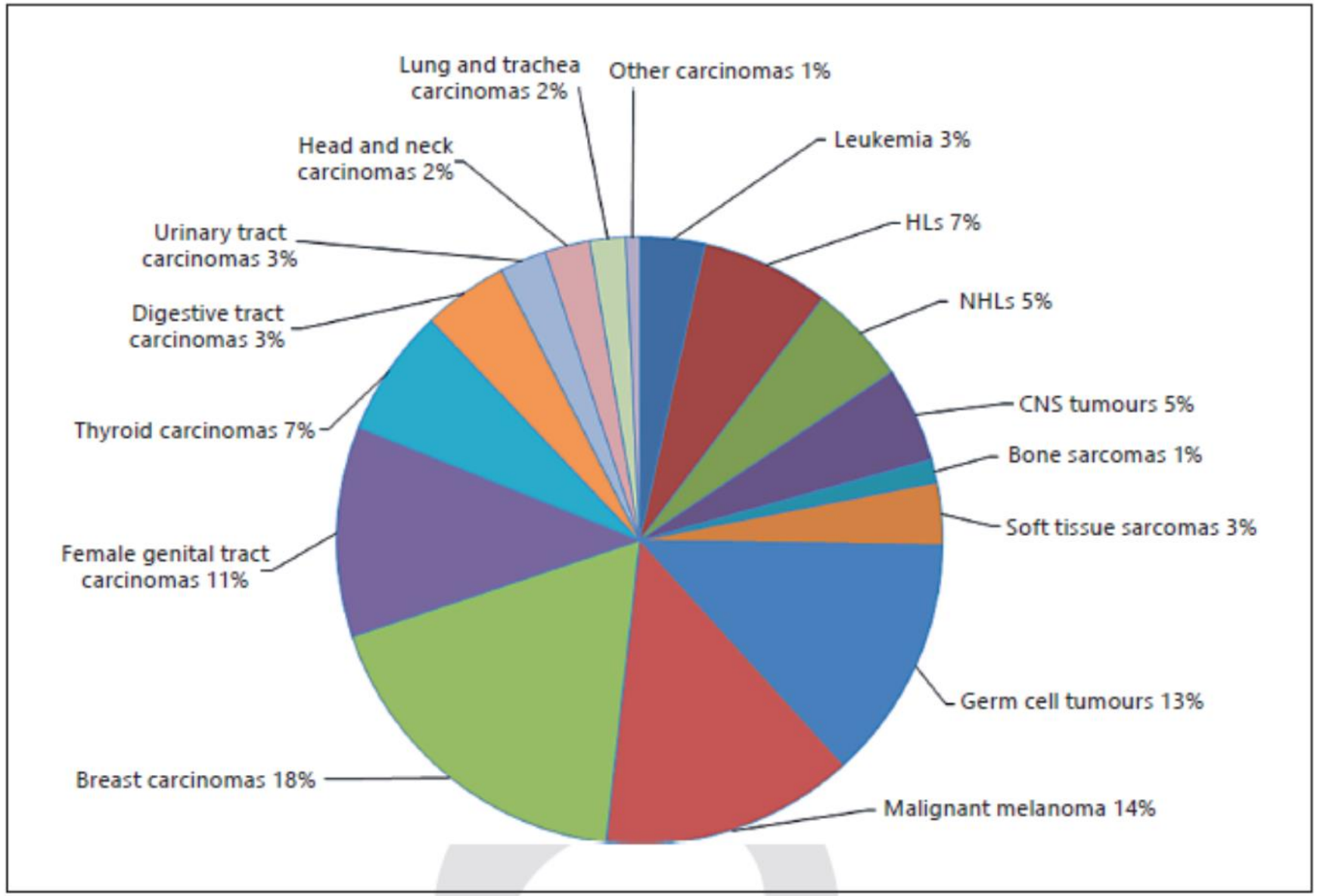


FIg. 2. The distribution of cancer in 15–39 years of age Europeans by main diagnostic group EUROCARE-5.

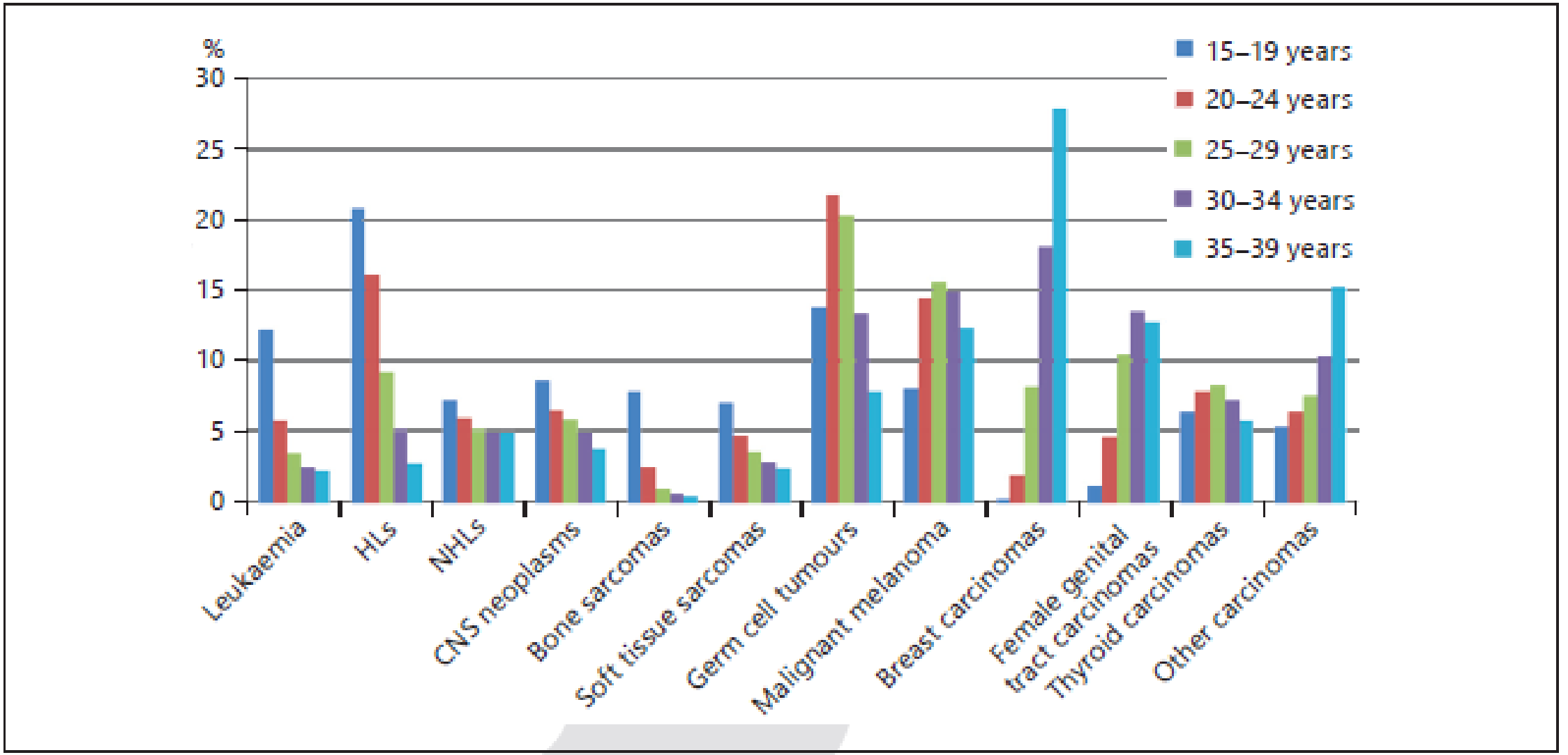
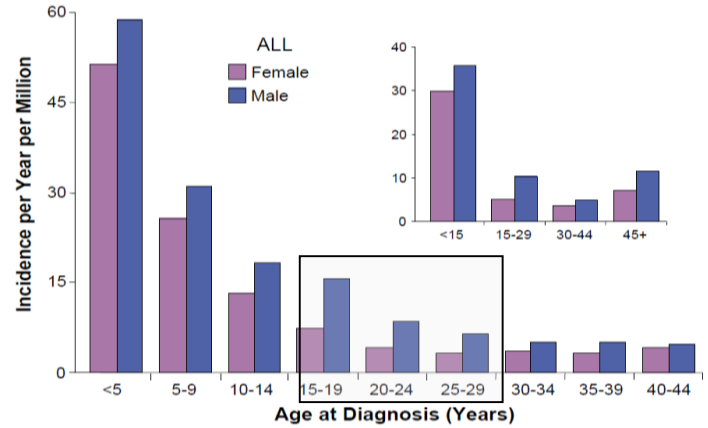
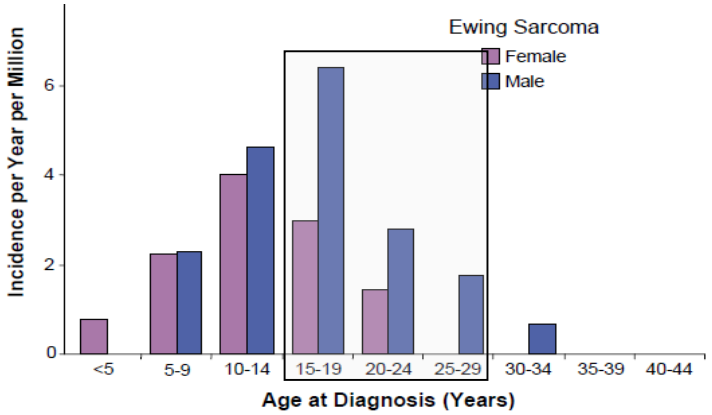


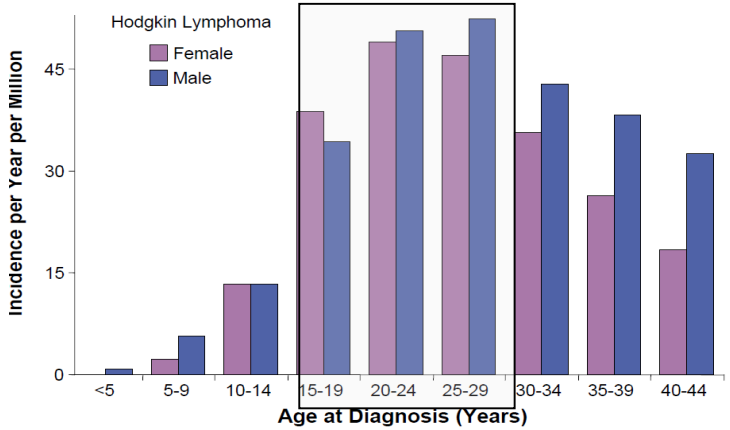
Fig. 3. The distribution of malignant disease among AYAs by main diagnostic group and age group EUROCARE-5.

No diseases begin or end at age 18 years [1]

But: In many countries the age of 18 defines the beginning of adulthood, with important biological (physical and gonadal maturation) and clinical (legal independence and ability to sign consent form, insurance coverage for treatment in adult services) implications.







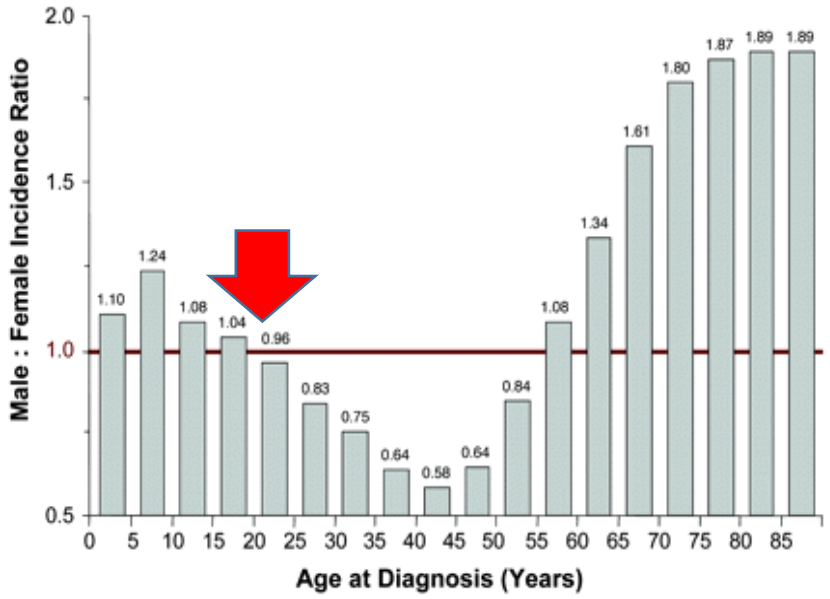
[1] Sallan S. Hematology 2006;128-132
Graphs: Cancer Epidemiology in AYA, SEER

Epidemiology: Not an adult, not a child

- Hodgkin's disease (HD) and Germ-cell tumours present 3-6 times more frequently in adolescents than in the pediatric population.
- Epithelial carcinomas, nasopharyngeal carcinomas, thyroid cancer and melanomas are seen in AYA.
- NHL and CNS tumours are almost as common in adolescents as in childhood.
- ALL is less frequent, whereas osteosarcoma is most frequent in AYA.
- Embryonal Rhabdomyosarcoma, Wilms Tumours, and neuroblastomas are rarely seen true "pediatric type" tumours occurring in AYA.
- Epithelial tumours (breast, colon, cervical etc) are seen in adolescents but significantly more often in young adults.

Bleyer A *et al*. Oncologist 2006;11(6):590-601

Epidemiology and sex



Slightly higher incidence in males

More common in males:

- ALL
- NHL
- Ewing/PNET
- Osteosarcomas
- CNS

More common in females:

- Thyroid cancer
- Melanoma
- Hodgkin's disease

Bleyer A *et al*. Oncologist 2006;11(6):590-601

Aetiological associations

- Leukaemia in young childhood has been strongly linked with an infectious aetiology
  - Much more pronounced male leukaemia excess between the ages of 15-29 years compared to both younger children and older adults- biologically distinct within AYA ?
  - Male hormonal factors may also be implicated
    - Higher incidence rates in males occur during the adolescent growth spurt.
- The role of viruses has been linked to the development of HL and NHL, including Epstein-Barr virus (EBV), HIV1 and HTLV1 [34-35].
  - Polyoma viruses such as the BK, JC and simian virus 40 may also be involved in the aetiology of specific CNS cancers
  - nasopharangeal carcinoma within south-east Asian countries with clear associations attributable to EBV infection
  - The herpes simplex virus type 2 and human papilloma virus have been associated with the onset of carcinoma of the uterus and cervix in young women
- Germline
  - CNS tumours APC and TP53 mutations - medulloblastoma, glioblastoma and anaplastic astrocytoma
  - Genetic factors are almost certainly involved in the aetiology of Ewing sarcoma
    - incidence rates in black populations are tiny
    - Osteosarcoma and soft tissue sarcoma have both been reported in families with germ-line TP53 mutations
  - Breast cancer , including Li-Fraumeni syndrome
  - STK11 mutations in Peutz-Jeghers syndrome and PTEN mutations in Cowden syndrome
  - Neurofibromatosis (*NF1 and NF2*)
  - Xeroderma pigmentosum (*XP*)
  - Ataxia-telangiectasia (*ATM*)
  - Fanconi pancytopenia

Environmental exposures

In rare cases environmental factors have been observed in the pathogenesis of AYA cancer:

- Clear-cell adenocarcinoma of the vagina or cervix (Maternal exposure to diethylstilbestrol during pregnancy)
- Second primary tumours (childhood exposure to chemo-radiation)

Aetiological associations 3

- Bone and soft tissue sarcoma, especially osteosarcoma, may be related to growth during adolescence
  - Specific bony sites are those which undergo the largest growth
  - Sex pattern reflects age at puberty
  - AYAs presenting with osteosarcoma and Ewing sarcoma might be taller than the non-cancer population
    - diet, physical activity, hormones?
  - Postnatal growth has been implicated in the onset of testicular GCTs
    - adult height shown to be associated with an increased risk
- Melanoma of skin - extended exposure to sunlight and ultraviolet radiation.
- However

The vast majority of cancers in AYA are sporadic events of unknown etiology.

Those managing AYA cancers need expertise in taking a full family history

Survival

Table 3. The 5-year survival estimates (%) by age at diagnosis and sex for all cancers combined diagnosed in Europe in 2000–2007, EUROCARE-5 [13]

Age at diagnosis, years	5-Year RS, %		
	male and female	male	female
15–19	79.5	77.4	82.0
20–24	83.3	81.5	85.4
25–29	83.6	83.2	84.1
30–34	81.7	80.0	82.8
35–39	78.7	73.9	81.3

Table 2. Five-year relative survival with standard error within the major diagnostic groups for European AYAs diagnosed in 2000–2007 inclusive, EUROCARE-5, compared to younger children with diseases in the same groups [13]

Diagnostic groups	AYAs		Children (0–14 years)	
	5-year RS, %	SE	5-year RS, %	SE
Leukemia				
Acute lymphoid leukemia	55.7	0.9	85.8	0.4
Acute myeloid leukemia	49.7	0.8	60.5	1.0
Lymphoma				
HL	92.9	0.2	95.1	0.5
NHL	77.4	0.4	83.0	0.9
CNS tumors	56.7	0.5	57.2	0.6
Medulloblastomas	69.3	2.3	63.2	1.3
Embryonal tumors	60.5	2.0	56.3	1.1
Astrocytomas	46.5	0.7	61.9	1.1
Bone sarcomas				
Chondrosarcomas	82.6	1.4	89.4	3.4
Osteosarcomas	61.3	1.5	66.8	1.5
Ewing tumor	49.3	1.8	66.6	1.5
Soft tissue sarcomas	69.8	0.5	69.3	0.9
Fibrosarcomas	81.4	1.9	83.8	3.6
Rhabdomyosarcomas	37.7	2.2	66.6	1.3
GCTs	94.7	0.1	91.5	0.8
Malignant melanoma	89.0	0.3	90.1	1.7
Carcinomas				
Thyroid carcinomas	99.2	0.1	–	
Breast carcinomas	83.5	0.2	–	
Urinary tract carcinomas	82.9	0.5	–	
Female genital tract carcinomas	81.6	0.3	–	
Male genital tract carcinomas	80.1	1.8	–	
Head and neck carcinomas	71.6	0.5	–	
Colon and rectum carcinomas	63.0	0.5	–	
Lung and trachea carcinomas	32.1	0.7	–	
Liver carcinomas	25.2	1.4	–	

Survival and age

Survival by geography

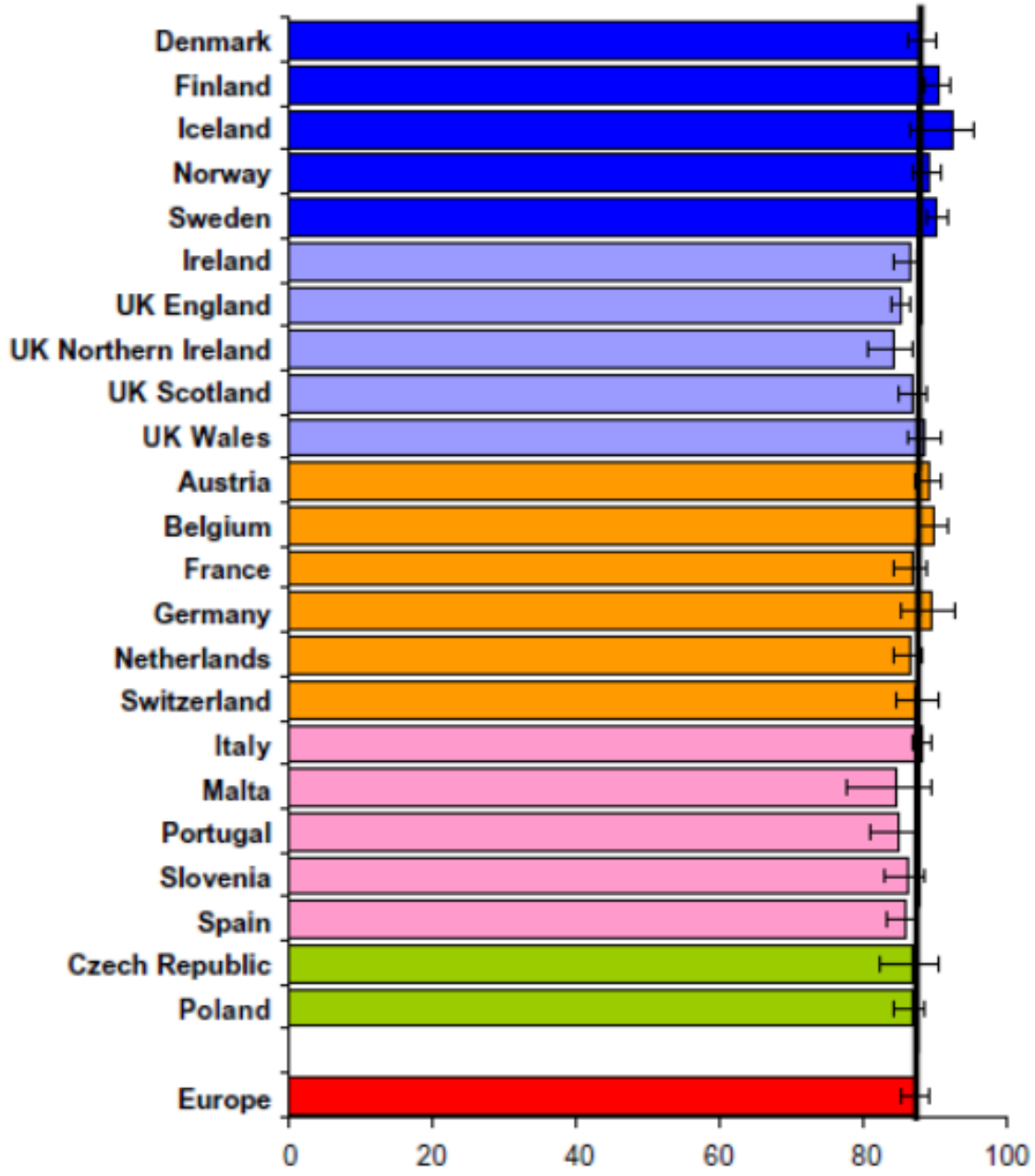


Fig. 2 – Five-year survival for all cancers combined, by country, in young Europeans (15–24 years) of both the sexes diagnosed in 1995–2002. The data are adjusted by age, sex, case mix and period of diagnosis using a Cox proportional hazards model.

Survival over time

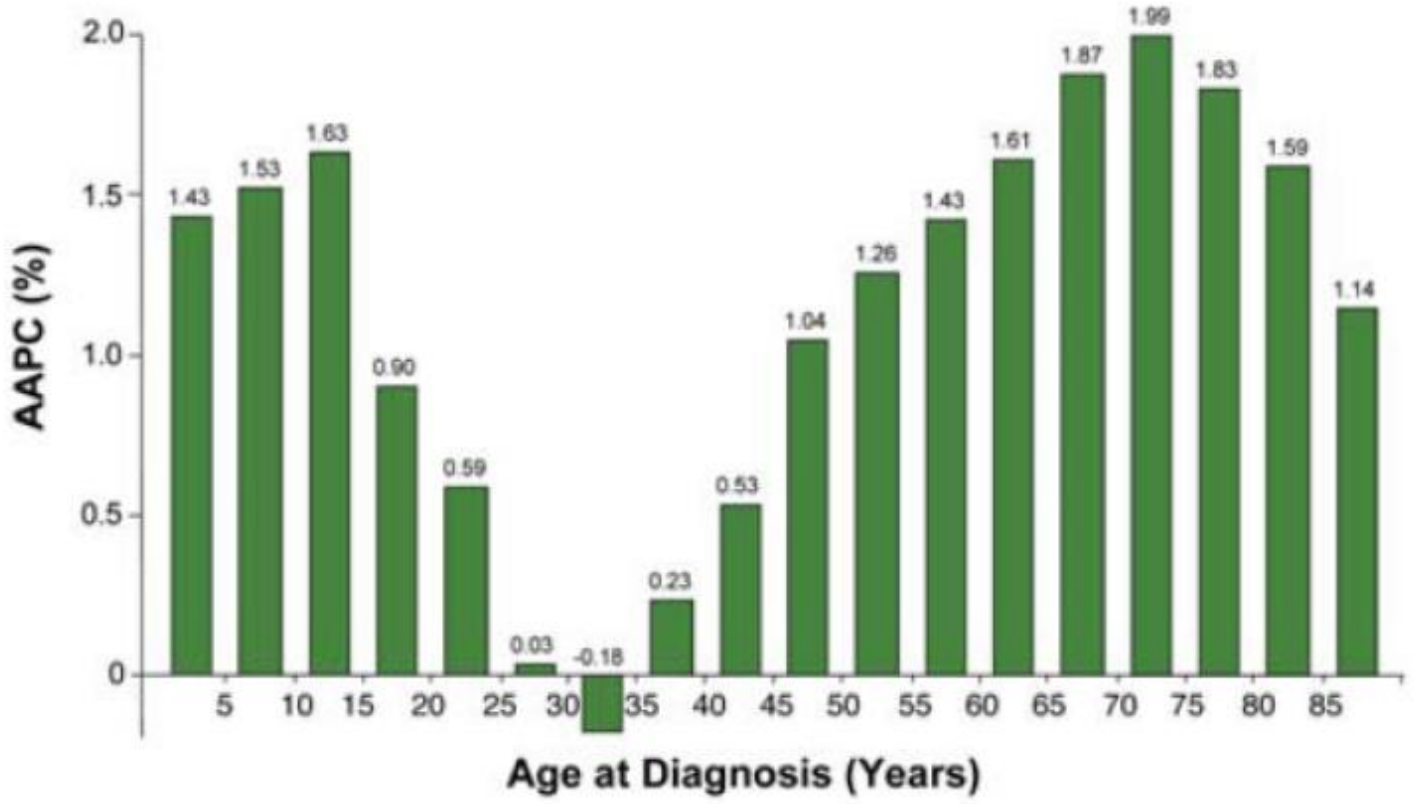
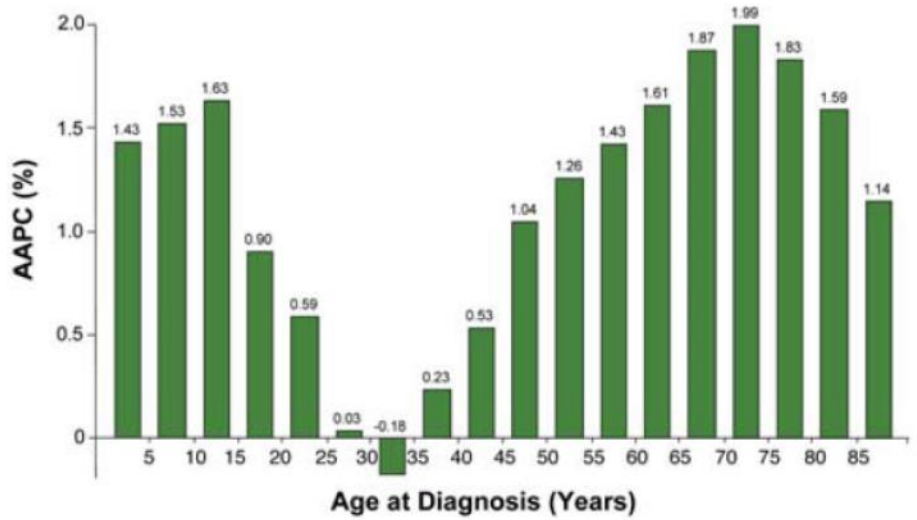


Figure 28. Average annual percent change (AAPC) in 5-year relative survival for all invasive cancers, SEER 1975–1997.

Survival over time



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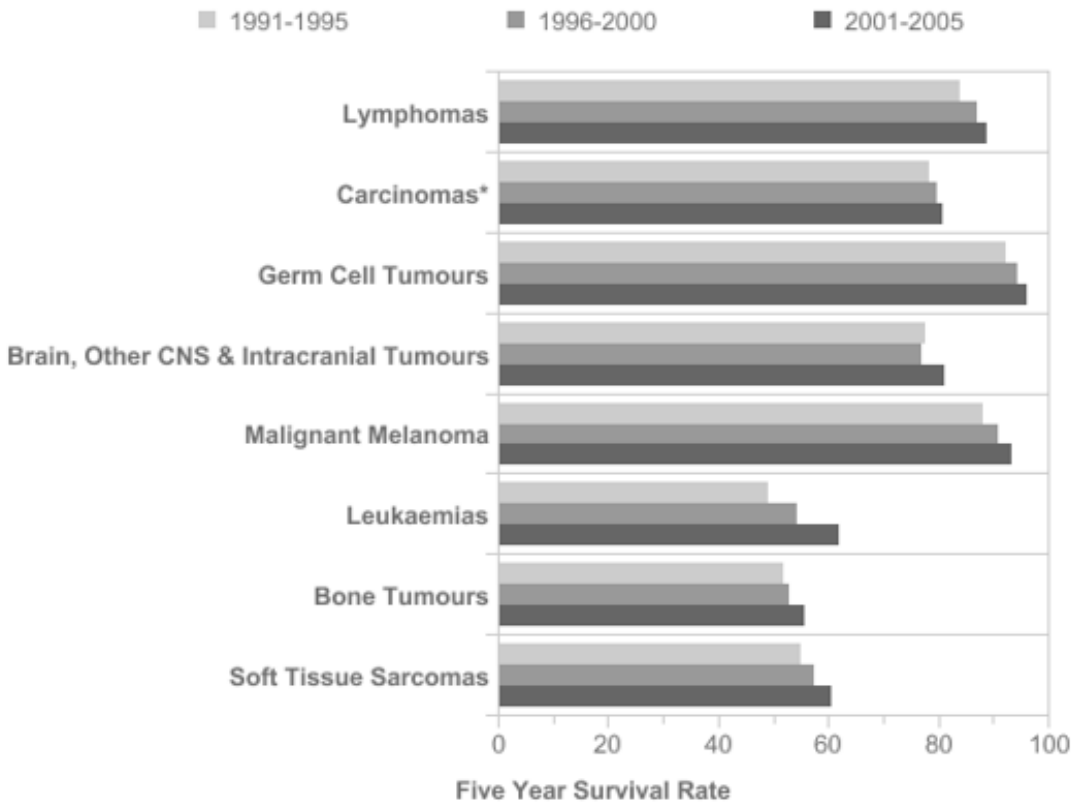
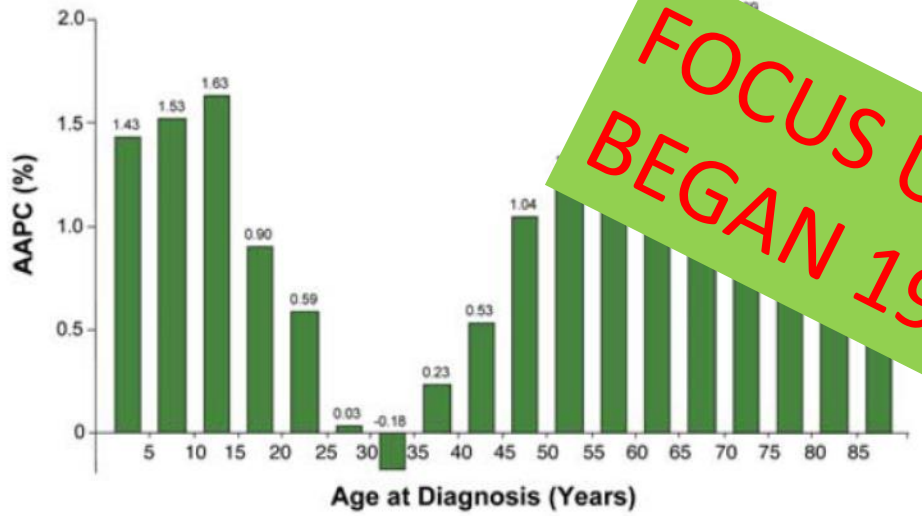


Figure 1.2: Five-year relative survival for AYA diagnosed 2000-2007 in Europe.

Survival over time



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FOCUS UPON TYA SERVICES BEGAN 1995

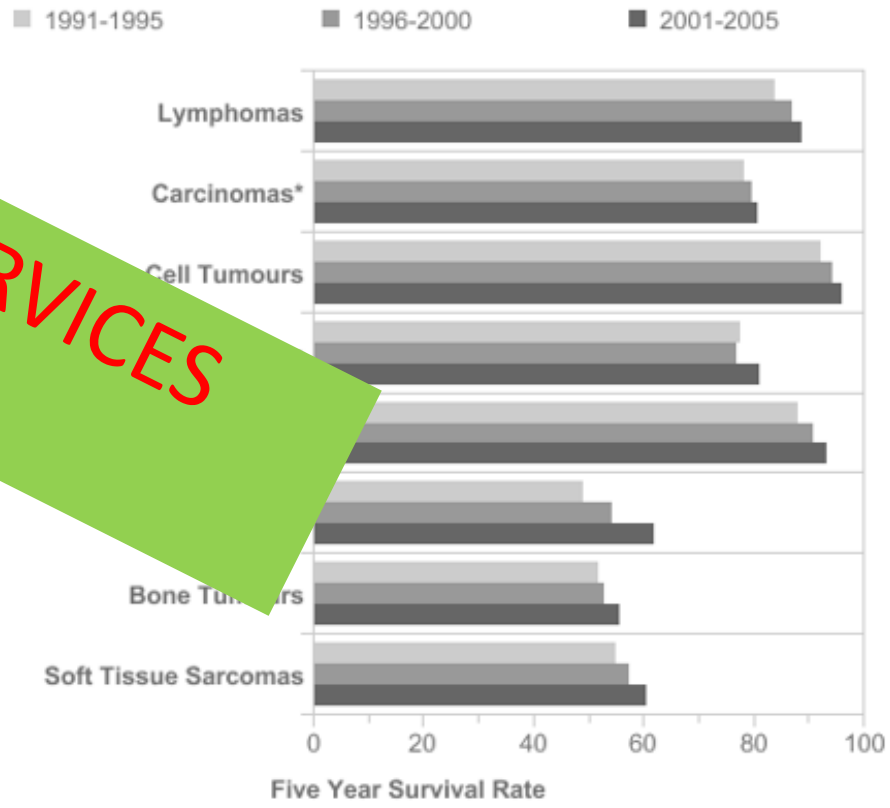

Figure 1.2: Five-year relative survival for AYA diagnosed 2000-2007 in Europe.

What is important and is not known

- Prevention techniques, especially for survivors of childhood cancer
- Biology of the developing tumour host

Summary

- Compared to older adults, the AYA cancer incidence is low. However
  - those effected have many years of life remaining to contribute to society, when successfully treated
  - for several cancers onset at this age is usual, including osteosarcoma, germ cell tumours and Hodgkin lymphoma
- A pathologically-driven (eg Ewing sarcoma, yolk sac tumour) is more useful than a ‘site-of-onset’ driven (eg chest wall cancer, testicular cancer) classification of AYA cancers.
  - This may well be the case soon for many other adult cancers as biological factors and biological target-specific therapies mature, such as in BRAF-positive melanoma.
- National variations in incidence should influence the local design of health services
- Tumours with higher mortality or variation in mortality by age or geography, represent key opportunities for improvement
  - BUT ONLY THROUGH clinical or biological research and the potential for biological or health services research to improve outcomes
  - When the AYA community began its research, then outcomes began to improve, slowly.
- A knowledge of the epidemiology can help the clinician recognise presentations at unusual ages, and direct clinicians to explore specific cases for unusual biology. Examples include a genetic predisposition in an adolescent breast adenocarcinoma or an unusual translocation in a Ewing Sarcoma in a 38 year-old AYA.
- A family history is a key skill for any clinician seeing AYA patients.