Childrens and Young Peoples Cancers

Multidisciplinary Team Coordinators Conference, Bristol

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Epidemiology

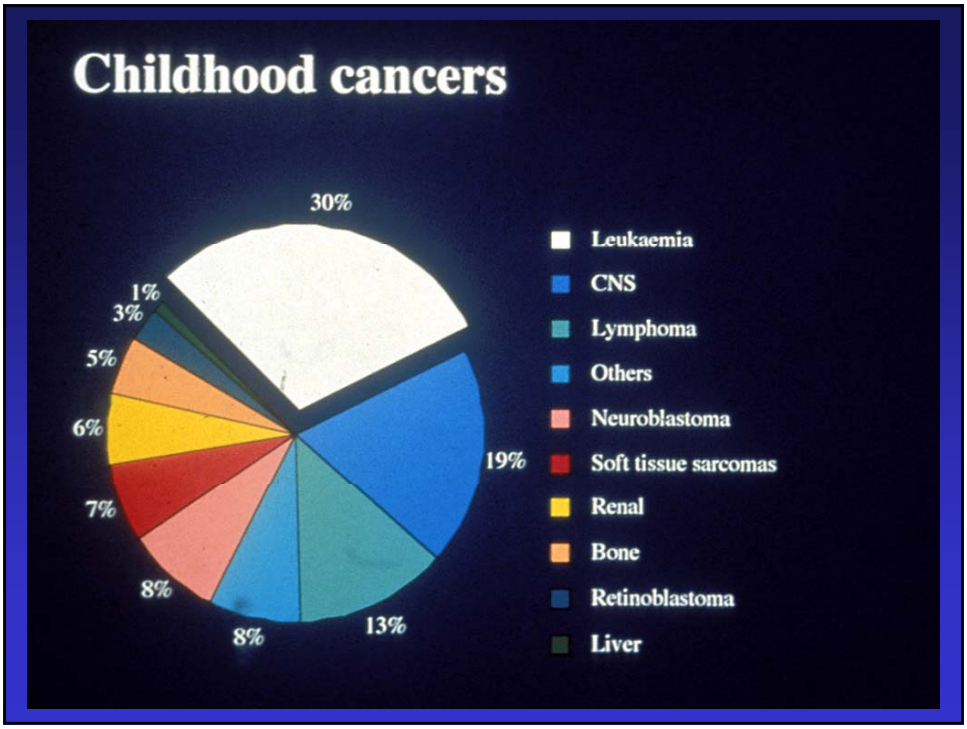
Cancer prevalence in adults:
1 in 3 lifetime risk

Cancer prevalence in children under 15:
1 in 700 children by age of 15

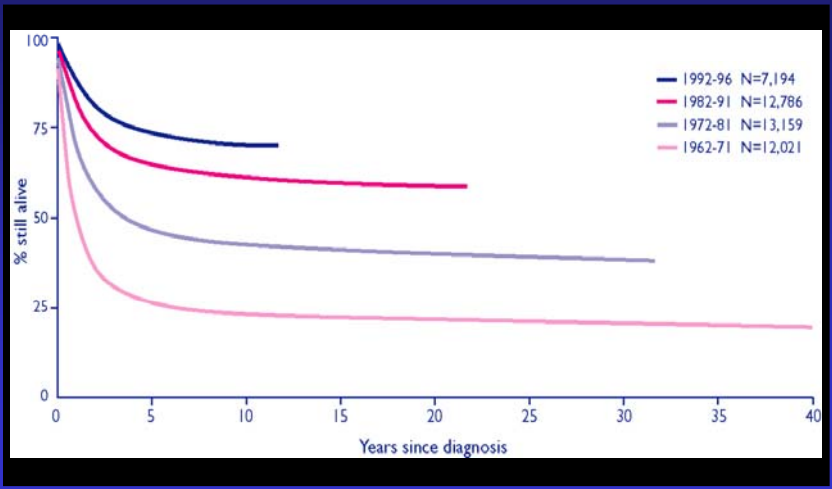
1400 children are diagnosed with cancer in the UK each year

Types of Tumour

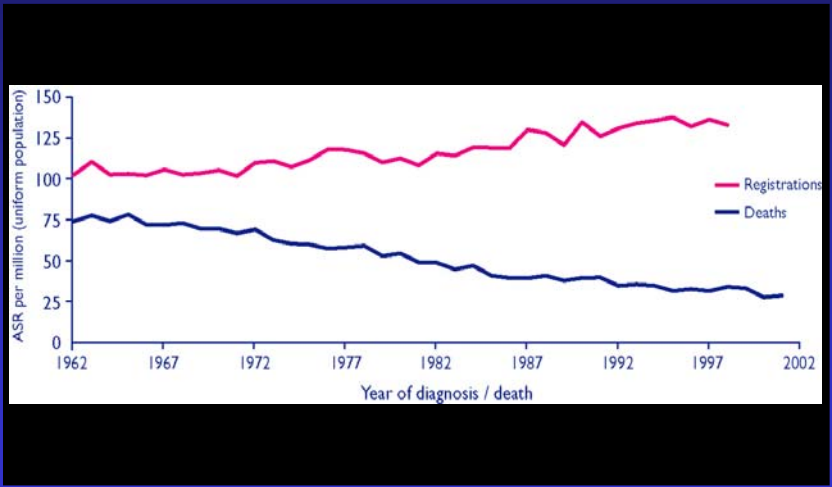
Adults	Children	
Carcinoma of bronchus, breast, prostate, stomach, colon	Leukaemia	30%
Leukaemia	Brain tumours	19%
Brain tumours	Lymphoma	13%
Lymphoma	Neuroblastoma	8%
Ewing's sarcoma	Wilms' tumour	5%
Osteosarcoma	Rhabdomyosarcoma	
	Ewing's sarcoma	
	Osteosarcoma	



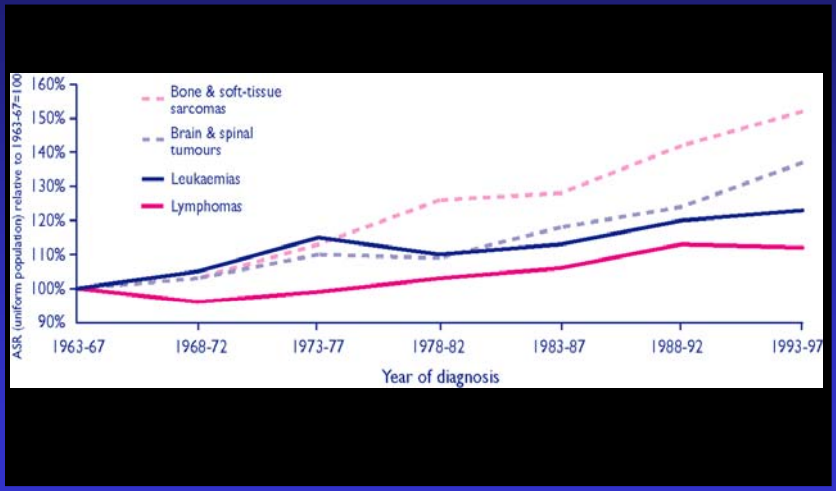
Survival of childhood cancer patients diagnosed in successive periods, Great Britain, 1962-96



Trends in age standardised (uniform population) cancer registration and death rates, children and 0-14 years, Great Britain, 1962-1998/2001



Registration rates for successive calendar periods, expressed as proportions of the rate for 1963-67, children aged 0-14, Great Britain 1963-97



Treatment of Childhood Cancer

- Chemotherapy
  - Most childhood tumours are sensitive
  - Intensive multidrug regimens often used
    - More effective but
    - Overlapping toxicities seen
- Radiotherapy
  - Used for 'local control'
  - Brain, sarcomas, Hodgkins
  - Side effects depend on area targeted
    - May have significant late effects in children
- Surgery

Chemotherapy side effects

Gut	Diarrhoea
	Nutrition
Bone Marrow	Red - Anaemia
	White - Immune function
	Platelets - Bleeding
Kidneys	Electrolyte leaks
Liver	Cell damage
CNS	Vomiting
Hair	Alopecia

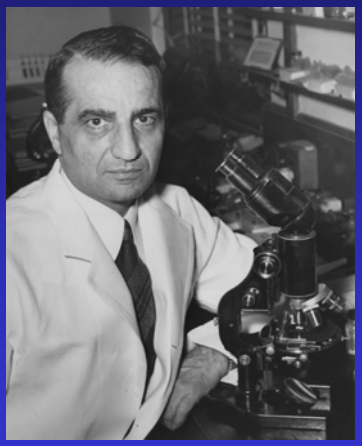
Acute lymphoblastic leukaemia

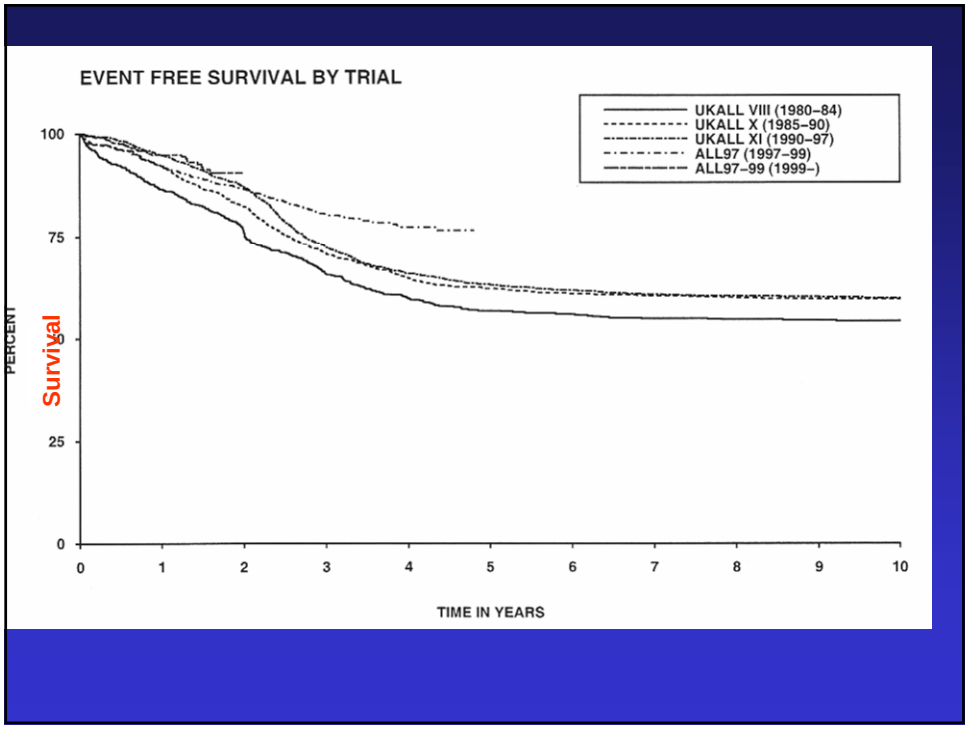
- 15-20% of childhood cancer
- Survival rates steadily improving
- Majority of children in UK in clinical trials
- Changes in approaches to therapy over time

Childhood ALL: a brief history

- 1860 report of use of microscope to make diagnosis of acute leukaemia in a 5 year old girl from Wurzburg, Germany
- 1960s multi - agent chemotherapy regimes
  - but less than 5% of children were cured even if treated for 5 years
- 1967 cranial radiation introduced, cure rates of 50% reported
- 1970 - 2000 improvement of cure rates to 85%
  - due to the use of “intensification blocks” for all children BUT many patients probably over treated
  - Use of cranial radiotherapy reduced
- 2005 measurement of sub microscopic levels of leukaemia to predict relapse,
  - Treatment modified for individual patients

Temporary remissions in acute leukaemia in children produced by folic acid antagonist, 4-aminopteroyl-glutamic acid (administering)
Faber S, Diamond LK, Mercer RD, Sylvester RF, Wolf JA *N Engl J Med* 1948;238:787-793

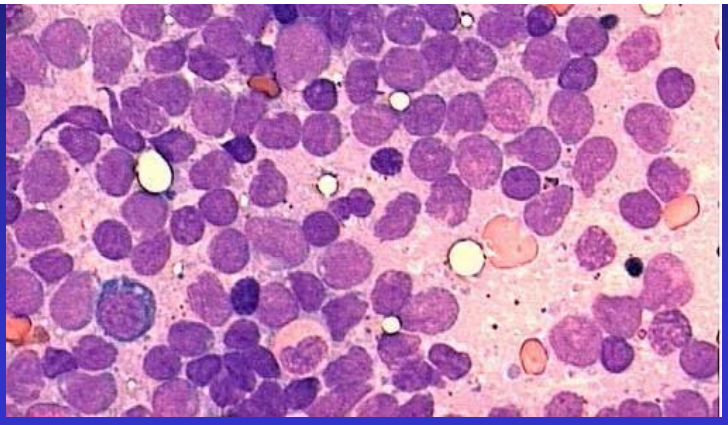




Prognostic factors directing therapy

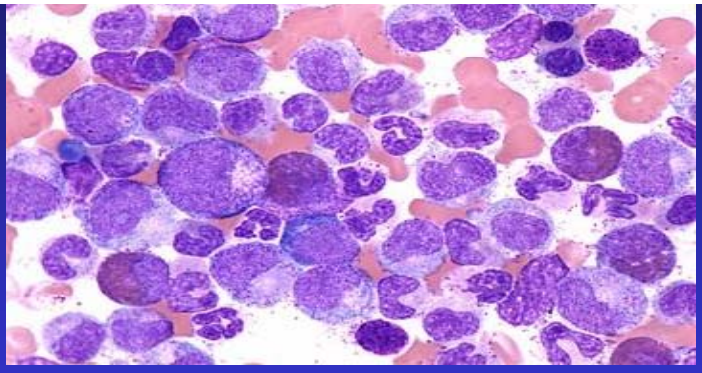
- Fixed factors
  - Age, sex, white cell count at diagnosis, cytogenetics
- Dynamic factors
  - response to treatment correlates with prognosis

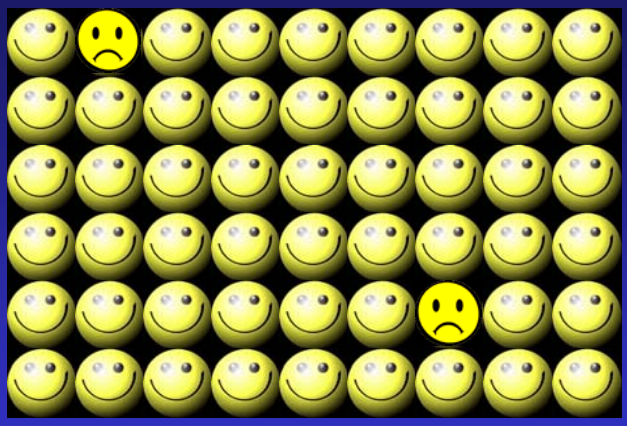
Acute Lymphoblastic Leukaemia



Bone marrow in ALL at diagnosis a factory making nothing useful

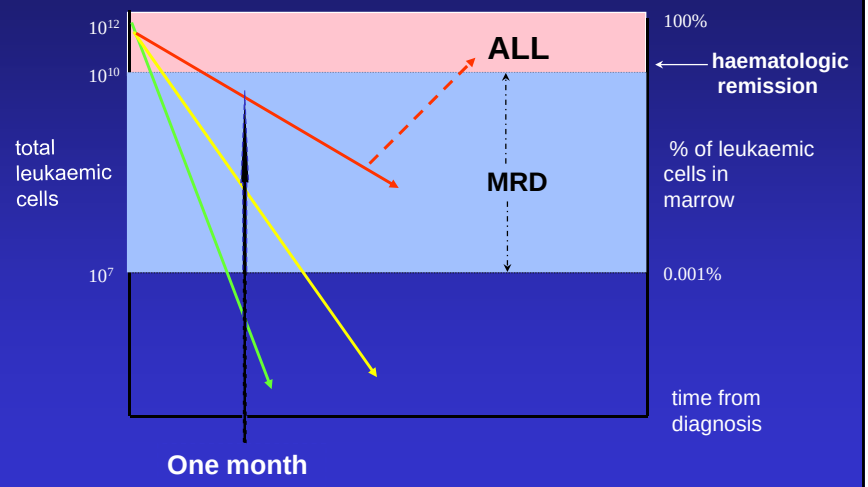
Acute lymphoblastic leukaemia in remission





Bone marrow in remission after one month of treatment for ALL

Minimal Residual Disease



MRD based treatment reduction: - an update

- Retrospective studies
  - Event free survival 92-95% in patients 'MRD negative' by day 35
- Prospective IBFM studies
  - 974 patients MRD low risk (day 35 and week 12), 14 (1.5%) relapse
- Prospective UK studies
  - No relapse in MRD negative day 28 and week 11 (134 patients)

MRD based treatment intensification: - an update

- Retrospective studies
  - 70% 3 year EFS in MRD high risk (day 35 and week 12), I-BFM 90
  - 72% 5 year EFS in MRD positive at day 28 of ALL 97 (one marker)

Acute lymphoblastic leukaemia

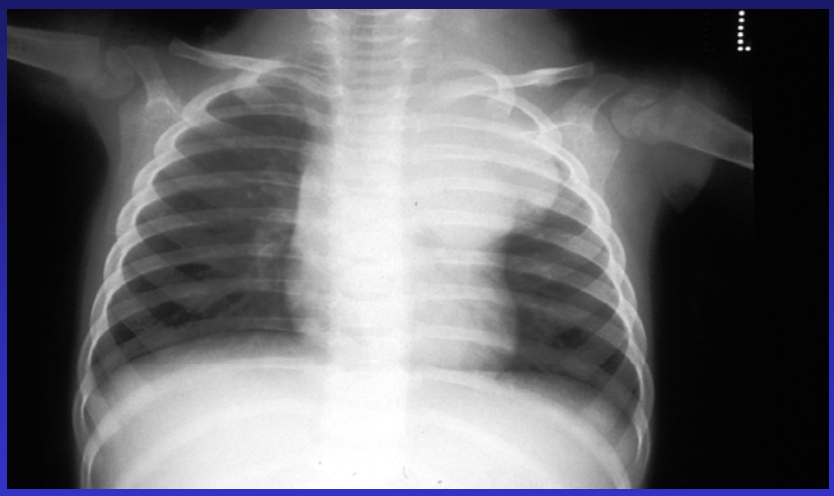
- Treatment now directed by *response* to chemotherapy
- Significant reduction in late effects with only few patients receiving cranial radiotherapy
- Some patients still require very intensive therapy, including transplantation

‘Embryonal tumours’

- Neuroblastoma
- Wilms’ tumour
- Rhabdomyosarcoma
- Primitive neuroectodermal tumour
- Retinoblastoma

Neuroblastoma

- Worldwide classification
- Age
  - <18 months good, >18 months poor
- MYCN status
  - Amplified: poor risk
- Stage of disease
- Studies can now be formally compared



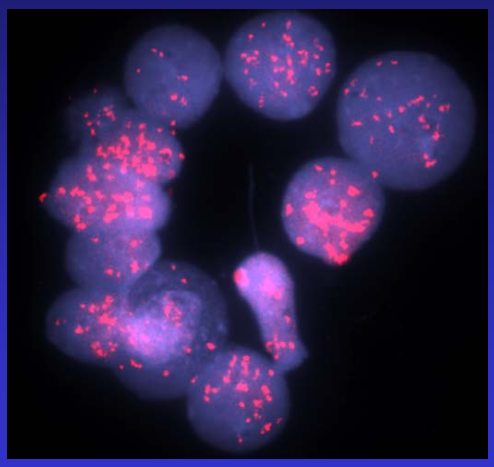
Neuroblastoma – good risk

- Observation only
  - of congenital neuroblastoma – even high stage
  - Low stage, non amplified
- Minimal chemotherapy
  - Usually patients under 18 months
  - If surgery deemed to carry risk
- Or ‘Watch and wait’ if surgery likely to cause morbidity

Neuroblastoma – high risk

- Patients over 18 months age
- Poor cytogenetic markers
  - MYCN amplification
- Stage 4 disease
  - With bony metastases

MYCN amplification – normally 2 copies per cell



Neuroblastoma – high risk

- Intensive induction chemotherapy
- High dose therapy with
  - Autologous stem cell (bone marrow) transplant
- Retinoic acid
  - 'Matures' cells
- Anti GD2
  - Not yet available in UK – targeted therapy

Lymphoma

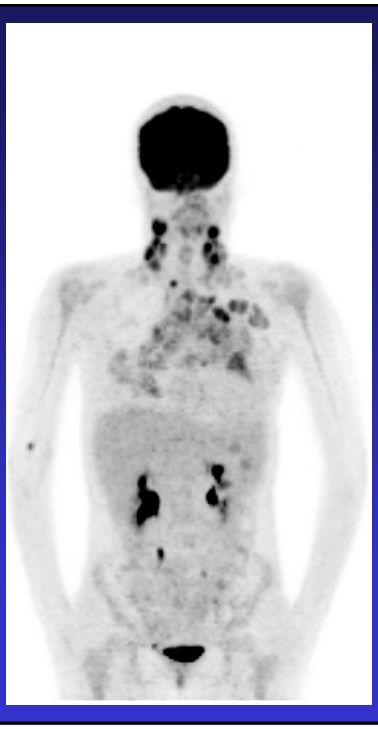
- Rapidly growing
- Chemosensitive
  - No XRT
- Can occur in any lymph node group

Lymphomas

- Rapidly progressive
- Very responsive to therapy
- Progress in monitoring response
  - PET scanning

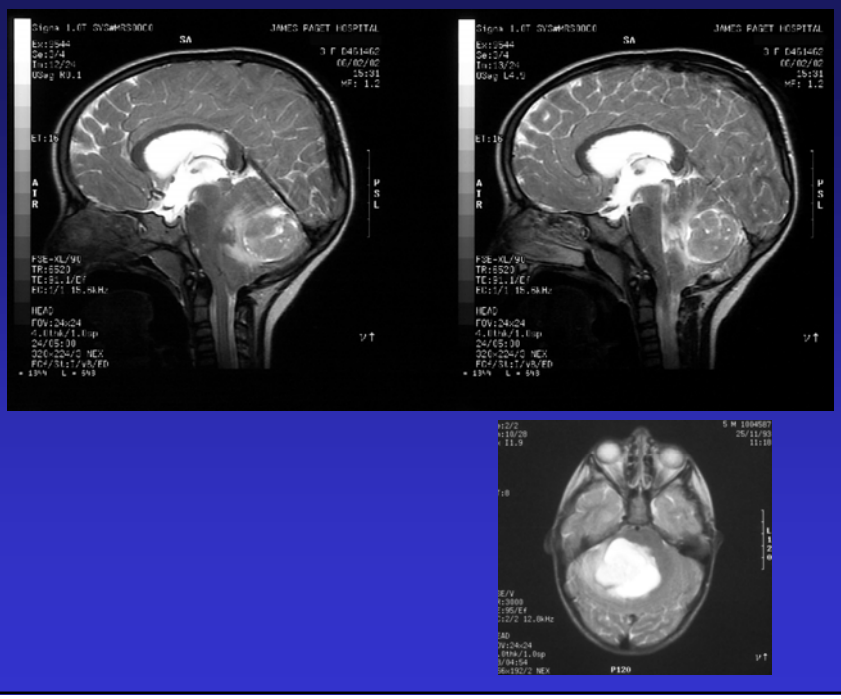
Positron Emission Tomography

- Labelled FDG taken up in active tumour cells
- Identifying site of disease
- Of real value in evaluating disease response
  - When a mass remains – is it active?
    - Hodgkins
    - Wilms
    - Sarcomas
- Helps in disease stratification, avoiding over/ under treatment of patients



Brain tumours

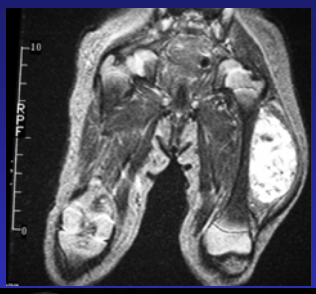
- Overall 50% survival
- Improving survival for children with more aggressive tumours
- Radiotherapy important part of therapy
- Increasing use of chemotherapy
  - With increasing intensity
- Role of MDT critical

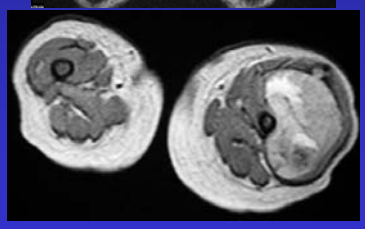


Late effects of therapy

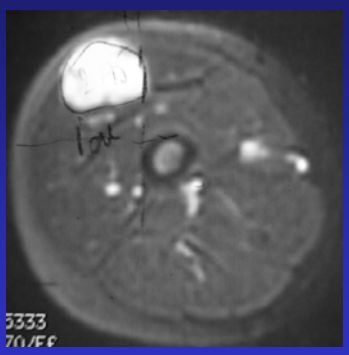
- Chemotherapy
  - Anthracyclines (cardiac disease)
  - Alkylating agents
    - Fertility
    - Renal fuction (ifosfamide)
  - Cisplatin/carboplatin
    - Hearing
- Radiotherapy
  - Age, dose and field

Site age and size important risk factors – however…





2 yr 3.3cm x 2.7cm x 5.2cm Volume = 23ml



7 yr 2.9cm x 2.5cm x 5.4cm Volume = 20 ml

Limb Length Discrepancy

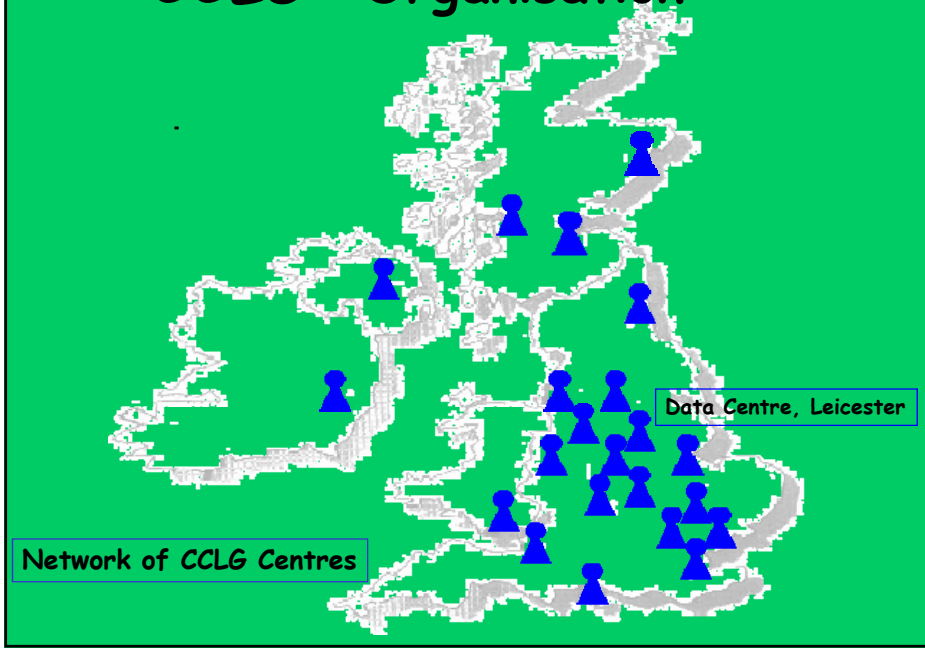
TABLE 17. *Buttock-knee length (cm)*

Age (yrs)	No.	Mean	SD
Females			
2.0–3.5	98	28.4	1.9
3.5–4.5	108	31.9	2.1
4.5–5.5	126	34.2	1.9
5.5–6.5	124	36.1	2.3
6.5–7.5	124	39.2	2.6
7.5–8.5	94	41.3	2.4
8.5–9.5	140	44.0	2.6
9.5–10.5	134	46.1	2.9
10.5–11.5	138	48.8	3.5
11.5–12.5	133	50.8	3.3
12.5–13.5	160	52.9	3.0
13.5–14.5	116	54.1	3.0
14.5–15.5	132	55.5	2.8
15.5–16.5	97	55.2	2.7
16.5–17.5	116	55.3	2.6
17.5–19.0	68	55.4	2.6

MDT working in paediatric oncology

- Longstanding history of mulitdisciplinary working
  - Clinical multidisciplinary clinical care
- NICE Service guidance formally identified other MDTs
  - Diagnostic (most closely related to site specific)
  - Psychosocial
  - Late effects

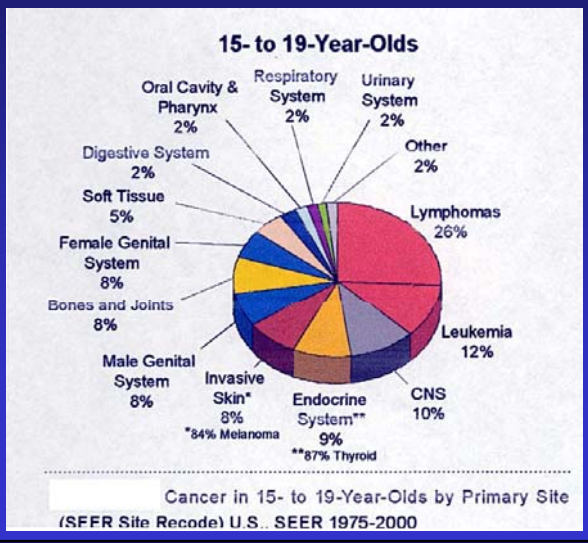
CCLG: Organisation

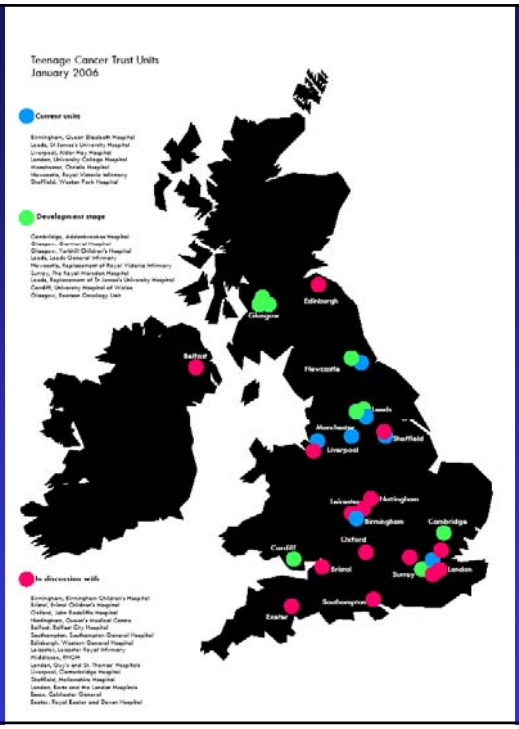


Teenagers and Young adults

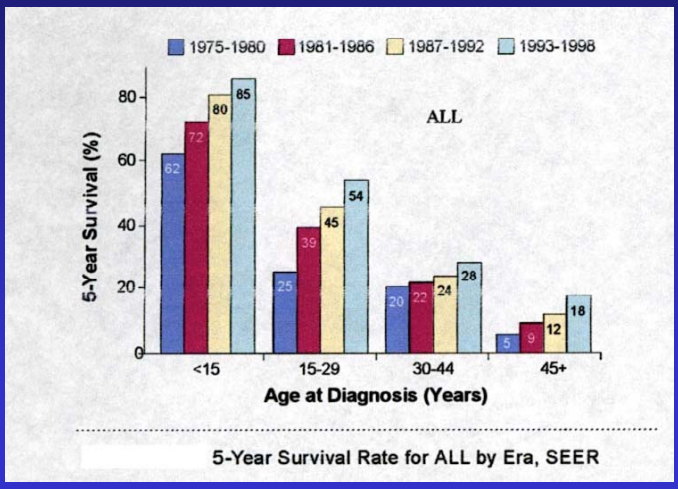
- Included in standards in England and Wales
  - Recognised as groups with different needs
  - Treatment may also differ – poorer outcome
  - Not comfortable within paediatric or adult setting
  - Teenage Cancer Trust has pioneered the development of specialised units
  - Patient choice is at centre of guidance
    - Disease specific expertise essential
    - 'age appropriate' facilities should be available

Patterns of cancers seen in TYA





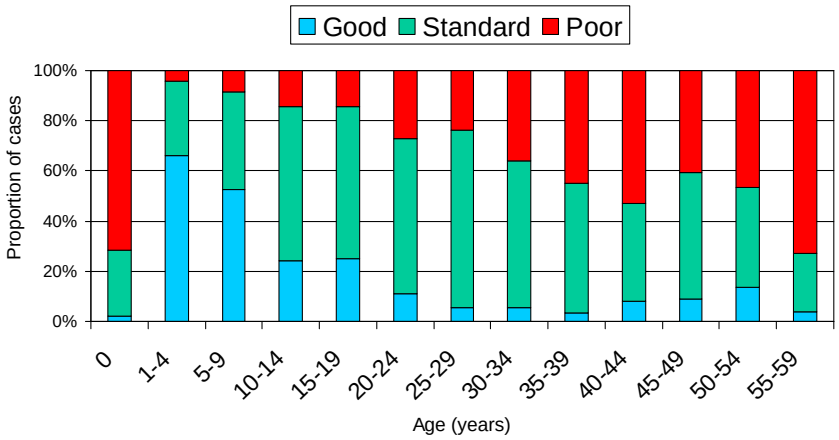
Cancer survival by age

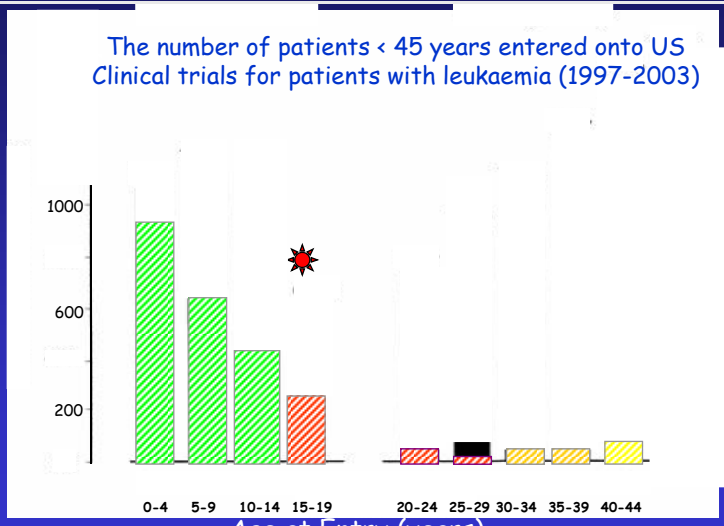


Survival in Teenagers and Young adults

- Types of cancer seen
- Biology of cancer e.g. leukaemia
- ?Compliance
- ?Entry onto clinical trials
  - Lower rates than in children

Age and cytogenetic risk group





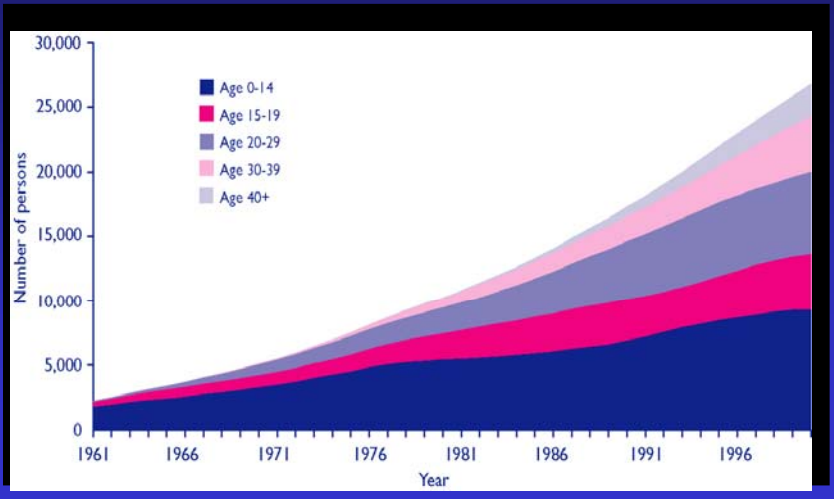
Cancer standards

- Rare Cancer - therefore development of standards has lagged behind other 'sites'
- NICE Service Guidance for England
  - Published August 2005
- Opportunity
  - Historical distribution of services
  - Services can now be planned to reflect need
  - Centre size and viability under review
  - MDTs formally idenified
  - Need for 'Shared care'
  - Needs of teenagers and young people recognised

Cancer standards

- DoH cancer measures shortly to be published (recent consultation)
- Cancer standards to be published in Scotland and Wales
- To be followed by standards for the treatment of cancer in young people

Number of people in the specified age group alive at the end of each calendar year who had previously had a diagnosis of childhood cancer, Great Britain, 1961-2000



Risk stratification for follow up (more than 5 years from completion of treatment)

(Taylor et al 2004)

Level	Treatment	Method of Follow up	Frequency	Examples of Tumours
1	- Surgery alone - Low risk chemotherapy	Postal or telephone	1-2 years	- Wilms Stage I or II - Low risk LCH - Germ cell tumours
2	-Chemotherapy - Low dose cranial irradiation (<24Gy)	Nurse or Primary Care led	1-2 years	Majority of patients (e.g. ALL in first remission)
3	-Radiotherapy, except low dose cranial irradiation - Megatherapy	Medically supervised late effects clinic	Annual	- Brain tumours - Post BMT - Stage 4 patients (any tumour type)

The future

- European and worldwide collaboration
  - Rare tumours require international clincal trials
- More treatment for some, less for others
  - Curing more
  - Reducing late effects of therapy
- New imaging
- New standards for care
- Prevention and screening……..