Causation Issues

Delay in Diagnosis of Cancer Cases

Prof Pat Price
Imperial College London
office@patprice.co.uk
www.patprice.co.uk

Faculty of Advocates
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EVIDENCE BASED

Medicine

Research

Law

Medical Errors

- Delay in diagnosis cancer third largest medical negligence cases in the UK

- ***Medical error—the third leading cause of hospital death in the US (after cardiovascular and cancer. BMJ May 2016***

http://www.bmj.com/content/353/bmj.i2139

- Call for more research and more recording

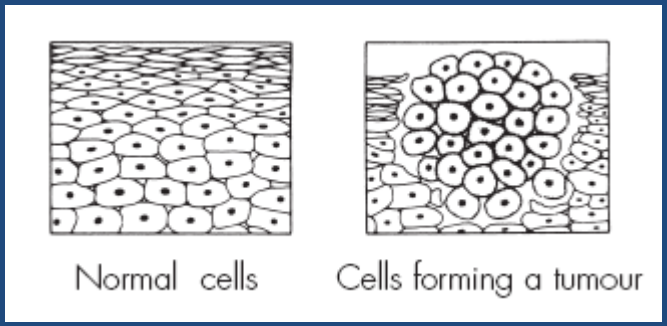
Cancer Facts

- 1 in 2 people get cancer at some time in lifetime
- 1 in 3 people die of their cancer
- Most cancers occur in the over 75 year olds
- Large body of research in tumour biology

What is Cancer

Basic Biology

- Cells grow uncontrolled and abnormally
  - Abnormalities in genes
  - Production of local growth factors
- Grow to develop a tumour. All tumours are different
- Tumour spreads locally
- Tumour metastases-lymphatics/blood/other



Main Causation Issues

- **Delay in diagnosis**
  - Most common issue
  - All cancers are different
  - **Usually most difficult to assess**
- **Failure of screening**
  - Cervical /breast/colon/follow up
- **Side effects of treatment**
  - Negligent or not/consent
- **Life Expectancy**
- **Montgomery consent**
- **[Causes of cancer]**

Main arguments in Cancer Cases

- What is stage of the cancer & prognostic factors → treatment & prognosis

  -medical records

  -radiology and detailed histopathology reports

- What is the natural history/behaviour/ growth rate of the tumour

  -detailed serial chronology from medical records

  -symptoms -witness evidence

  -Litterature and opinion as to departure from average

Main arguments in Cancer Cases

- What is the treatment guidelines of individual cancer for stage/grade/prognostic features

  -literature

- What does the literature say about prognosis

  -literature

  *Main evidence is medical records and literature

  *Need to define natural history of individual tumour

  -needs time and full paper medical records

Natural History of Cancer

Curable: screening
Cervical: 3-10yrs
Breast: 3-10yrs
Bowel: 5-10yrs
Oesophagus: 2-3yrs

Surgery/adjuvant therapy

Radical radiation

Curable:
Teratoma/Lymphoma

Chemo increase survival
Lung: 2months
Colon 3.7+ months
Gastric: 3months
Ovary: years

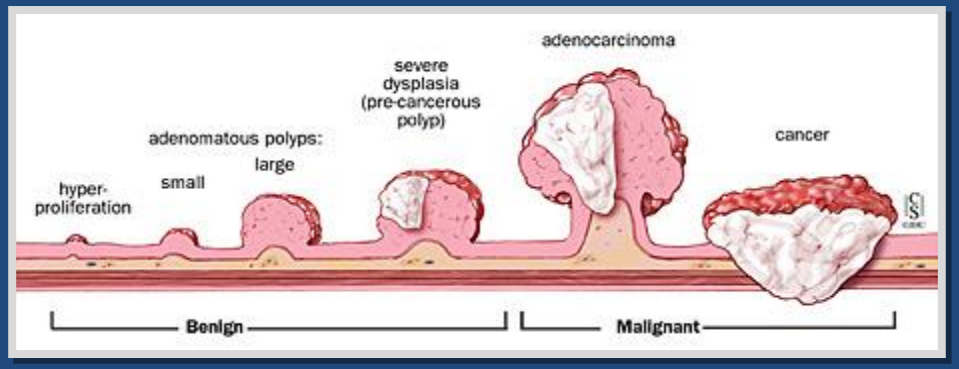
Chemo given early increase survival: ???

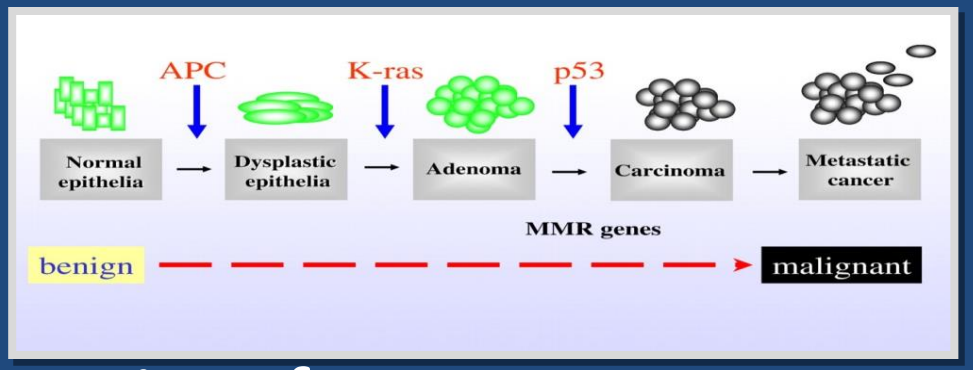
Premalignant stage

-screening programmes

Adenoma-carcinoma sequence

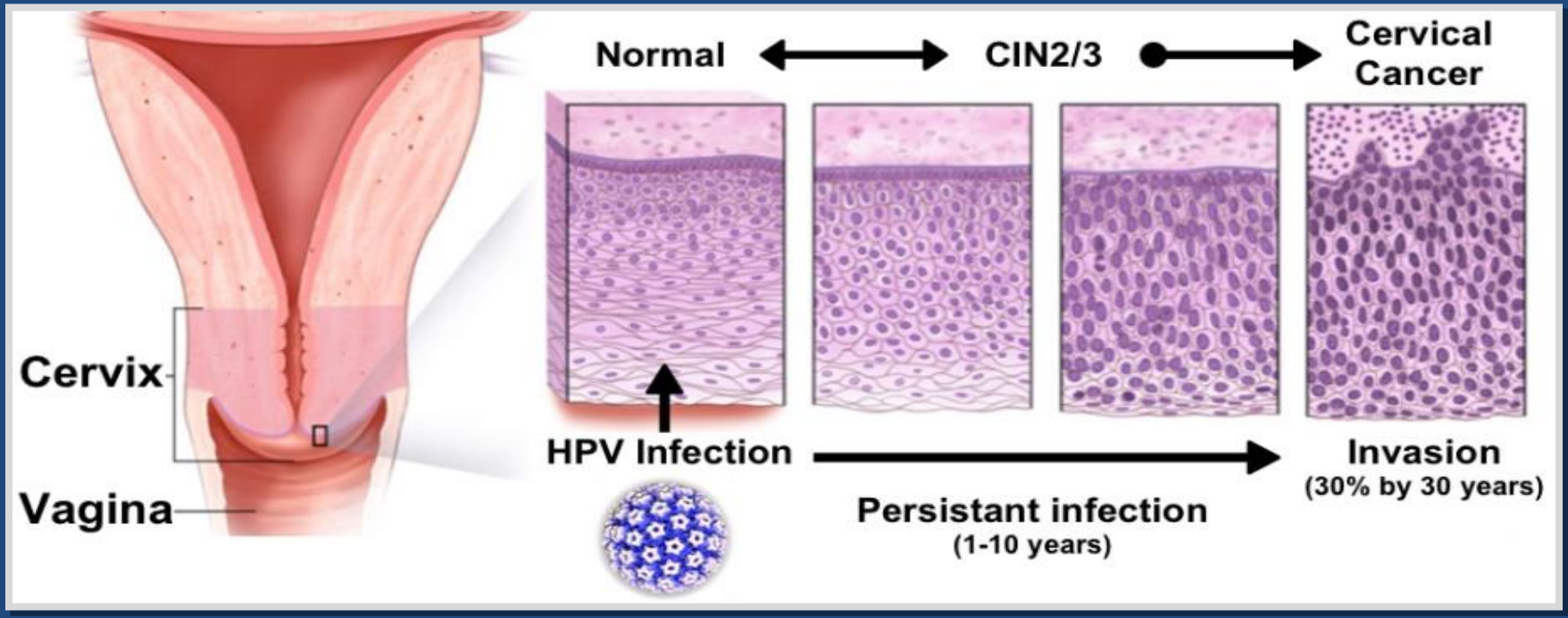
- Classical “sporadic” colorectal cancer pathway



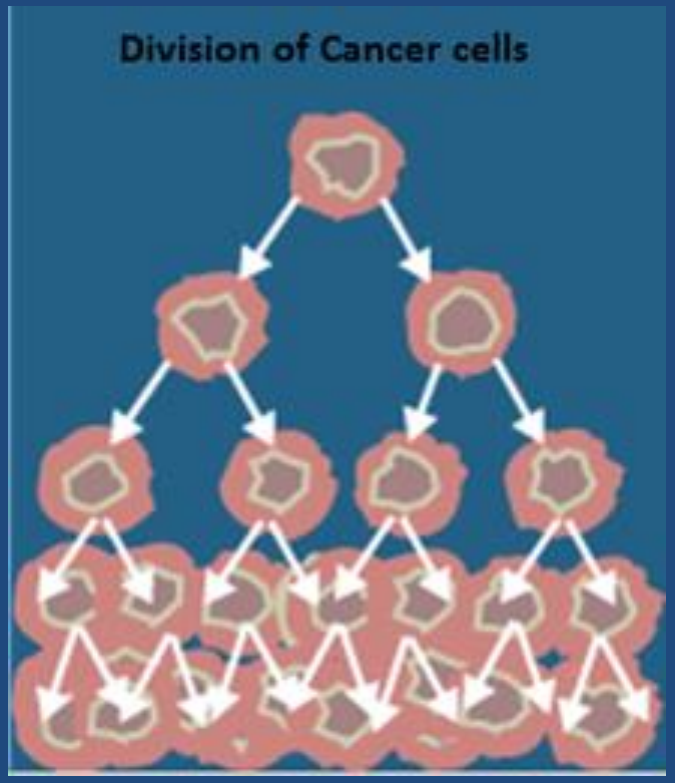


- 5 – 10 year time frame

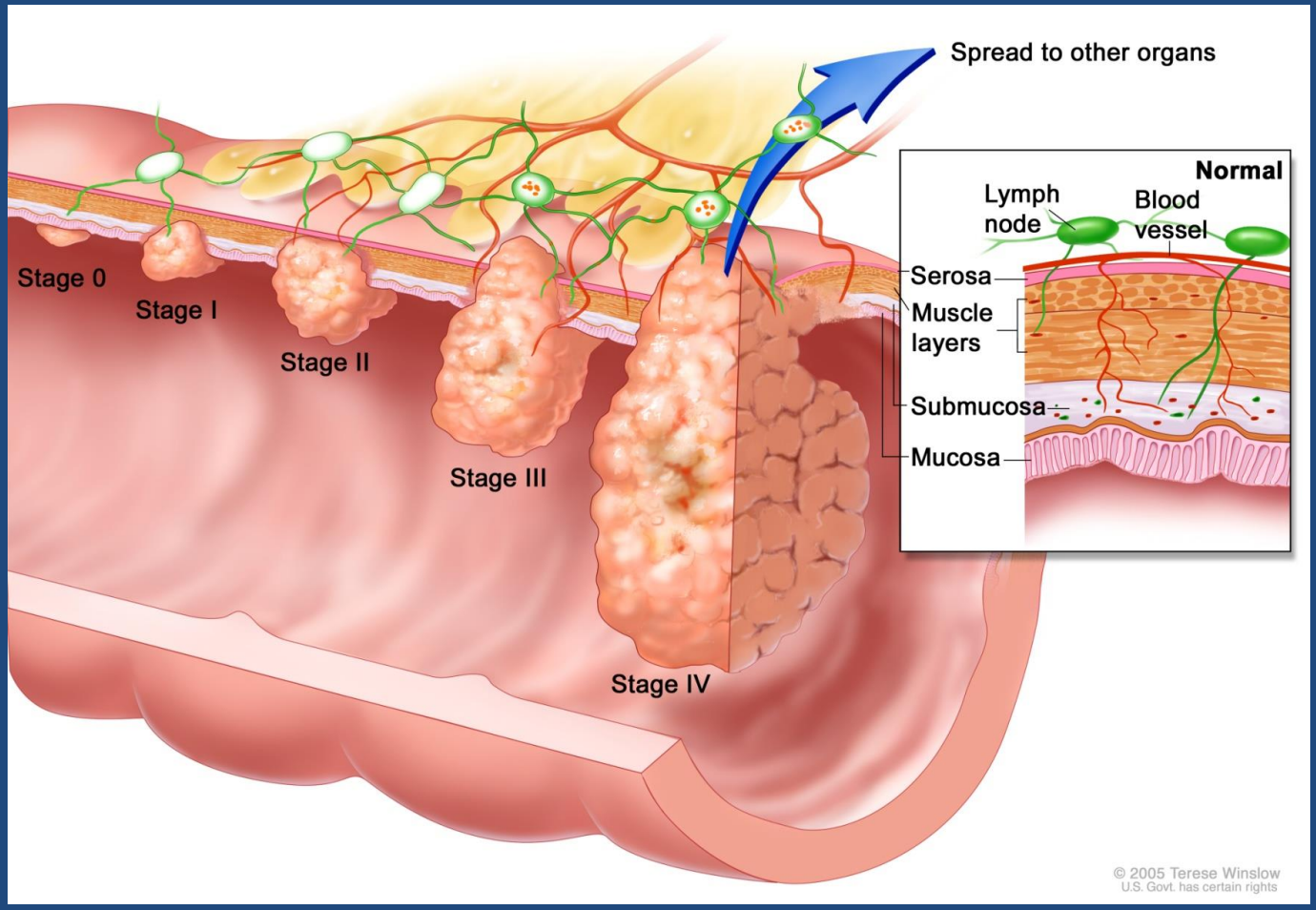
Development of Cervical Cancer



Tumour cell growth



Colorectal cancer growth and spread



Staging of cancer

TNM classification

Cancer TNM

- Primary Tumour T
- Regional Lymph nodes N
- Blood borne spread M

Staging of cancer

TNM UICC classification 8th edition

- Absolute definition
- Clinical vs pathological
- Stage Determines treatment and prognosis

Alternative summaries

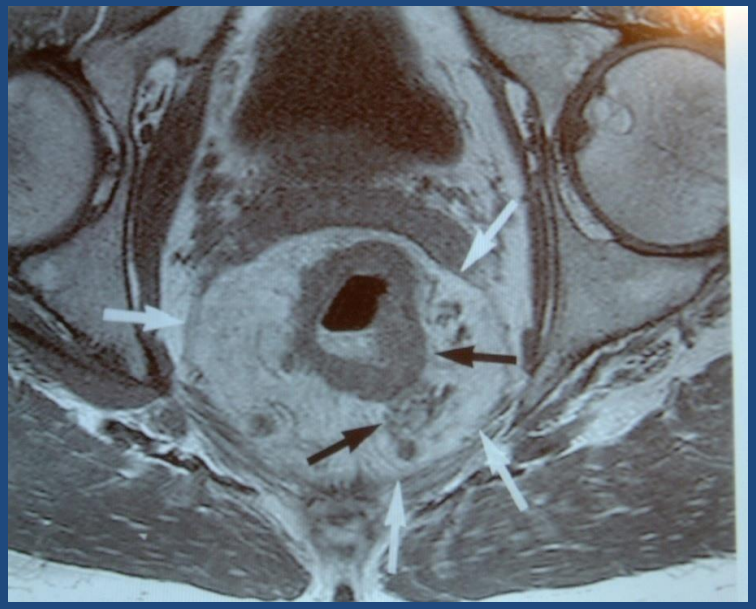
– e.g Dukes classification in colon cancer

TNM Classification (American Joint Commission on Cancer)				Dukes' Classification
Stages	T	N	M	Stages
Stage 0	Tis	N0	M0	
Stage I	T1	N0	M0	A
	T2	N0	M0	B1
Stage II	T3	N0	M0	B2
	T4	N0	M0	B2
Stage III	T1, T2	N1 or N2	M0	C1
	T3, T4	N1 or N2	M0	C2
Stage IV	Any T	Any N	M1	D

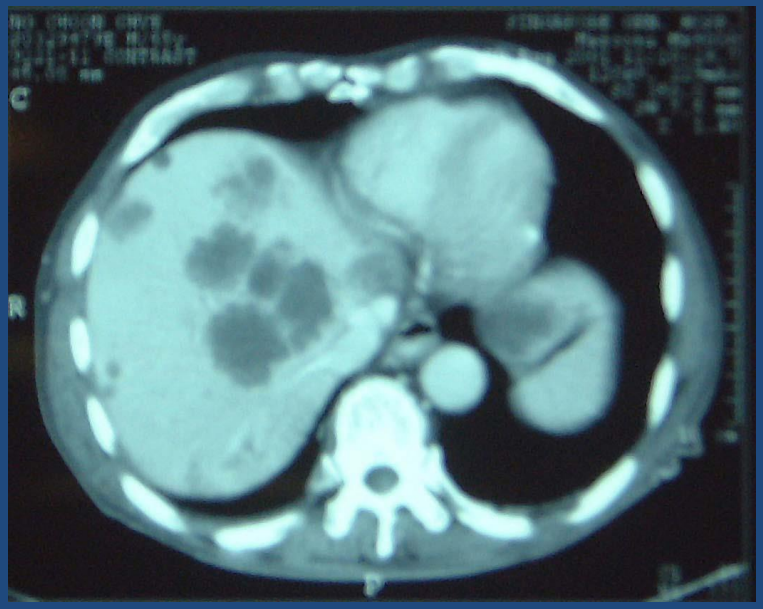
A comparision of TNM and Dukes' Classification

Clinical Staging of Tumours

- Assess
  - Local cancer spread /Distant metastatic spread
  - Decide on treatment at MDT meeting



MRI: Rectal cancer



CT: Liver metastases

Histopathology

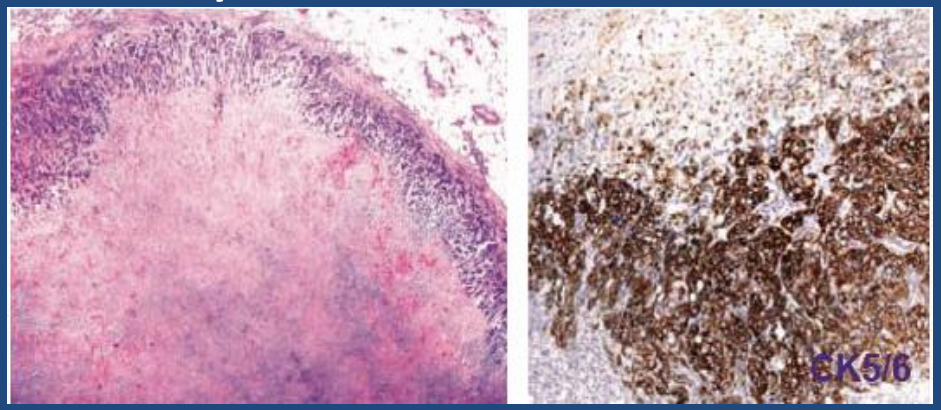
Cancer under the microscope

- Prognosis and treatment

-Pathological staging pTNM

-Grading: G1/2/3

-Immunohistochemistry

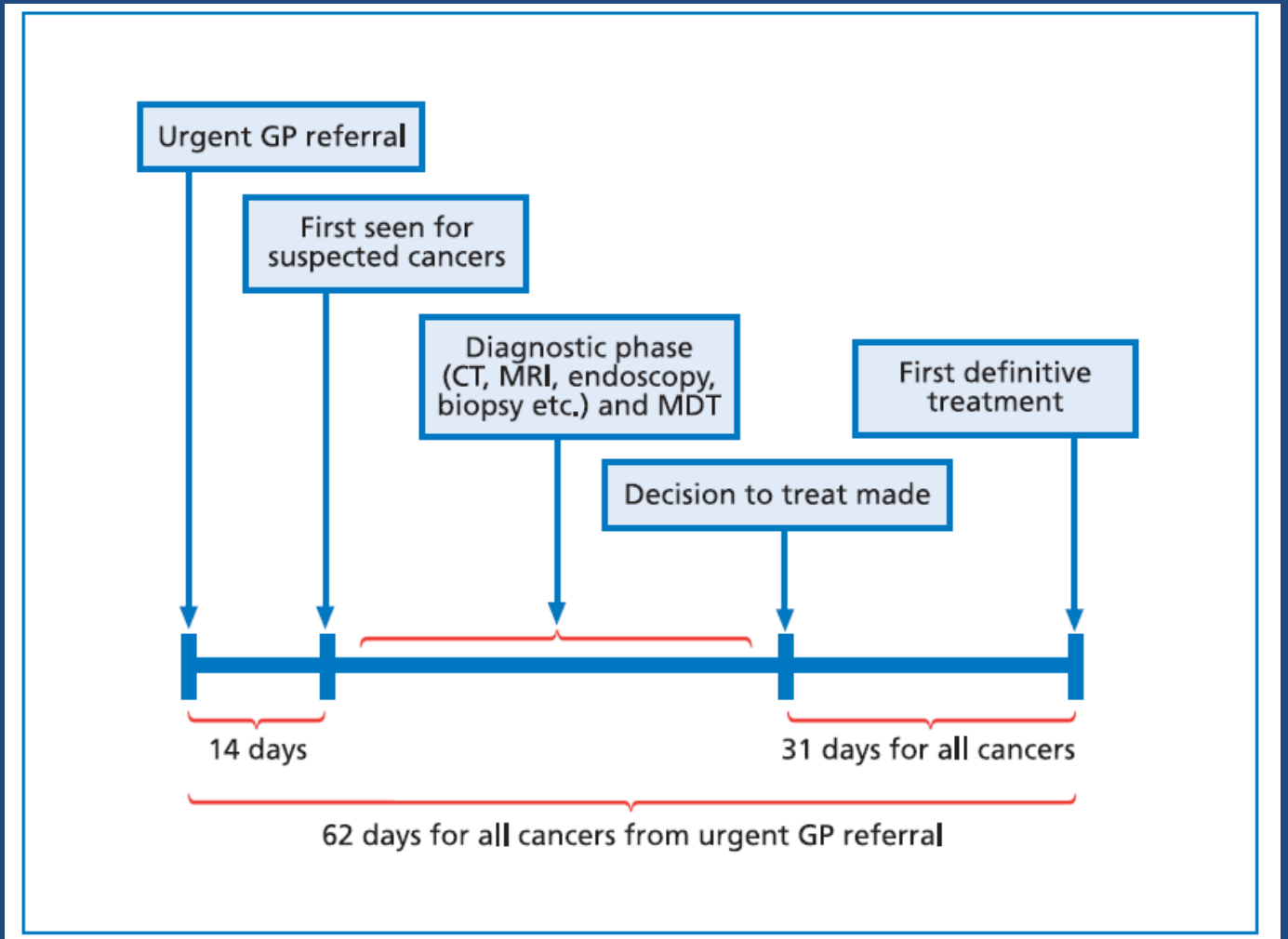


Diagnosis & Management plan

Multidisciplinary Team Meeting

- MDT clinicians present
- TNM staging
- Histology
- Treatment plan
- Time to Treatment: TTT-31 days

Treatment Targets



Source: Department of Health 2008

Delay in Diagnosis
Basic structure of arguments

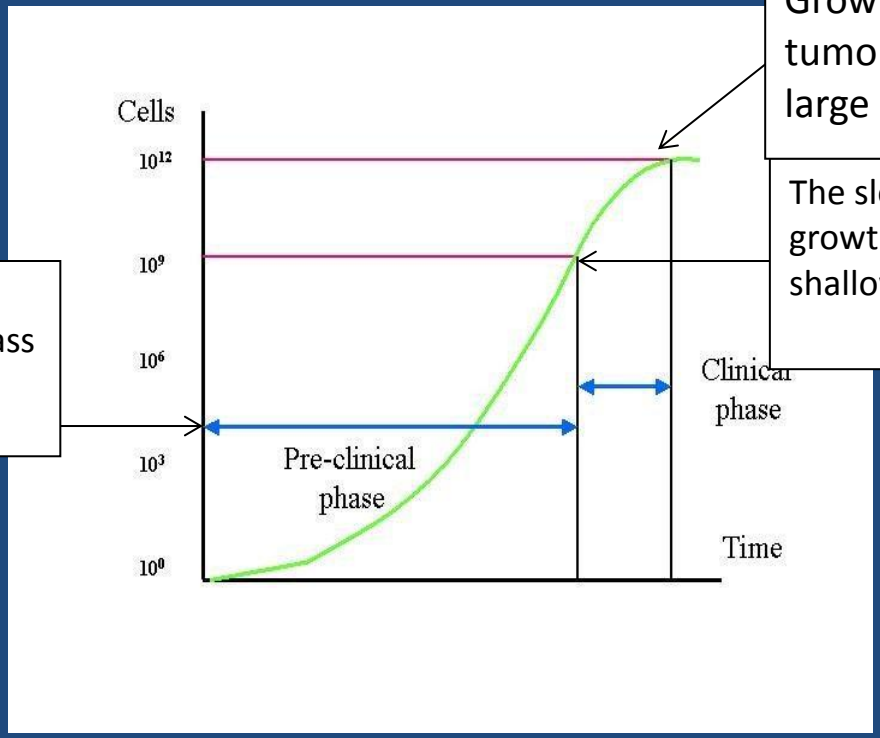
Opinion on earlier tumour status

- **TNM stage**
- **Grade**
- **Other biological factors-PSA level, ER and HER2 status**
- **In situ components**

Earlier TNM stage based on:

- **Clinical experience**
- **Known natural history-literature based and individual tumour information**
- **Back extrapolation of size of tumour**

Tumour Growth & delay in Diagnosis



Growth slows as tumours get very large and necrotic

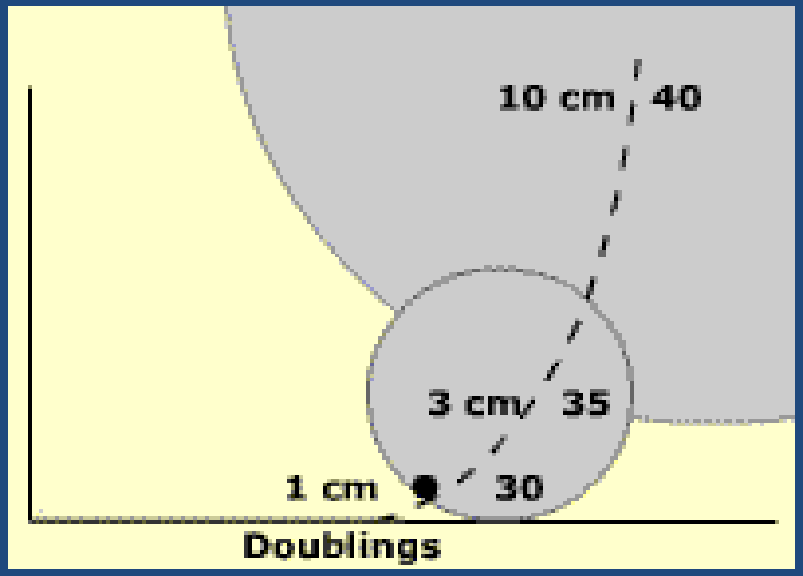
The slope of this line is the growth rate-steep for faster and shallower for slower

Below this line the tumour mass is not seen on scan

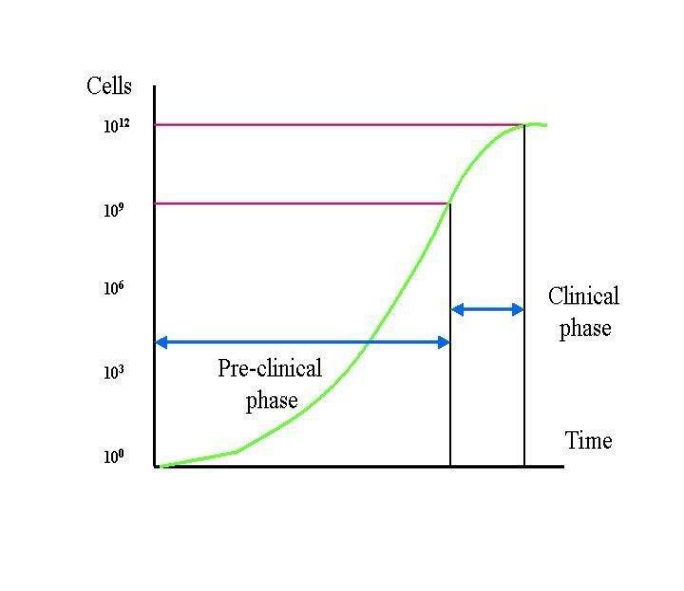
Half empty glass

Natural History of Growth

Doublings	Cells	Diameter	
0	1	10 um	microscopic
20	1×10^{6}	1 mm	microscopic
30	1×10^{9}	1 cm	Detectable XR
35	$1 \times 10^{10.5}$	3 cm	Average Diagnosis
40	1×10^{12}	10 cm	Death



Back extrapolation calculation



Equation for Doubling time = $T_i \times \log 2 / 3 \times \log(D_f/D_o)$ or $(\ln 2 \times T_i)/(\ln(V_f/V_o)$

- T_I = interval time
- D_I = initial diameter
- D_0 = final diameter
- V_I = initial volume
- V_0 = final volume

Volume doubling time: Literature average or individual serial measurements.
Plus reality check

Volume doubling time

Based on literature based assessments

Table 3. Tumor Volume Doubling Time of Primary Breast Cancer According to Age

Age at diagnosis (yr)	Geometric mean in days (95% confidence limits)	68% range*
< 50	80 (44–147)	24–273
50–70	157 (121–204)	46–533
> 70	188 (120–295)	55–640

Likelihood ratio test: $P = 0.06$

* Sixty-eight percent of the tumor volume doubling times are between the presented limits: 16% is smaller than the lower limit, 16% is larger than the upper limit.

Or

Serial clinical measurements with no intervening treatment

Earlier nodal disease

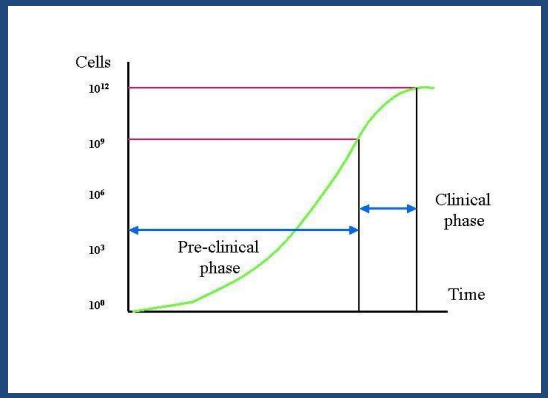
- Based on nodal status at diagnosis
- Back extrapolation more difficult as clumps of cells and exiting cells
- Clinical experience
- Disease free interval
- Probability of spread to nodes based on T stage and prognostic factors

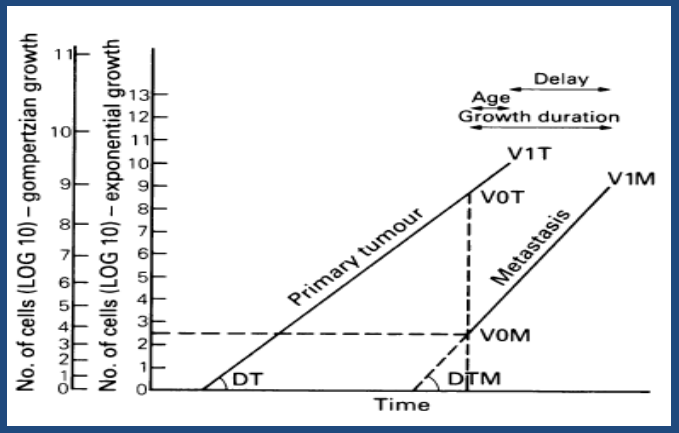
Earlier Metastatic disease

- Often extent of clinical metastatic disease can be underestimated
- Important to consider subclinical disease

Growth rate of metastases

- **Back extrapolation technique**



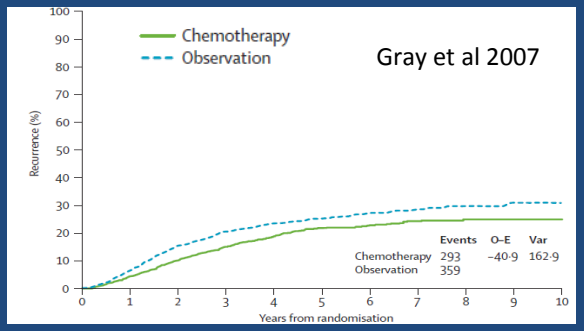


Using known or literature based-only go so far

Unknown use x2 primary growth rate

- **Disease free interval**

Time to image metastases following resection
= growth rate of subclinical disease



Pitfalls in **Back extrapolation of tumour**

T stage

- Based on mathematical models of tumour biology –exact figure v.s broad guide
- Reality check from subsequent natural history
- Poor understanding of biology and mathematics confused with invalidity
- Concept vs maths. VDT vs growth rate

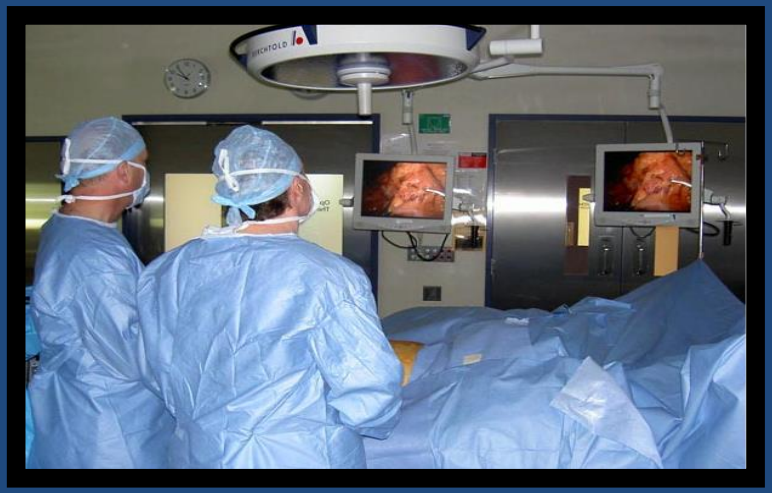
Estimate Previous TNM stage

- Know Clinical/pathological/subclinical TNM
- Treatment strategy at MDT based on TNM/prognostic factors-need guidelines
- M is rarely curable
- Prognosis based in TNM/prognostic factors/literature

Treatment of Cancer

-and results of delay in diagnosis

Development of surgery



Surgery

- 50% patients cure by surgery
- Open/laparoscopic/endoscopic/robotic
- Complete resection needed R0 (not R1 or R2)
- Complications of surgery
  - Premature death
  - Not allowing adjuvant therapy
  - Anastomotic leak

Adjuvant Therapy

- Definition
  - Treatment given at the same time as primary treatment
- Treatment of micro-metastatic disease
- Improves local control –Gynea/rectal/breast
- Improves survival-breast/colon
- Radiotherapy /chemotherapy/hormone

Radiotherapy

External Beam Radiotherapy

Brachytherapy

Medico Legal Issues: Radiotherapy

- Acute late side effects
  - —-5% severe
- Given incorrectly
  - —-IMER guidelines and regulations/medical physicists
- Overdose to critical structures
- Given unnecessarily

Medicolegal Issues: Chemotherapy

- Too late-delay in diagnosis
- Not given, given
- Over-dosage
- Toxicity of individual agents
- Acute side effects
- Long term side effects

Other Therapy

Hormone Therapy

- Breast and prostate

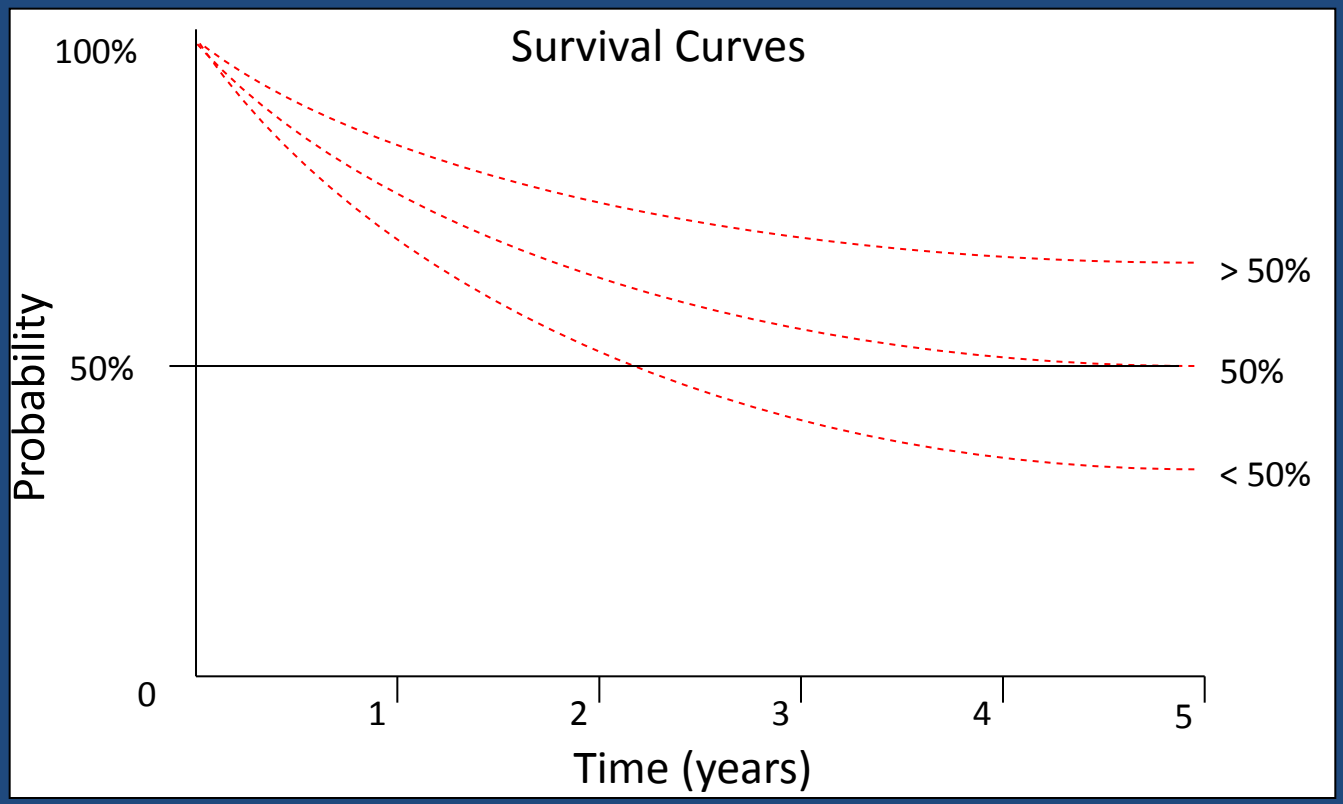
Immunotherapy

- Significant developments in melanoma

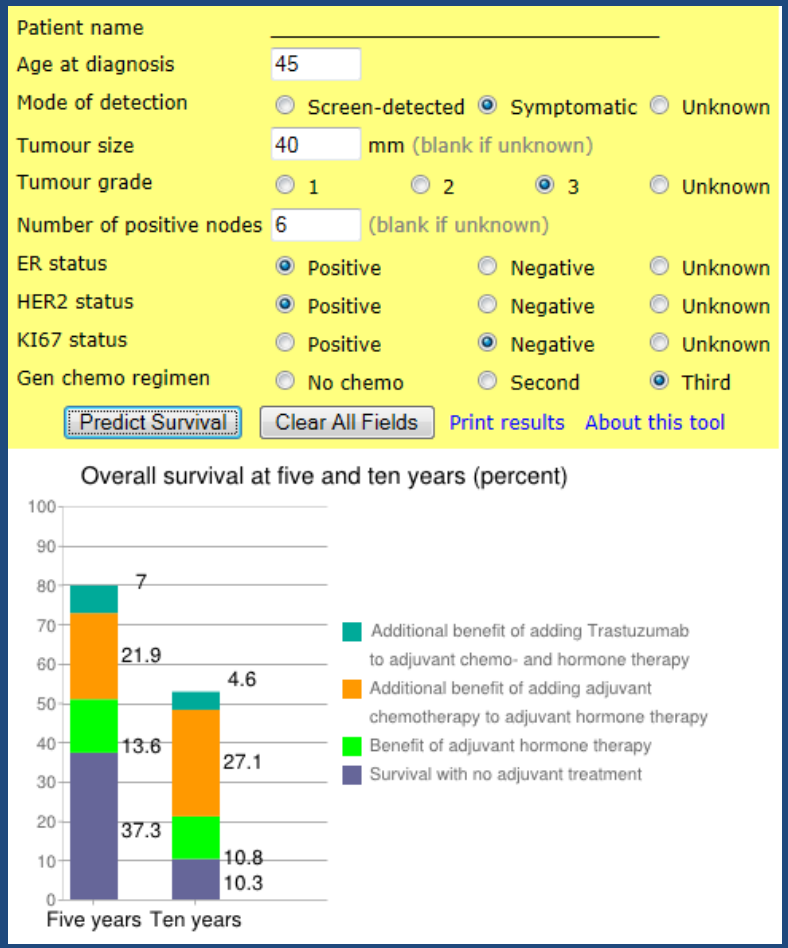
Prognosis and Life expectancy

Prognosis Issues:
Survival Rates

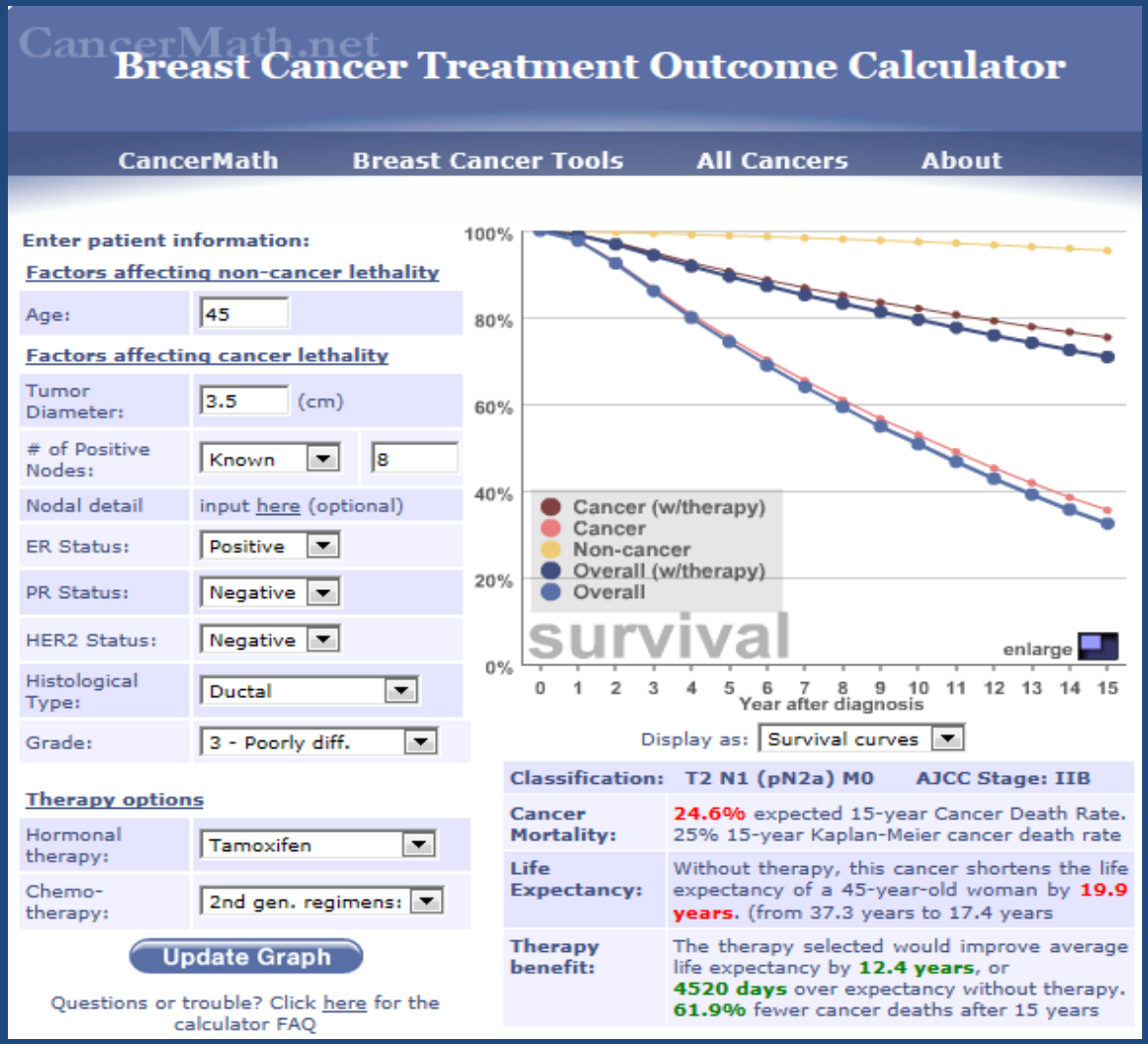
- TNM used to express the probability of survival (with range)
- For most legal cases 5 year survival without disease is taken as "cure", as probability of relapse after is < 50%. Some not



Web based tools to predict survival

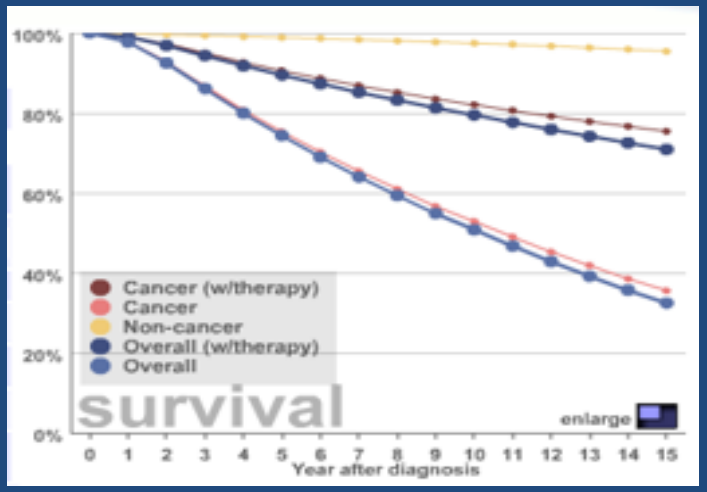


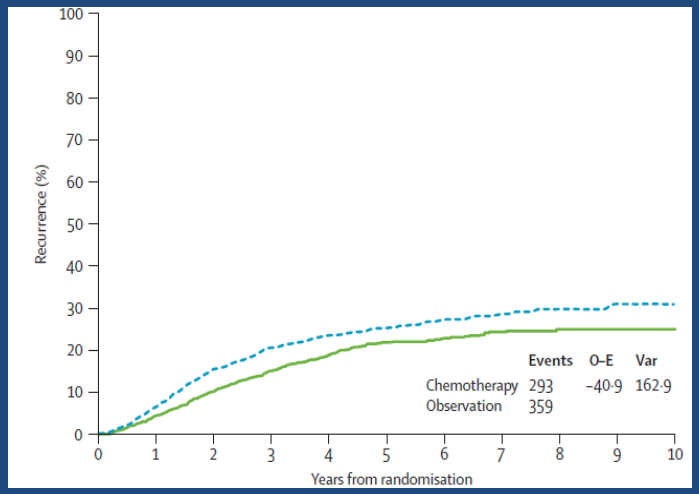
Life Expectancy
JD vs Mather 2012 EWHC 3063 (QB)



Conditional survival

- Prognosis at diagnosis vs prognosis at a later time
- Assess when most recurrences occur
- Loss of LE may disappear over time





When claims difficult to defend

Failure of Care

- Guidelines not adhered to
- Serial radiology is available
- Results not acted on
- There has been a SUI report identifying failure

When claims difficult to defend

Causation

- Incorrect treatment given
- Delays starting treatment (31 day ITT)
- Significant delay in diagnosis (often years)
  - tumour would have been pre-invasive
  - significantly different TNM stage eg not metastasised.
- Cant always trust SIR

Change in case profile -related to change in NHS last 10 years

Hospital

- Increase in administrative failure
  - -Cancelled appointment/tests
- Results not communicated to team
- Lack of continuity of care
- Failure of responsibility e.g. MDT meeting
- X-rays not routinely reported

GP

- Interpretation of guidelines

References

Cancer and the Law: Waxman and Simons

Treatment of Cancer: Price & Sikora 6th edition on line

http://cancerhelp.cancerresearchuk.org/about-cancer/

http://www.cancer.gov/statistics/glossary

www.actionradiotherapy.org