Medical Student Training in Oncology

Lecture 1

❖ Key competencies in cancer care

Learning objectives

❖ The Cancer Pathway & Cancer Journey

❖ Red flag symptoms, differential diagnosis

❖ Staging

❖ Co-factors for decision making, treatment intent

❖ Planning and prognosticating

❖ Treatment initiation

❖ Considerations for cancer screening

Cancer pathways

Mike Richards
Erstwhile Cancer Tsar

❖ Before the NHS Cancer plan
- Primary care doctors had to work out which doctor they should contact to see a patient with suspected cancer
- Cancer was often managed by surgeons, who made decisions on referral for ongoing treatment

❖ The NHS Cancer plans set targets for patient referral and treatment times, and mandated standardised pathways for patient care.

❖ Multidisciplinary team meeting meet regularly, offer electronic referral proformas and employ coordinators to ensure all patients are discussed and relevant plans are put into place.

Cancer pathways

❖ How quickly should a patient with suspected cancer be seen by a specialist?

❖ How quickly should a patient start treatment having been seen by an appropriate specialist, once a diagnosis of cancer has been established?

Cancer pathways

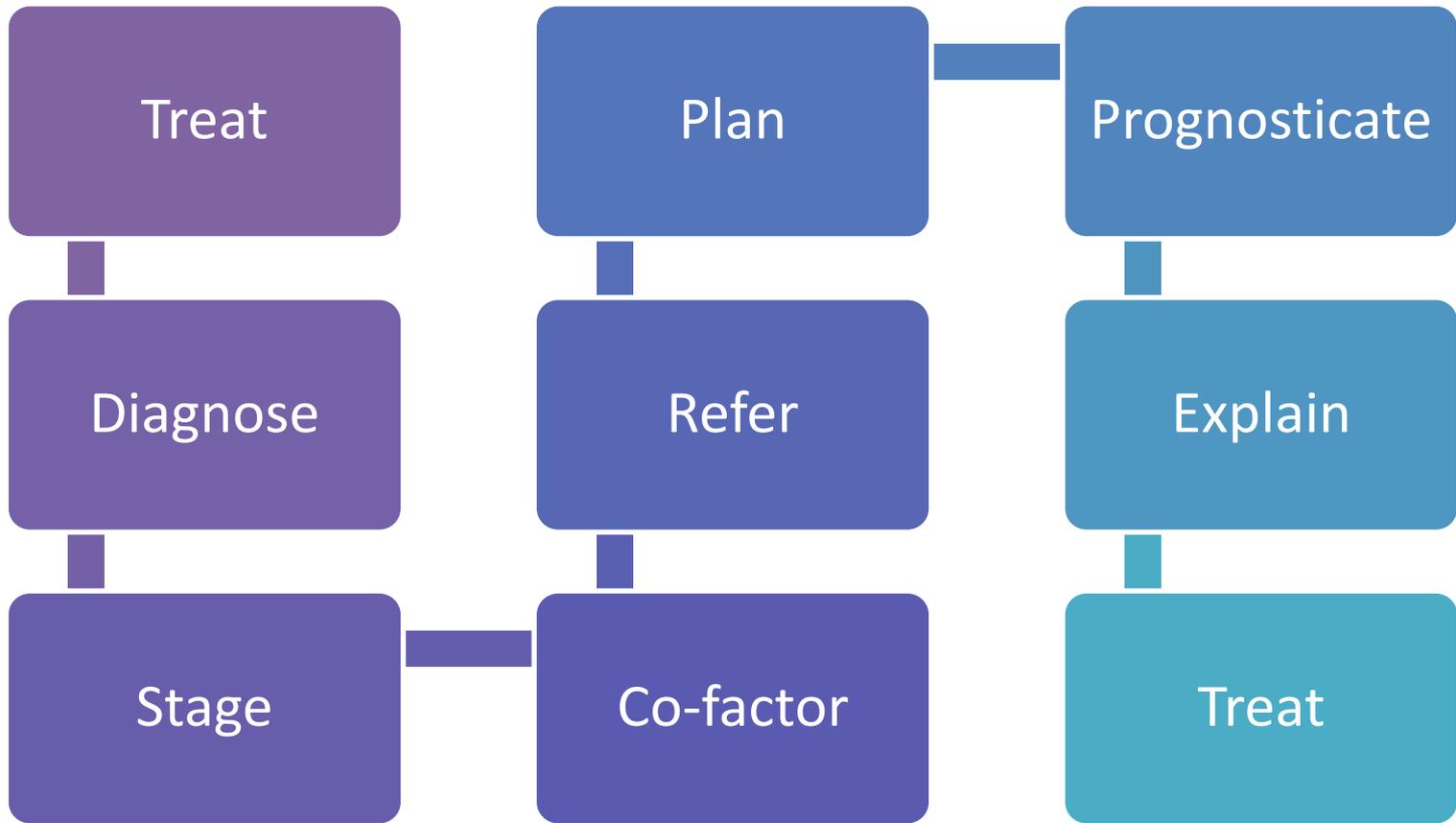❖How quickly should a patient with suspected cancer be seen by a specialist?

❖Within 2 weeks

❖How quickly should a patient start treatment having been seen by an appropriate specialist, once a diagnosis of cancer has been established?

❖Within 28 days

Cancer Journey

❖ Consider from a patient's point of view

Treat	Plan	Prognosticate
Diagnose	Refer	Explain
Stage	Co-factor	Treat

Treat immediate symptoms

❖ Sounds obvious but in the rush of trying to diagnose a suspected cancer, the symptoms of the patient may be overlooked

❖ These need to be considered and treated in a holistic fashion

❖ What are the commonest immediate symptoms?

Treat immediate symptoms

❖ Sounds obvious but in the rush of trying to diagnose a suspected cancer, the symptoms of the patient may be overlooked

❖ These need to be considered and treated in a holistic fashion

❖ What are the commonest immediate symptoms?
- Acute Pain
- Headache
- Breathlessness
- Bleeding
- Visceral obstruction

Establish a (cancer) diagnosis

❖ Cancer must enter your differential diagnosis when you see the patient

❖ Think about 'Red Flag' symptoms:
- Each red flag has a PPV >25% for a cancer diagnosis

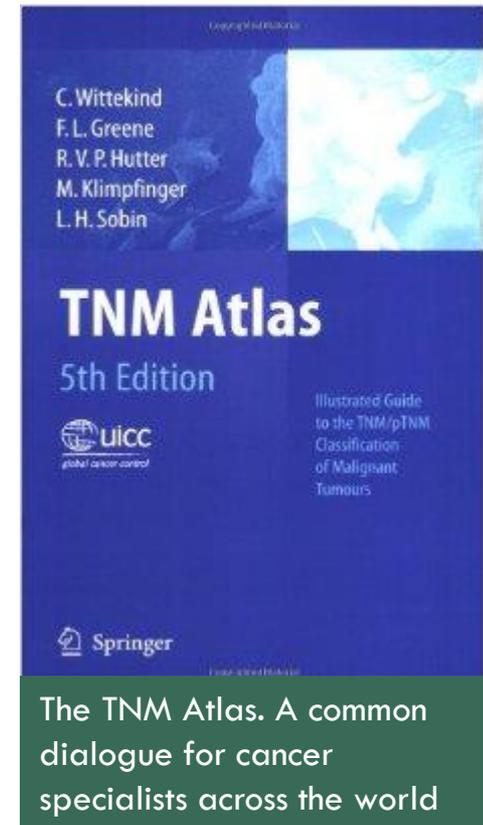❖ Undertake appropriate imaging or diagnostic investigations

Confirm diagnosis

❖ Confirmation of diagnosis is usually within the remit of a specialist MDT, but there are some exceptions

- Bronchoscopy / endoscopic biopsies
- Punch biopsies for skin lesions
- Blood film / bone marrow aspirate
- Tumour markers
- Radiological diagnosis where biopsy is not safe / possible
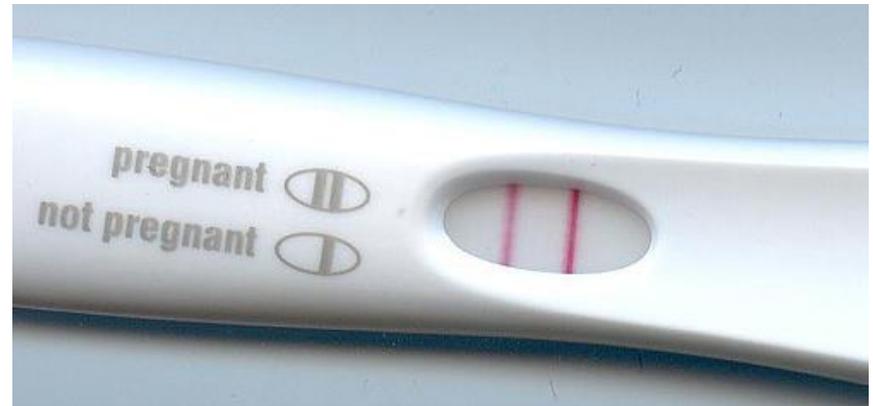
What is the cancer diagnosis?

Staging

❖ Staging involves performing necessary investigations (usually imaging) to assess extent of disease spread

❖ UICC TNM staging system used for many cancers
  - T = tumour stage
  - N = nodal stage
  - M = metastatic disease spread
  - TNM stages often then merged into clinical stages (1-4)
❖ Useful as a common dialogue (e.g. T3 N2 M0 lung cancer)
❖ Essential for guiding management and establishing treatment intent
❖ Useful for prognosis

❖ Consider that staging may be revised radiological, pre-operative, post-operative

C. Wittekind
F. L. Greene
R. V. P. Hutter
M. Klimpfinger
L. H. Sobin

TNM Atlas

5th Edition

Illustrated Guide to the TNM/pTNM Classification of Malignant Tumours

uicc
global cancer control

Springer

The TNM Atlas. A common dialogue for cancer specialists across the world

Treatment intent

❖ Very important to establish the intent of treatment after diagnosis and staging is complete

❖ Curative intent
- Benign conditions (meningioma)
- Localised disease
- Metastatic disease in very sensitive tumours (Lymphoma, Germ cell tumour)

- Accept *significant* acute toxicity if cure is possible
- Consider long term effects of therapy
- Support patient through side effects, even if this requires ITU admission

❖ Palliative intent
- Metastatic disease (solid tumours)
- Locally advanced disease
- Patient co-factors preclude radical treatment

- May still need intensive therapy to achieve palliation (e.g. Head & Neck Cancer)
- Balance side effects of treatment with QOL
- Ceiling of supportive care

Treatment scenarios

❖ Radical and palliative have been discussed

❖ Primary treatment : using Chemo or RT in place of surgery (e.g. RT for Head & Neck Cancer)

❖ Neo-adjuvant : using Chemo or RT to shrink (downstage) a tumour prior to definitive surgery (e.g. Colorectal cancer)

❖ Adjuvant : using Chemo or RT after surgery to improve loco-regional control and survival (e.g. Breast cancer)

❖ Concomitant : Using chemotherapy in combination with radiotherapy (e.g. Glioblastoma)

Co-factors and Performance Status

❖ Cannot consider tumour factors *in isolation* from patient factors
❖ Oncologists like to know performance status of patient (we use mainly WHO PS)
❖ PS is usually the most important prognostic factor after disease stage
❖ WHO PS works well but focuses on mobility rather than global function

❖ Co-factors are important in establishing suitability for treatment
❖ Consider Physical, Cognitive, and Social co-factors

WHO PS	Explanation of activity
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

Making the referral

❖ An important process. Your referral starts the clock for cancer waits. Incomplete referrals introduce delays for definitive treatment

❖ Find out which MDT to refer to (not always easy. Does a patient with meningeal metastases go to the CNS MDT or the skull base MDT)?

❖ Every MDT has a coordinator. Contacting them for advice is often a good idea

❖ Some MDTs move to electronic referral systems. They will often not let you progress the referral until you place an answer in every box. Whilst this is frustrating it prevents incomplete referrals and ultimately results in better service for your patient.

Request for Referral to Breast MDT Discussion Cases.

Cambridge Breast Unit, Box 97.
MDT co-ordinator: Teresa Smith.
Email: teresa.smith@addenbrookes.nhs.uk
Telephone: 01223 596179x 6179
Fax: 01223 257219

Referred by:...
Dept...

Patient Name...
Date of birth...
Hospital Number...

Date of MDM (if known).................................

Reason for referral:

Imaging results   YES / NO

Mammogram
Ultrasound
CT
MRI

Oncology Management YES / NO

Neo Adjuvant
Trial Name
Cycle Number
Reason for Discussion

Other: Please specify

Pathology review required

Yes
No

Other (please specify)

Prognosticating and weighing up treatment options

❖ Prognosis relates both to patient factors and treatment factors
❖ Need to evaluate treatment options before discussing them with the patient
  ▪ Consider level of evidence
  ▪ Consider level of efficacy
❖ Recommendations made by NICE are strongly influenced by evidence level

| Evidence category	Source
Ia	Systematic review and meta-analysis of randomised controlled trials
Ib	At least one randomised controlled trial
IIa	At least one well-designed controlled study without randomisation
IIb	At least one other type of well-designed quasi-experimental study
III	Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies or case studies
IV	Expert committee reports or opinions and/or clinical experience of respected authorities

Adapted from Eccles M, Mason J (2001) How to develop cost-conscious guidelines. Health Technology Assessment 5 (16).

Randomised controlled trials are considered the best form of evidence, but technically an RCT should only be used to evaluate two treatments considered on the basis of available evidence to be iso-effective

Assessing efficacy

❖ Most interventions will report overall survival as primary endpoint

❖ Usual analysis is a Kaplan-Meier survival curve

❖ Useful to understand how these work as they give a lot of data
- Survival rates at different periods of time after an intervention
- Deal with censored data (survival time is not known at the time the study ends)
- Maximise use of follow-up data

K-M curves initially reported for a landmark study of chemoradiation in 2005. Look at the magnitude of survival benefit at 36 months. (Stupp NEJM 2009)
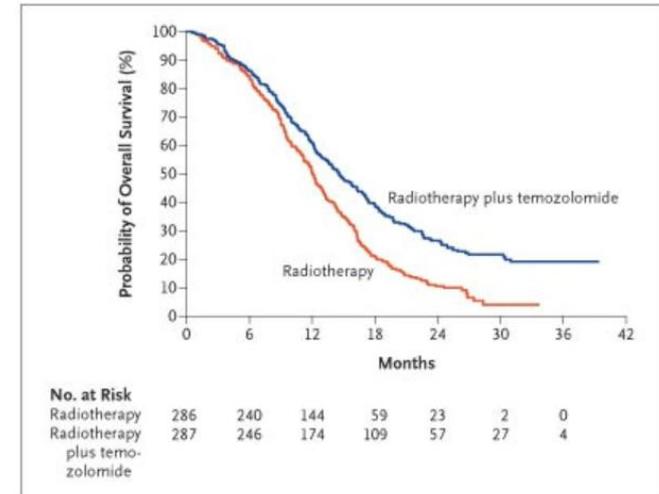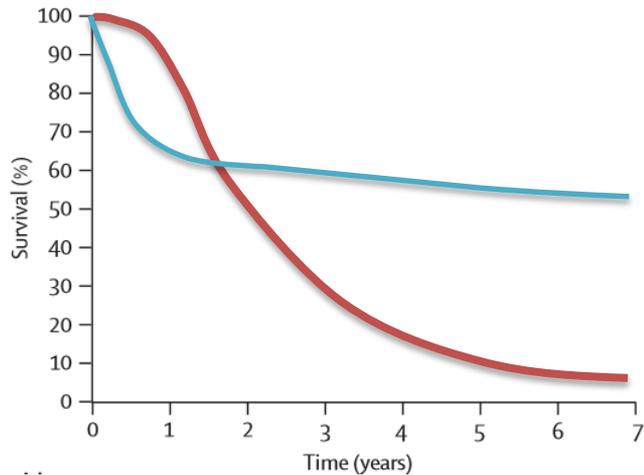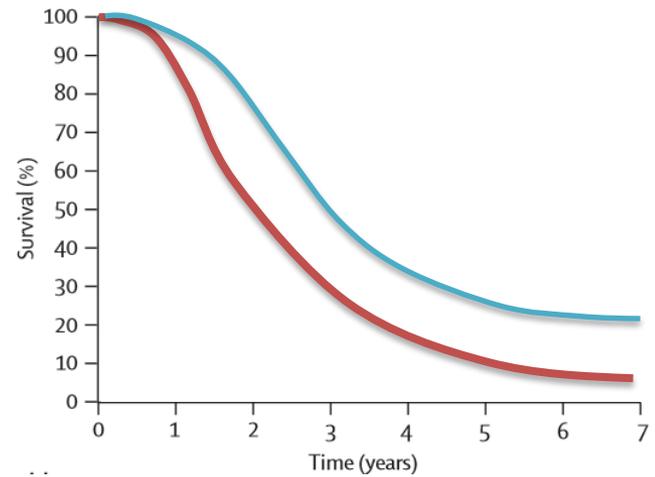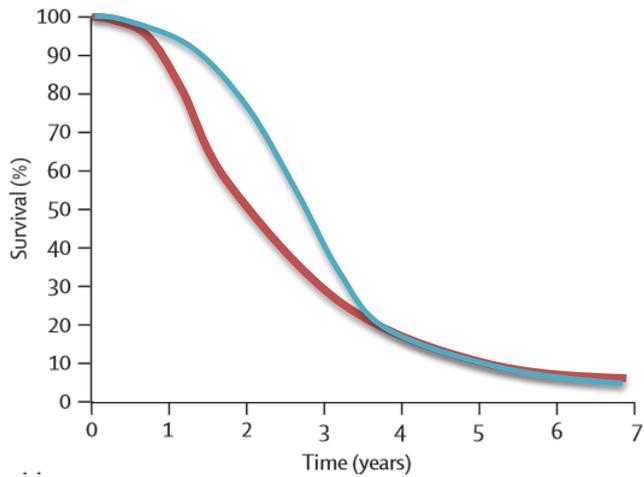

K-M curves for 5 year follow-up. The survival benefit is not maintained (Stupp NEJM 2009)
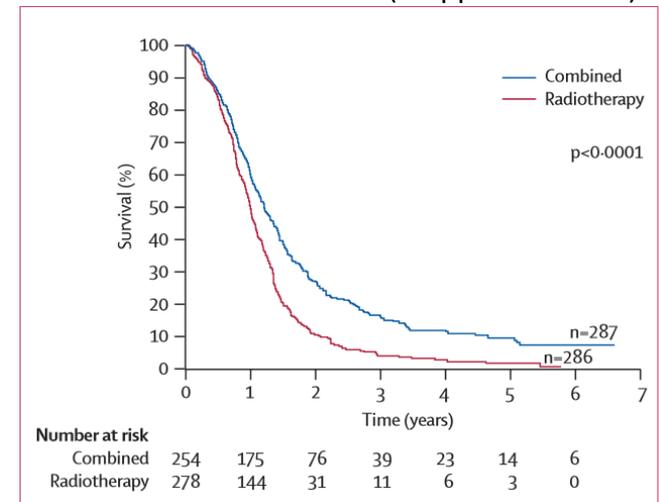
What do these K-M curves indicate?

Blue line = investigation arm | Red line = control arm
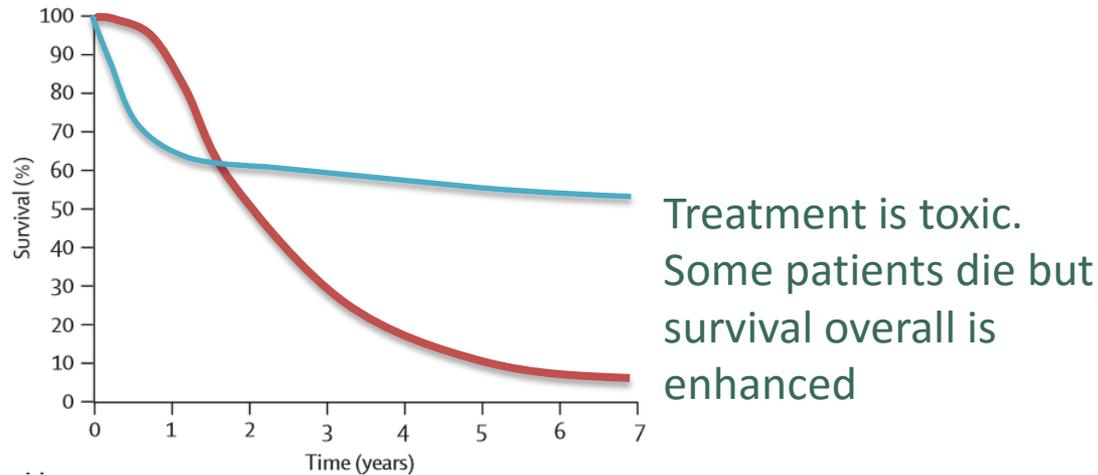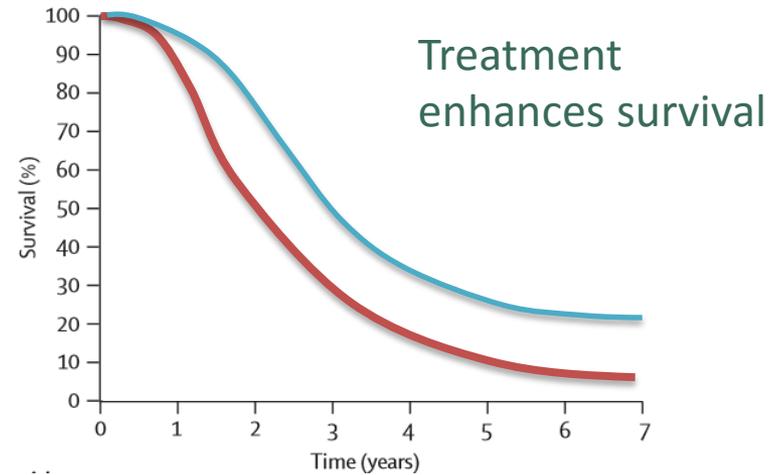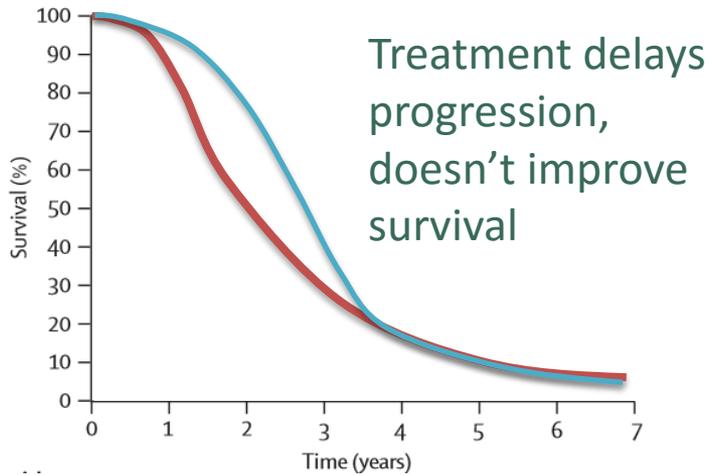
What do these K-M curves indicate?

Treatment delays progression, doesn't improve survival

Treatment enhances survival

Treatment is toxic. Some patients die but survival overall is enhanced

Meta-analysis

❖ Individual RCTs are prone to bias and effects of the study protocol
❖ Meta-analyses analyse effects of multiple RCTs. This should be done by going back to individual patient data from each RCT and producing summary statistics (though often this is not the case)

❖ What is an odds ratio?

❖ What is a hazard ratio?

Meta-analysis

❖ Individual RCTs are prone to bias and effects of the study protocol
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❖ What is an odds ratio?
❖ Relative risk of an event in each arm of the study, *independent* of time. Calculated by looking at the total number of events in a trial (e.g. odds ratio of vomiting). Not good for survival.

❖ What is a hazard ratio?
❖ Takes into account time. Hazard = rate at which events happen. Hazard in one arm of a study is a constant proportion of the hazard in the other arm of a study. This is the hazard ratio.

Meta-analysis

❖ Confidence interval + hazard ratio often expressed in a Forrest (box-whisker) plot

Study or Subgroup	Weight	Odds Ratio, [95% CI]
Years 5-9		
ATLAS	20.5%	0.90 [0.78 to 1.02]
aTTom	19.4%	0.90 [0.78 to 1.05]
ECOG E4181/E5181	3.0%	0.44 [0.21 to 0.92]
NSABP B14	5.9%	1.80 [1.11 to 2.93]
Scottish Trial	4.8%	1.57 [0.90 to 2.74]
Subtotal	**53.7%**	**1.01 [0.79 to 1.29]**

Heterogeneity: $P = 0.005$; $I^2 = 73\%$
Test for overall effect: $Z = 0.05$ ($P = 0.96$)

Years 10 and beyond		
ATLAS	22.1%	0.83 [0.74 to 0.92]
aTTom	17.1%	0.76 [0.63 to 0.91]
ECOG E4181/E5181	0.8%	0.58 [0.12 to 2.68]
NSABP B14	3.9%	0.59 [0.31 to 1.10]
Scottish Trial	2.5%	0.98 [0.43 to 2.22]
Subtotal	**46.3%**	**0.80 [0.73 to 0.88]**

Heterogeneity: $P = 0.74$; $I^2 = 0\%$
Test for overall effect: $Z = 4.72$ ($P < 0.001$)

Total	**100.0%**	**0.88 [0.77 to 1.01]**

Heterogeneity: $P = 0.01$; $I^2 = 58\%$
Test for overall effect: $Z = 1.83$ ($P = 0.07$)
Test for subgroup differences: $Chi^2 = 2.78$, ($P = 0.10$)

0.5   0.7   1   1.5   2
Favours >5 years   Favours 5 years

Look at this plot – would you recommend extended adjuvant tamoxifen on the basis of this data?

Communicating data to patient

❖ Best example of balancing up the Scholar and the Physician in a Doctor

❖ Even in a common indication with evidence from meta-analyses, there is no right answer

❖ Need to include patient factors in prognostication

❖ Consider patient's information needs

 The 'Internet patient' : Comes to clinic with reams of paper or an Ipad. Wants to know all of the details leading to the decision making process.

 The 'accepting patient' : Comes to clinic with the expectation that the doctor knows best and will decide on the best course of treatment.

❖ Try and observe how complex data is discussed with patients in our clinics

A word on screening

❖ Happens upstream from us in Oncology, but it is very important for us to understand

❖ Can you name the Wilson criteria for a screening programme?
- ▪ Condition should present a significant health problem to the population
- ▪ Natural history of the disease must be understood
- ▪ Early and late stages of disease must be recognisable
- ▪ Available screening test that is sensitive and specific
- ▪ An accepted policy should be available for who needs treatment
- ▪ Accepted treatment options for the disease should be available
- ▪ Treatment in early stage must impact on survival
- ▪ Screening should be cost effective

❖ Key concept to remember is that screening detects occult malignancy in patients that are well. Prognosis will be better than patients presenting with symptoms.

Summary

❖ In the department we have 40+ oncologists dealing with range of cancers

❖ All will use these key competencies, and follow this approach to a cancer patient

❖ Understanding this will allow you to help your patients with suspected cancer to obtain rapid and appropriate treatment

❖ Balance of the scholar and the physician is needed to get the process right

❖ During your attachment do try to attend at least one consultation where initial treatment options are discussed with the patient, and follow this process through.