Screening Populations for Cancer

- Commonplace for clinician to observe

  ‘If only the patient had presented earlier’ or

  ‘... had already spread too far when treatment started’

- The idea of screening, namely:

  to examine ostensibly healthy members of a population for subclinical signs of a disease,

  is attractive

Screening for Influenza

- Why would this be ridiculous?

1 Time from catching ‘flu to symptoms appearing is short
2 Can’t do anything even when you know you’ve got ‘flu
3 For most people ‘flu is unpleasant rather than serious

Requirements for screening

- Period in which disease is present, clinically undetectable *and* detectable by proposed screening method, must be substantial
- Must be thought that early detection confers therapeutic advantage
- Disease must be serious

Use in Chronic Disease

- Since demise of infectious disease, cancers and cardiovascular disease (CVD) are main health fear in developed world
- Previous requirements make screening a prime candidate for the use in these areas
- Screening in CVD is usually for ‘risk-factors’

Screening for Cancer

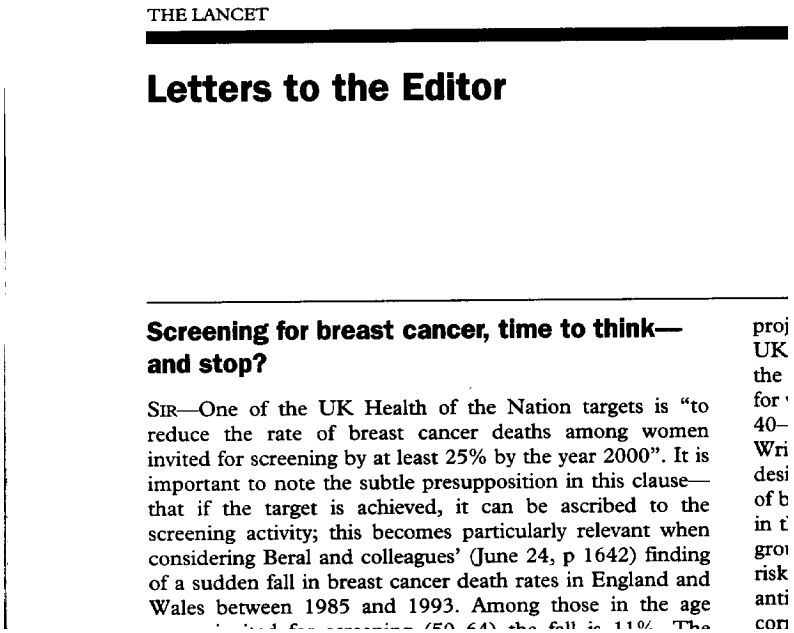
- Consider screening for cancer, rather than for risk-factors for CVD
- Provides hope in areas of considerable public health concern
- It ‘must’ be better to try to find early cases than not, so large population programmes come into being.

Screening for Cancer

- Take screening for breast cancer (e.g. using mammography) as example
- Issues similar to those for other cancers

Does it work?
Is it worth it?

- Considerable controversy
- Multidisciplinary problem, with *ethical, economic, statistical, sociological* as well as *clinical* aspects



THE LANCET

Letters to the Editor

Screening for breast cancer, time to think—and stop?

SIR—One of the UK Health of the Nation targets is "to reduce the rate of breast cancer deaths among women invited for screening by at least 25% by the year 2000". It is important to note the subtle presupposition in this clause—that if the target is achieved, it can be ascribed to the screening activity; this becomes particularly relevant when considering Beral and colleagues' (June 24, p 1642) finding of a sudden fall in breast cancer death rates in England and Wales between 1985 and 1993. Among those in the age

Is it worth it?

- Screening is certainly expensive
- Considerable debate about costs
- Costs often presented as cost per life saved: vary between $100 000 and $1.48m

Does it work?

- Even this is difficult
- What are the main problems?

Use mammographic screening for breast cancer as an example, although most aspects apply to most cancer screening programmes

Does it work?

- Even this is difficult
- What are the main problems?

Assessment of Screening

1. Is it practical?

2. Is it beneficial?

3. Is it harmful?

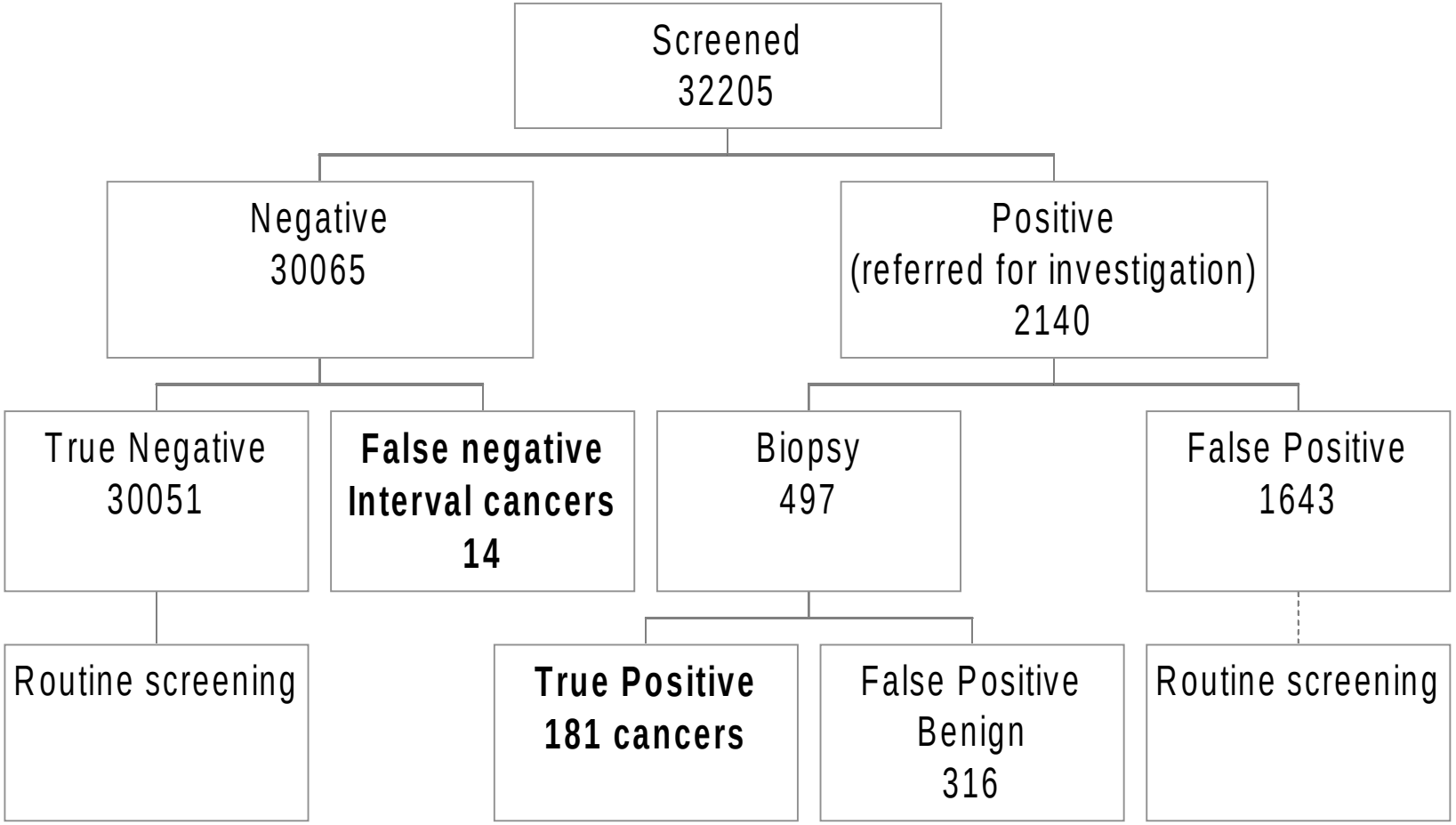
Is it practical?

- Breast screening programme will make two types of error:
  Refer well women
  Miss women with cancer
- Second obviously important
- First can be more so
  will facilities for further treatment be able to cope?

Sensitivity & Specificity

- Sensitivity:
  Probability a case will screen positive
- Specificity:
  Probability a non-case will screen negative
- Attributes of screening procedure:
  e.g.. mammography and physical examination

UK Trial of Early Detection: Edinburgh and Guildford centres



Calculating Sensitivity & Specificity

	Cancer Present	Cancer Absent	Total
Screened Positive	a = 181	b = 1959	a+b = 2140
Screened Negative	c =	d =	c+d = 30065
Total			32205

$$Sensitivity = a/(a+c) \qquad 1-Specificity = b/(b+d)$$

$$Positive\ Predictive\ Value = a/(a+b) = 181/2140 = 8.4\%$$

Calculating Sensitivity & Specificity

	Cancer Present	Cancer Absent	Total
Screened Positive	a = 181	b = 1959	a+b = 2140
Screened Negative	c = 14	d =30051	c+d = 30065
Total	195	32010	32205

$$Sensitivity = a / (a + c) = 181 / 195 = 93\%$$

$$1 - Specificity = b / (b + d) = 1959 / 32010 = 6.1\% \approx 1959 / 32205$$

Calculating Sensitivity & Specificity

- Calculation of specificity and sensitivity requires knowledge of *c* and *d*
- Only *c*+*d* known
- Using *c*+*d* in place of *d* does not lead to large errors in specificity
- Using number of ‘interval cancers’

  (those coming to light in 1 or 2 years after screening)

  can be inaccurate

Ranges of values

- Working Party on Breast Cancer screening considered several screening programmes

  Specificity ranged between 96 & 97%

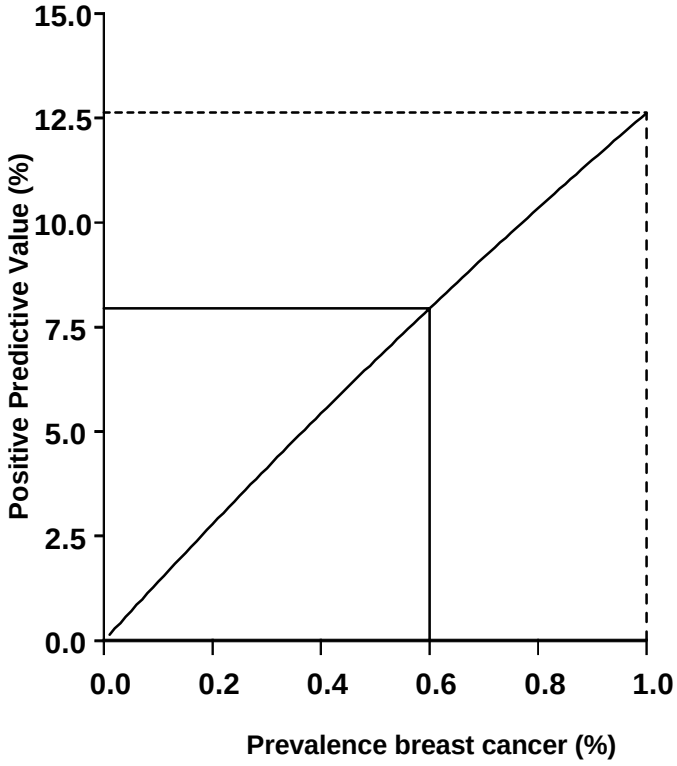
  Sensitivity ranged between 78 & 94%

Positive Predictive Value (PPV)

- Probability a woman screened positive actually has cancer
- Depends on sensitivity and specificity *and* on *prevalence* (proportion in population with disease)
- Breast cancer prevalence about 0.6%

PPV

- For prevalence of 0.6%, PPV = 8% (*at 1%, 12.5%)*
- For every case found, over 11 screen positives need to be investigated
- Increases as prevalence increases
- Why screening should focus on groups with higher prevalence



Is it beneficial?

- How can we tell?
- Compare breast cancer mortality in those screened and those unscreened?
- There are three reasons why this would be a bad idea

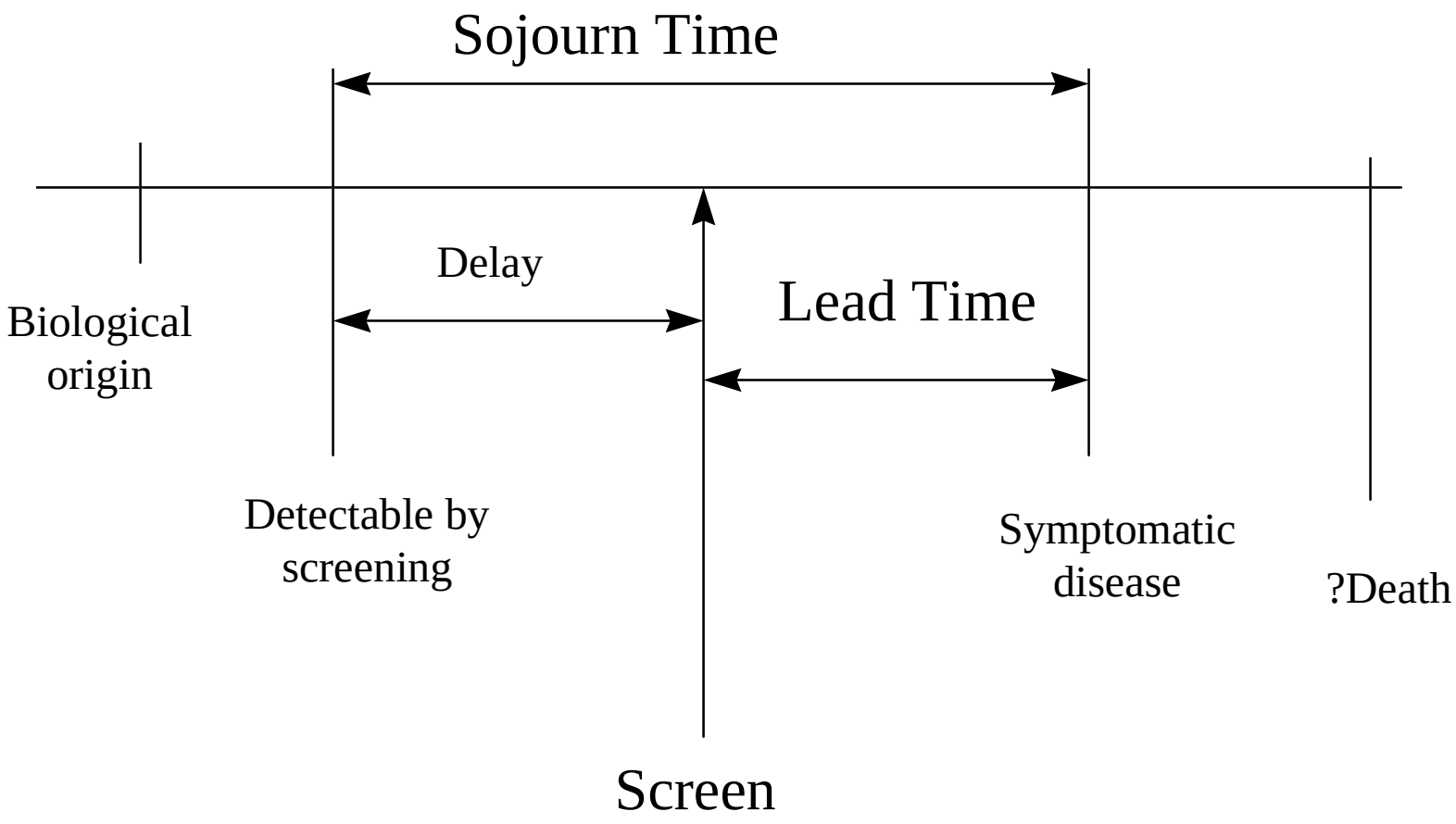
1. Those Screened are Healthier

- Observed that those accepting invitation to be screened are more ‘health-aware’
- Health Insurance Plan of New York (HIP)

Deaths /10000 person years

Controls 58.2 Refusers 83.7

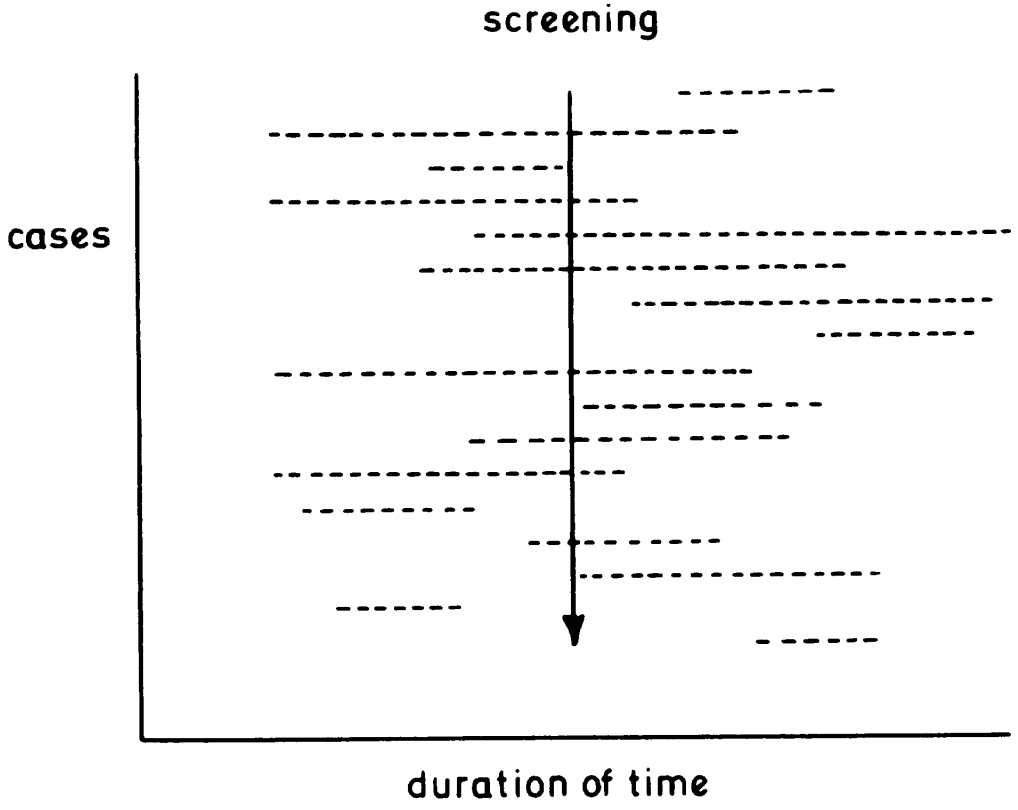
Notional History of Cancer



Lead-Time Bias

- Survival time is time from diagnosis to death
- Statistical techniques available to deal with cases where death has not yet happened
- BUT cases detected by screening will have increased survival time, even if death not delayed, because diagnosis is made earlier

Length Biassed Sampling



Length Biassed Sampling

- Screening more likely to detect cases with longer sojourn times
- It may be these are of a different type, e.g. they may be less aggressive
- If so, early detection may not be as useful as might be supposed

Correct Assessment

- Requires women to be enrolled in trial
- Women, or groups of women, randomised to programmes of screening
- Compare survival times from date of entry to study
- Compare all women, whether they accepted invitation for screening or not
- Include in mortality in screened group all cases, not just screen detected cases

Present Position

- Early studies showed some evidence of benefit
- Later studies less convincing, but may be methodological reasons for this
- Some debate about use of *relative* or *absolute* mortality:

Is it harmful?

- False Positives can cause unnecessary anxiety
- Confirmed cases may not have developed into ‘cancer’
- Size of benefit may not justify cost:
  10,000 screened expect 11 deaths
  10,000 controls, expect 15 deaths
  screening gives 30% reduction,
  but screening saves only 4 deaths /10,000