Screening

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Prevention

- *Live sensibly, among a thousand people only one dies a natural death, the rest succumb to irrational modes of living. Maimonides, 1135 - 1204*

Three lines of prevention

- Primary prevention
- Secondary prevention
- Tertiary prevention

Primary prevention

- Keep disease from occurring at all by removing the risk factors
- Examples:
  - immunization for communicable diseases
  - stop smoking

Secondary prevention

- Detects disease early when it is still asymptomatic and when early treatment can stop the disease from progressing
- Example: Pap smears for cervical cancer

Tertiary prevention

- Clinical activities that prevent further deterioration or reduce complications after a disease has become evident
- Example: use of beta-blocking drugs to decrease the risk of death in patients who have recovered from myocardial infarction

Levels of prevention

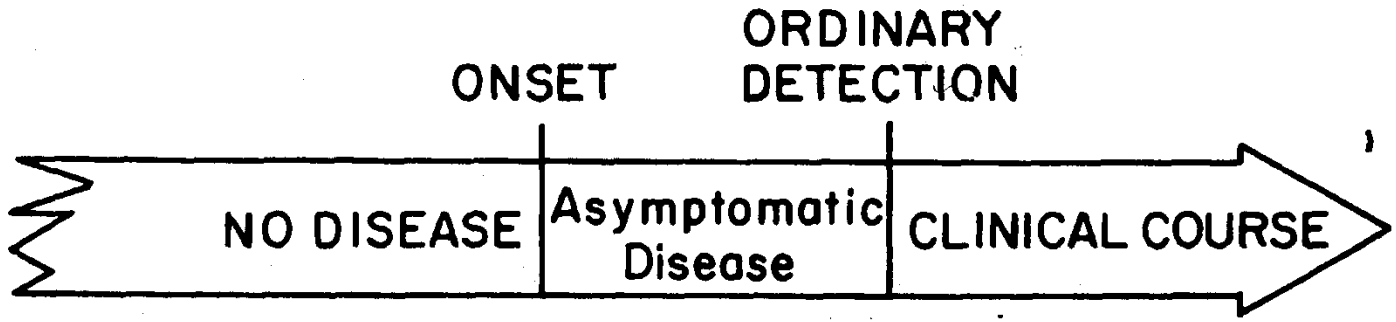

Figure 8.1. Levels of prevention.

Screening

- Presumptive identification of an unrecognized disease by the application of tests, examinations, or other procedures which can be applied rapidly
- Sorts out persons who have a disease from those who probably do not
- Person with positive or suspicious findings must be referred for further diagnosis and treatment

Which disease?

- First decide which disease one wants to screen for
- Many time we order exams without knowing exactly what we are looking for
- Example: urinalysis ordered in a routine check up. What are we interested in: diabetes or urinary tract infections or calculi, etc?
- Which condition is it worth screening for?

Is early treatment effective?

- If early treatment is not effective it is not worth screening for the disease
- Effective treatment
  - it must work
  - the patients accept it
  - results of treatment are better early in the course of the disease (asymptomatic) than later when disease is symptomatic and the patient seeks medical care
- The best way to establish efficacy is by RCTs (it may take a long time)

Biases again!

- When evaluating effectiveness of a screening program it is important to consider several sources of biases:
- Lead time bias
- Length/time bias
- Patient compliance

Lead time bias

- Lead time is the period of time between the detection of a medical condition by screening and when it ordinarily would have been diagnosed because of symptoms
- People who are diagnosed by screening for deadly disease will live longer from the time of diagnosis than people who are diagnosed because of symptoms, even if early treatment is ineffective (disease time vs. survival time)

Lead time bias

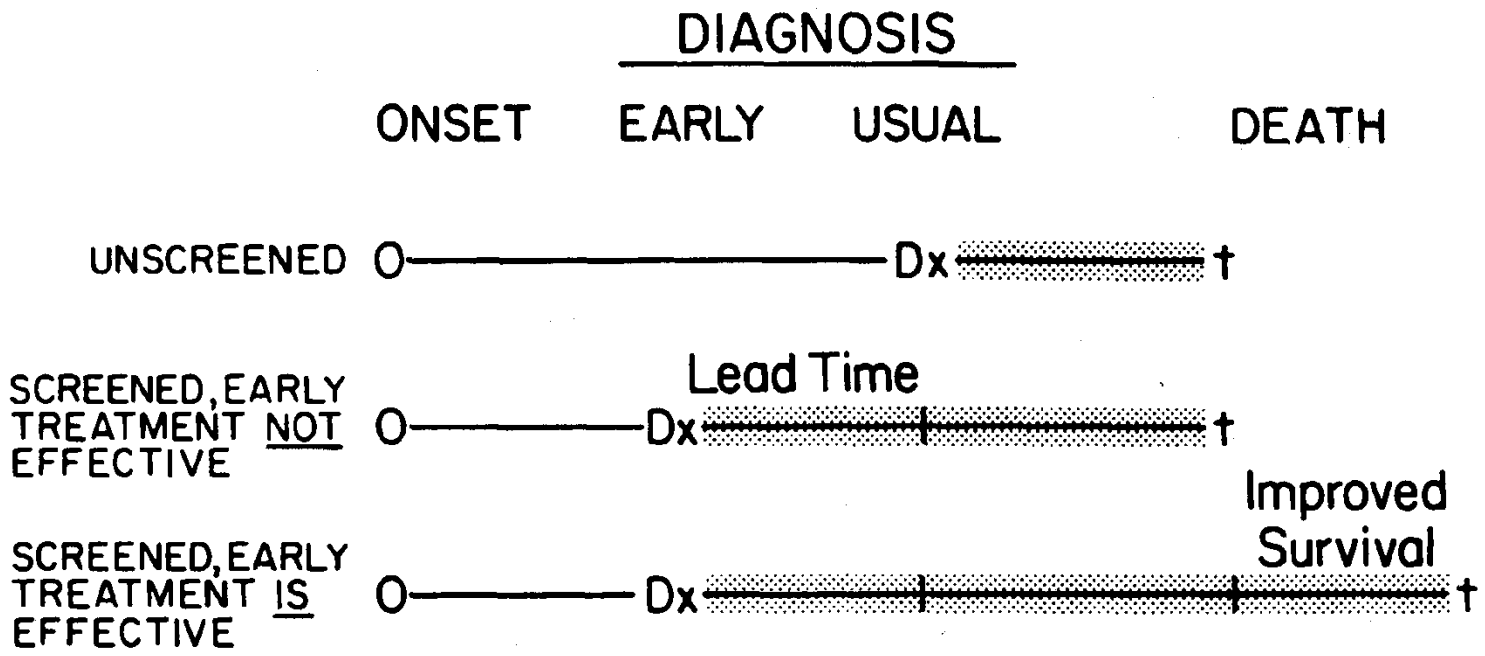

Figure 8.2. How lead time affects survival time after screening; *shaded areas* indicate length of survival.

Length/time bias

- A disease may be fast growing or slow growing
- Screening is more likely to find slow growing conditions (fast growing will have already caused symptoms at the time of screening)
- Therefore, screening is more likely to detect diseases with better prognosis (but the fact that screened persons have better prognosis is not related to screening itself)

Length/time bias

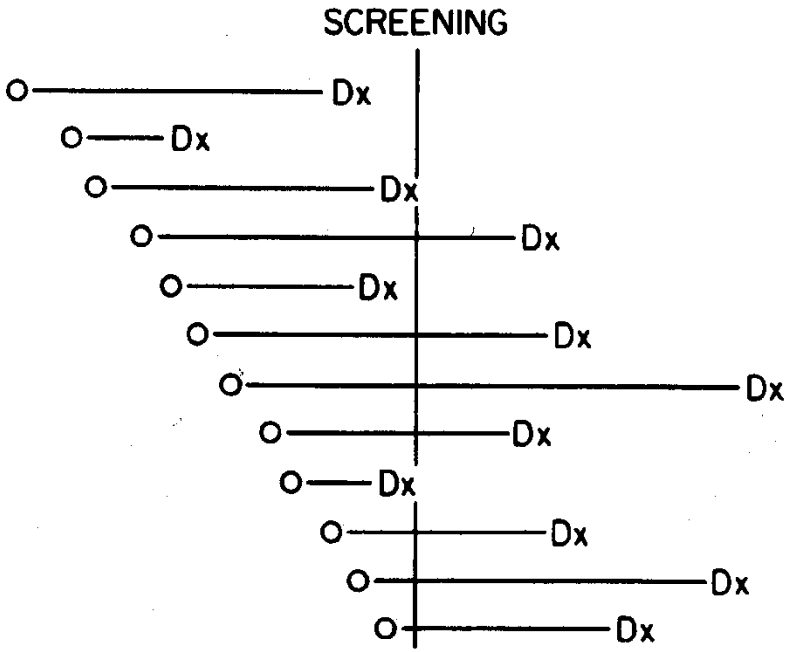

Figure 8.3. Length/time bias. Cases that progress rapidly from onset (O) to symptoms and diagnosis (Dx) are less likely to be detected during a screening examination.

Patient compliance

- It depends on the propensity of patients to follow medical advice
- If we compare disease outcome between a group of people who volunteered for a screening program with outcomes in a group of people who did not volunteer, better results in the volunteers might be due to other differences and not to treatment after screening

Burden of suffering

- Is screening justified by the severity of the medical condition in terms of mortality, morbidity and suffering caused by the disease?
- Only conditions posing threats to life and health should be sought.

Which test?

- Sensitivity and specificity (how the test performs)
- Simplicity and low cost
- Safety
- Acceptable to both patients and clinicians
- The labelling effect

Specificity and sensitivity

- Describe how the test performs

Accuracy of test results

- The test gives the correct answer when it is positive in the presence of a disease or negative in the absence of the disease
- The test is misleading if it is positive when the disease is absent (false positive) or negative when the disease is present (false negative)

The gold standard

- The assessment of the test's accuracy rests on its relationship to some way of knowing whether the disease is truly present or not (the gold standard)
- Why we want another test if we have already the gold standard?
- The gold standard is often elaborate, expensive, risky (biopsies) or is available too late (autopsies)

Screening for asymptomatic bacteriuria

- We want to know how good is a urine dipstick to detect asymptomatic bacteriuria
- The gold standard is urine culture

These are the results of the study

- of 37 persons with bacteriuria 27 tested positive with the dipstick (true positives)
- of 112 persons with no bacteriuria, 77 tested negative with the dipstick (true negative)
- of 112 persons with no bacteriuria, 35 tested positive with the dipstick (false positives)
- of 37 persons with bacteriuria 10 tested negative with the dipstick (false negatives)

This is not a new problem

Appearances to the mind are of four kinds.
Things either are what they appear to be;
or they neither are not appear to be;
or they are and do not appear to be;
or they are not, yet appear to be.
Rightly to aim in all these cases
is the wise man's task
Epictetus 2nd century AD

How to organize the data

	Disease +	Disease -	Total
Test +	True positives	False positives	
Test -	False negatives	True negatives	
Total			

Definitions

We are interested in knowing:

- The proportion of individuals with the disease who have a positive test for the disease (*Sensitivity*)
- The proportion of people without the disease who have a negative test (*Specificity*)

Back to bacteriuria

	Culture +	Culture -	Total
Dipstick +	27	35	62
Dipstick -	10	77	87
Total	37	112	149

How the test performs?

- Sensitivity: individuals with positive result/individuals with bacteriuria 27/37=73%
- Specificity: individuals with negative result/individuals with no bacteriuria 77/112=69%

What sensitivity and specificity tell us?

- A sensitive test will rarely miss people with the disease (chose a sensitive test when there is an important penalty for missing the disease - rule out the disease -, as in dangerous but treatable conditions)
- A specific test will rarely misclassify people without the disease as diseased (use when you want to rule in a disease, e.g. when confirming a diagnosis before starting a treatment)

To recap

- A test could be misleading (to some extent)
- Patients with the disease may test negative (false negative)
- Patients without the disease may test positive (false positive)
- Sensitivity: how good is the test in detecting as positive patients with the disease
- Specificity: how good is the test in detecting as negative patients with no disease

Sensitivity and specificity in a screening test

Ideally the test should be:

- highly sensitive (not to miss the usually few cases of disease that are present)
- highly specific (to reduce the number of people with false positive results who require further investigations)

Simplicity and low cost

The test should:

- take minimum time to perform
- require minimum preparation
- depend on no special appointment
- be inexpensive (think about further evaluation)

- Example: blood pressure determination

Other important issues

- Safety (a test considered safe in clinical practice when dealing with symptomatic patients, could be seen as dangerous when used for screening purposes in the general population)
- Acceptable to
  - patients
  - clinicians

The labelling effect

- We do not know much about the psychological impact of test results
- The effect could be either
  - positive (positive attitudes are reinforced)
  - negative (the patient assumes the sick role)

Important concepts

- Disease can be prevented by primary or secondary prevention
- Screening makes sense if:
  - early treatment is more effective than treatment at the usual time
  - the disease causes a substantial burden of suffering
  - a good screening test is available (sensitive and specific enough)

1) For many diagnostic or screening tests, there is a trade-off between sensitivity and specificity. True statements include which of the following?

A) Sensitivity would be extremely important when testing for amyothrophic lateral sclerosis (ALS) because there is no good treatment for it

B) Because hypothyroidism in infancy is devastating if missed, a screening test for it should be highly specific

C) Specificity is more important than sensitivity for screening tests

D) In evaluating the potential usefulness of a screening test, the effectiveness of the treatment for the disease screened for is important

E) None of the above

2) A radiologist develops a new screening test for cancer of the ovary. The sensitivity and specificity of the test are said to be "very high, at least 98%." You are asked to determine whether it would be useful to screen everyone in your primary care practice with this test in the next year. To answer, you need to know all the following EXCEPT

A) The incidence of asymptomatic ovarian cancer

B) The prevalence of asymptomatic ovarian cancer

C) The exact values of the sensitivity and specificity of the test

D) The cost of the test

E) The survival rate from ovarian cancer cases detected by the new test

3) A doctor has developed a new diagnostic test for cholera. He performs the test on 100 patients known to have cholera and 100 patients known not to have cholera with the following results:

	Cholera +	Cholera -	Total
Test +	**91**	**12**	**103**
Test -	**9**	**88**	**97**
Total	**100**	**100**	**200**

Which of the following is true:

A) The test categorized 9 individuals as true positive

B) The specificity of the test is 12%

C) the test categorized 88 individuals as false negative

D) the sensitivity of the test is 91%

E) None of the above

Receiver operating characteristic curves