Faculty of Medicine

Introduction to Community Medicine Course

(31505201)

Unit 4 Epidemiology

Introduction to Epidemiology

Screening for diseases

By

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15 +17 -11- 2016
Introduction to unit 4 Epidemiology

• Definition, History of Epidemiology
• Purpose/Use of Epidemiology
• Concepts in the infectious diseases
• Disease Causation
• Measurements of Morbidity and Mortality
• Levels of prevention and vaccination
• Screening for diseases
• Sources of Data and methods of data collection
• Epidemic Investigation and Management
• Epidemiological Surveillance
# Presentation outline

<table>
<thead>
<tr>
<th>Topic</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening for diseases: definition</td>
<td>12:00 to 12:10</td>
</tr>
<tr>
<td>Requirements of Tests used for Screening</td>
<td>12:10 to 12:20</td>
</tr>
<tr>
<td>Considerations before Launching a Screening Program</td>
<td>12:20 to 12:40</td>
</tr>
<tr>
<td>Serial (Sequential) and Parallel (Simultaneous) Screening Tests</td>
<td>12:40 to 12:50</td>
</tr>
<tr>
<td>Public Health Officer’s Check List while Planning a Screening Program</td>
<td></td>
</tr>
<tr>
<td>Evaluation of Screening Programs</td>
<td></td>
</tr>
</tbody>
</table>
World Health Day 2016: Beat diabetes

World Diabetes Day 2016- 14 November

7% of people with diabetes are at risk of blindness

#diabetes
www.who.int/whd/diabetes
DIABETES

DIABETES IS ON THE RISE

3.7 MILLION
deaths due to diabetes and high blood glucose

1.5 MILLION
deaths caused by diabetes

422 MILLION
adults have diabetes

THAT'S 1 PERSON IN 11

Main types of diabetes

**TYPE 1 DIABETES**
Body does not produce enough insulin

**TYPE 2 DIABETES**
Body produces insulin but can't use it well

**GESTATIONAL DIABETES**
A temporary condition in pregnancy

Consequences
Diabetes can lead to complications in many parts of the body and increase the risk of dying prematurely.

- Stroke
- Blindness
- Heart attack
- Kidney failure
- Amputation

Risk factors for type 2 diabetes
Genetics, age and family history of diabetes can increase the likelihood of becoming diabetic and cannot be changed. But some behaviours that increase risk can:

- Unhealthy diet
- 1 in 3 is overweight

- Physical inactivity
- 1 in 10 is obese

KEY ACTIONS

**FOR EVERYONE**

- Eat healthily
- Be physically active
- Avoid excessive weight gain
- Check blood glucose if in doubt
- Follow medical advice

**FOR GOVERNMENTS**

- Ensure Healthy Environments
- Better Diagnosis & Treatment
- Better Data

www.who.int/diabetes/global-report

#diabetes
Objectives - Concepts

- 1. Primary, Secondary, and Tertiary prevention
- 2. Population-level vs. individual-level prevention
- 3. Screening (secondary prevention)
  - Mass screening vs. case-finding
- 4. Screening concepts
  - Pre-clinical phase, lead time, test Se & Sp, importance of trials, DSMR
- 5. Screening Biases (Observational studies)
  - Lead-time, Length-time, and Compliance
- 6. Assessing the feasibility of screening
- 7. Risks (Harms) vs. Benefits
Relationship between Continuum and Health Promotion & Disease Prevention

• Health Promotion – **optimize overall health**. LEFT side
• Disease Prevention – **reduce occurrence and impact of specific diseases**. RIGHT side
# Levels of Prevention Table

<table>
<thead>
<tr>
<th>Disease:</th>
<th>Primary</th>
<th>Secondary</th>
<th>Tertiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>General or At-risk</td>
<td>Exposed or Early disease</td>
<td>Advanced disease or Complications</td>
</tr>
<tr>
<td>Goal</td>
<td>↓ new cases</td>
<td>↓ severity ↓ complications</td>
<td>↓ impact ↓ deaths</td>
</tr>
<tr>
<td>Rationale</td>
<td>↓ risk by ↓ exposure</td>
<td>Early identification allows earlier treatment</td>
<td>Minimize impact of disease on person</td>
</tr>
<tr>
<td>Interventions</td>
<td>Education Prophylaxis</td>
<td>Screening Early treatment Access to care</td>
<td>Treatment Rehabilitation</td>
</tr>
<tr>
<td></td>
<td>Health promotion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation (Outcomes)</td>
<td>↓ incidence of exposure</td>
<td>↓ incidence of disease ↓ morbidity</td>
<td>↓ prevalence ↓ morbidity ↓ mortality</td>
</tr>
</tbody>
</table>
Secondary Prevention

- **Defn:** measures available for the *early detection and prompt treatment of health problems*

- **Objectives:**
  - To reduce the consequences of disease (death or morbidity) by *screening asymptomatic* patients to identify disease in its early stages and intervening with a treatment which is *more effective* because it is being applied *earlier*.
  - It *cannot* reduce disease incidence

- **Where and how do we screen?:**
  - Population-level or mass screening
  - Individual-level screening or case finding
Screening for diseases: definition and objectives

• “the presumptive identification of unrecognized defect or disease by the application of tests, examinations or procedures which can be applied rapidly, to sort out apparently well persons who probably have a disease, from those who probably do not”.

Screening is the testing of apparently healthy populations to identify previously undiagnosed diseases.
Screening for diseases: definition and objectives

• To ensure **early detection of a disease** among individuals, so that prompt treatment may be instituted; e.g. screening for cervical cancer, breast cancer, hypertension etc. This is also called “Prescriptive Screening”.

• To **protect the community from disease** that the person being screened has, also called “Prospective Screening”; e.g. screening the blood units for HIV.

• For **entry into certain forms of occupations** (armed, industries, etc.) with a view to “weed out” those who are **unfit or whose existing** health status may be adversely affected by occupational conditions.
Definitions

1. **Screening program** -- *comprehensive disease control activity* based on the identification and treatment of persons with either unrecognized disease or unrecognized risk factors for disease.

2. **Screening test** -- *specific technology*:
   
   (survey questionnaire, physical observation or measurement, laboratory test, radiological procedure, etc.)

   used to help identify persons with unrecognized disease or unrecognized risk factors for disease.
Screening – two different approaches

- **Population-level screening**
  - National level policy decision to offer *mass screening* to a whole sub-group of a population
    - e.g., mammography screening (women 40+)
    - e.g., Vision and hearing screening of all Michigan 2nd graders

- **Individual-level screening**
  - Occurs at the *individual patient-physician level*
  - Also refereed to *case finding*
    - e.g., BP screening every time you visit MD
    - e.g., PSA screening
  - Also a component of the PHE.
  - Focus is on identifying existing disease in patients *who don’t know* they have it.
Generalities

1. Screening often implies a public health related activity involving asymptomatic or healthy subjects coming from the general population.

2. Case-finding refers to special clinical efforts to recognize disease among persons who consult a health professional.

3. Screening is an important aspect of prevention, but not all diseases are suitable for screening.
• Effective screening involves both **diagnostic** and **treatment** components
• Screening differs from diagnostic testing:

<table>
<thead>
<tr>
<th>Screening</th>
<th>Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy non-patients</td>
<td>Sick patients</td>
</tr>
<tr>
<td>No diagnostic intent</td>
<td>Diagnostic intent</td>
</tr>
<tr>
<td>Very low to low disease prevalence</td>
<td>Low to high disease prevalence</td>
</tr>
</tbody>
</table>
# Screening and case finding

## Screening:
- **testing for disease** in average (or low) risk, **asymptomatic population**
- may be considered a form of primary prevention
- goals:
  - early detection
  - treating to reduce morbidity or mortality
- **no diagnostic intent**
- average prevalence (by definition)

## Case-finding:
- **testing in patients at higher risk**
  - patients seeking medical care because of a complaint
  - patients with familial risks / exposures / other diagnosis
- **may be a form of secondary prevention**
  - disease present, reduce mortality / recurrence rate
- **diagnostic intent**
- usually higher than average disease prevalence
Important Concepts in Screening

The Pre-Clinical Phase (PCP)

• the period between when early detection by screening is possible and when the clinical diagnosis would normally have occurred.

Pathology begins → Disease detectable → Clinical Presentation

| ← Pre-Clinical Phase → |
Lead Time

Lead time = amount of time by which diagnosis is advanced or made earlier

Pathology → Disease detectable → Normal Clinical Presentation

Screen

Lead Time
Lead Time

• Equals the *amount of time by which treatment is advanced or made “early”*

• Not a theory or statistical artifact but what is expected and must occur with early detection

• *Does not imply improved outcome!!*

• *Necessary but not sufficient condition for effective screening.*
Requirements of Tests used for Screening

- **Valid**: It should be “accurate”, i.e. should measure correctly what it intends to. It should have high sensitivity, specificity, and positive & negative predictive values.

- **Reliable (Precise)**: It should give consistent results when repeated applications are made.

- **Yield**: It should give enough number of cases to commensurate with the expenditure and inputs involved. Yield will depend on Sensitivity of the test, Prevalence of the disease (If screening is applied to a high risk group, the yield will be better) and availability of medical care (if medical care has not been available to the community being screened, a large number of people with the disease will be diagnosed).
Requirements of Tests used for Screening

• **Practical**: The test should be easily administered by even persons with ordinary training, should be innocuous, acceptable and should give fairly quick results.

• **Efficient**: The amount of inputs (in terms of expenses and time) should result in reasonable amount of outputs in terms of improved health & satisfaction
Considerations before Launching a Screening Program for any Disease

• The condition should be an important health problem.
• There should be an acceptable and effective treatment.
• Facilities for confirming the diagnosis and for treatment should be available.
• There should be recognizable latent / early symptomatic stage.
• There should be a suitable screening test or examination available.
• The test should be acceptable.
Considerations before Launching a Screening Program for any Disease

● The natural history of the condition, including development from latent to apparent disease, should be adequately understood.

● There should be an agreed policy regarding whom to treat as patients.

● The cost of case finding (including final diagnosis and treatment) should be economically balanced vis-a-vis the expenditure on medical care as a whole.

● Case finding should be a continuing process and not “once and for all” project.
The Principles of Screening

• The choice of disease for which to screen;
• The nature of the screening test or tests to be used;
• The availability of a treatment for those found to have the disease;
• The relative costs of the screening.
Summary

• **Screening** is the testing of **apparently healthy populations to identify previously undiagnosed diseases or people at high risk of developing a disease.**

• Principles of Screening: disease, test, treatment and cost.

What is the next step?

Define the validity of the screening test and put screening to use in the population.
Screening

Screening is the process in which we use a test to determine whether an individual likely has a particular health indicator or not or is likely to develop a particular health indicator or not.

Screening is not the same as diagnosis; screening tests give us information about whether the disease is \textit{likely to be present}.

A screening test assesses the presence of an underlying marker that is associated with outcome of interest.
Screening, examples

• Women receive regular screening tests beginning in young adulthood for cervical cancer *(Pap smear)*
• Physicians assess **blood pressure and cholesterol** as screening tools for the development of cardiovascular disease
• Women use home **pregnancy tests** to screen for presence of an embryo or fetus
• ..........................
When to screen

We screen for disease when we have the opportunity to reduce costs and risk associated with diagnoses on large proportions of at-risk individuals.

1. We screen for health indicators that affect population health principally, not for rare diseases (although there are exceptions for rare diseases screen in utero).

2. There should be sufficient time between biological onset of disease and appearance of signs and symptoms of the disease exist so that screening could detect the presence of the disease earlier than it would come to clinical attention.

3. There should be available treatment for the disease so that early detection improves the lives of affected.

4. Screening tests should be cheaper and less invasive than best available diagnostic tool.
When to screen?
## Outcomes of a Screening Test

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>True Positives (TP)</td>
<td>False Positives (FP)</td>
<td>TP+FP</td>
</tr>
<tr>
<td>Negative</td>
<td>False Negatives (FN)</td>
<td>True Negatives (TN)</td>
<td>FN+TN</td>
</tr>
<tr>
<td>Total</td>
<td>TP+FN</td>
<td>FP+TN</td>
<td>TP+FP+FN+TN</td>
</tr>
</tbody>
</table>

### True Disease Status
- **Positive**: True Positives (TP) and False Positives (FP)
- **Negative**: False Negatives (FN) and True Negatives (TN)
time for a break!
Screening test evaluation

1. Sensitivity
2. Specificity
3. Positive predictive value
4. Negative predictive value
## Diagnostic and Screening Tests

### Test properties

<table>
<thead>
<tr>
<th></th>
<th>DISEASE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>(+)</td>
<td>A + C (All ill)</td>
</tr>
<tr>
<td>TEST (+)</td>
<td>(Š)</td>
<td>B + D (All healthy)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A + B + C + D (Grand Total)</td>
</tr>
</tbody>
</table>

|                  |          |
| DISEASE (Š)      |          |
|                  | C (FN)   |
|                  | D (TN)   |

|                  | (+)      | (Š)      |
|                  | A (TP)   | B (FP)   |

- **TP**: True Positive
- **FP**: False Positive
- **FN**: False Negative
- **TN**: True Negative
### Diagnostic and Screening Tests

#### Test properties

<table>
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<tr>
<th>DISEASE</th>
<th>(+)</th>
<th>(Š)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEST</td>
<td>A</td>
<td>B</td>
<td>A+B</td>
</tr>
<tr>
<td>(+)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Š)</td>
<td>C</td>
<td>D</td>
<td>C+D</td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td>A+B+C+D</td>
</tr>
</tbody>
</table>

**(True) prevalence**: Proportion of persons with disease in the population.

Prevalence = \( \frac{A+C}{A+B+C+D} \)

Of 1000 kids, 78 have head lice. Prevalence = 7.8%
### Diagnostic and Screening Tests

#### Test properties

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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<tr>
<td>TEST</td>
<td>A</td>
<td>B</td>
<td>A+B</td>
</tr>
<tr>
<td></td>
<td>(TP)</td>
<td>(FP)</td>
<td></td>
</tr>
<tr>
<td>(Š)</td>
<td>C</td>
<td>D</td>
<td>C+D</td>
</tr>
<tr>
<td></td>
<td>(FN)</td>
<td>(TN)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td>A+B+C+D</td>
</tr>
</tbody>
</table>

**Sensitivity**: Likelihood a diseased person will have a positive test

\[
\text{Sensitivity} = \frac{TP}{\text{All disease}} = \frac{A}{A+C}
\]

Of 100 men with prostate cancer, 90 have (+) PSA. Sensitivity=90%
### Diagnostic and Screening Tests

#### Test properties

<table>
<thead>
<tr>
<th>TEST</th>
<th>(+)</th>
<th>(Š)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>A (TP)</td>
<td>B (FP)</td>
<td>A+B</td>
</tr>
<tr>
<td>(Š)</td>
<td>C (FN)</td>
<td>D (TN)</td>
<td>C+D</td>
</tr>
</tbody>
</table>

Total: A+C, B+D, A+B+C+D

**Specificity**: Likelihood a healthy person will have a negative test

\[
\text{Specificity} = \frac{\text{TN}}{\text{All healthy}} = \frac{D}{B+D}
\]

Of 100 healthy kids, 3 have a false (+) strep test. Specificity = 97%
Example: **Diabetes**

Diabetes is diagnosed based on a fasting blood sugar $\geq 126$ mg/dL. If we raise the cutoff to 180 mg/dL, we make it more difficult to have a positive diabetes test, i.e., a diagnosis of DM.

We have made our test less sensitive (some true diabetics won’t have blood sugar that high) and more specific (normal people may get their blood sugar to 126, but are unlikely to get it to 180).

The opposite applies to lowering the cutoff: we become more sensitive but less specific.
Sensitivity and specificity give us likelihood of the test result among persons known to be diseased or healthy.

As clinicians, we need to know the opposite: the likelihood of being diseased or healthy among persons with a known test result.
**Diagnostic and Screening Tests**

<table>
<thead>
<tr>
<th>Test properties</th>
<th>DISEASE</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(⁺) TEST</td>
<td>A</td>
<td>B</td>
<td>A+B</td>
</tr>
<tr>
<td>(Š) TEST</td>
<td>C</td>
<td>D</td>
<td>C+D</td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td>A+B+C+D</td>
</tr>
</tbody>
</table>

**Predictive value of (⁺):** Likelihood that a person with a positive test actually has the disease

\[
PV(+) = \frac{TP}{All \ positives} = \frac{A}{A+B}
\]

Two-thirds of patients with a (+) Exercise Stress Test will have atherosclerosis on angiography  \[ PV(+) = 66\% \]
## Diagnostic and Screening Tests

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>(+)</th>
<th>(Š)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEST</td>
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<tr>
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<td>D</td>
<td>C+D</td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td>A+B+C+D</td>
</tr>
</tbody>
</table>

**Predictive value of (−):** Likelihood that a person with a negative test is free of the disease

\[ PV(−) = \frac{TN}{All \; negatives} = \frac{D}{C+D} \]

99 of 100 patients with a (−) syphilis test are free of syphilis

\[ PV(−) = 99\% \]
Diagnostic and Screening Tests

Consider: What is the likelihood that a person with a positive test will actually have the disease (i.e., what is the PV+) when...

Prevalence=20% in a population of $10^4$
Sensitivity=90%
Specificity=90%
## Diagnostic and Screening Tests

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>(+)</th>
<th>(Š)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens x 2000</td>
<td>1800</td>
<td>800</td>
<td>2600</td>
</tr>
<tr>
<td>Spec x 8000</td>
<td>200</td>
<td>7200</td>
<td>7400</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2000</td>
<td>8000</td>
<td>10,000</td>
</tr>
</tbody>
</table>

Population: 10,000  
Prevalence: 20%  
Sensitivity: 90%  
Specificity: 90%

\[
PV(+) = \frac{TP}{All\ Positives} = \frac{1800}{2600} = 69.2\%
\]

Conclude: Only 69.2% of persons with a positive test actually have the disease. (Tests ain’t perfect!)
Let’s see what happens when we make this a **rare disease**. Test properties stay the same. . .

**Prevalence=0.1%** in a population of $10^4$

Sensitivity=90%

Specificity=90%
## Diagnostic and Screening Tests

<table>
<thead>
<tr>
<th></th>
<th>DISEASE</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)</td>
<td>(Š)</td>
<td>Total</td>
</tr>
<tr>
<td>TEST</td>
<td>Sens x 10</td>
<td>Spec x 9,990</td>
<td></td>
</tr>
<tr>
<td>(+)</td>
<td>9</td>
<td>1</td>
<td>1,008</td>
</tr>
<tr>
<td>(Š)</td>
<td>999</td>
<td>8,991</td>
<td>8,992</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>9,990</td>
<td>10,000</td>
</tr>
</tbody>
</table>

**Population:** 10,000

**Prevalence:** 0.1%

**Sensitivity:** 90%

**Specificity:** 90%

**PV(+) = TP/All Positives =** 9/1,008 = 0.89%

Conclude: Less than 1%(!!) of persons with a positive test actually have the disease.
Diagnostic and Screening Tests

Although a positive test result identifies a group with increased prevalence of the disease, the prevalence may still be very low when you are starting with a rare disease.

Implication: Don’t do cardiac stress tests on marathon runners! Any positive is likely to be a false positive.

Tests should be limited to situations in which there is some intermediate probability of disease, where the result will affect your approach. (See following slide.)
Diagnostic and Screening Tests

Two other test attributes:

**Validity** = Accuracy: The likelihood that a test result will be correct, *on average*.

**Precision** = repeatability = reliability: The likelihood that repeated measures on the same sample or subject will yield the same result.

Ideal tests have high validity and high precision.
### Diagnostic and Screening Tests

Consider validity and precision for five repeated measurements where the true value is 120

<table>
<thead>
<tr>
<th>Results of five measurements</th>
<th>Validity</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>120, 120, 119, 121, 120</td>
<td><strong>High</strong> (average is 120)</td>
<td><strong>High</strong> (results all very close together)</td>
</tr>
<tr>
<td>120, 100, 140, 90, 150</td>
<td><strong>High</strong> (average is still 120!)</td>
<td><strong>Low</strong> (results all over the place)</td>
</tr>
<tr>
<td>100, 100, 99, 101, 100</td>
<td><strong>Low</strong> (average is way off at 100)</td>
<td><strong>High</strong> (results all very close together)</td>
</tr>
<tr>
<td>100, 80, 120, 70, 130</td>
<td><strong>Low</strong> (average is way off at 100)</td>
<td><strong>Low</strong> (results all over the place)</td>
</tr>
</tbody>
</table>
Sometimes we use tests in combination:

**Series testing**: The second test is given only to those positive on the first. To be positive for the combination, one must be positive on both the first **AND** second test. **This saves money, lowers sensitivity, and raises specificity.**

Example: HIV is first tested with a sensitive (but not specific) serological test. This catches all positives, but includes many false positives. The Western blot is done only on positives. It is very specific and identifies the false positives.
Diagnostic and Screening Tests

Sometimes we use tests in combination:

**Parallel testing:** *Both tests are given to everyone.* To be positive for the combination, a positive for either one of the tests will suffice.

This raises sensitivity and lowers specificity.

Example: Ischemic heart disease is diagnosed on the basis of a positive exercise tolerance test **OR** a positive exercise ECHO scan. (Many other tests are also available.) A positive result from either of these establishes the diagnosis.
II. Characteristics of screening tests

a) Sensitivity (Se) (Prob T+ | D+)

– Defn: the proportion of cases with a positive screening test among all individuals with pre-clinical disease

– Want a highly Se test in order to identify as many cases as possible...... but there’s a trade off with......
II. Characteristics of screening tests

b) **Specificity (Sp) (Prob T- | D-)**
   
   – *Defn: the proportion of individuals with a negative screening test result among all individuals with no pre-clinical disease*
   
   – *The feasibility and efficiency of screening programs is acutely sensitive to the PVP which is often very low due to the very low disease prevalence*
   
   – *e.g., PVP of +ve FOBT for CR CA = < 10%*
III. Evaluation of Screening Outcomes
How do we know if screening is helpful?

- Compare **disease-specific mortality rate (DSMR)** between those randomized to screening and those not

- Eliminates all forms of bias (theoretically)

- But, problems of:
  - Expense, time consuming, logistically difficult, contamination, non-compliance, ethical concerns, changing technology.

- Can also evaluate screening programmes using Cohort and Case-control studies, but they are difficult to do and very susceptible to bias.
The only valid measure of screening is...

**Disease-specific Mortality Rate (DSMR)**

the number of deaths due to disease
Total person-years experience

– *The only gold-standard outcome measure for screening*
– NOT affected by lead time
– when calculated from a RCT - not affected by compliance bias or length-time bias.
– However, there can be problems with the correct assignment of cause of death (hence some researchers advocate using only all-cause mortality as the outcome).
Example of a RCT reporting DSMR to measure efficacy of FOBT screening on Colorectal CA Mortality (Mandel, NEJM 1999)
IV. Biases that effect screening studies

• Observational studies and especially survival data are acutely sensitive to:

• 1. **Compliance bias** (Selection bias):
  • Volunteers or compliers are better educated and more health conscious – thus they have inherently better prognosis

• 2. **Lead-time bias**
  • *Apparent* increased survival duration introduced by the *lead time* that results from screening.
  • Screen-detected cases survive longer event without benefit of early treatment (review Fig 2 in course notes).

• 3. **Length-time bias**
  • Screening preferentially identifies slower growing or less progressive cases that have a better prognosis.
V. Pseudo-disease and Over-diagnosis

• **Over-diagnosis**
  – Limited malignant potential
  – Extreme form of length-biased sampling
  – Examp: Pap screening and cervical carcinoma

• **Competing risks**
  – Cases detected that would have been interrupted by an unrelated death
  – Examp: Prostate CA and CVD death

• **Serendipity**
  – **Chance detection due to diagnostic testing for another reason**
  – Examp: PSA and prostate CA, FOBT and CR CA
VI. Assessing the feasibility of screening

- **Burden of disease**
  - Effectiveness of treatment without screening

- **Acceptability**
  - Convenience, comfort, safety, costs (= compliance)

- **Efficacy of screening**
  - Test characteristics (Se, Sp)
  - Potential to reduce mortality

- **Efficiency**
  - Low PVP
  - Risks and costs of follow-up of test positives
  - Cost-effectiveness
    - Annual Mam screening (50-70 yrs) = $30 – 50,000 /YLS
    - Annual Pap screening (20-75 yrs) = $1,300,000 YLS

- **Balance of risks (harms) vs. benefits**
Feasibility

- **Efficacy**
- **Effectiveness**
- **Cost-effectiveness**

• Should we screen? (scientific)
• Can we screen? (practical)
• Is it worth it? (scientific, practical, policy, political)
Summary

• Screening for health indicators is integral part of improving population health

• Screening predicts who will develop a specific disease and detects disease among those in early stages

• Screening tests need to be studied for validity (sensitivity and specificity)

• We often have a trade-off between sensitivity and specificity

• Predictive value of screening test is maximized in populations with high prevalence of health indicator of interest

• Value of screening program will depend on cost-effectiveness, minimal invasiveness, availability of effective treatment