The public and clinicians frequently endorse cancer screening tests based on the argument that early detection leads to better survival. The intuitive appeal of this reasoning has led to widespread use of screening technologies that have not been fully tested and even of some that have been associated with substantial harm….

-- Barnett S. Kramer

Visanou Hansana MD; MCTM
LEARNING OBJECTIVES

- Define the purpose of screening tests and name criteria for their use in populations
- Define terms used to evaluate screening test effectiveness
- Identify and define the types of bias characteristic of cancer screening studies
- Describe how the principles of evidence-based medicine apply to counseling individuals on cancer screening tests
WHAT IS CANCER SCREENING?

- A test performed on asymptomatic individuals that allows for early detection, therapeutic intervention, and decreased mortality from the disease
- Positive result on screening test often leads to further testing and possibly to diagnostic workup
- Considered a secondary preventive intervention
Criteria for Use of a Screening Test

- Significant burden of disease in population
- Preclinical stage is detectable and prevalent
- Early detection improves outcome (mortality) with acceptable morbidity
- Screening tests are acceptable to population, inexpensive, and relatively accurate
- Effective treatment available for detected disease
CHARACTERISTICS OF SCREENING TESTS

- Test effectiveness measured as
  - Sensitivity: ability to confirm disease
  - Specificity: ability to identify disease absence

- Clinical importance related to predictive ability
  - Positive Predictive Value: proportion testing positive who actually have the disease
  - Negative Predictive Value: proportion testing negative who do not have the disease
APPLICATION OF SCREENING TO POPULATIONS

The 2x2 Table describes screening test outcomes:

<table>
<thead>
<tr>
<th></th>
<th>Disease present</th>
<th>Disease absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive result</td>
<td>Group (a) True Positive</td>
<td>Group (b) False Positive</td>
</tr>
<tr>
<td>Negative result</td>
<td>Group (c) False Negative</td>
<td>Group (d) True Negative</td>
</tr>
</tbody>
</table>
CHARACTERISTICS OF SCREENING TESTS

1) **Sensitivity**: proportion of those with disease who test positive in the screened group

\[
\frac{(a)}{(a) + (c)}
\]

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease present</strong></td>
<td><strong>Disease absent</strong></td>
</tr>
<tr>
<td>Group (a) True Positive</td>
<td>Group (b) False Positive</td>
</tr>
<tr>
<td>Group (c) False Negative</td>
<td>Group (d) True Negative</td>
</tr>
</tbody>
</table>
CHARACTERISTICS OF SCREENING TESTS

2) **Specificity**: proportion of those without disease who test negative in screened group

\[
\frac{(d)}{(b) + (d)}
\]

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease present</td>
<td>Group (a) True Positive</td>
</tr>
<tr>
<td>Disease absent</td>
<td>Group (b) False Positive</td>
</tr>
</tbody>
</table>
### The Ideal Situation -- 100% Agreement

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Disease present</th>
<th>Disease absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 200</td>
<td>200 True positive</td>
<td>0 False positive</td>
</tr>
<tr>
<td>Negative result</td>
<td>0 False negative</td>
<td>800 True negative</td>
</tr>
</tbody>
</table>
### A More Likely Outcome

<table>
<thead>
<tr>
<th>Disease present</th>
<th>Disease absent</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>n</em> = 200</td>
<td><em>n</em> = 800</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>170</strong> True Positive</td>
<td><strong>30</strong> False Negative</td>
</tr>
<tr>
<td><strong>30</strong> False Positive</td>
<td><strong>770</strong> True Negative</td>
</tr>
</tbody>
</table>
SENSITIVITY AND SPECIFICITY

- Consequences of a False Positive
  - Even 3-5% will be large on a population level
  - Follow-up tests, cost, potential harm, anxiety
  - Periodic screening increases lifetime risk

- Consequences of a False Negative
  - Even one person can have tragic implications
  - At best, a false sense of security
  - Might neglect future screening tests
THE TRADEOFF: SENSITIVITY vs. SPECIFICITY

- If missing cancers is a concern, sensitivity can be raised by adjusting the diagnostic cut point for a positive result
- But, the false positive rate will also increase
- How will this affect screening program costs?
- Specificity may be the determining factor in the success of screening programs
**Understanding Predictive Values**

- Clinician’s perspective: If a test result is positive, how likely is it that this individual has the disease?
- Predictive value varies with the prevalence of the disease in the screened population.
- *Bayes’ theorem*: As the prevalence of a disease increases, the positive predictive value of the test increases (PPV) and its negative predictive value (NPV) decreases.
Characteristics of Screening Tests

3) Positive Predictive Value (PPV): The likelihood that a positive test result indicates the existence of the disease

\[
\frac{(a)}{(a) + (b)}
\]

<table>
<thead>
<tr>
<th>Positive result</th>
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<tbody>
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<td>Group (a) True Positive</td>
<td>Group (b) False Positive</td>
<td></td>
</tr>
<tr>
<td>Group (c) False Negative</td>
<td>Group (d) True Negative</td>
<td></td>
</tr>
</tbody>
</table>
4) Negative Predictive Value (NPV): The likelihood that a negative test result indicates the absence of the disease

\[
\frac{(d)}{(c) + (d)}
\]
# Predictive Values and Prevalence

**Sensitivity** = ? ; **Specificity** = ?

<table>
<thead>
<tr>
<th>Prevalence = ?</th>
<th>Disease Yes</th>
<th>Disease No</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive result</td>
<td>99</td>
<td>495</td>
<td></td>
</tr>
<tr>
<td>Negative result</td>
<td>1</td>
<td>9405</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>9900</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prevalence = ?</th>
<th>Disease Yes</th>
<th>Disease No</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive result</td>
<td>495</td>
<td>475</td>
<td></td>
</tr>
<tr>
<td>Negative result</td>
<td>5</td>
<td>9025</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>500</td>
<td>9500</td>
<td></td>
</tr>
</tbody>
</table>
## Predictive Values and Prevalence

**Sensitivity = 99%; Specificity = 95%**

<table>
<thead>
<tr>
<th>Prevalence = 1%</th>
<th>Disease Yes</th>
<th>Disease No</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive result</td>
<td>99</td>
<td>495</td>
<td></td>
</tr>
<tr>
<td>Negative result</td>
<td>1</td>
<td>9405</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>9900</td>
<td>17%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prevalence = 5%</th>
<th>Disease Yes</th>
<th>Disease No</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive result</td>
<td>495</td>
<td>475</td>
<td></td>
</tr>
<tr>
<td>Negative result</td>
<td>5</td>
<td>9025</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>500</td>
<td>9500</td>
<td>51%</td>
</tr>
</tbody>
</table>
Evaluating a Cancer Screening Test

- Goal is reduced mortality, not early case detection
- Survival is not an adequate surrogate endpoint
- Natural history of screen-detected cancers not identical to that of clinically detected cancers
- Effectiveness and morbidity of screening tests cannot be separated from subsequent treatments for the disease
Evaluation of Screening Programs

- Bias is any systematic error that affects the evaluation of screening test performance
- “Stage shift” biases
  - **Lead time bias**: screening advances the diagnosis of cancer and leads to longer survival, but no benefit in mortality reduction
  - **Length bias**: screening detects less aggressive cancers with long preclinical phases (and better prognoses)
EVALUATION OF SCREENING PROGRAMS

- Overdiagnosis bias
  - Benign or indolent cancers are often detected
  - Cancers diagnosed have malignant potential but not likely to cause death

- Selection bias: individuals who participate in screening trials are fundamentally different from those who do not
  - Randomized study design minimizes effect
  - “Healthy volunteer effect”
Risks of Screening

- The principle “do no harm” applies
- Risk often attached to follow-up testing
  - CRC screening—positive FOBT leads to risks of colonoscopy, including heavy blood loss and bowel perforation
  - Evaluation of the false positive—more harm than benefit to individuals?
- Treatment for any detected cancer will significantly affect quality of life
Barriers to Screening

Patient barriers

- Social & cultural norms
- Psychological factors (fear and anxiety)
- Access to the health care system and insurance status
- Behavioral factors
- Perceptions of personal risk for disease
- Self-efficacy
Barriers to Screening

Physician barriers

- Lack of time and competing priorities
- No reimbursement for counseling on preventive behaviors
- Mobile populations—documentation and follow up difficult
- Lack of professional consensus on benefits of some screening tests
- Organizational or systems problems
INDIVIDUALIZING THE SCREENING DECISION

- Patient must share in screening decision
  - Informed consent essential
  - Partners in health with the clinician
- Eliciting patient preferences is key
  - Incorporate patient’s values, past experiences, and attitudes
  - Discuss barriers and problem solve
- Adherence to screening the goal
CONCLUDING COMMENTS

- Cancer screening tests require optimal performance characteristics for effective use in screening programs within populations.
- Understanding the scientific evidence for screening recommendations promotes best clinical care for individual patients.
- Preventive medicine requires the active participation of clinician and patient in a partnership for health.
Thank You

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