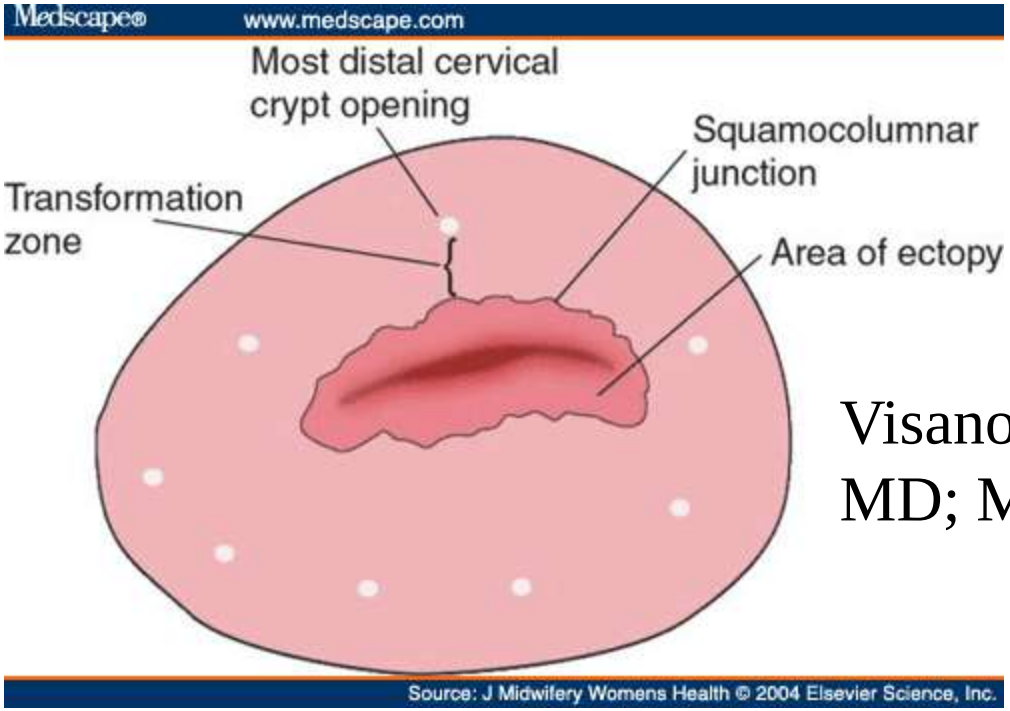
Principles of Cancer Screening



Visanou Hansana
MD; MCTM

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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

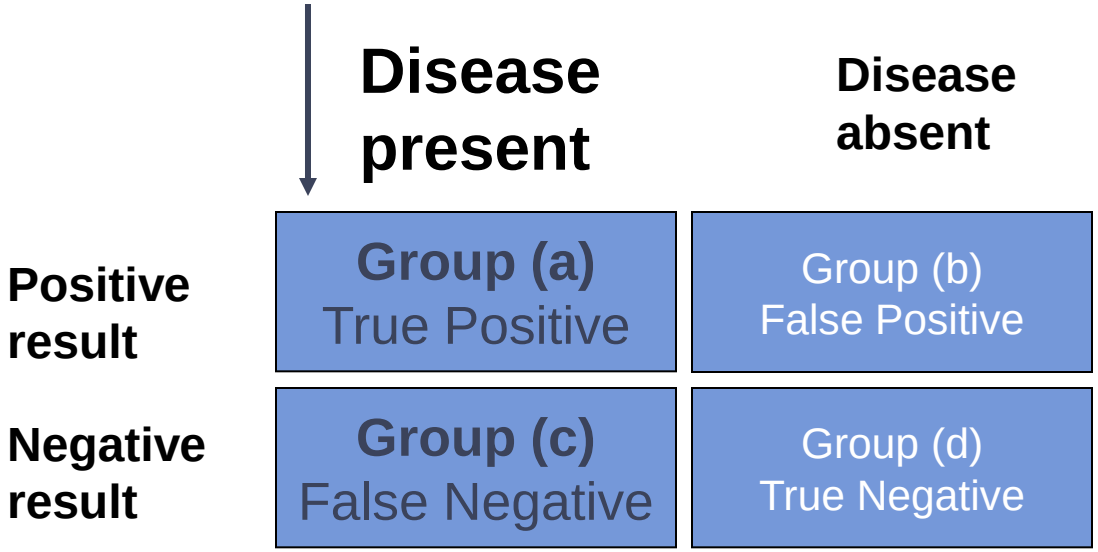
The 2x2 Table describes screening test outcomes:

	Disease present	Disease absent
Positive result	Group (a) True Positive	Group (b) False Positive
Negative result	Group (c) False Negative	Group (d) True Negative

Characteristics of Screening Tests

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

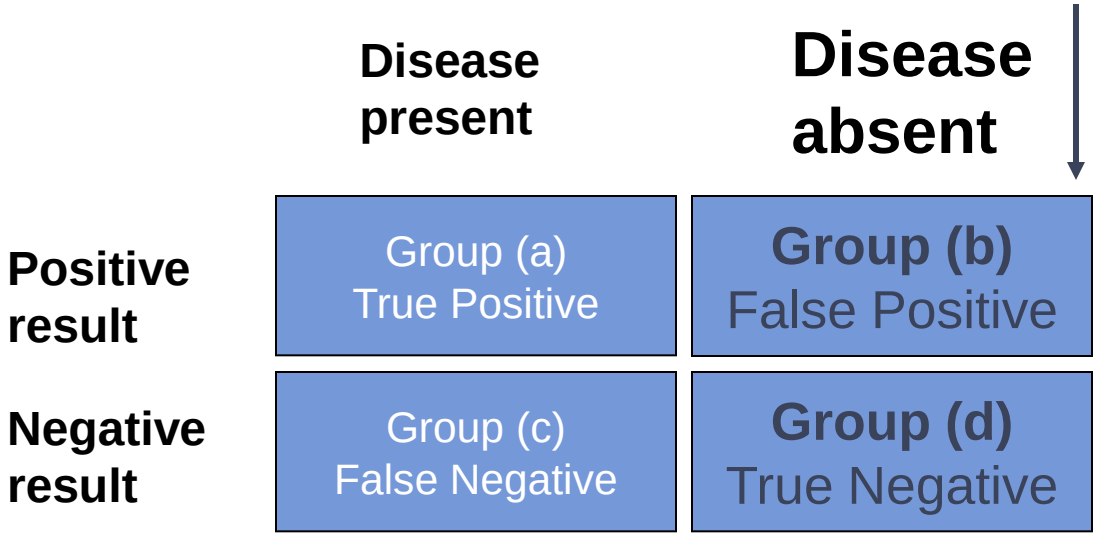
$$\frac{(a)}{(a) + (c)}$$



Characteristics of Screening Tests

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

$$\frac{(d)}{(b) + (d)}$$



The Ideal Situation--100% Agreement

	Disease present n = 200	Disease absent n = 800
Positive result	**200** True positive	0 False positive
Negative result	0 False negative	**800** True negative

A More Likely Outcome

	Disease present n = 200	Disease absent n = 800
Positive result	170 True Positive	**30** **False Positive**
Negative result	**30** **False Negative**	770 True Negative

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

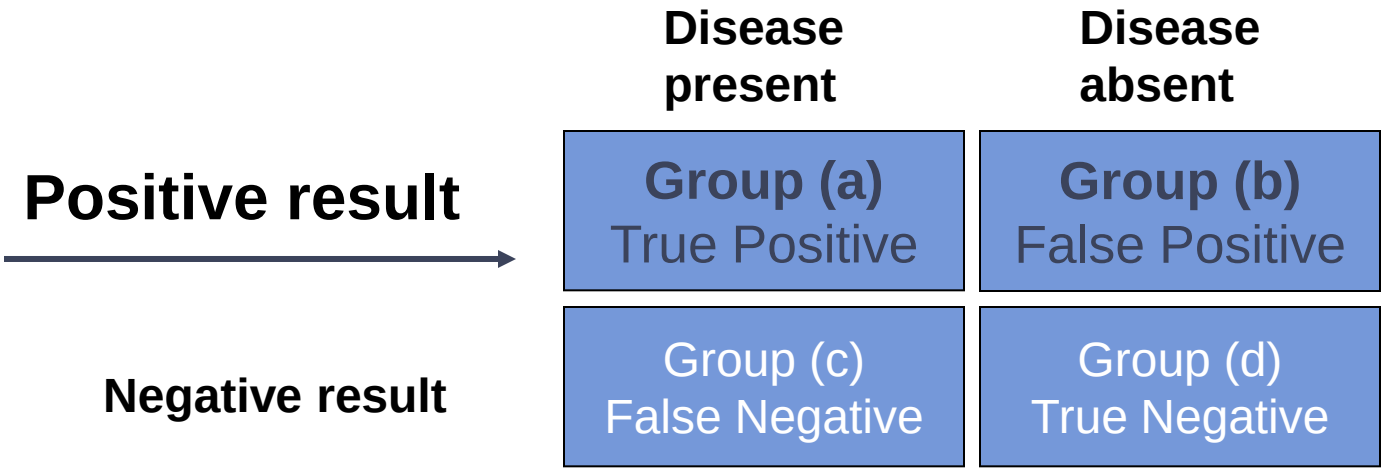
Understanding Predictive Values

- 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

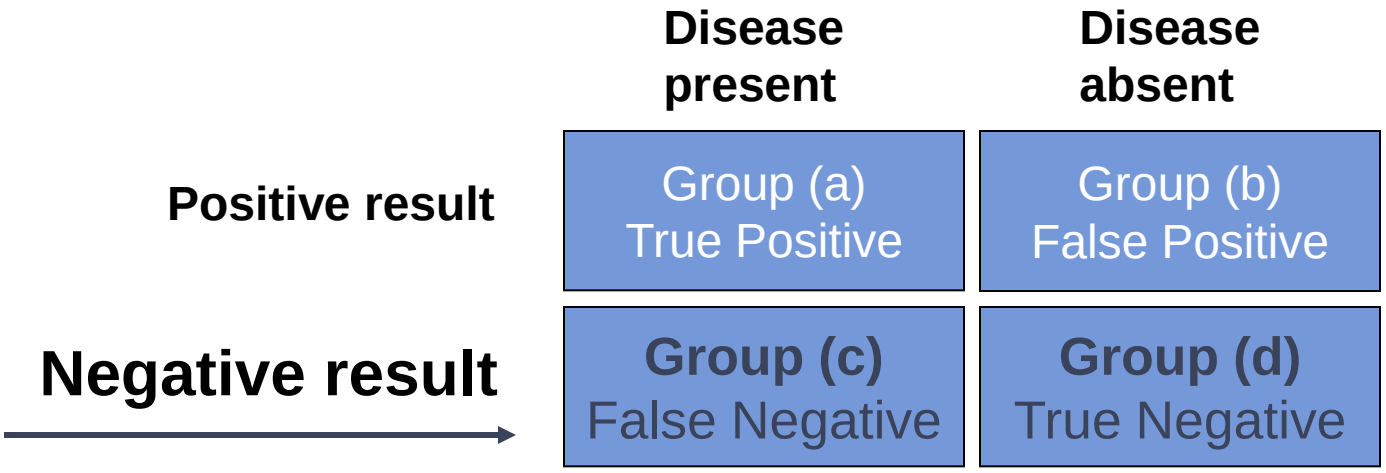
$$\frac{(a)}{(a) + (b)}$$



Characteristics of Screening Tests

4) Negative Predictive Value (NPV): The likelihood that a negative test result indicates the absence of the disease

$$\frac{\mathbf{(d)}}{\mathbf{(c) + (d)}}$$



Predictive Values and Prevalence

Sensitivity = ? ; Specificity = ?

Prevalence = ?	**Disease Yes**	**Disease No**	**PPV**
Positive result	99	495	
Negative result	1	9405	
Total	100	9900	?
Prevalence = ?			
Positive result	495	475	
Negative result	5	9025	
Total	500	9500	?

Predictive Values and Prevalence

Sensitivity = 99%; Specificity = 95%

Prevalence = 1%	**Disease Yes**	**Disease No**	**PPV**
Positive result	99	495	
Negative result	1	9405	
Total	100	9900	**17%**
Prevalence = 5%			
Positive result	495	475	
Negative result	5	9025	
Total	500	9500	**51%**

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