Foundations in Biostatistics and Epidemiology

Session 4: Screening and Diagnostic Testing Methods

The following provides a summary of the calculations used in this module.

Part I: Definitions and Criteria

a. Definition of screening programs

- The identification of disease in asymptomatic individuals by application of rapid tests to separate persons who probably have the disease from those who probably do not have the disease
- Not intended to be diagnostic
- Positive or suspicious findings must be referred for diagnosis and treatment

b. WHO Criteria for Effective Screening

1. The condition being screened for must be serious.
2. The condition being screened for must be treatable.
3. The condition must be detectable while asymptomatic and timely treatment must reduce morbidity and mortality more effectively than treatment after the appearance of symptoms.
4. The screening test must be accurate.
5. The screening test must be acceptable to the patient and inexpensive.
6. The condition must be sufficiently prevalent to warrant screening.

Part II: Evaluation of Screening Tests

- **Sensitivity and Specificity**
  - Sensitivity = P(+ test|Disease)
  - Specificity = P(- test|No Disease)
  - False positive rate = P(+ test|No Disease) = 1-Specificity
- **Likelihood Ratios**

$$PLR = \frac{Prob(+test|Disease)}{Prob(+test|No\ Disease)} = \frac{sensitivity}{1-specificity}$$

– **Values > 1 indicate that those with disease are more likely to have a positive test compared to those without the disease**

$$NLR = \frac{Prob(-test|Disease)}{Prob(-test|No\ Disease)} = \frac{1-sensitivity}{specificity}$$

- **Values < 1 indicate that those with disease are less likely to have a negative test compared to those without the disease**

Post-test odds of disease = pre-test odds x PLR
= prob(D)/[1-prob(D)] x PLR

Part III: Identifying cut-points for positive screening tests

a. **ROC Curves**

1. For each possible cut-point, plot the sensitivity (y-axis) by 1-specificity (x-axis) [could be interpreted as a plot of the true positive by false positive rate]
2. If costs of a false positive and false negative are equal, the best cut-point will correspond to the upper, left-most point of the curve
3. For each possible cut-point, plot the sensitivity (y-axis) by 1-specificity (x-axis) [could be interpreted as a plot of the true positive by false positive rate]
4. If costs of a false positive and false negative are equal, the best cut-point will correspond to the upper, left-most point of the curve
5. The area under the ROC curve is 0.5 for a test with no screening capability. The maximum area under the ROC curve is 1.

b. Reliability

Percent agreement = [(# tests in which observers agree)/(total # tests read)] * 100%

Kappa = (% observed agreement) – (% agreement expected by chance alone)

$$\frac{\text{(\% observed agreement) – (\% agreement expected by chance alone)}}{\text{100\% - (\% agreement expected by chance alone)}}$$

c. Positive and Negative Predictive Value

PPV = P(Disease | + test) = TP / (TP+FP)

NPV = P(No Disease | - test) = TN / (TN+FN)

NOTE: PPV and NPV depend on the test sensitivity, test specificity and the prevalence of the disease. Lower prevalence → lower PPV; Higher prevalence → higher PPV when considering test with fixed sensitivity and specificity.

Part IV: Value of a screening program and possible biases

- Volunteer Bias
  - Self-selected volunteers; "Worried well"
  - May be healthier or at higher risk of developing the disease than those that don't participate
- Lead-time Bias
  - Survival may falsely appear to be increased among screened group simply because the diagnosis was made earlier in the course of the disease
- Length-biased Sampling
  - Less aggressive forms of a disease are more likely to be picked up by screening because they have a longer preclinical phase
  - Less aggressive forms of disease usually have better survival
  - Thus, screen detected cases appear to have better survival