Evidence-Based Medicine Diagnosis

Component 2 / Unit 5

Using EBM to assess questions about diagnosis

- Diagnostic process involves logical reasoning and pattern recognition
- Consists of two essential steps
  - Enumerate diagnostic possibilities and estimate their relative likelihood, generating *differential diagnosis*
  - Incorporate new information from *diagnostic tests* to change probabilities, rule out some possibilities, and choose most likely diagnosis
- Two variations on diagnosis also to be discussed
  - Screening
  - Clinical prediction rules

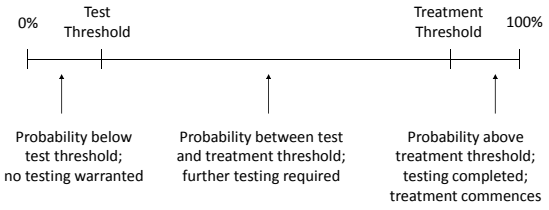
Diagnostic (un)certainty can be expressed as probabilities

- Probability is expressed from 0.0 to 1.0
  - Probability of heads on a coin flip = 0.5
- Alternative expression is odds
  - Odds = Probability of event occurring / Probability of event not occurring
  - Odds of heads on a coin flip = 0.5/0.5 = 1
- Rolling a die
  - Probability of any number = 1/6
  - Odds of any number = 1/5

Some other probability principles

- Sum of all probabilities should equal 1
  - e.g., p[heads] + p[tails] = 0.5+0.5 = 1
- Bayes' Theorem in diagnosis
  - Post-test (posterior) probability a function of pre-test (prior) probability and results of test
  - Post-test probability variably increases with positive test and decreases with negative test

Diagnostic and therapeutic thresholds (Guyatt, 2008)



Using EBM to assess questions about diagnostic tests

- Assessing the diagnostic value of a test
- Single-test version of Bayes' Theorem
- Example application of Bayes' Theorem
- Screening tests

Assessing the diagnostic value of a test

	Disease present	Disease absent	Total
Test positive	True positive (TP)	False positive (FP)	All with positive test (TP+FP)
Test negative	False negative (FN)	True negative (TN)	All with negative test (FN+TN)
Total	All with disease (TP+FN)	All without disease (FP+TN)	All (TP+FN+ FP+TN)

Sensitivity and specificity

- Sensitivity or true positive rate (TPR) is proportion of patients with disease who have positive test
  - TPR = TP/(TP+FN)
  - "Positivity in disease" (PID)
  - Better at ruling out disease – SnNout
- Specificity or true negative rate (TNR) is proportion of patients without disease who have negative test
  - TNR = TN/(TN+FP)
  - "Negativity in health" (NIH)
  - Better at ruling in disease – SpPin

Other statistics to calculate disease probability

- Prevalence of disease is the proportion of people with a disease
  - Prevalence = Total with disease / Total
  - Prevalence = (TP+FN)/(TP+FN+FP+TN)
  - Can be a good starting point for pre-test probability of disease
- Likelihood ratio positive measures how many times more likely test is positive in disease
  - LR+ = Sensitivity/(1-Specificity) = TPR/FPR
- Likelihood ratio negative measures how many times more likely test is negative in health
  - LR- = (1-Sensitivity)/Specificity = FNR/TNR

Calculating probability of disease with Bayes' Theroem

- Need pre-test probability
  - Can be prevalence, known risk, or estimate
- Convert to pre-test odds
  - Pre-test odds = (pre-test prob)/(1-pre-test prob)
- Calculate post-test odds with LR
  - Post-test odds = pre-test odds * LR+ (or LR-)
- Convert to post-test probability
  - Post-test prob = post-test odds/(1+post-test odds)

Other statistics – predictive value

- Predictive value positive is proportion of people with positive test who have disease
  - PV+ = TP/(TP+FP)
  - Note: Sensitivity is TP/(TP+FN)
- Predictive value negative is proportion of people with negative test who do not have disease
  - PV- = TN/(TN+FN)

Limitations of diagnostic tests

- There are many real and potential sources of bias (Whiting, 2004)
- Diagnostic tests improve probability estimations of diseases but still require diagnostic judgment
- Results can be influenced by pre-test probability estimation that may be incorrect
- Bayes' Theorem assume conditional independence of all data, but clinicians often have multiple pieces of evidence and tests, which can
  - Make calculations very complex
  - Violate assumptions of independence

Example of Bayes' Theorem application

- Detection of colonic polyps >6 mm in size in patients at high risk for colon cancer (Rockey, 2005)
- Air-contrast barium enema (ACBE)
  - Sens = 41%, spec = 82%, LR+ = 2.28, LR- = 0.72
- Computer colonic tomography
  - Sens = 55%, spec = 89%, LR+ = 5.00, LR- = 0.51
- Colonoscopy
  - Sens = 99%, spec = 99.6%, LR+ = 248, LR- = 0.01
- Number of polyps detected in this study of 614 patients was 155 patients with 234 lesions, 152 of which were adenomas or cancer

Comparing ACBE and colonoscopy

- Estimate pre-test probability = 0.25
- Pre-test odds = 0.25/(1-0.25) = 0.33
- With positive tests
  - ACBE
    - Post-test odds = 0.33*2.28 = 0.75
    - Post-test probability = 0.75/(1+0.75) = 0.43 (43%)
  - Colonoscopy
    - Post-test odds = 0.33*248 = 81.8
    - Post-test probability = 81.8/(1+81.8) = 0.99 (99%)

Comparing ACBE and colonoscopy

- With negative tests
  - ACBE
    - Post-test odds = 0.33*0.72 = 0.24
    - Post-test probability = 0.24/(1+0.24) = 0.19 (19%)
  - Colonoscopy
    - Post-test odds = 0.33*0.01 = 0.0033
    - Post-test probability = 0.0033/(1+0.0033) = 0.0033 (0.3%)

Screening tests for disease

- "Identification of unrecognized disease"
- Aim to keep disease (or complications) from occurring (1° prevention) or stop progression (2° prevention)
- Requirements for a screening test
  - Low cost
  - Intervention effective
  - High sensitivity – do not want to miss any cases; usually follow up with test of high specificity

Americans love screening tests despite lack of evidence

- Despite their limitations, screening tests for cancer are very popular with Americans (Schwartz, 2004)
- But cost of FP tests is substantial; in one study of screening for prostate, lung, colorectal, and ovarian cancer (Lafata, 2004)
  - 43% of sample had at least one FP test
  - Increased medical spending in following year by over $1000
- Despite lack of evidence for benefit of Pap smear in women with hysterectomy, procedure is still widely done (Sirovich, 2004)
- Despite lack of evidence for benefit of annual physical exam, two-thirds of physicians still believe it is necessary (Prochazka, 2005)

Clinical prediction rules

- Use of results of multiple "tests" to predict diagnosis
- Best evidence establishes rule in one population and validates in another independent one
- Examples of clinical prediction rules
  - Predicting deep venous thrombosis (DVT) (Wells, 2000; Wells, 2006)
    - High sensitivity, moderate specificity
    - Better for ruling out than ruling disease
  - Coronary risk prediction – newer risk markers do not add more to known basic risk factors (Folsom, 2006)