Topic 3 Outline

- Biomedical Decision Process
- Probability assessment
  - Pre-test probability
  - Post-test probability
- Measurement of Diagnostic Tests
Two Questions

- What is the complexity in the medical decision process?
- How probability assists to improve the medical decision process?
Topic 3 Outline

- Biomedical Decision Process
- Probability assessment
  - Pre-test probability
  - Post-test probability
- Measurement of Diagnostic Tests
The Nature of Clinical Decisions

- Clinical data are imperfect (p69)
- Outcomes of treatment are uncertain
- Medical choices are difficult
- Probabilistic Medical Reasoning – Approach to help dealing with uncertainty in medical decisions
- Medical practice is medical decision making
- How can HIS assist in the process?
Case: Mr. James is a 59-year-old man with coronary artery disease (narrowing or blockage of the blood vessels that supply the heart tissue). When the heart muscle does not receive enough oxygen (hypoxia) because blood cannot reach it, the patient often experiences chest pain (angina). Mr. James has twice undergone coronary artery bypass graft (CABG) surgery, a procedure in which new vessels, usually taken from the leg, are grafted onto the old ones such that blood is shunted past the blocked region. Unfortunately, he has again begun to have chest pain, which becomes progressively more severe, despite medication. If the heart muscle is deprived of oxygen, the result can be a heart attack (myocardial infarction), in which a section of the muscle dies.
The Nature of Clinical Decisions

- What is the best decision for previous case?
  - Surgery?
  - Do nothing?
  - Increase medication?
  - Cost factors? Patient safety?
  - Other approaches (e.g. diet, exercise, meditation)?

- An incorrect decision, may increase chances of death

- How can the use of probability and decision analysis help to make the best decision? Benefits vs harms?
The Nature of Clinical Decisions – Ambiguity & Probability -> Uncertainty

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 3rd Edition, Chapter 3, Figure 3.1
The Nature of Clinical Decisions – Overview of the Diagnostic Process

- ID – Patient Identification
- CC – Chief Complaint
- HPI – History of Present Illness
- PMH – Past Medical History
- FH – Family History
- ROS – Review of Systems
- PE – Physical Examination

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 3rd Edition, Chapter 3, Figure 2.11
Case: Mr. Smith, a 60-year-old man, complains to his physician that he has pressure like chest pain that occurs when he walks quickly. After taking his history and examining him, his physician believes there is a high enough chance that he has heart disease to warrant ordering an exercise stress test. In the stress test, an electrocardiogram (ECG) is taken while Mr. Smith exercises. Because the heart must pump more blood per stroke and must beat faster (and thus requires more oxygen) during exercise, many heart conditions are evident only when the patient is physically stressed. Mr. Smith’s results show abnormal changes in the ECG during exercise—a sign of heart disease.
The Nature of Clinical Decisions – Overview of the Diagnostic Process

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 3, Figure 3.1a
The Nature of Clinical Decisions – Overview of the Diagnostic Process

- Tests reduce uncertainty
- Some tests reduce uncertainty more than others?
  - Cost factor to test
  - Which test is appropriate?
- The more uncertainty is reduced the better the value of the test
- Multiple tests are required to increase certainty
- Probability is used to express uncertainty

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 3rd Edition, Chapter 3, Figure 3.2
The Nature of Clinical Decisions – Overview of the Diagnostic Process

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 3, Figure 3.1
Topic 3 Outline

- Biomedical Decision Process
  - Probability assessment
    - Pre-test probability
      - Subjective method
      - Objective method
    - Post-test probability
  - Measurement of Diagnostic Tests
Pre-test Probability

• How can we determine the pre-test probability?

• How to adjust the pre-test probability?

• Two methods
  • Subjective method
  • Objective method
Clinicians use probability of disease to assist in decision making.

Probability $p$ is clinician’s opinion on the likelihood of an event outcome, values are between $[0,1]$

Probability of an event outcome $A$ is $p[A]$

E.g. Event - flipping a coin, outcomes – head, tail

$p[\text{head}] = 0.5$
$p[\text{tail}] = 0.5$

$p[\text{head}] + p[\text{tail}] = 1.0 \quad \leftarrow $ Sum of all possible outcomes probabilities should add 1

Probability Assessment – Independent Events

- Independent event outcomes A and B
- Occurrence of A does not influence occurrence of B and vice versa
- E.g. Probability of two consecutive head coin tosses is 0.5 x 0.5 = 0.25
Conditional probability is the probability of event A given that event B is known, is denoted $p[A|B]$.

E.g. $p[\text{female student} \mid \text{CS student}] = 0.2$ ?

How can we estimate probability to express uncertainty?

Two methods
  - Subjective
  - Objective
Probability Assessment – Subjective Assessment

- Personal experience assessment is frequently used

- Cognitive heuristics – mental processes of learning, processing and recalling

→ Heuristics as rules of thumb
Probability Assessment –
Subjective Assessment: Heuristics Types

• Representativeness
  • E.g. what is the probability that object A belongs to class B?
  • Physician recollects previous observation (mental image) was related to a specific diagnosis

• Availability
  • E.g. Probability influenced by recalling events capability
  • i.e. Family/personal history, repeated infections, “runs in the family…”

• Anchoring and adjustment
  • Additional information suggests initial probability is higher

• What is the issue with heuristics?
  Rare cases, persons memory, lack of experience
Subjective Assessment: Heuristics

- What is the issue with heuristics?
  - Rare cases
  - Persons memory
  - Lack of experience
Probability Assessment –
Objective Assessment

• Published research results as objective estimates of probability
  E.g. \( p[\text{prostate cancer} \mid \text{man} \& \text{50 yr old}] \) is between 5 -> 14% (published reports)

• Symptoms to allocate patient into a clinical subgroup guided by clinical prediction rules

• How can information systems assist in the objective assessment process?
  • Knowledge base, Research, Analytics...
Probability Assessment – Objective Assessment

- Case: Ms. Troy, a 65-year-old woman who had a heart attack 4 months ago, has abnormal heart rhythm (arrhythmia), is in poor medical condition, and is about to undergo elective surgery.

- What is the probability of cardiac complication for Ms. Troy?

### Table 3.2. Clinical prediction rule for diagnostic weights in Table 3.1.

<table>
<thead>
<tr>
<th>Total score</th>
<th>Prevalence (%) of cardiac complications&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–15</td>
<td>5</td>
</tr>
<tr>
<td>20–30</td>
<td>27</td>
</tr>
<tr>
<td>&gt;30</td>
<td>60</td>
</tr>
</tbody>
</table>

<sup>a</sup>Cardiac complications defined as death, heart attack, or congestive heart failure.

Table source: Shortliffe et al, ‘Biomedical Informatics’, 4<sup>th</sup> Edition, Chapter 3, Table 3.2, p 74
### Table 3.1. Diagnostic weights for assessing risk of cardiac complications from noncardiac surgery.

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Diagnostic weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age greater than 70 years</td>
<td>5</td>
</tr>
<tr>
<td>Recent documented heart attack</td>
<td></td>
</tr>
<tr>
<td>&gt;6 months previously</td>
<td>5</td>
</tr>
<tr>
<td>&lt;6 months previously</td>
<td>10</td>
</tr>
<tr>
<td>Severe angina</td>
<td>20</td>
</tr>
<tr>
<td>Pulmonary edema&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Within 1 week</td>
<td>10</td>
</tr>
<tr>
<td>Ever</td>
<td>5</td>
</tr>
<tr>
<td>Arrhythmia on most recent ECG</td>
<td>5</td>
</tr>
<tr>
<td>&gt;5 PVCs</td>
<td>5</td>
</tr>
<tr>
<td>Critical aortic stenosis</td>
<td>20</td>
</tr>
<tr>
<td>Poor medical condition</td>
<td>5</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>10</td>
</tr>
</tbody>
</table>

ECG = electrocardiogram; PVCs = premature ventricular contractions on preoperative electrocardiogram.

<sup>a</sup>Fluid in the lungs due to reduced heart function.

Table source: Shortliffe et al, ‘Biomedical Informatics’, 4<sup>th</sup> Edition, Chapter 3, Table 3.1, p 74
Case: Ms. Troy, a 65-year-old woman who had a heart attack 4 months ago, has abnormal heart rhythm (arrhythmia), is in poor medical condition, and is about to undergo elective surgery.

What is the probability of cardiac complication for Ms. Troy?

-> Total score of 20 for a 27% for severe cardiac complication

Probability Assessment – Objective Assessment: Issues

- May be subject to error due to original study bias (newer analysis highlights flaws in study)

- May not be directly applicable to patient

- Tests may involve risk, discomfort and cost

- Referral bias issue when study was done (p74)
Probability Assessment

- Goal: Reasonable estimate of the pre-test probability

- Combining
  - Subjective assessment
  - Objective assessment

- Next step in diagnostic process is to gather further information (e.g. formal diagnostic tests like lab, radiology, etc) to determine post-test probability
The Nature of Clinical Decisions – Overview of the Diagnostic Process

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 2, Figure 2.12

ID – Patient Identification
CC – Chief Complaint
HPI – History of Present Illness
PMH – Past Medical History
FH – Family History
ROW – Review of Systems
PE – Physical Examination
Topic 3 Outline

- Biomedical Decision Process
- Probability assessment
  - Pre-test probability
  - Post-test probability
- Measurement of Diagnostic Tests
Measurement of Diagnostic Tests

- Challenge: How do we know if the test results are normal or abnormal?

- Method
  - Contingency tables to measure test performance
  - Receiver-Operating Characteristics (ROC) curves to evaluate among tests
Measurement of Diagnostic Tests – Classification of Test Results

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 3, Figure 3.2, p 76
Measurement of Diagnostic Tests – Classification of Test Results

- **True Positive Test** – the result of the test correctly proves the patient has the disease or condition

- **True Negative Test** – the result of the test correctly proves the patient does not have the disease or condition

- **False Positive Test** – the test incorrectly proves the patient has the disease or condition

- **False Negative Test** – the test incorrectly proves the patient does not have the disease or condition
Measuring the effectiveness of a Clinical Test
Step 1: +ve Distribution Curve

Add Positive results - patient has the disease
Step 2: –ve Distribution Curve

Add Negative results - patient does not have disease
Measurement of Diagnostic Tests - Classification of Test Results

• What is the ideal test?

• Contingency tables – Once we know the cut-off value, we can summarize test performance in contingency tables

<table>
<thead>
<tr>
<th>Table 3.3. A 2 × 2 contingency table for test results.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results of test</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Positive result</td>
</tr>
<tr>
<td>Negative result</td>
</tr>
<tr>
<td>TP + FN</td>
</tr>
</tbody>
</table>

TP = true positive; TN = true negative; FP = false positive; FN = false negative.

Table source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 3, Table 3.3, p 76
Measurement of Diagnostic Tests – Test Performance Measurement (p77)

- Two types
  - Measures of *concordance*
    - E.g. TP, TN
  - Measures of *discordance*
    - E.g. FP, FN
Measurement of Diagnostic Tests – Sensitivity & Specificity

- Critical parameters that flag abnormal tests
- Sensitivity
  - Likelihood that a given datum will be observed in a patient with a given disease or condition
- Specificity
  - Observation is highly specific for a given disease

- TPR – True Positive Rate or Sensitivity is the likelihood that a diseased patient has a positive test
  - \( p \left[ \text{positive test} \mid \text{disease} \right] \)
  - \( \text{TPR} = \frac{\text{number of diseased patients with positive test}}{\text{total number of diseased patients}} \)
  - \( \text{TPR} = \frac{TP}{TP + FN} \)


- **TNR** – True Negative Rate or Specificity is the likelihood that a non-diseased patient has a negative test
  - \( p [ \text{negative test} | \text{no disease} ] \)
  - \[ TNR = \frac{\text{number of nondiseased patients with negative test}}{\text{total number of nondiseased patients}} \]
  - \[ TNR = \frac{TN}{TN + FP} \]

Measurement of Diagnostic Tests – Test Performance Measurement Case

• Case

Example 6. Consider again the problem of screening blood donors for HIV. One test used to screen blood donors for HIV antibody is an enzyme-linked immunosorbent assay (EIA). So that the performance of the EIA can be measured, the test is performed on 400 patients; the hypothetical results are shown in the 2 \times 2 table in Table 3.4.\textsuperscript{5}

<table>
<thead>
<tr>
<th>EIA test result</th>
<th>Antibody present</th>
<th>Antibody absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive EIA</td>
<td>98</td>
<td>3</td>
<td>101</td>
</tr>
<tr>
<td>Negative EIA</td>
<td>2</td>
<td>297</td>
<td>299</td>
</tr>
</tbody>
</table>

\text{Total} \quad 100 \quad 300

EIA = enzyme-linked immunosorbent assay.

• What is the test performance? i.e. What is the TPR (Sensitivity) & TNR (Specificity) of the test?

Case source: Shortliffe et al, ‘Biomedical Informatics’, 4\textsuperscript{th} Edition, Chapter 3, p 78
Example: Screening Blood Donors

![Graph showing the screening of blood donors with a healthy and diseased population, cutoff value, and test results. The graph illustrates the number of individuals with false positives and false negatives.]

Insert values from results table (2*2 Matrix)
Measurement of Diagnostic Tests – Test Performance Measurement Case

- TPR
  \[
  \frac{TP}{TP + FN} = \frac{98}{98 + 2} = 0.98.
  \]

- TNR
  \[
  \frac{TN}{TN + FP} = \frac{297}{297 + 3} = 0.99
  \]

- How do we interpret these results?
Measurement of Diagnostic Tests – Implications of Sensitivity & Specificity

• How the cut-off value affects test sensitivity and specificity?

• How do we choose among tests?

Measurement of Diagnostic Tests – Decreasing cut-off value?

- Higher Sensitivity produces more +ve test results
- Therefore more FP’s and more patients misclassified

TPR = 98/98+1 = 98/99 = 0.989 and now TNR = 297/ 297 + 4 = 297/ 301 = 0.986
Increase Specificity produces more -ve test results
Therefore more FN’s and more patients will be missed diagnosed

\[ TPR = \frac{98}{98+4} = \frac{98}{102} = 0.96 \]
\[ \text{and now } TNR = \frac{297}{297 + 1} = \frac{297}{298} = 0.996 \]
Do we want more FNs (i.e. missed cases)?
Or do we want more FPs (i.e. misclassifying patients as diseased)

Answer will depend on disease and purpose of testing
- Disease serious and therapy available, minimize FNs
- Disease not serious and therapy dangerous, minimize FPs
Measurement of Diagnostic Tests – Implications of Sensitivity & Specificity

• How do we choose among tests?
Measurement of Diagnostic Tests – Implications of Sensitivity & Specificity

- Receiver-operating characteristic (ROC) curve
  - Graph that characterizes a test by a range of values of sensitivity and specificity that it can take on over a range of possible cut-off values
  - ROC curves assist to decide among tests
  - Other factors might need to be considered in what test to choose though
measurement of diagnostic tests – implications of sensitivity & specificity

- ROC curve, which test is better?

Figure source: Shortliffe et al, ‘Biomedical Informatics’, 4th Edition, Chapter 3, Figure 3.3, p 79
Measurement of Diagnostic Tests – Implications of Sensitivity & Specificity

- How do we choose among tests?
  - Select test with highest sensitivity and specificity, assuming other factors (costs, risks) are equal
Gold-standard test – procedure utilized to define the presence or absence of a disease with high probability, i.e. best known test

- But usually riskier, costly and more difficult to apply

- E.g. Sleep apnea test performed at sleep labs
Which test do we choose?

Figure sources: http://www.examiner.com/article/sleep-apnea-testing-what-to-expect and http://1800cpap.com/home-sleep-testing-for-sleep-apnea.aspx