Question 1

100 women over the age of 50 received mammograms at a mobile breast cancer screening unit. 27 women had findings suspicious for malignancy on the mammogram: 19 of these women were confirmed as having breast cancer by biopsy. 1 woman had a negative mammogram but in the subsequent year developed breast cancer, and is assumed to have had the disease at the time of screening.

What is the sensitivity of the mammogram? the specificity? the predictive value of a positive result?

\[
\begin{array}{c|c|c|}
\text{Screening Test} & \text{Yes} & \text{No} \\
\hline
+ & a & b \\
\hline
- & c & d \\
\hline
 & a + c & b + d \\
\end{array}
\]

Sensitivity = \( \frac{T+}{Dx+} = \frac{a}{a + c} \)

Specificity = \( \frac{T-}{Dx-} = \frac{d}{b + d} \)
What influences sensitivity, specificity, and predictive value?

Breast Cancer

\[
\begin{array}{cc}
+ & - \\
\hline
19 & 8 \\
1 & 72 \\
\end{array}
\]

Mammogram

\[
\begin{array}{cc}
+ & - \\
\hline
19 & 8 \\
1 & 72 \\
\end{array}
\]

Sensitivity = \( \frac{T+}{Dx+} = \frac{19}{20} = 95\% \)

Specificity = \( \frac{T-}{Dx-} = \frac{72}{80} = 90\% \)

PV (+) = \( \frac{Dx+}{T+} = \frac{19}{27} = 70\% \)

PV (-) = \( \frac{Dx-}{T-} = \frac{72}{73} = 99\% \)

Question 2

In a Mantoux tuberculosis screening program in a high risk population, a positive test was defined as 10 mm of induration. If a positive test is now defined as only 5 mm of induration, which of the following will be true? More than one answer may be correct.

A. Sensitivity will increase
B. Specificity will decrease
C. Positive predictive value will increase
D. False positives will increase
E. False negatives will decrease

“Criterion of positivity” influences both sensitivity and specificity of the screening test:

↓ Criterion of positivity  ➔ sensitivity
↓ Specificity

↑ Criterion of positivity  ➔ sensitivity
↑ Specificity

PV+ increased mainly by increase in underlying disease prevalence (like screening a higher risk group)
Question 2
In a Mantoux tuberculosis screening program in a high risk population, a positive test was defined as 10 mm of induration. If a positive test is now defined as only 5 mm of induration (i.e., ↓ the criterion of positivity), which of the following will be true? More than one answer may be correct.
A. Sensitivity will increase
B. Specificity will decrease
C. Positive predictive value will increase
D. False positives will increase
E. False negatives will decrease
Correct answers: A, B, D, E

What are issues in the interpretation of screening results?

Question 3
A randomized trial was conducted to evaluate the effectiveness of a new screening program for colon cancer. Among those patients whose cancers were detected by the screening program, average age at diagnosis was 54 years and average age at death was 60 years: thus, average survival from diagnosis to death was 6 years. For patients whose cancers were detected by clinical symptoms, average age at diagnosis was 56 years and average age at death was 60 years: thus, average survival from diagnosis to death was 4 years. The investigators reported a statistically significant 2 year increase in survival from colon cancer associated with screening. This mistaken conclusion is most likely due to:
A. The play of chance
B. Confounding by stage of disease at diagnosis
C. Lead time bias
D. Length bias

MEASURING DATA
• Measures of association
• Measures of disease frequency
Question 4
In each statement below, data are presented based on the Framingham Study of coronary heart disease. Choose the measure which best describes each of these statements.
A. Prevalence measure
B. Incidence measure
C. Standardized morbidity ratio
D. Age-specific measure
E. Age-adjusted measure

Prevalence = \frac{\text{number of existing cases at a point in time}}{\text{total population}}

Incidence = \frac{\text{number of new cases during a period of time}}{\text{population at risk}}

Rates can be category-specific (e.g. age-specific) or category-adjusted (e.g. age-adjusted)

Standardized morbidity ratio: \frac{\text{observed cases}}{\text{expected cases}}

1. At the initial examination, 17 persons per 1,000 had evidence of coronary heart disease:
   Prevalence measure

2. Among heavy smokers, the observed frequency of angina pectoris was 1.6 times as great as the expected frequency during the first 12 years of the study:
   Standardized morbidity ratio
3. During the first eight years of the study, 45 persons developed coronary heart disease per 1,000 persons who entered the study free of disease:

Incidence measure

4. At the initial examination, 31 persons aged 45 to 62 had coronary heart disease per 1,000 persons examined in this age group:

Age-specific prevalence measure

How do we calculate incidence and prevalence?

Question 5
At the beginning of 2009, 800 people diagnosed with diabetes lived in City X, which had a mid-year population estimated at 10,000. During that year, 200 new cases of diabetes were diagnosed in the city and 40 people died of complications of diabetes.
In 2009, 200 new cases diagnosed
Estimated midyear population = 10,000
On 1/1/09, 800 diabetics in city
During 2009, 40 died from diabetes

A. Incidence measure per 1,000 during 2009:
\[ I = \frac{200}{10,000} = \frac{20}{1,000} \]

B. Prevalence measure per 1,000 on 1/1/09:
\[ P = \frac{800}{10,000} = \frac{80}{1,000} \]

C. Prevalence measure per 1,000 on 12/31/09:
C. Prevalence measure per 1,000 on 12/31/09:

\[ P = \frac{800+200-40}{10,000} = \frac{96}{1,000} \]

- In 2009, 200 new cases diagnosed
- Estimated midyear population = 10,000
- On 1/1/09, 800 diabetics in city
- During 2009, 40 died from diabetes

D. Mortality due to diabetes per 1,000 during 2009:

\[ M = \frac{40}{10,000} = \frac{4}{1,000} \]

- In 2009, 200 new cases diagnosed
- Estimated midyear population = 10,000
- On 1/1/09, 800 diabetics in city
- During 2009, 40 died from diabetes

E. If the prevalence of diabetes in 2009 is less than that in 1999, this could be due to:

A. A change in the incidence rate
B. A change in the duration of the disease
C. Both (1) and (2)

E. The proportion of the population that has a disease at a point in time (prevalence) depends on both the rate of development of the disease in the population (incidence) as well as the duration of the disease from onset to termination. Thus, a change in prevalence can reflect a change in incidence, a change in duration, or both. (Answer “C”)

How do we calculate measures of association?
Question 6

The table below gives the annual mortality rates from lung cancer and coronary heart disease among cigarette smokers in a cohort study of British male physicians.

### Annual Mortality Rates per 100,000

<table>
<thead>
<tr>
<th></th>
<th>Lung Cancer</th>
<th>Coronary Heart Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette smokers</td>
<td>140</td>
<td>669</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>10</td>
<td>413</td>
</tr>
</tbody>
</table>

Relative Risk = \( RR = \frac{I_e}{I_o} \)

- Measure of the strength of association
- If no association, \( RR = 1 \)

**Attributable Risk in the Exposed = \( ARe = I_e - I_o \)**

- Assuming exposure causes outcome, measure of public health impact among the exposed
- If no association, \( AR = 0 \)

\[
RR (\text{Lung Cancer}) = \frac{140/100,000}{10/100,000} = 14
\]

Those who smoke have 14x the risk of dying from lung cancer as nonsmokers

\[
RR (\text{CHD}) = \frac{669/100,000}{413/100,000} = 1.6
\]

Those who smoke have 1.6x the risk (or 60% increased risk) of dying from CHD, compared to nonsmokers

\[
ARe (\text{Lung Cancer}) = I_e - I_o = 140/100,000 - 10/100,000 = 130/100,000
\]

Assuming smoking causes lung cancer, for every 100,000 smokers, 130 cases of lung cancer are due to their smoking

\[
ARe (\text{CHD}) = I_e - I_o = 669/100,000 - 413/100,000 = 256/100,000
\]

Assuming smoking causes heart disease, for every 100,000 smokers, 256 cases of CHD are due to their smoking
Based on these data, is smoking a stronger risk factor for lung cancer or CHD?

Lung cancer, since the RR for lung cancer is greater than for heart disease.

But if smoking were eliminated, could more deaths be saved among smokers from lung cancer or CHD?

Coronary heart disease, since the ARe for heart disease is greater than for lung cancer (because the baseline risk of CHD is higher than lung cancer).

Number Needed to Treat

<table>
<thead>
<tr>
<th></th>
<th>Number Needed to Treat (NNT) = ( \frac{1}{AR_e} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>= ( \frac{1}{0.03} ) = 33</td>
</tr>
</tbody>
</table>

We would need to treat 33 patients over 5 years (median duration of follow-up) in order to prevent one nonfatal MI or CHD death.

INTERPRETATION OF DATA

- Types of studies
- Association vs. Causation
Question 7
The association between low birth weight and maternal smoking during pregnancy can be studied by obtaining smoking histories from women at the time of their first prenatal visits and then correlating subsequent birth weight with these smoking histories. What type of study is this?
A. Clinical trial
B. Cross-sectional survey
C. Case-control study
D. Prospective cohort study

Correct answer: D

Question 8
A case-control study was undertaken to evaluate the relationship between maternal smoking during pregnancy and low birth weight. A total of 350 mothers of low birth weight babies and 400 mothers of normal weight babies were interviewed. Of the mothers of low birth weight babies, 200 reported smoking during the pregnancy, while 200 of the mothers of the normal weight babies also reported such a history.

What is the magnitude of the association between smoking and birth weight? Is the observed association valid?

Measure of association in a case-control study is the odds ratio (OR), which is a valid estimate of the relative risk:
\[ \text{OR} = \frac{ad}{bc} \]

Mothers who smoke during pregnancy have a 30% increased risk of low birth weight babies.
Validity of an Association

To determine if an association observed in a study is valid, we need to rule out alternative explanations for the findings:

- Chance: sampling variability
- Bias: systematic error which distorts the association between exposure and outcome
- Confounding: mixture of effect between the association under study and a third variable, which may be responsible in part or totally for the association seen

B. It is suggested that mothers of low-birth weight babies who smoked would tend to deny such an activity due to feelings of guilt. This would be an example of the effects of:
   1. Chance
   2. Selection bias
   3. Recall bias
   4. Confounding

Correct answer: 3

C. The effect of the situation described in (B) would be to result in an observed relative risk which is an:
   1. Underestimate of the true relative risk
   2. Overestimate of the true relative risk
   3. The same as the true relative risk

Correct answer: 1
D. It was also observed that mothers of low birth weight babies tended to be younger than the mothers of the normal-weight children. Moreover, smoking rates are known to be higher in younger women in this population. This would be an example of the effects of:

1. Chance
2. Selection bias
3. Recall bias
4. Confounding

Correct answer: 4

E. In comparing the difference between the two groups, the p-value is found to be 0.20. The correct interpretation of this result is:

1. The null hypothesis is rejected
2. The difference is statistically significant
3. The difference occurred by chance
4. The difference is compatible with the null hypothesis
5. Sampling variation is an unlikely explanation of the difference

Correct answer: 4

The p-value is the probability that the observed data (or data more extreme) would occur due to the effects of chance alone, given that the null hypothesis is true (H₀, that there is truly no difference, no association between the two groups).

- If P <0.05, reject H₀, difference is statistically significant at 0.05 level
- If P >0.05, cannot reject H₀, difference is not statistically significant at 0.05 level
- P-value does not mean due to chance, or mean chance is ruled out - just related to likelihood of effect of chance

Correct answer: 4
How do we interpret graphical data?

Question 9
The figures show the results of a recently published 20-year trial of adjuvant combination chemotherapy for women with node-positive breast cancer. 179 women were randomized to the control group and 207 women to the adjuvant chemotherapy group (CMF).
What is the median relapse-free survival for CMF-treated women? By how much did treatment increase median overall survival? What is the absolute increase in 20-year survival associated with CMF?

Question 1: What was the median relapse-free survival for CMF-treated women?

Question 2: By how much did treatment increase median overall survival?
Question 2: By how much did treatment increase median overall survival?

4 year increase (12-8)

Question 3: What was the absolute increase in 20-year survival for CMF?

0.1 or 10% (0.32 - 0.22)

TAKE HOME MESSAGE

TRUST YOUR INSTINCTS

References