Epidemiology

Typical Board Question

A research study is done to determine if intravenous (IV) ibandronate sodium (Boniva) will decrease the incidence rate of hip fractures in perimenopausal women. There are 2,600 women in the ibandronate sodium group of whom 130 develop hip fractures. Of the 2,600 women in the placebo group 260 develop hip fractures. Based on these data, how many women need to be treated with ibandronate sodium to prevent one hip fracture?

A. 1
B. 5
C. 10
D. 15
E. 20

(See "Answers and Explanations" at end of chapter.)

I. EPIDEMIOLOGY: INCIDENCE AND PREVALENCE

Epidemiology is the study of the factors determining the occurrence and distribution of diseases in human populations.

A. Incidence

Incidence rate is a ratio of the number of individuals in the population who develop an illness in a given time period (commonly 1 year) divided by the total number of individuals at risk for the illness during that time period (e.g., the number of IV drug abusers newly diagnosed with AIDS in 2008 divided by the number of IV drug abusers in the population during 2008).

B. Prevalence

Prevalence rate is the number of individuals in the population who have an illness (e.g., AIDS) divided by the total number of individuals at risk for the illness.

1. **Point prevalence** is the number of individuals who have an illness at a specific point in time (e.g., the number of people who have AIDS on August 31, 2008, divided by the total population who could have the illness on that date).
2. **Period prevalence** is the number of individuals who have an illness during a specific time period (e.g., the number of people who have AIDS in 2008 divided by the total population who could have the illness mid-year in 2008).

C. Relationship between incidence and prevalence

1. Prevalence rate is equal to incidence rate multiplied by the average duration of the disease process (if incidence and duration are stable).
2. Prevalence rate is greater than incidence rate if the disease is long term. For example, because diabetes lasts a lifetime, its prevalence is much higher than its incidence. In contrast, the prevalence of influenza, an acute illness, is approximately equal to the incidence.
3. Health interventions that prevent disease (i.e., primary prevention, see Chapter 24) decrease the incidence rate of an illness and ultimately its prevalence rate as well.
4. People with a specific illness can leave the population of prevalent cases either **by recovering or by dying.**

II. RESEARCH STUDY DESIGN

Research studies identify relationships between factors or variables. Types of research studies include cohort, case-control, and cross-sectional studies.

A. Cohort studies

1. Cohort studies begin with the identification of specific populations (cohorts), who are **free of the illness** under investigation at the start of the study.
2. Following assessment of exposure to a risk factor (a variable linked to the cause of an illness [e.g., smoking]), incidence rates of illness between exposed and unexposed members of a cohort are compared. An example of a cohort study would be one that followed healthy adults from early adulthood through middle age to compare the health of those who smoke versus those who do not smoke.
3. Cohort studies can be **prospective** (taking place in the present time) or **historical** (some activities have taken place in the past).
4. **A clinical treatment trial** is a special type of cohort study in which members of a cohort with a specific illness are given one treatment and other members of the cohort are given another treatment or a placebo. The results of the two treatments are then compared. An example of a clinical treatment trial would be one in which the differences in survival rates between men with lung cancer who receive a new drug and men with lung cancer who receive a standard drug are compared.

B. Case-control studies

1. Case-control studies begin with the identification of subjects who have a specific disorder (cases) and subjects who do not have that disorder (controls).
2. Information on the **prior exposure of cases and controls to risk factors** is then obtained. An example of a case-control study would be one in which the smoking histories of women with and without breast cancer are compared.

C. Cross-sectional studies

1. Cross-sectional studies begin when information is collected from a group of individuals who provide a **snapshot in** time of disease activity.
2. Such studies can provide information on the relationship between risk factors and health status of a group of individuals at one specific point in time (e.g., a random telephone sample conducted to determine if men who smoke have more upper respiratory infections than men who do not smoke). They can also be used to calculate the prevalence of a disease in a population.

III. QUANTIFYING RISK

A. Risk factors are variables that are linked to the cause of a disease.

1. **Measures.** Absolute risk, relative risk, attributable risk, and the odds (or odds risk) ratio are measures used to quantify risk in population studies.
    a. **Absolute, relative, and attributable risk** are calculated for **cohort** studies.
    b. **The odds ratio** is calculated for **case-control** studies.

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2. **Absolute risk** is equal to the incidence rate.
3. **Absolute risk reduction** is the difference in absolute risks. For example, if the incidence rate of lung cancer among people in Newark and in Trenton, New Jersey, in 2008 are 20:1,000, and 15:1,000 respectively, the absolute risk is 20:1,000, or 2.0%, in Newark and 1.5% in Trenton, and the absolute risk reduction is 0.5%.
4. **Relative risk.** Relative risk compares the incidence rate of a disorder among individuals exposed to a risk factor (e.g., smoking) with the incidence rate of the disorder in unexposed individuals.
    a. For example, the incidence rate of lung cancer among smokers in a city in New Jersey is 20/1,000, while the incidence rate of lung cancer among nonsmokers in this city is 2/1,000. Therefore, the fold increase in risk of lung cancer (the relative risk) for smokers vs. nonsmokers in this New Jersey population is 20/1,000 divided by 2/1,000, or 10.
    b. A relative risk of 10 means that in this city, if an individual smokes, his or her risk of getting lung cancer is 10

times that of a nonsmoker.

5. **Attributable risk**
    a. Attributable risk is useful for determining what would happen in a study population if the risk factor were removed (e.g., determining how common lung cancer would be in a study if people did not smoke).
    b. To calculate attributable risk, the incidence rate of the illness in unexposed individuals is subtracted from the incidence rate of the illness in those who have been exposed to a risk factor.
    c. For the example above, the risk of lung cancer attributable to smoking (the attributable risk) in this New Jersey city's population is 20/1,000 minus 2/1,000, or 18/1,000.
6. **Odds ratio** Since incidence data are not available in a case-control study, the odds ratio (i.e., odds risk ratio) can be used as an estimate of relative risk (Example 25.1) in such studies.

Example 25.1 Calculating the Odds Ratio

Of 200 patients in the hospital, 50 have lung cancer. Of these 50 patients, 45 are smokers. Of the remaining 150 hospitalized patients who do not have lung cancer, 60 are smokers. Use this information to calculate the odds ratio for smoking and lung cancer.

	Smokers	Nonsmokers
People without lung cancer	A = 45	B = 5
People with lung cancer	C = 60	D = 90

$$\frac{(AD) = (45)(90)}{(BC) = (5)(60)} = 135 = 0(\text{Jdsratio}$$

An odds ratio of 13.5 means that in this population, a person with lung cancer was 13.5 times more likely to have smoked than a person without lung cancer.

B. Number needed to treat and number needed to harm

1. Number needed to treat **(NNT)**
    a. NNT is the number of persons who need to take a treatment for one person to benefit from the treatment.
    b. NNT is 1 divided by the absolute risk reduction.
    c. NNT allows comparison of the effectiveness of different treatments or of treatment versus no treatment or placebo (Example 25.2).
2. Number needed to harm **(NNH)**
    a. NNH is the number of persons who need to be exposed to a risk factor for one person to be harmed who would otherwise not be harmed
    b. NNH is 1 divided by the attributable risk.

Example 25.2 Number Needed to Treat

- A new drug (Drug S) was designed to prevent stroke in men aged 55-65 with hypertension.
- Four hundred hypertensive men in this age group were randomly assigned to a group taking Drug S (n = 200) or a placebo (n = 200).

- After 10 years there were 100 strokes in the placebo group and 20 strokes in the Drug S group.
- The absolute risk of stroke in the placebo group was therefore 100/200 = 50%.
- The absolute risk of stroke in the Drug S group was 20/200 = 10%.
- The absolute risk reduction is therefore 50% - 10% = 40%.
- If 40% of hypertensive men were saved from stroke by the drug, the NNT is 1/0.4 = 2.5.
- Therefore, 2.5 men would have to be treated with Drug X to prevent one case of stroke.

IV. Bias, Reliability, and Validity

To be useful, testing instruments must be bias-free, reliable, and valid.

A. Bias

1. A biased test or study is one constructed so that **one outcome is more likely to occur than another.** Selection, recall, or sampling bias can flaw all types of research studies.
2. **Selection bias**
    a. Selection bias can occur if the subjects are permitted to choose whether to go into a drug group or placebo group rather than being assigned to one or the other randomly. **For example,** in a study on the effectiveness of estrogen replacement therapy (ERT) on menopausal symptoms, menopausal women who have many hot flashes would be more likely to choose the ERT group rather than the placebo group because they would want relief. Thus, women with more symptoms would end up in the ERT group, making it more difficult to show a positive effect of ERT.
    b. Selection bias can also occur if, rather than making random assignments, the investigator purposely chooses which patients go into the drug group and which patients go into the placebo group. **For example,** a physician investigator, believing that a new drug for relief of menopausal symptoms being tested in clinical trials will be effective, would put her most serious cases into the new drug group. Thus, women with more symptoms would end up in the new drug group, making it more difficult to show a positive effect of the new drug.
3. **Recall bias.** In recall bias, knowledge of the presence of a disorder alters the way the subject remembers his or her history. For example, if mothers of children with neural tube defects overestimate how much medication they took during pregnancy, the overestimation can make it appear (erroneously) that certain medications are related to formation of neural tube defects.
4. Sampling bias. In sampling bias, subjects who volunteer to be in a study may not be representative of the population being studied. Factors unrelated to the subject of the study may have led them to volunteer, but could also distinguish the subjects from the rest of the population. Because of these factors, the results of the study may not be true for that whole population (i.e., the results are not generalizable). **For example, if** college students who volunteer for an experiment on the physiological bases of sexual response are more sexually active than students who do not volunteer, the students who volunteered may not be representative of the entire population of college students.
5. **Late-look** bias. In late-look bias, people who have already died of a disease are not included in the sample. **For example,** if tuberculosis patients who were most ill in a study have already died, those tuberculosis patients still alive have symptoms that are not severe.
6. Surveillance bias. In surveillance bias, people who are aware that they are being followed for the development of a disease are more likely to seek testing for and thus to be identified with the disease. **For example,** if a cohort of people is being followed for the development of melanoma, those people have heightened concern about developing

    melanoma. This heightened concern leads to increased surveillance, e.g., physical examinations or skin biopsies, leading to diagnoses of melanoma that may be missed in the general population who do not have such increased concern.

B. Reducing bias in clinical treatment trials

Blind studies, placebos, crossover studies, and randomized studies are used to reduce bias.

1. **Blind studies.** The expectations of patients can influence the effectiveness of treatment. Blind studies attempt to reduce this influence.

a. In a **single-blind study,** the subject does not know what treatment he or she is receiving.

b. In a **double-blind study,** neither the subject nor the clinician-evaluator knows what treatment the subject is receiving.

2. **Placebo responses**

a. In a blind drug study, a patient may receive a placebo (an inactive substance) rather than the active drug.

b. People receiving the **placebo** are the **control group;** those receiving the **active drug** are the **experimental group.**

c. A number of patients in research studies respond to treatment with placebos alone (the placebo effect).

3. **Crossover studies**

a. In a crossover study, subjects are randomly assigned to one of two groups. Subjects in group 1 first receive the drug and subjects in group 2 first receive the placebo.

b. Later in the crossover study, the groups switch—those in group 1 receive the placebo, and those in group 2 receive the drug.

c. Because subjects in both groups receive both drug and placebo, **each subject acts as his or her own control.**

4. **Randomization.** In order to ensure that the proportion of sicker and healthier people is the same in the treatment and control (placebo) groups, patients are randomly assigned to the groups. The number of patients in each group does not have to be equal.

C. Reliability and validity

1. Reliability refers to the reproducibility or dependability of results.

a. **Interrater reliability** is a measure of whether the results of the test are similar when the test is administered by a different rater or examiner.

b. **Test-retest reliability** is a measure of whether the results of the test are similar when the person is tested a second or third time.

2. **Validity** is a measure of the appropriateness of a test, i.e., whether the test assesses what it was designed to assess (e.g., Does a new IQ test really measure IQ or does it instead measure educational level?) (see Chapter 8). Sensitivity and specificity are components of validity.

D. Sensitivity and specificity

(Example 25.3)

1. **Sensitivity** measures how well a test identifies truly ill people.

a. **True positives** (TP) are ill people whom a test has correctly identified as being ill.

b. **False negatives** (FN) are ill people whom a test has incorrectly identified as being well (i.e., healthy).

c. **Sensitivity** is calculated using only people who are, in fact, ill (TP and FN) by dividing TP by the sum of TP and FN.

(1) Tests with high sensitivity identify most or all possible cases.

(2) They are most useful when identifying an ill person as healthy can lead to severe consequences (e.g., cancer which can metastasize if not identified early).

2. **Specificity** measures how well a test identifies truly well people.

a. **True negatives (TN)** are well people whom a test has correctly identified as being well.

b. **False positives** (FP) are well people whom a test has incorrectly identified as being ill.

c. **Specificity** is calculated by dividing TN by the sum of TN and FP.

(1) Tests with high specificity identify most or all well people.

(2) They are most useful when identifying a healthy person as ill can lead to dangerous, painful, or

unnecessary treatment.

E. Predictive value

(Example 25.3)

1. The predictive value of a test is a measure of the percentage of test results that match the actual diagnosis. Predictive values (but not sensitivity or specificity) vary according to the prevalence of the disorder in the population.
    a. Positive predictive value (PPV) is the probability that someone with a positive test is actually ill. PPV is calculated by dividing TP by the sum of TP and FP.
    b. Negative predictive value (NPV) is the probability that a person with a negative test is actually well. NPV is calculated by dividing TN by the sum of TN and FN.
2. The higher the prevalence of a disorder in the population, the higher the PPV and the lower the NPV of a test used to detect it. If the prevalence of a disorder in the population is low, even tests with very high specificity may have a low PPV because there are likely to be a high number of FP relative to TP.

Example 25.3 Sensitivity, Specificity, Predictive Value, and Prevalence

A new blood test to detect the presence of HIV was given to 1,000 patients. Although 200 of the patients were actually infected with the virus, the test was positive in only 160 patients (true +); the other 40 infected patients had negative tests (false -) and thus were not identified by this new test. Of the 800 patients who were not infected, the test was negative in 720 patients (true -) and positive in 80 patients (false +).

Use this information to calculate sensitivity, specificity, positive predictive value, and negative predictive value of this new blood test and the prevalence of HIV in this population.

	Patients Infected with HIV	Patients Not Infected with HIV	Total Patients	
Positive HIV blood test	160 (true +)	80 (false +)	240 (those with + test)	B = 5
Negative HIV blood test	40 (false -)	720 (true -)	760 (those with - test)	B = 5
Total patients	200	800	1,000	B = 5

$$\text{Sensitivity} = \frac{160\ (\text{true +})}{160\ (\text{true +}) + 40\ (\text{false -})} = \frac{160}{200} = 800\%$$

$$\text{Specificity} = \frac{720\ (\text{true -})}{720\ (\text{true -}) + 80\ (\text{false +})} = \frac{720}{800} = 90\_0\%$$

$$\text{Positive predictive value} = \frac{160\ (\text{true +})}{160\ (\text{true +}) + 80\ (\text{false +})} = \frac{160}{240} = 66.67\%$$

$$\text{Negative predictive value} = \frac{720\ (\text{true -})}{720\ (\text{true -}) + 40\ (\text{false -})} = \frac{720}{760} = 94.7\%$$

$$\text{Prevalence} = \frac{200\ (\text{total of those infected})}{1000\ (\text{total patients})} = 20.0\%$$

V. CLINICAL PROBABILITY AND ATTACK RATE

A.

Clinical probability is the number of times an **event actually occurs** divided by the number of times the **event** can **occur** (Example 25.4).

Example 25.4 Clinical Probability

After 3 years of clinical trials of a new medication to treat migraine headache, it is determined that 20% of patients taking the new medication develop hypertension. If two patients (patients A and B) take the drug, calculate the following probabilities.

1. **The probability that both patient A and patient B will develop hypertension:**

   This is calculated by multiplying the probability of A developing hypertension by the probability of B developing hypertension (the multiplication rule for independent events).

   The probability of A developing hypertension = 0.20.

   The probability of B developing hypertension = 0.20.

   The probability of both A and B developing hypertension = 0.20 x 0.20 = 0.04.

2. **The probability that at least one of the two patients (either A or B or both A and B) will develop hypertension:**

   This is calculated by adding the probability of A developing hypertension to the probability of B developing hypertension and then subtracting the probability of both A and B developing hypertension (the addition rule).

   0.20 + 0.20 - 0.04 = 0.36

   The probability that neither patient A nor patient B will develop hypertension:

   This is calculated by multiplying the probability of patient A being normotensive by the probability of patient B being normotensive: probability of both being normotensive = (1 - probability of A being hypertensive) x (1 - probability of B being hypertensive) = 0.80 x 0.80 = 0.64.

B. Attack rate

is a type of incidence rate used to describe disease outbreaks. It is calculated by dividing the number of people who become ill during a study period by the number of people at risk during the study period. **For example,** if 20 out of 40 people who drank apple juice and 10 out of 50 people who drank orange juice become ill after a picnic, the attack rate is 50% for apple juice and 20% for orange juice.

Review Test

Directions: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the **one** lettered answer or completion that is **best** in each case.

1. A type of gynecological cancer has the same incidence rate in white women and African American women in the United States, but the prevalence rate of this type of cancer is lower in African American than in white women. The most likely explanation for this difference in prevalence rates is that when compared to white women, African American women are more likely to

(A) recover from this type of cancer

(B) have natural immunity to this type of cancer

(C) have increased access to treatment for this type of cancer

(D) be resistant to this type of cancer

(E) die from this type of cancer

2. Two separate randomized double-blind trials were done to see if administration of vitamin C after a myocardial infarction (MI) decreased risk for another MI. Both trials showed that vitamin C reduced the risk by 5%. This reduction was significant in one trial ($P < 0.05$); in the other, it was not significant. The best explanation for this difference between the results of the two trials is that

(A) the researchers were "blind" in one trial but not in the other

(B) randomization did not evenly distribute the risk factors between the two trials

(C) the sample sizes in the two trials were different

(D) there was a placebo effect in one trial but not in the other

(E) the concentration of vitamin C was different between the two trials

Questions 3 and 4

A town in the western United States has a population of 1,200. In 2007, 200 residents of the town are diagnosed with a disease. In 2008, 100 more residents of the town are discovered to have the same disease. The disease is lifelong and chronic but not fatal.

3. The incidence rate of this disease in 2008 among this town's population is

(A) 100/1,200

(B) 200/1,200

(C) 300/1,200

(D) 100/1,000

(E) 300/1,000

4. The prevalence rate of this disease in 2008 among the town's population is

(A) 100/1,200

(B) 200/1,200

(C) 300/1,200

(D) 100/1,000

(E) 300/1,000

5. A study is designed to determine the relationship between emotional stress and ulcers. To do this, the researchers used hospital records of patients diagnosed with peptic ulcer disease and patients diagnosed with other disorders over the period from July 1988-July 1998. The amount of emotional stress each patient was

exposed to was determined from these records. This study is best described as a

(A) cohort study

(B) cross-sectional study

(C) case-control study

(D) historical cohort study

(E) clinical treatment trial

6. A study is done to determine the effectiveness of a new antihistamine. To do this, 25 allergic patients are assigned to one of two groups, the new drug (13 patients) or a placebo (12 patients). The patients are then followed over a 6-month period. This study is best described as a

(A) cohort study

(B) cross-sectional study

(C) case-control study

(D) historical cohort study

(E) clinical treatment trial

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7. An intelligence quotient (IQ) test has high interrater reliability. This means that

(A) the test involves structured interviews

(B) a new assessment strategy is being used

(C) the test actually measures IQ and not educational level

(D) the results are very similar when the test is administered a second time

(E) the results are very similar when the test is administered by a different examiner

8. There are 100,000 people in Hobart, Tasmania. On January 1, 2006, 50 of these people have Disease Y. Fifty divided by 100,000 on that date gives which of the following measures for Disease Y?

(A) Point prevalence

(B) Period prevalence

(C) Incidence rate

(D) Odds ratio

(E) Relative risk

9. In which of the following infectious illnesses is prevalence most likely to exceed incidence?

(A) Measles

(B) Influenza

(C) Leprosy

(D) Rubella

(E) Rabies

Questions 10-13

A patient is given a new screening test for tuberculosis. Although the patient is infected, the test indicates that the patient is well.

10. This test result is known as

(A) false positive

(B) false negative

(C) true positive

(D) true negative

(E) predictive

11. To identify all patients infected with tuberculosis, the cutoff point for this test should be set at the point of highest

(A) sensitivity

(B) specificity

(C) positive predictive value

(D) negative predictive value

(E) accuracy

12. If this new screening test has a sensitivity of 90% and a specificity of 70% in a group of young Russian prisoners in which the prevalence of tuberculosis is 50%, the positive predictive value of this test is best estimated as

(A) 12.5%

(B) 25%

(C) 30%

(D) 75%

(E) 90%

13. If the test is given only to old prisoners in which the incidence and prevalence of tuberculosis is higher than in young prisoners, the positive predictive value (PPV) and sensitivity of this screening test will respectively change in which of the following ways?

Positive Predictive Value Sensitivity

(A) Increase Increase

(B) Decrease Decrease

(C) Increase Not change

(D) Not change Not change

(E) Increase Decrease

Questions 14-16

A study is undertaken to determine if prenatal exposure to marijuana is associated with low birth weight in infants. Mothers of 50 infants weighing less than 5 lbs (low birth weight) and 50 infants weighing more than 7 lbs (normal birth weight) are questioned about their use of marijuana during pregnancy. The study finds that 20 mothers of low-birth-weight infants and 2 mothers of normal-birth-weight infants used the drug during pregnancy.

14. In this study, the odds ratio associated with smoking marijuana during pregnancy is

(A) 2

(B) 16

(C) 20

(D) 30

(E) 48

15. An odds ratio of X, calculated in the preceding question, means that

(A) the incidence of low birth weight in infants whose mothers smoke marijuana is X

(B) an infant of low birth weight was X times as likely as an infant of normal birth weight to have had a mother who used marijuana during pregnancy

(C) a child has a 1/X chance of being bom of low birth weight if its mother uses marijuana

(D) the risk of low birth weight in infants whose mothers use marijuana is no different from that of infants whose mothers do not use the drug

(E) the prevalence of low birth weight in infants whose mothers smoke marijuana is X

16. This study is best described as a

(A) cohort study

(B) cross-sectional study

(C) case-control study

(D) historical cohort study

(E) clinical treatment trial

17. A case-control study is done to determine if elderly demented patients are more likely to be injured at home than elderly patients who are not demented. The results of the study show an odds ratio of 3. This figure means that if you are an elderly patient who was injured at home, you

(A) should be placed in an extended-care facility

(B) are one-third more likely to be demented than a patient who was not injured at home

(C) are no more likely to be demented than a patient who was not injured at home

(D) are three times more likely to be demented than a patient who was not injured at home

(E) should be kept at home

Questions 18-21

A new blood test to detect prostate cancer by measuring prostate specific antigen (PSA) was given to 1,000 male members of a large HMO. Although 50 of the men actually had prostate cancer, the test was positive in only 15; the other 35 patients with prostate cancer had negative tests. Of the 950 men without prostate cancer, the test was positive in 200 men and negative in 750.

18. The specificity of this test is approximately

(A) 15%

(B) 30%

(C) 48%

(D) 79%

(E) 86%

19. The positive predictive value of this blood test is

(A) 7%

(B) 14%

(C) 21%

(D) 35%

(E) 93%

20. If the cutoff value indicating a positive test is lowered from 4 ng/mL PSA to 3 ng/mL PSA, this change would

(A) increase negative predictive value

(B) decrease sensitivity

(C) increase false negative rate

(D) increase positive predictive value

(E) increase specificity

21. With this change in the cutoff value, the incidence and prevalence of prostate cancer would

Incidence Prevalence

(A) Increase Increase

(B) Decrease Decrease

(C) Increase Not Change

(D) Not Change Not Change

(E) Increase Decrease

22. A study is designed to compare a new medication for Crohn disease with a standard medication. Each of 50 Crohn disease patients is allowed to decide which of these two treatment groups to join. The major reason that the results of this study may not be valid is because of

(A) selection bias

(B) recall bias

(C) sampling bias

(D) differences in the sizes of the two groups

(E) the small number of patients in the study

23. After a new antidepressant has been on the market for 5 years, it is determined that of 2,400 people who have taken the drug, 360 complained of persistent nausea. If a physician has two patients on this antidepressant, the probability that both of them will experience persistent nausea is approximately

(A) 2%

(B) 9%

(C) 24%

(D) 30%

(E) 64%

24. A blood test reveals that a 35-year-old woman at 18 weeks gestation has increased serum alpha-fetoprotein (AFP). Of the following measures, which has the greatest influence in determining the predictive value of this test for neural tube defects in the fetus?

(A) Absolute concentration of AFP in the maternal serum

(B) Family history of dizygotic twin pregnancy

(C) Prevalence of neural tube defects in the population in question

(D) Specificity of the blood test

(E) Sensitivity of the blood test

25. In people with no known risks for tuberculosis, a positive reaction to the purified protein derivative (PPD) tuberculin skin test requires 15 mm or more of hard swelling at the site. A group of physicians decide that they are going to change the criterion for a positive test in a group of people with no known risk for tuberculosis to a hard swelling of 10 mm or more at the site. With respect to the PPD test, this change in the cutoff point is most likely to

(A) increase sensitivity

(B) decrease sensitivity

(C) decrease negative predictive value

(D) increase positive predictive value

(E) decrease positive predictive value

Answers and Explanations

Typical Board Question

The answer is E. Twenty women need to be treated with IV ibandronate sodium to prevent one hip fracture. Number needed to treat is calculated as 1/absolute risk reduction. Of the 2,600 women in the placebo group 260 develop hip fractures. Of the 2,600 women in the ibandronate sodium group 130 develop hip fractures. The incidence rate of hip fractures in the placebo group is therefore 260/2,600 (= 0.1 or 10%) and the incidence rate of hip fractures in the ibandronate sodium group is 130/2,600 (= 0.05 or 5%). Therefore, absolute risk reduction (ARR) is 10 - 5 = 5. If 5% of women were prevented from having a hip fracture by the drug, the NNT is 1 divided by 5, or 20.

The answer is E. Prevalence rate of an illness is decreased either when patients recover or when they die. Because when compared to white patients, African American patients tend to have lower incomes and decreased access to health care (see Chapter 18), they are less likely to receive early treatment for disorders such as cancer, and thus more likely to die. Decreased prevalence in African American women is thus more likely to be due to early death than to recovery from this type of cancer. Resistance to an illness or immunity to an illness affects incidence rate, which is equal in both groups of women in this example.

The answer is C. The best explanation for this difference between the studies is that the sample sizes in the two studies were different. The larger the sample size, the higher the power, and the less likely a type I error. This decreased likelihood is reflected in a lower P value, and thus, a higher likelihood of significance for studies with a large sample size. Problems with randomization, efficacy, blinding, or placebo effects would have differentially affected the risk. However, the risk was equal (5%) in the two studies (see Chapter 26).

The answer is D. 4. The answer is C. The incidence rate of the disease in 2008 is 100/1,000, the number diagnosed with the illness divided by the number of people at risk for the illness. Because the 200 people who got the disease in 2007 are no longer at risk for getting the illness in 2008, the denominator in the equation (number of people at risk) is 1,000 (rather than 1,200). The prevalence rate of this disease in 2008 is 300/1,200. This figure represented the people who were diagnosed in 2008 (100) plus the people who were diagnosed in 2007 and still have the disease (200) divided by the total population at risk (1,200).

The answer is C. Case-control studies begin with the identification of subjects who have a specific disorder (cases, i.e., ulcer patients) and subjects who do not have that disorder (controls, i.e., those diagnosed with other disorders). Information on the prior exposure of cases and controls to risk factors is then obtained. In this case-control study, the investigators used cases (ulcer patients), and controls (patients with other disorders), and looked into their histories (hospital records), to determine the occurrence of the risk factor (i.e., emotional stress) in each group. Cohort studies begin with the identification of specific populations (cohorts), who are free of illness at the start of the study and can be prospective (taking place in the present time) or historical (some activities have taken place in the past). Clinical treatment trials are cohort studies in which members of a cohort with a specific illness are given one treatment and other members of the cohort are given another treatment or a placebo. The

results of the two treatments are then compared. Cross-sectional studies involve the collection of information on a disease and risk factors in a population at one point in time.

The answer is E. This study is best described as a clinical treatment trial, a study in which a cohort receiving a new antihistamine is compared with a cohort receiving a placebo (see answer 5).

The answer is E. Interrater reliability is a measure of how similar test findings are when used by two different examiners.

The answer is A. Point prevalence is the number of people who have an illness at a specific point in time (e.g., January 1, 2006) divided by the total population at that time. Incidence rate is the number of individuals who develop an illness in a given time period (commonly 1 year) divided by the total number of individuals at risk for the illness during that time period. Period prevalence is the number of individuals who have an illness during a specific time period. Relative risk compares the incidence rate of a disorder among individuals exposed to a risk factor (e.g., smoking) with the incidence rate of the disorder in unexposed individuals. The odds ratio is an estimate of the relative risk in case-control studies.

The answer is C. In leprosy, a long-lasting, infectious illness, the number of people in the population who have the illness (prevalence) is likely to exceed the number newly developing the illness in a given year (incidence). Measles, influenza, rubella, and rabies are shorter-lasting illnesses than leprosy.

The answer is B. 11. The answer is A. 12. The answer is D. 13. The answer is C. A false negative result occurs if a test does not detect tuberculosis in someone who truly is infected. True positives are ill people whom a test has correctly identified as being ill. True negatives are well people whom a test has correctly identified as being well. False positives are well people whom a test has incorrectly identified as being ill. In order to identify all truly infected people (TP and FN), the cutoff point for the test should be set at the point of highest sensitivity, i.e., the point at which there are the fewest number of FN. Calculations shown below indicate that the positive predictive value (TP/TP + FP) of this test is 90/120 = 75%.

	Disease Present	Disease Absent	Total
Positive test	90 (TP)	30 (FP)	120
Negative test	10(FN)	70 (TN)	80
Total	100	100	200

Positive predictive value: 90 TP/(90 TP + 30 TP) = 90/120 = 75%.

Calculations shown below indicate that if prevalence of the disease is increased in a population (e.g., old men), positive predictive value increases, but sensitivity does not change.

	Disease Present	Disease Absent	Total
Positive test	172(TP)	6(FP)	178
Negative test	18(FN)	14 (TN)	32
Total	180	20	200

If the prevalence of the disease is increased, both TP and FN will increase to the same extent, and sensitivity will not change. However, with increased prevalence, TP will increase and FP will decrease, so PPV will increase. Also, because with increased prevalence, FN increases but TN decreases, NPV will decrease.

The answer is B. 15. The answer is B. 16. The answer is C. The odds ratio is 16 and is calculated as follows:

	Mother Smoked Marijuana	Mother Did Not Smoke Marijuana
Low-birth-weight babies	A = 20	B = 30
Normal-birth-weight babies	C = 2	D = 48
Odds ratio = (AD)/(BC) or (20)(48)/(30)(2) = 960/60 = 16.		

The odds ratio of 16 means that an infant of low birth weight was 16 times as likely as an infant of normal birth weight to have had a mother who used marijuana during pregnancy. This study is best described as a case-control study; the risk factor here is fetal exposure to marijuana (see also the explanation for question 5).

The answer is D. An odds ratio of 3 means that an elderly patient who was injured at home was three times more likely to be demented than a patient who was not injured at home.

This number does not indicate whether or not certain people should remain at home or be cared for by others.

The answer is D. 19. The answer is A. 20. The answer is A. 21. The answer is D. Calculations shown below indicate that the specificity of this blood test is 79%.

	Those Who Have Prostate Cancer	Those Who Do Not Have Prostate Cancer	Total
Positive blood test	15 (true +)	200 (false +)	215
Negative blood test	35 (false -)	750 (true -)	785
Total patients	50	950	1000

Specificity: 750 (true -)/[750 (true -) + 200 (false +)] = 0.789 or 78.9%. The calculations shown below indicate that the positive predictive value of this test is 7%.

Positive predictive value: 15 (true +)/(15 + 200) (those with + test) = 0.07 or 7.0%. Decreasing the lower limit of this reference test value (i.e., the cutoff value) can be expected to both decrease the number of false negatives and increase the number of false positives. Such alterations will both increase sensitivity (TP/TP. + FN) and negative predictive value (TN/TN. + FN) and decrease specificity (TN/TN. + FP) and positive predictive value (TP/TP. + FP) of the test. A change in the reference interval would not affect the incidence or prevalence of prostate cancer in the population.

The answer is A. The major reason that the results of this study are not valid is because of selection bias (i.e., the subjects were able to choose which group to go into). If very ill people were more likely to choose the standard treatment, people in the experimental treatment group (who were healthier to begin with) would have had a better outcome. In recall bias, knowledge of the presence of a disorder alters the way subjects remember their histories. In sampling bias, subjects are chosen to be in a study because of factors that may be unrelated to the subject of the study but distinguish them from the rest of the population. A study can be valid even though two groups may be of different sizes or there is a small number of patients in a study.

The answer is A. The probability of both patients (A and B) taking this antidepressant experiencing nausea equals the probability of A experiencing nausea. (360/2400 = 0.15) times the probability of B experiencing nausea (360/2400 = 0.15) = 0.15 x 0.15 = 0.0225 = about 2%.

The answer is C. The prevalence of neural tube defects in the population in question has the greatest influence in

determining the predictive value of this test for this patient since prevalence is directly related to predictive value. The higher the prevalence, the higher the positive predictive value (PPV) and the lower the negative predictive value (NPV). Sensitivity and specificity relate to whether the test indicates that there is a neural tube defect in an affected fetus (sensitivity) or the absence of a neural tube defect in a healthy fetus (specificity). While AFP in the maternal serum or family history of dizygotic twin pregnancy may be related to whether or not the fetus has a neural tube defect, they are not related to the predictive value of a screening test.

The answer is A. With respect to the PPD test, this change in the cutoff point is most likely to increase sensitivity. This is because there will be fewer false negatives, i.e., fewer people who are actually at risk for TB will be identified as not at risk. Having fewer false negatives can also increase the negative predictive value of the test but is less likely to affect specificity or positive predictive value.