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Item 20 of 40 Question Id: 1174

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ARR represents the actual difference in control and experimental group event rates. The data is *not* presented in the standard format of a [contingency \(2 × 2\) table](#), so care should be exercised in selecting the appropriate values. In this example, the event of interest is myocardial infarction. There were  $25 + 975 = 1,000$  patients in the control group; of those, 25 had a myocardial infarction. Similarly, there were  $10 + 990 = 1,000$  patients in the treatment (ie, Superstatin) group; of those, 10 had a myocardial infarction. Therefore:

$$\text{Control event rate} = 25 / 1,000 = 0.025$$

$$\text{Experimental event rate} = 10 / 1,000 = 0.01$$

ARR can then be calculated:

$$\text{ARR} = \text{Control event rate} - \text{Experimental event rate} = 0.025 - 0.01 = 0.015, \text{ or } 1.5\%$$

Finally, NNT is found by dividing 1 by 0.015:

$$\text{NNT} = 1 / 0.015 = 66.6 \approx 67$$

Rounding up the result to the nearest whole number, **67 patients** need to be treated with Superstatin to prevent an additional myocardial infarction.

The ideal NNT would be 1, meaning that all patients in the treatment group benefit from the treatment. A **low NNT** implies that a treatment is **more beneficial** because fewer patients need to be treated to prevent an additional negative outcome. For instance, if a third hypolipidemic medication had an NNT of 40, it would be more beneficial than Superstatin, as only 40 patients would need to be treated over a given period to prevent an additional myocardial infarction.

#### Educational objective:

The number needed to treat (NNT) is the number of patients that need to be treated with a medication to avoid an additional negative outcome.

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**Experimental event rate =  $10 / 1,000 = 0.01$**

ARR can then be calculated:

ARR = Control event rate – Experimental event rate =  $0.025 - 0.01 = 0.015$ , or 1.5%

Finally, NNT is found by dividing 1 by 0.015:

$$\text{NNT} = 1 / 0.015 = 66.6 \approx 67$$

Rounding up the result to the nearest whole number, **67 patients** need to be treated with Superstatin to prevent an additional myocardial infarction.

The ideal NNT would be 1, meaning that all patients in the treatment group benefit from the treatment. A **low NNT** implies that a treatment is **more beneficial** because fewer patients need to be treated to prevent an additional negative outcome. For instance, if a third hypolipidemic medication had an NNT of 40, it would be more beneficial than Superstatin, as only 40 patients would need to be treated over a given period to prevent an additional myocardial infarction.

### Educational objective:

The number needed to treat (NNT) is the number of patients that need to be treated with a medication to avoid an additional negative outcome. NNT is calculated by dividing 1 by the absolute risk reduction (the difference between the control and experimental group event rates). Lower NNT values represent more beneficial treatments.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Number Needed To Treat  
Topic

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Item 21 of 40 Question Id: 1299

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A researcher is interested in assessing the blood folate level of women who live in a population with a high incidence of neural tube defects. She takes a large random sample ( $n$ ) of women age 18-45 and measures their blood folate levels. The researcher finds that the data are normally distributed, and she reports the mean and standard deviation (SD) of the sample. To account for sampling variation, she decides to calculate a 95% confidence interval to estimate the mean of the entire population. The researcher concludes that 2.4 to 4.6 ng/mL might be a likely range for the true, unknown population mean. Which of the following calculations was most likely used to compute this interval estimate of the population mean?

- A. Mean  $\pm 1.96 \times SD$  (18%)
- B. Mean  $\pm 1.96 \times (SD/\sqrt{n})$  (63%)
- C. Mean  $\pm 2.58 \times SD$  (4%)
- D. Mean  $\pm 2.58 \times (SD/\sqrt{n})$  (8%)
- E. Mean  $\pm (SD/n)$  (5%)

Omitted  
Correct answer  
B

63%  
Answered correctly

01 sec  
Time Spent

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Version

### Explanation

The **normal distribution** is a continuous distribution that follows a bell-shaped curve with a single peak at the mean value. One of the most important properties of the normal distribution is its **symmetry** about its mean,

The screenshot shows a mobile application interface for a study. At the top, there's a header bar with icons for back, forward, and search. Below it is a toolbar with various functions: Item 21 of 40, Question Id: 1299, Mark, Previous, Next, Full Screen, Tutorial, Lab Values, Notes, Calculator, Reverse Color, Text Zoom, and Settings. The main content area contains text about the normal distribution and its properties, such as the 68/95/99 rule and standard error calculations.

The **normal distribution** is a continuous distribution that follows a bell-shaped curve with a single peak at the mean value. One of the most important properties of the normal distribution is its **symmetry** about its mean, which allows for determination of the percentage of all observations that lie within 1, 2, or 3 standard deviations (SDs). The "68/95/99 rule" states that 68% of all observations lie within 1 SD of the mean, 95% within 2 SDs of the mean, and 99.7% within 3 SDs of the mean. These are helpful approximations; however, when considering the normal distribution, exactly **95% of the observations** lie within **1.96 SDs** of the mean and 99% of the observations lie within 2.58 SDs (1.96 and 2.58 represent z-scores for 95% and 99% of the distribution, respectively).

Most research is done using **samples** rather than entire populations. This introduces some variability when calculating population parameters such as mean value (eg, when different samples are drawn from the same population, the means from all possible samples will often be slightly different). The **variability between sample means** can be calculated in a way analogous to calculating the SD of a group of observations in a single sample. The "standard deviation" of a series of sample means is known as the **standard error (SE)** of the mean, and it estimates how far the sample mean is likely to be from the unknown population mean. The SE is estimated considering both the SD and the size of the sample ( $n$ ) in the following manner:  **$SD/\sqrt{n}$** .

A sample mean is a point estimate of the true population mean; however, a **confidence interval (CI)** better accounts for the variability due to sampling by including the SE in its calculation. The CI of the mean can be calculated as follows:

$$\text{CI of mean} = \text{mean} \pm [\text{z-score for confidence level}] \times [\text{SE}]$$

where the z-score for confidence level represents the number of SEs containing the desired percentage of observations around the mean (eg, 95%, 99%). In this case, the 95% CI can be calculated:

$$\text{CI of mean} = \text{mean} \pm 1.96 \times (\text{SD}/\sqrt{n})$$

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$$\text{CI of mean} = \text{mean} \pm [z\text{-score for confidence level}] \times [\text{SE}]$$

where the z-score for confidence level represents the number of SEs containing the desired percentage of observations around the mean (eg, 95%, 99%). In this case, the 95% CI can be calculated:

$$\text{CI of mean} = \text{mean} \pm 1.96 \times (\text{SD}/\sqrt{n})$$

The sample size and the SD of the sample determine the magnitude of the variability due to sampling. As  $n$  increases, SE decreases, and the CI becomes narrower and more precise. Conversely, as the SD increases, SE increases, and the CI becomes wider and less precise.

**(Choice A)** CI estimates use the SE of the mean, which takes into account the SD and the size of the sample ( $n$ ). As such, the equation divides the SD by the square root of  $n$ .

**(Choices C, D, and E)** As noted, the SD reflects the spread of individual values in a normal distribution. Multiplying the SD by a specific constant (z-score) gives us a range of values that encompass a certain proportion of the observations. The mean  $\pm 1 \times \text{SD}$  would cover 68% of the observations, and the mean  $\pm 2.58 \times \text{SD}$  would cover 99% of the observations. However, the question is asking for a 95% CI, so the equation should use a z-score of 1.96 and the SE (ie,  $\text{SD}/\sqrt{n}$ ).

### Educational objective:

The standard deviation reflects the spread of individual values in a normal distribution (ie, it measures the variability of the observations within a single sample). The standard error of the mean reflects the variability of means (ie, variance between the means of different samples) and helps estimate the true mean of the underlying population.

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Item 22 of 40 Question Id: 1301

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A study to assess spironolactone's efficacy in patients with heart failure is performed. 450 patients receive either spironolactone or placebo for two years. Neither the patients nor physicians are aware of who takes the drug or placebo. The study setup described above is most effective in preventing:

- A. Beta error (2%)
- B. Recall bias (2%)
- C. Observer bias (75%)
- D. Effect modification (7%)
- E. Selection bias (12%)

Omitted  
Correct answer  
C

75%  
Answered correctly

03 secs  
Time Spent

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Version

### Explanation

Blinding technique is commonly used in clinical trials. The blinding can involve patients exclusively or both patients and physicians (double blinding). The main purpose of blinding is to prevent patient or researcher expectancy from interfering with the determination of an outcome. For example, a researcher's belief in a positive outcome in treated patients can potentially result in observer bias.

**(Choice A)** Beta error refers to a conclusion that there is no difference between the groups studied when a difference truly exists. Beta error is a random error, not a systematic error (i.e., bias).

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Item 22 of 40 Question Id: 1301

Mark

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Correct answer C

75% Answered correctly

03 secs Time Spent

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### Explanation

Blinding technique is commonly used in clinical trials. The blinding can involve patients exclusively or both patients and physicians (double blinding). The main purpose of blinding is to prevent patient or researcher expectancy from interfering with the determination of an outcome. For example, a researcher's belief in a positive outcome in treated patients can potentially result in observer bias.

**(Choice A)** Beta error refers to a conclusion that there is no difference between the groups studied when a difference truly exists. Beta error is a random error, not a systematic error (i.e., bias).

**(Choice B)** Recall bias results from the inaccurate recall of past exposure by subjects. It applies mostly to case-control studies.

**(Choice D)** Effect modification is not a bias and should not be controlled.

**(Choice E)** Selection bias results from the manner in which people are selected for the study, or from the selective losses from follow-up.

### Educational Objective:

The main purpose of blinding is to prevent patient or researcher expectancy from interfering with an outcome.

Biostatistics

Biostatistics & Epidemiology

Bias

Subject

System

Topic

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Item 23 of 40 Question Id: 19315

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A new study is conducted to investigate the efficacy of intravenous immunoglobulin versus analgesics on pain alleviation in patients with idiopathic small fiber neuropathy. A total of 100 eligible patients who fulfilled the inclusion/exclusion criteria are assigned to one of two groups based on random selection by a computer. The method of assigning patients to treatment groups in this study is most likely intended to produce which of the following?

- A. One group in which participants are blinded to the intervention they receive and another in which participants are not (1%)
- B. One group in which researchers but not participants are aware of the intervention received and another in which participants but not researchers are aware of the intervention received (1%)
- C. Two groups of participants that will only be analyzed based on their initial treatment allocation (24%)
- D. Two groups that have equal numbers of participants (29%)
- E. Two groups in which participants are similar in underlying characteristics (42%)

Omitted  
Correct answer  
E

42%  
Answered correctly

03 secs  
Time Spent

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### Explanation

**Randomization** refers to the process of **randomly** (ie, by chance) **assigning subjects** to experimental groups (eg, treatment vs control group). Randomization **prevents selection bias** and potentially produces **comparable**



assignments. Although this study used randomization to assign patients to treatment groups, no information is provided regarding the awareness of participants or researchers to treatment assignments. By itself, randomization does not make a study blind.

**(Choice C)** A study that analyzes all participants as initially allocated after randomization, regardless of what happens during the study period, is using an intention-to-treat (ITT) analysis. ITT is not a result of randomization; instead, it is used to preserve the effect of randomization.

**(Choice D)** Depending on the randomization method (eg, simple, complete) used to allocate participants into experimental groups, a study may or may not result in groups that are similar in sample size. Regardless, the goal of randomization is not to create groups of similar size (which can be done trivially by alternating group assignment as patients enroll) but rather to make the underlying characteristics of experimental groups as similar as possible.

### Educational objective:

Randomization refers to the process of using random methods to assign subjects to experimental groups. Its purpose is to make experimental groups as similar as possible (except for the treatment assignment) to ensure that any difference observed between the groups is due exclusively to the treatment and not to other underlying factors.

### References

- Randomized allocation to treatment groups and the importance of adjusting for covariates.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Randomized control trials  
Topic

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A pediatric cardiologist decides to determine whether there is a relationship between body composition and blood pressure in a random sample of children and adolescents age 5-15. He used standard procedures to collect anthropometric measurements that included weight, height, hip circumference (HC), and waist circumference (WC). Systolic blood pressure (SBP) and diastolic pressure (DBP) readings were taken at least 3 times at 5-minute intervals after the participants had been seated, and average SBP and DBP readings were calculated based on these measurements. Which of the following statistical tests is adequate to determine whether there is a relationship between WC and average DBP?

- A. Analysis of variance (5%)
- B. Chi-square test (9%)
- C. Correlation analysis (55%)
- D. Meta-analysis (1%)
- E. Two-sample *t*-test (27%)

Omitted  
Correct answer  
C

55%  
Answered correctly

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### Explanation

#### Dependent variable

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		Dependent variable	
		Qualitative (categorical)	Quantitative
<b>Independent variable</b>	Qualitative (categorical)	Chi-square, logistic regression*	<i>t</i> test, ANOVA, linear regression
	Quantitative	Logistic regression*	Correlation, linear regression

\*Dependent variable must be dichotomous.

**ANOVA** = analysis of variance.

Variables are broadly classified as qualitative (ie, categorical) or quantitative (ie, continuous) based on their scale of measurement. **Qualitative variables** (eg, type of treatment, blood type) represent categories or groups whereas **quantitative variables** (eg, temperature, glucose levels) represent numerical values. The scale of measurement of the dependent (eg, outcome) and independent (eg, exposures, risk factors) variables in a study determines the correct statistical test for any given situation.

**Correlation analysis** is a statistical technique **used to assess** the strength and direction of a **linear relationship between 2 quantitative variables** (often, but not always, a dependent and an independent variable). In this study:

- The quantitative dependent variable was diastolic pressure (DBP).
- The quantitative independent variable was waist circumference (WC).

Correlation analysis can determine whether there is a relationship between DBP and WC. A statistically significant **correlation coefficient** indicates that DBP and WC have a linear relationship (ie, the null hypothesis is

The screenshot shows a mobile application interface for a test item. At the top, there is a header bar with the URL "apps.uworld.com". Below the header is a toolbar with various icons: a left arrow, a right arrow, a double arrow, a magnifying glass, a question mark, a calculator, a reverse color button, a text zoom button, and a settings gear icon. The main content area displays a list of bullet points:

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- The quantitative dependent variable was diastolic pressure (DBP).
- The quantitative independent variable was waist circumference (WC).

Correlation analysis can determine whether there is a relationship between DBP and WC. A statistically significant [correlation coefficient](#) indicates that DBP and WC have a linear relationship (ie, the null hypothesis is rejected) that is either positive (as WC increases, DBP increases) or negative (as WC increases, DBP decreases).

**(Choice A)** The analysis of variance (ANOVA) test compares the mean of a quantitative variable of  $\geq 3$  independent groups, as in a study comparing serum ferritin concentrations (ie, quantitative variable) in children (age 0-12), adolescents (age 13-17), adults (age 18-59), and seniors (age  $\geq 60$ ).

**(Choice B)** The chi-square test evaluates the association between 2 categorical variables, as in a study evaluating the association between sex (ie, "male" and "female") and myocardial infarction (ie, presence of myocardial infarction, absence of myocardial infarction).

**(Choice D)** Meta-analysis is a quantitative statistical technique used to combine and analyze data from several studies to conduct an analysis with a greater statistical power than that of the individual studies.

**(Choice E)** The two-sample *t*-test compares the mean of a quantitative variable between 2 groups, as in a study comparing serum ferritin concentrations (ie, quantitative variable) in male and female patients.

#### Educational objective:

Correlation analysis is a statistical technique used to describe the strength and direction of a linear relationship between 2 quantitative variables.

#### References

- Correlation coefficients: appropriate use and interpretation.

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A physician is conducting a double-blind randomized controlled trial to determine the effect of a new cream in reducing the risk of relapse in chronic recurrent atopic dermatitis. A total of 30 patients with moderate to severe atopic dermatitis who were experiencing a flare are randomly divided into 2 groups: 15 patients will receive the new cream, and 15 patients will receive emollient alone. The rate of relapse after 2 weeks of treatment is 25% in the group who received the new cream and 50% in the group who received emollient alone. However, the difference is found to be not statistically significant ( $p = 0.14$ ). The physician concludes that use of the new cream does not reduce the risk of relapse in chronic recurrent atopic dermatitis. Which of the following is most likely to explain the results of the study?

- A. Ascertainment bias (3%)
- B. Confounding bias (5%)
- C. Ecologic fallacy (1%)
- D. Insufficient statistical power (89%)
- E. Recall bias (0%)

Omitted

Correct answer

D



89%

Answered correctly



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Time Spent



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Version

### Explanation

**Statistical power** represents a study's **strength to detect a difference** (ie, effect size) between treatment

**Statistical power** represents a study's **strength to detect a difference** (ie, effect size) between treatment groups when one truly exists. It **depends** on **sample size** (among other factors): studies with **greater sample sizes** have **greater power** than studies with smaller sample sizes. An excessively large sample size may determine that a clinically irrelevant difference between groups is statistically significant (ie,  $p < 0.05$ ), while an inappropriately small sample may fail to determine that a clinically relevant difference between groups is statistically significant (ie,  $p > 0.05$ ).

In this case, the rate of relapse in the group receiving the new cream is 25% and the rate in the group receiving the emollient alone is 50%. This represents a **relative risk reduction (RRR) of 50%** (ie,  $[50\% - 25\%] / 50\%$ ); therefore, the new cream reduced the risk of relapse by 50% (ie, effect size) compared to emollient alone. A 50% risk reduction may be considered **clinically relevant**; however, it was **not statistically significant** (ie,  $p = 0.14 > 0.05$ ) in the study.

The most likely explanation is that the sample size (ie, 15 per group) provided **insufficient power** to detect the observed difference between groups (ie, effect size, RRR = 50%). A larger sample size would increase the power of the study (ie, its ability to detect the difference), and the  $p$ -value would reach statistical significance (ie,  $p < 0.05$ ).

**(Choice A)** Ascertainment bias occurs when the results of a study are distorted by awareness of treatment assignment, as in an unblind study. This study is double-blinded, thereby minimizing potential ascertainment bias.

**(Choice B)** Confounding distorts the relationship between exposures (eg, treatments) and the outcome (eg, disease) of interest, and can wholly or partially account for observed effects. This study is a randomized trial, thereby minimizing potential confounding bias by generating groups that are comparable with respect to known and unknown confounding variables.

$p < 0.05$ .

**(Choice A)** Ascertainment bias occurs when the results of a study are distorted by awareness of treatment assignment, as in an unblind study. This study is double-blinded, thereby minimizing potential ascertainment bias.

**(Choice B)** Confounding distorts the relationship between exposures (eg, treatments) and the outcome (eg, disease) of interest, and can wholly or partially account for observed effects. This study is a randomized trial, thereby minimizing potential confounding bias by generating groups that are comparable with respect to known and unknown confounding variables.

**(Choice C)** Ecological fallacy occurs when conclusions are made about individuals based on studies where the unit of analysis is a group (ie, the conclusions of a study assessing population groups do not necessarily apply to individuals). In this study, the unit of analysis is the individual, not the group.

**(Choice E)** Recall bias results from the inaccurate recollection of past exposure status. It is a potential problem for case-control studies, particularly when questionnaires are used to inquire about distant past exposure. However, this study is an experiment in which patients are exposed to treatments and then assessed for the outcome.

#### Educational objective:

An inappropriately small sample will fail to identify important clinically significant differences as statistically significant because of a lack of sufficient statistical power.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Power and sample size  
Topic

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A study is conducted to assess the relationship between smoking status and forced expiratory volume in one second (FEV<sub>1</sub>). Subjects are randomly selected and categorized based on smoking status. Group A consists of 200 nonsmokers, group B consists of 200 light smokers (1-7 cigarettes per day), group C consists of 200 moderate smokers (8-22 cigarettes per day), and group D consists of 200 heavy smokers (23+ cigarettes per day). FEV<sub>1</sub> is quantitatively measured in all participants using properly calibrated office spirometers. Which of the following is the most appropriate statistical method to compare the mean FEV<sub>1</sub> results among all 4 groups?

- A. Analysis of variance (63%)
- B. Chi-square test (21%)
- C. Meta-analysis (4%)
- D. Multiple logistic regression (2%)
- E. Pearson correlation coefficient (4%)
- F. Two-sample t-test (2%)

Omitted  
Correct answer  
A

63% Answered correctly

03 secs Time Spent

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### Explanation

#### Analysis of variance (ANOVA)

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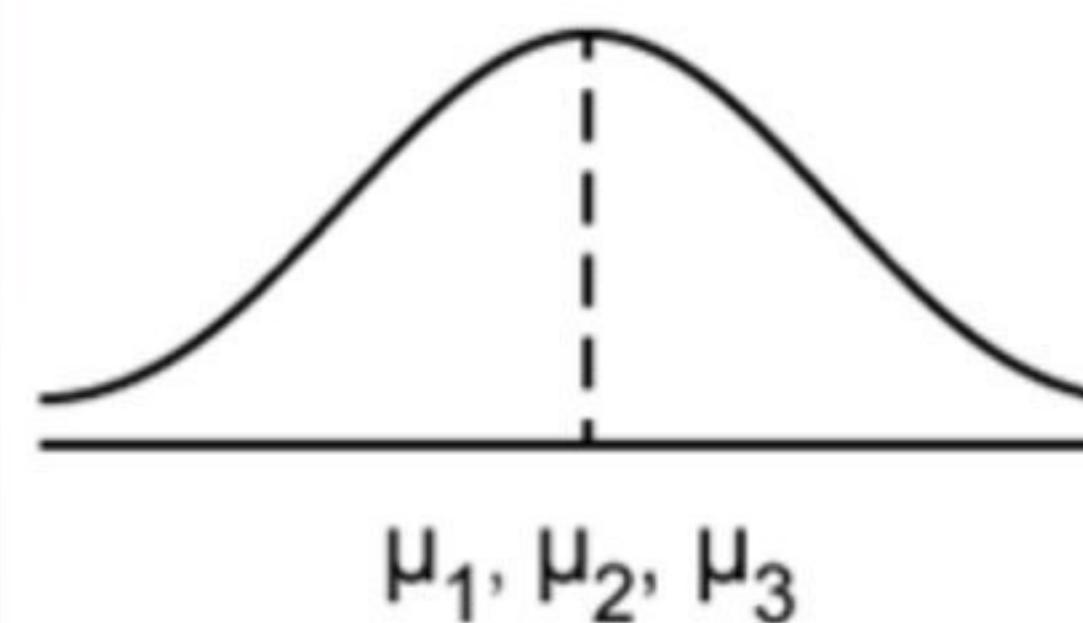
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## Analysis of variance (ANOVA)

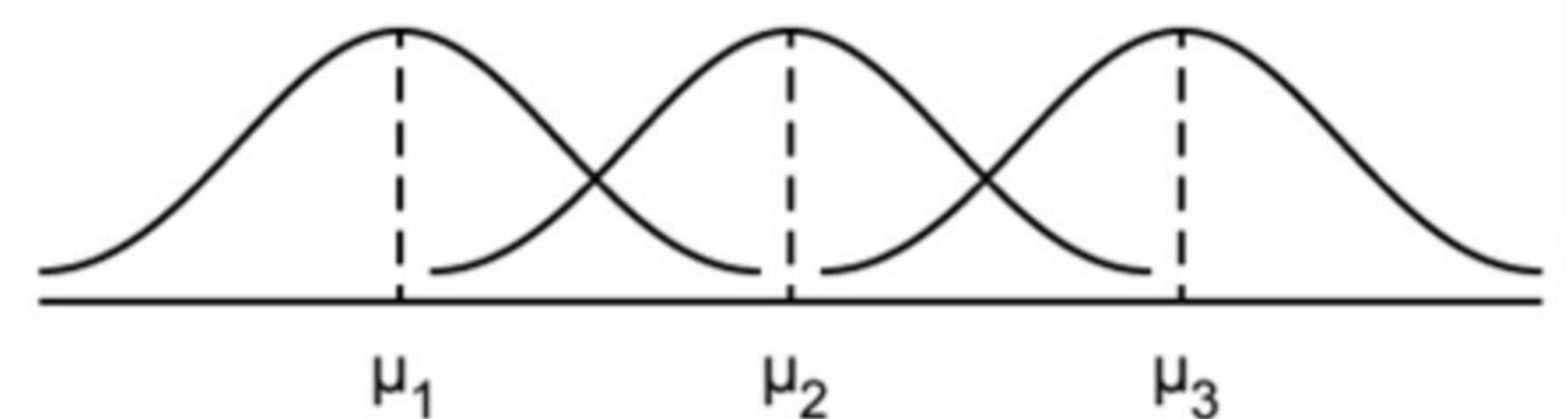
### Null hypothesis

All samples drawn from the same population  
 $(\mu_1 = \mu_2 = \mu_3)$

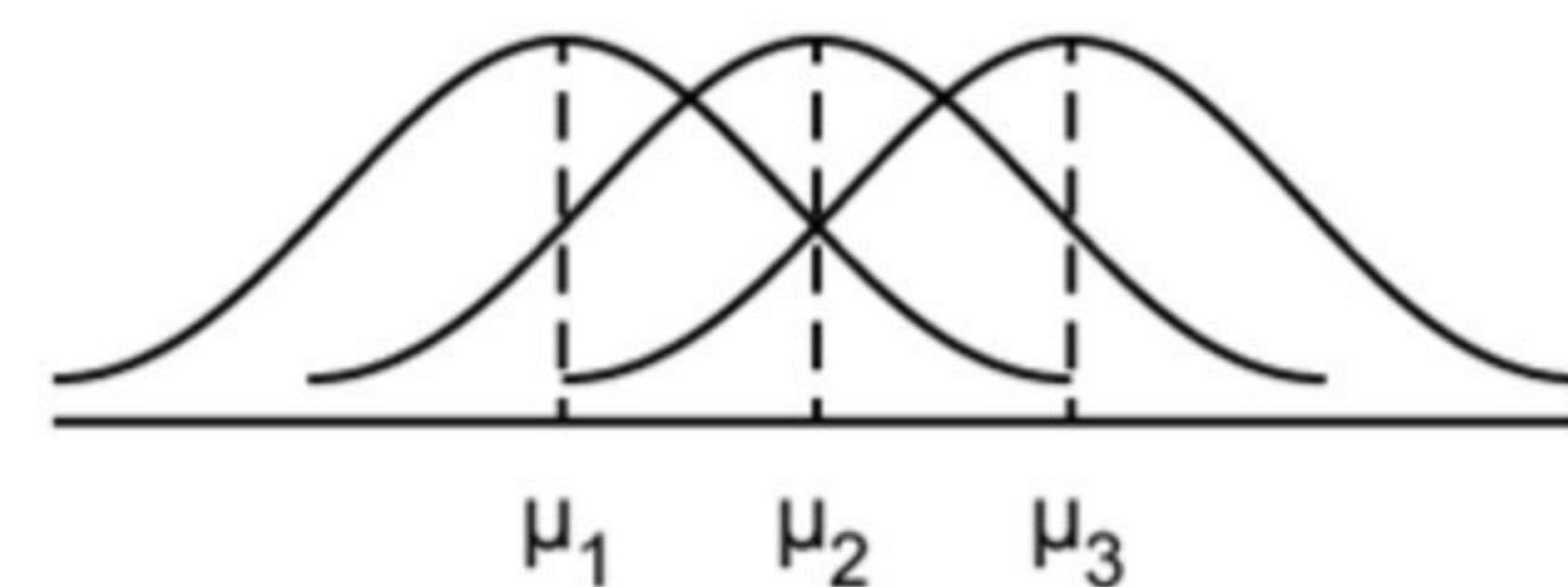


### Alternate hypothesis

Samples drawn from different populations  
 $(\mu_1 \neq \mu_2 \neq \mu_3)$



Small apparent differences between the means of the samples:  
null hypothesis not rejected



Large apparent differences between the means of the samples:  
null hypothesis rejected

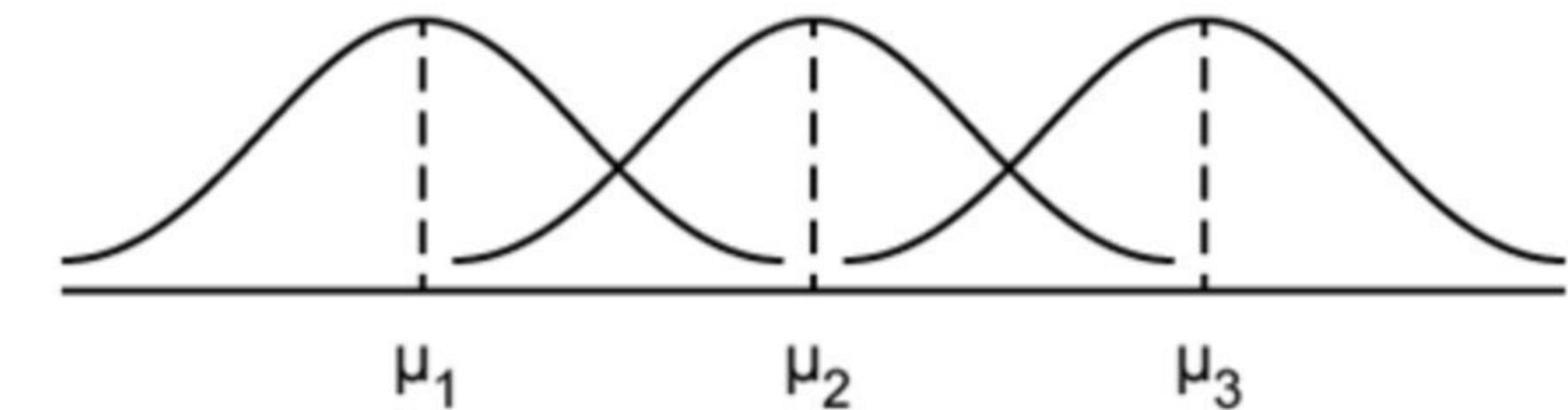


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Large apparent differences between the means of the samples:  
null hypothesis rejected



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**Analysis of variance (ANOVA)** is used to determine whether there are any significant **differences between the means of several independent groups**.

ANOVA compares the means between the groups relative to the variability within groups (F-test) and determines whether any of those means are significantly different from one another. Specifically, it tests the **null hypothesis** that all groups are simply random samples of the same population (ie, the **means are the same**). The null hypothesis is rejected when there are at least 2 group means that are significantly different from one another.

ANOVA can be used to compare  $\geq 2$  groups but is generally used to compare  **$\geq 3$  groups** (because other equivalent methods exist to compare 2 groups). For example, the 2 independent samples *t*-test is a special case of the F-test in ANOVA. The assumptions for both tests and their resulting *p*-values are the same.

**(Choice B)** Chi-square tests can be used to evaluate the association between 2 *categorical* variables. For example, if  $FEV_1$  is measured as a categorical variable (eg, normal or low), then a chi-square test could be used to determine if there is an association between  $FEV_1$  and smoking status. However, this study is specifically comparing the mean  $FEV_1$  results (a *quantitative* variable) between groups.

**(Choice C)** Meta-analysis involves the pooling of data from several studies to perform an analysis with greater

to determine if there is an association between FEV<sub>1</sub> and smoking status. However, this study is specifically comparing the mean FEV<sub>1</sub> results (a *quantitative* variable) between groups.

**(Choice C)** Meta-analysis involves the pooling of data from several studies to perform an analysis with greater statistical power than the individual studies alone. For example, individual studies assessing the effects of aspirin on certain cardiovascular events may be inconclusive. However, analysis of data compiled from multiple clinical trials may reveal a significant benefit.

**(Choice D)** Multiple logistic regression is a method used to predict the probability of a binary outcome (eg, presence or absence of gastric cancer) based on 1 or more independent variables that can be either continuous or categorical. For example, this test could be used to predict the probability of gastric cancer based on alcohol consumption, tobacco use, and charred food consumption.

**(Choice E)** The Pearson correlation coefficient is a measure of the strength and direction of a linear relationship between 2 quantitative (ie, continuous) variables. For example, a study may report a correlation coefficient describing the association between hemoglobin A1c levels and average blood glucose levels.

**(Choice F)** A two-sample *t*-test can be used when 2 group means are compared. This test could have been used for the example in the question if the study participants were divided into smoking and nonsmoking groups only (ie, 2 groups instead of 4).

#### Educational objective:

A *t*-test is used to compare the difference between the means of 2 groups. Analysis of variance (ANOVA) compares the difference between the means of 2 or more groups. Results from a *t*-test and ANOVA test will be equivalent when comparing the difference between the means of 2 groups.

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An epidemiologist wants to conduct a study on hepatitis C (HCV) transmission in a country with limited healthcare resources. She has access to a cohort of adults newly diagnosed with HCV and a cohort of age-matched HCV-negative adults. She plans to use these 2 cohorts of adults to conduct a case-control study. Which of the following would be the most appropriate measure of interest for this researcher's study?

- A. The average death rate in each cohort (3%)
- B. The frequency of past blood transfusions in each cohort (69%)
- C. The incidence rate of liver cancer in HCV-positive participants (10%)
- D. The rate of eventual HCV infection in HCV-negative participants (14%)
- E. The rate of treatment-related adverse effects in HCV-positive participants (1%)

Omitted  
Correct answer  
B

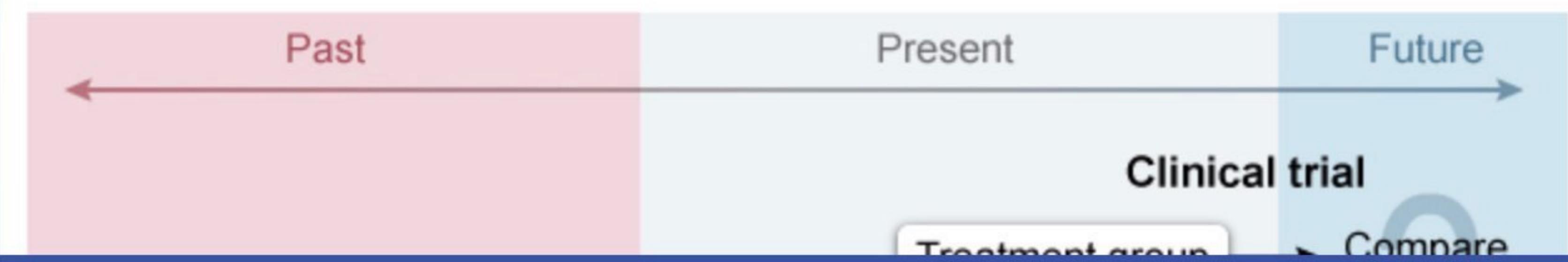
69%  
Answered correctly

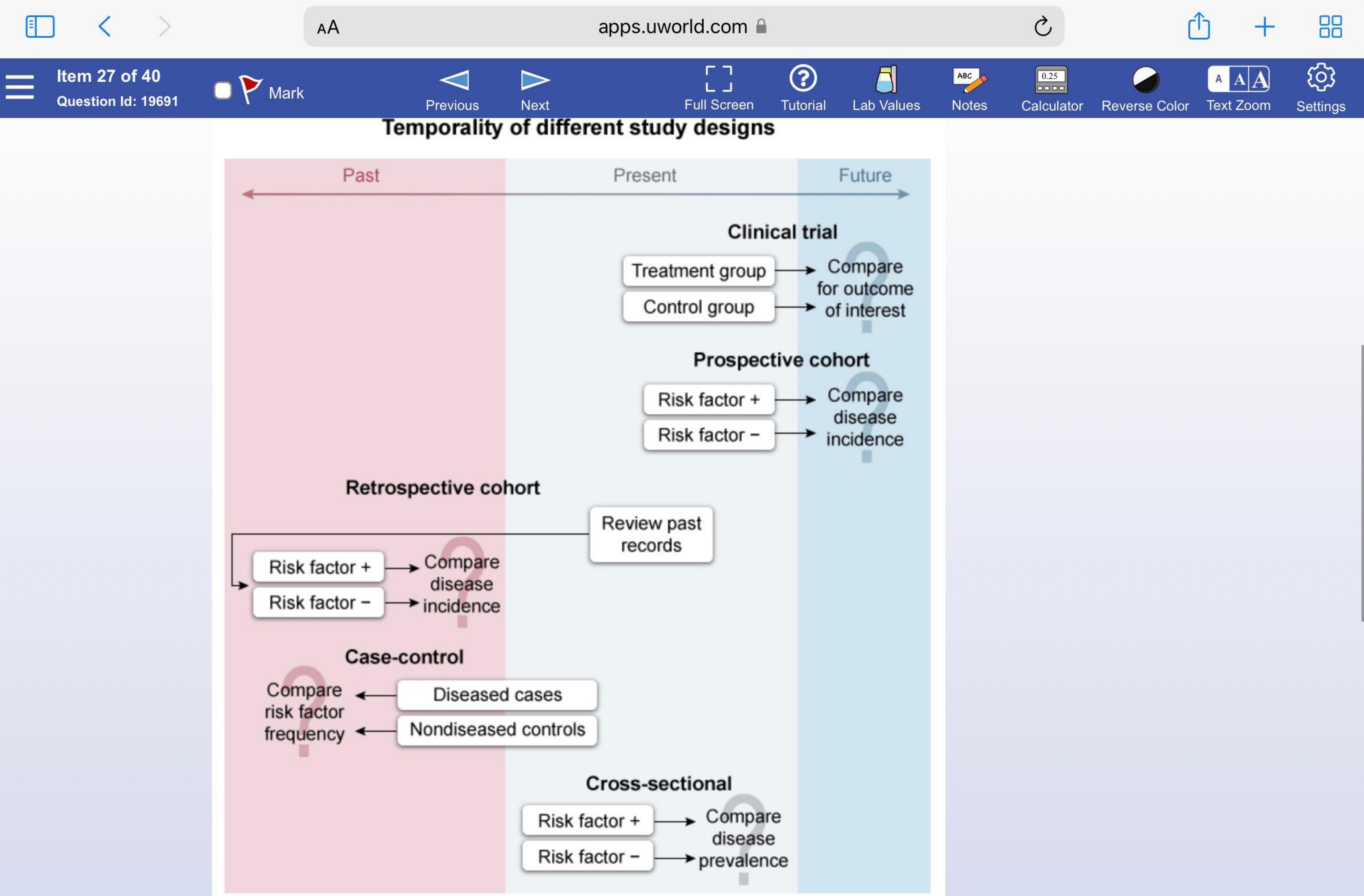
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Version

### Explanation

#### Temporality of different study designs





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A **case-control** study is an observational study design in which potential participants are initially identified as **cases or controls** according to their **disease status** (ie, have or do not have the disease of interest). In the study described above, a cohort of adults newly diagnosed with hepatitis C (HCV) represents the cases, and a cohort of HCV-negative adults represents the controls. Note that "cohort" in this case refers to a group of individuals with similar characteristics (eg, HCV-positivity), not to a "cohort study," in which a group of individuals are followed over time.

Once cases and controls are identified, the **frequency** of past exposure to  $\geq 1$  **risk factors** of interest is compared between cases and controls to estimate the **association** between the risk factors and the outcomes. Therefore, an **appropriate measure** for the proposed study would be any event that **preceded HCV infection**. Among the given choices, a history of **past blood transfusions** precedes HCV infection.

Because of the retrospective nature of a case-control study, this study design is not able to compare the frequency (ie, incidence, risk, rate) of any event that occurs after a disease has been diagnosed (ie, prospective outcomes). Prospective outcomes are reasonable in cohort studies and experimental designs (**Choices A, C, D, and E**).

**Educational objective:**

In a case-control study, potential participants are initially identified as cases or controls according to their disease status. The frequency of past exposure to  $\geq 1$  risk factors of interest is then compared between cases and controls to estimate the association between the risk factors and the outcomes.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Case control studies  
Topic

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Item 28 of 40 Question Id: 19632

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A research group is studying the correlation between BMI and blood pressure in a random sample of children age 12-16. After collecting data, they conduct a correlation analysis at a 1% significance level. The researchers find that BMI correlates with systolic blood pressure with a coefficient of  $r = 0.46$  ( $p < 0.001$ ) and diastolic blood pressure with a coefficient of  $r = 0.37$  ( $p < 0.001$ ). Which of the following is the most accurate interpretation of these results?

- A. An increase in BMI causes a statistically significant increase in blood pressure in children (8%)
- B. Childhood obesity significantly increases the risk of cardiovascular disease later in life (0%)
- C. There is a statistically significant negative linear relationship between BMI and blood pressure (5%) in children
- D. There is a statistically significant positive linear relationship between BMI and blood pressure (73%) in children
- E. There is no statistically significant linear relationship between BMI and blood pressure in (11%) children

Omitted

Correct answer

D



73%

Answered correctly



02 secs

Time Spent



2023

Version

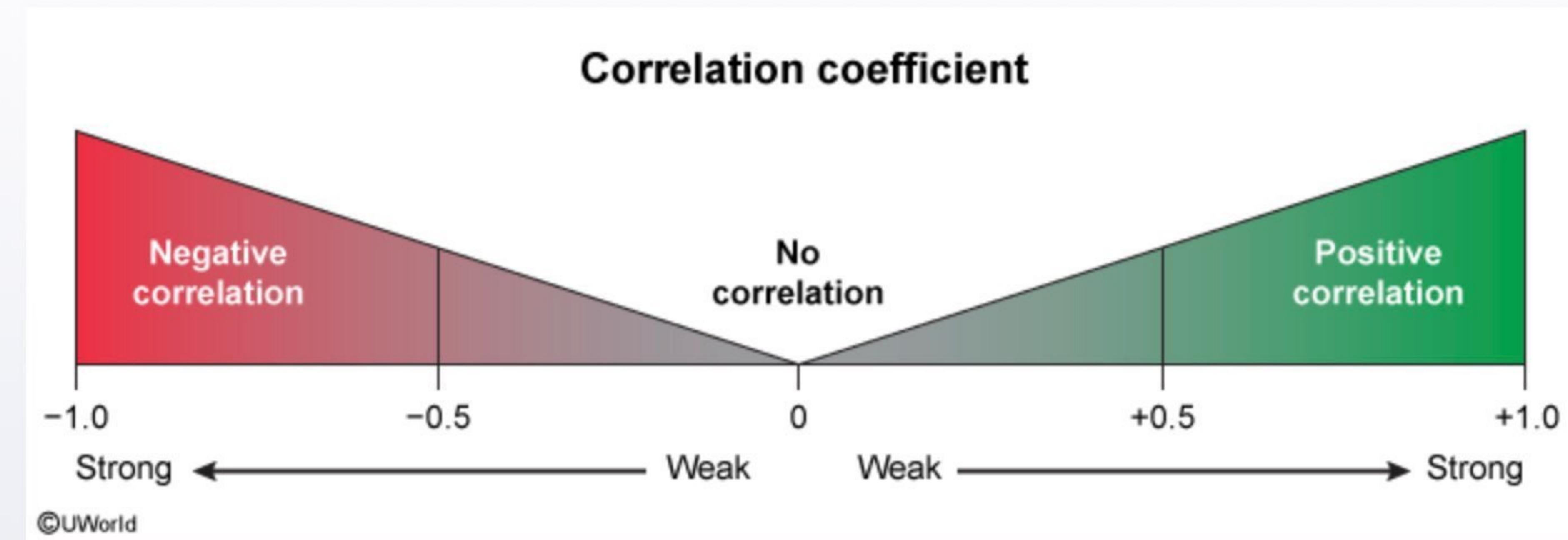
Explanation

### Correlation coefficient

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Item 28 of 40 Question Id: 19632

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The **correlation coefficient ( $r$ )** measures the direction and strength of a **linear relationship** (ie, association) between 2 variables (that are usually quantitative).

- **Direction:** When  $r < 0$ , the linear relationship is negative and one variable increases as the other decreases; when  $r > 0$ , the linear relationship is positive and both variables increase and decrease together.
- **Strength:** When  $r$  values are close to  $-1$  or  $1$ , the linear relationship is strong; when  $r$  values are close to  $0$ , the linear relationship is weak.

A **correlation analysis** evaluates whether a **linear relationship exists** between 2 variables. A  $p$ -value less than a given significance level indicates that there is a statistically significant linear relationship between the variables. However, a statistically significant linear relationship result does not imply that the relationship is causal (**correlation ≠ causation**) because when 2 variables are correlated, it does not necessarily mean that one is directly causing the other to change (**Choices A and B**).

In this study, researchers studied the correlation between BMI and blood pressure in a random sample of

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- **Direction:** When  $r < 0$ , the linear relationship is negative and one variable increases as the other decreases; when  $r > 0$ , the linear relationship is positive and both variables increase and decrease together.
- **Strength:** When  $r$  values are close to  $-1$  or  $1$ , the linear relationship is strong; when  $r$  values are close to  $0$ , the linear relationship is weak.

A **correlation analysis** evaluates whether a **linear relationship exists** between 2 variables. A  $p$ -value less than a given significance level indicates that there is a statistically significant linear relationship between the variables. However, a statistically significant linear relationship result does not imply that the relationship is causal (**correlation ≠ causation**) because when 2 variables are correlated, it does not necessarily mean that one is directly causing the other to change (**Choices A and B**).

In this study, researchers studied the correlation between BMI and blood pressure in a random sample of children. Study results showed that the correlation coefficients for BMI and systolic/diastolic blood pressure are both positive ( $r = 0.46$  and  $r = 0.37$ , respectively, are both  $>0$ ); therefore, there is a **positive linear relationship** between BMI and blood pressure (**Choice C**). Because the  $p$ -value for both coefficients ( $p < 0.001$ ) is less than 0.01 (the given significance level of 1%), the linear relationship is **statistically significant** (**Choice E**).

### Educational objective:

The correlation coefficient ( $r$ ) indicates whether there is a negative ( $r < 0$ ) or positive ( $r > 0$ ) linear relationship between 2 variables. The closer  $r$  is to  $-1$  or  $+1$ , the stronger the linear relationship. A statistically significant (ie,  $p$ -value < significance level) linear relationship between 2 variables does not imply that the relationship is causal.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Correlation coefficient  
Topic

apps.uworld.com

Item 29 of 40 Question Id: 14857

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Researchers want to explore the association between selective serotonin reuptake inhibitor (SSRI) use and pulmonary tuberculosis. A random sample of subjects age 20-84 with newly diagnosed pulmonary tuberculosis and an independent random sample of subjects without pulmonary tuberculosis are enrolled in the study. Subsequently, subjects who never had a prescription for an SSRI are defined as "never users," and those who have had a prescription for an SSRI are defined as "users." The study compares the frequency of SSRI use in subjects with and without a diagnosis of pulmonary tuberculosis and determines that SSRI use is not associated with pulmonary tuberculosis. Which of the following best describes the design of this study?

- A. Case-control study (62%)
- B. Cross-sectional study (13%)
- C. Prospective cohort study (2%)
- D. Randomized controlled trial (2%)
- E. Retrospective cohort study (18%)

Omitted  
Correct answer  
A

62%  
Answered correctly

02 secs  
Time Spent

2023  
Version

### Explanation

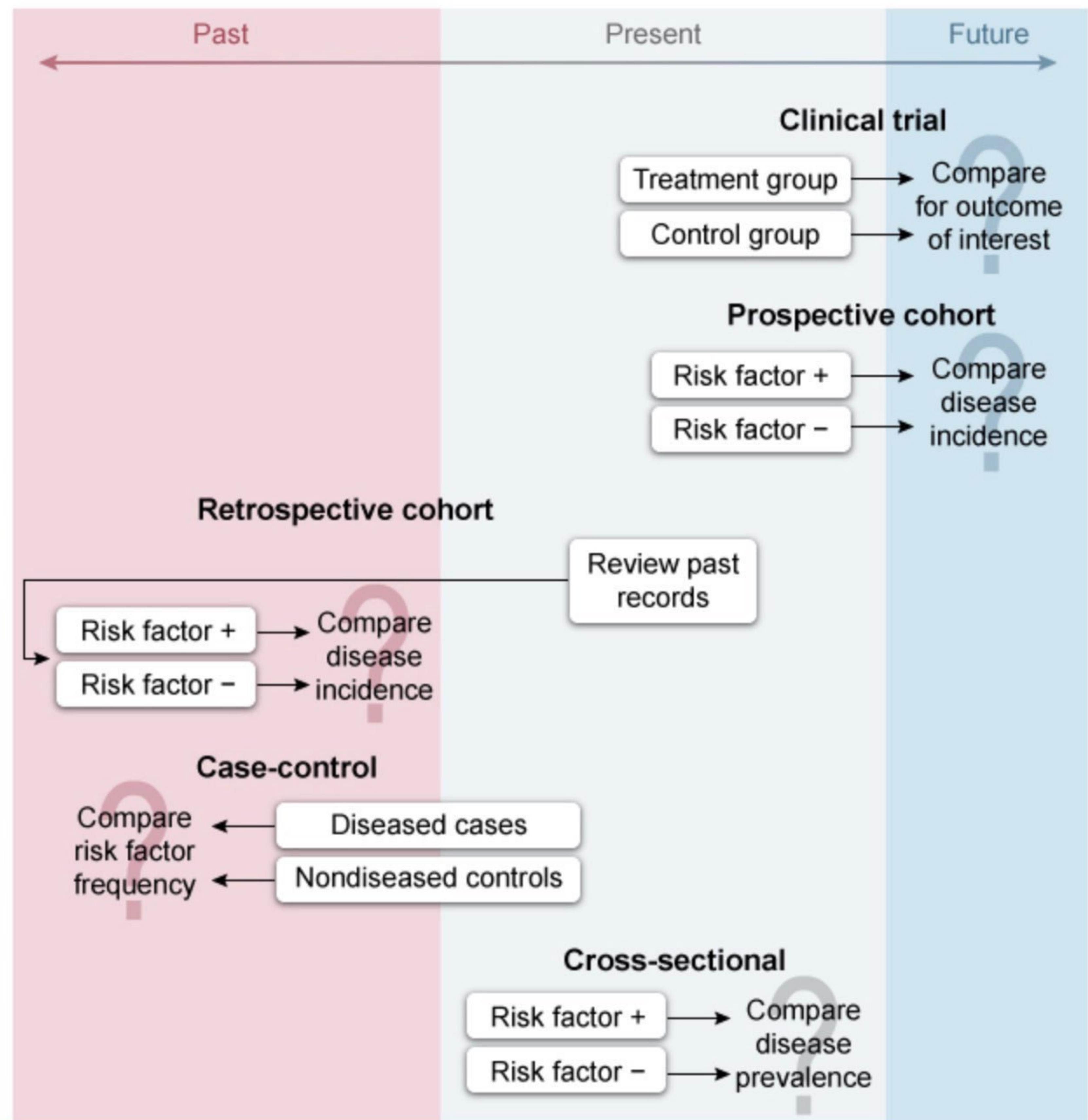
#### Temporality of different study designs

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Item 29 of 40 Question Id: 14857

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## Temporality of different study designs



The screenshot shows a mobile application interface for a medical question. At the top, there's a header with the URL "apps.uworld.com". Below the header is a toolbar with various icons: a left arrow, a right arrow, a double arrow, a magnifying glass, a 'Mark' icon, 'Previous' and 'Next' buttons, 'Full Screen', 'Tutorial', 'Lab Values', 'Notes', 'Calculator', 'Reverse Color', 'Text Zoom', and 'Settings'. The main content area contains text about research studies and their classification into observational and experimental designs. There are also sections for case-control studies and cohort studies.

**Research studies** are broadly classified as having an observational or experimental design depending on the control the researcher has over the independent variables (eg, exposure to risk factors, treatments).

- In **observational studies** (eg, case series, case-control studies, cohort studies, cross-sectional studies), the researcher has **no control** over the independent variables (eg, exposures, risk factors).
- In **experimental studies** (eg, randomized controlled trials), the researcher **controls** and randomly assigns the independent variables (eg, treatments, interventions).

A **case-control** study is an observational design in which potential participants are initially identified as **cases** or **controls** according to the **dependent variable or outcome** (eg, disease of interest). In the study described above, subjects age 20-84 newly diagnosed with pulmonary tuberculosis are cases, and subjects without pulmonary tuberculosis are controls. Once cases and controls are identified, the presence of past exposure to  $\geq 1$  **risk factors** of interest is determined in each group. In this study, the risk factor is selective serotonin reuptake inhibitor (SSRI) use ("never users" are subjects who never had a prescription for an SSRI, and "users" are subjects who have had a prescription for an SSRI). Finally, the **frequency** of exposure to the risk factor is compared between cases and controls to estimate the **association** between the risk factor and the outcomes. Conducted as designed, this study can determine if SSRI use is associated with pulmonary tuberculosis.

**(Choice B)** In contrast to participants in a case-control study, who are selected based on outcome status (eg, presence or absence of tuberculosis), participants in a cross-sectional study are randomly selected from a population of interest (eg, random sample from a region with high tuberculosis prevalence) and then simultaneously categorized according to risk factor (eg, SSRI use) and outcome (eg, tuberculosis) status. The goal is to determine prevalence by providing a snapshot of the population.

**(Choices C and E)** In a cohort study, 2 groups of individuals (ie, cohorts) are initially identified based on their

**(Choice B)** In contrast to participants in a case-control study, who are selected based on outcome status (eg, presence or absence of tuberculosis), participants in a cross-sectional study are randomly selected from a population of interest (eg, random sample from a region with high tuberculosis prevalence) and then simultaneously categorized according to risk factor (eg, SSRI use) and outcome (eg, tuberculosis) status. The goal is to determine prevalence by providing a snapshot of the population.

**(Choices C and E)** In a cohort study, 2 groups of individuals (ie, cohorts) are initially identified based on their exposure status to a specific risk factor (eg, SSRI use) rather than based on their outcome status (eg, pulmonary tuberculosis), as seen in this example. These 2 cohorts are then followed over time (ie, prospectively) to assess development of the outcome. Sometimes the exposure status is determined retrospectively, typically using medical records, and patients are tracked from the point of exposure onward.

**(Choice D)** A randomized controlled trial follows individuals who have been randomized to either a treatment arm or a control arm and compares the effect of the intervention.

### Educational objective:

A case-control study is an observational study design; it begins with individuals who have the outcome (cases) and compares them with individuals who do not have the outcome (controls) according to history of exposure to  $\geq 1$  risk factors.

### References

- Epidemiology in practice: case-control studies.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Study designs  
Topic

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Item 30 of 40 Question Id: 1280

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A prospective study evaluates the relationship between regular antioxidant supplement use (vitamins C and E) and the risk of stroke in healthy and physically active men age 40-60. The study compares the risk of stroke among men who consumed antioxidant supplements for  $\geq 5$  years and among men who consumed antioxidant supplements for  $< 5$  years, as compared to a reference group of men who never consumed antioxidant supplements. According to the study results, men who consumed antioxidant supplements for  $< 5$  years and men who consumed antioxidant supplements for  $\geq 5$  years have stroke relative risks of 0.95 ( $p = 0.45$ ) and 0.75 ( $p < 0.01$ ), respectively, when compared to the reference group. The results of the study were adjusted to account for baseline differences related to healthy behaviors and overall health. Which of the following factors most likely explains why the relative risk of stroke is lower with longer antioxidant use?

- A. Accumulation effect (44%)
- B. Lead-time bias (27%)
- C. Observer bias (5%)
- D. Rare disease assumption (2%)
- E. Selection bias (20%)

Omitted  
Correct answer  
A

44%  
Answered correctly

02 secs  
Time Spent

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Explanation

Item 30 of 40 Question Id: 1280

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**Antioxidant use for ≥5 years** was associated with a **statistically significant** ( $p < 0.01$ ) decreased risk of stroke (relative risk [RR] = 0.75 <1). By contrast, antioxidant use for <5 years demonstrated a **nonstatistically significant** ( $p > 0.05$ ) smaller reduction in risk (RR = 0.95); in other words, antioxidant use for <5 years seems to have no benefit on stroke risk reduction. This discrepancy can be explained if reduction in stroke risk is associated with the **duration of exposure** to antioxidant supplementation; in other words, a minimum cumulative exposure to antioxidants may be necessary for the exposure to have a significant effect on stroke risk.

This concept of **accumulation effect** can apply to both risk factors and risk reducers. The effect of exposure to risk factors may depend on the duration and intensity of the exposure; long-term exposure may be necessary well before an effect on the disease process is clinically evident (eg, lung cancer developing after decades of smoking exposure). Similarly, exposure to certain **risk reducers** must occur continuously over extended periods before disease outcome is affected. In this case, ≥5 years of continuous antioxidant use (risk reducer) were required to reveal their protective effect on stroke.

**(Choice B)** Lead time is the time between the initial detection of a disease and a specific outcome or measured endpoint. **Lead-time bias** can occur when a test detects or diagnoses the disease at an earlier stage than another test without impacting the natural history of the disease. A study comparing disease survival times may then erroneously conclude that using the earlier-detection test prolongs survival, when in actuality the increased survival time is due solely to earlier detection of the disease.

**(Choice C)** Observer bias occurs when an observer misclassifies data due to individual differences in interpretation or preconceived expectations regarding a study. It can be reduced by performing a double-blind study (ie, both observers and participants unaware of randomized parameters) and by having multiple observers encode and verify the recorded data.

**(Choice D)** Diseases with a very low incidence rate in the population will also have a very low prevalence.

another test without impacting the natural history of the disease. A study comparing disease survival times may then erroneously conclude that using the earlier-detection test prolongs survival, when in actuality the increased survival time is due solely to earlier detection of the disease.

**(Choice C)** Observer bias occurs when an observer misclassifies data due to individual differences in interpretation or preconceived expectations regarding a study. It can be reduced by performing a double-blind study (ie, both observers and participants unaware of randomized parameters) and by having multiple observers encode and verify the recorded data.

**(Choice D)** Diseases with a very low incidence rate in the population will also have a very low prevalence. According to the rare disease assumption, the odds ratio approximates RR when disease prevalence is low (eg, <10%).

**(Choice E)** Selection bias can occur with inappropriate (ie, nonrandom) selection methods or through selective attrition of the study participants. Although selection bias is a possible limitation of the study (eg, individuals who take vitamins daily may be more likely to be already healthy), the fact that the study was limited to healthy, physically active men and that it adjusted for baseline differences should considerably reduce the effect of this potential bias.

#### Educational objective:

The concept of accumulation effect can be applied to disease pathogenesis and exposure to risk modifiers. Cumulative exposure to a risk factor or risk reducer must sometimes occur for prolonged periods before a clinically significant effect is detected.

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Risk  
Topic

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Item 31 of 40 Question Id: 14861 

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A study aims to investigate the effectiveness of the topical application of tetracycline ointment in the prevention of surgical-site infection associated with resection of advanced oral cavity cancer. Fifty patients who underwent locoregional resection were assigned by chance to receive standard care alone or tetracycline-ointment in addition to standard care. The patients were then followed for 1 month and the number and severity of surgical-site infections were recorded for each group. Which of the following best describes the study design?

- A. Case-control study (7%)
- B. Crossover design (0%)
- C. Prospective cohort study (23%)
- D. Randomized control trial (68%)
- E. Retrospective cohort study (0%)

Omitted

Correct answer

D



68%

Answered correctly



02 secs

Time Spent



2023

Version

### Explanation

**Research studies** are classified as observational studies (eg, cross-sectional, case control, cohort) or experimental studies (eg, randomized control trials, factorial, crossover), depending on how much control a researcher has over the independent variables (eg, risk factors/exposures, interventions) in a study. The main differences between these 2 types of study designs are as follows:

Item 31 of 40  
Question Id: 14861

Mark

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Full Screen Tutorial Lab Values Notes Calculator Reverse Color Text Zoom Settings

**Research studies** are classified as observational studies (eg, cross-sectional, case control, cohort) or experimental studies (eg, randomized control trials, factorial, crossover), depending on how much control a researcher has over the independent variables (eg, risk factors/exposures, interventions) in a study. The main differences between these 2 types of study designs are as follows:

- In **observational designs**, the researcher **observes the effect** of naturally occurring risk factors/exposures on outcomes of interest.
- In **experimental designs**, the researcher **randomly assigns interventions** to potential participants to assess the effect of the controlled interventions.

A **randomized control trial** is one of the simplest subtypes of experimental designs; it is an experiment in which **participants are randomly allocated to ≥2 groups** to assess the effect of **specific interventions** (eg, treatments). In this example, 50 patients who underwent surgical resection of advanced oral cavity cancer were assigned by chance into either a tetracycline-ointment treatment group or a standard-of-care control group. The effectiveness of the topical application of tetracycline ointment for prevention of surgical-site infection was then assessed by recording the incidence and severity of infections in each group.

**(Choice A)** A case-control study is a type of observational study in which potential participants are initially identified as cases or controls according to outcome status (ie, developing the disease or condition of interest); the 2 groups are then assessed on their past exposure to specific risk factors.

**(Choice B)** A **crossover study** is an experiment in which subjects are exposed to different treatments or exposures sequentially. In the above scenario, patients are exposed to a single treatment only.

**(Choices C and E)** In prospective cohort studies, exposure status is determined in the present and patients are tracked over time for development of the outcome of interest; in retrospective cohort studies, exposure status is

Item 31 of 40 Question Id: 14861

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participants are randomly allocated to  $\geq 2$  groups to assess the effect of specific interventions (eg, treatments). In this example, 50 patients who underwent surgical resection of advanced oral cavity cancer were assigned by chance into either a tetracycline-ointment treatment group or a standard-of-care control group. The effectiveness of the topical application of tetracycline ointment for prevention of surgical-site infection was then assessed by recording the incidence and severity of infections in each group.

**(Choice A)** A case-control study is a type of observational study in which potential participants are initially identified as cases or controls according to outcome status (ie, developing the disease or condition of interest); the 2 groups are then assessed on their past exposure to specific risk factors.

**(Choice B)** A [crossover study](#) is an experiment in which subjects are exposed to different treatments or exposures sequentially. In the above scenario, patients are exposed to a single treatment only.

**(Choices C and E)** In prospective cohort studies, exposure status is determined in the present and patients are tracked over time for development of the outcome of interest; in retrospective cohort studies, exposure status is determined at a particular point in the past, and participants are tracked retrospectively, typically through their medical records. However, participants in cohort studies already have a definite exposure status; they are not randomly assigned to exposure groups as in the above example.

#### Educational objective:

A randomized control trial is an experiment in which participants are randomly allocated to  $\geq 2$  groups to assess the effect of specific interventions (eg, treatments).

Biostatistics  
Subject

Biostatistics & Epidemiology  
System

Study designs  
Topic

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Item 32 of 40 Question Id: 19105

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In a reference sample of hundreds of healthy subjects, the laboratory reference range for a novel marker of cardiac injury is 0.04-0.08 U/mL at the standard 95% level of probability. The marker has very high sensitivity and specificity for myocardial tissue. The clinical cardiology team would like to use a 99.7% reference range to assess patients who come to the emergency department with chest pain and have a high pretest probability of cardiac ischemia. An elevated value of the marker is defined as exceeding the 99.7th percentile of the reference sample. Assuming a normal (Gaussian) distribution with a mean of 0.06 U/mL, which of the following most closely approximates the corresponding reference range?

- A. 0.03 to 0.09 (73%)
- B. 0.035 to 0.085 (12%)
- C. 0.045 to 0.075 (5%)
- D. 0.05 to 0.07 (4%)
- E. 0.055 to 0.065 (3%)

Omitted  
Correct answer  
A

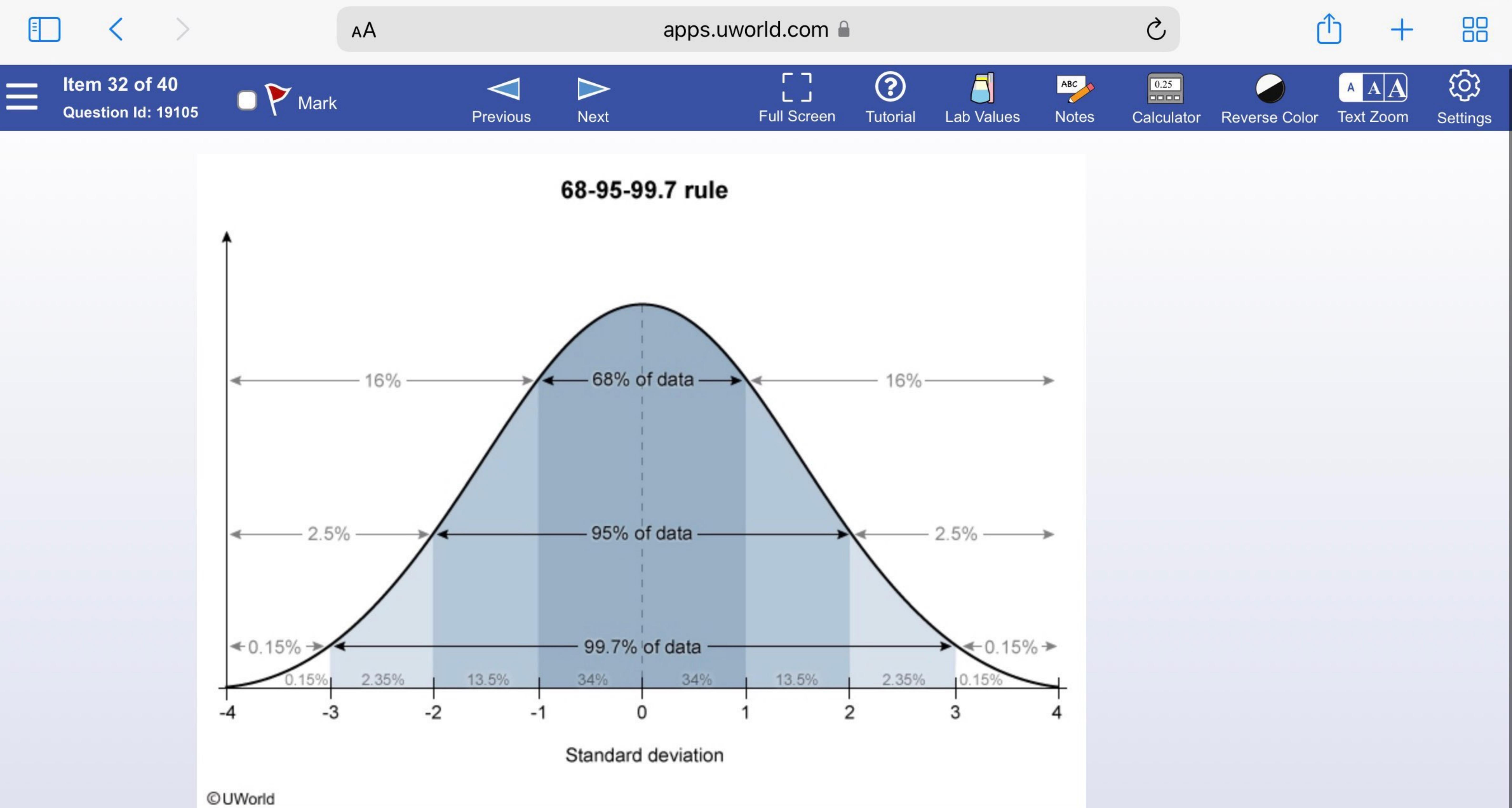
73%  
Answered correctly

01 sec  
Time Spent

2023  
Version

### Explanation

68-95-99.7 rule



A **normal (Gaussian) distribution** refers to a symmetrical, bell-shaped distribution with a fixed proportion of observations lying within a certain distance of the mean. This distance is called the **standard deviation (SD)** and reflects the **degree of dispersion** from the mean. According to the properties of this distribution, 68% of observations lie within 1 SD from the mean, with half (ie,  $68/2 = 34\%$ ) above and half (34%) below the mean. The remaining 32% ( $= 100\% - 68\%$ ) lie outside 1 SD from the mean, with half (ie,  $32/2 = 16\%$ ) above and the

The screenshot shows a mobile application interface for a medical reference guide. At the top, there's a header bar with a back arrow, a forward arrow, and a double arrow icon. The URL 'apps.uworld.com' is displayed in the center. On the right side of the header are icons for sharing, adding to a favorites list, and a grid view. Below the header is a blue navigation bar with various icons: a menu icon, 'Item 32 of 40', 'Question Id: 19105', a 'Mark' icon, 'Previous' and 'Next' arrows, 'Full Screen', 'Tutorial', 'Lab Values', 'Notes', 'Calculator', 'Reverse Color', 'Text Zoom', and 'Settings'. The main content area contains text about the standard deviation rule and its applications in laboratory measurements.

observations lying within a certain distance of the mean. This distance is called the **standard deviation (SD)** and reflects the **degree of dispersion** from the mean. According to the properties of this distribution, 68% of observations lie within 1 SD from the mean, with half (ie,  $68/2 = 34\%$ ) above and half (34%) below the mean. The remaining 32% ( $= 100\% - 68\%$ ) lie outside 1 SD from the mean, with half (ie,  $32/2 = 16\%$ ) above and the other half (16%) below 1 SD from the mean. In addition, 95% of all observations lie within 2 SD of the mean, and 99.7% of all observations lie within 3 SD from the mean. This is the **68-95-99.7 rule**.

The 95% range for this marker with a **mean of 0.06 U/mL** is 0.04 to 0.08 U/mL; given a normal distribution, this represents the range given by mean  $\pm$  2 SD. Therefore, **1 SD = 0.01** (because  $0.04 = \text{mean} - 2 \text{ SD} = 0.06 - 2 \text{ SD} = 0.06 - 2 \times 0.01$  and, similarly,  $0.08 = 0.06 + 2 \times 0.01$ ). The **99.7% range** is given by **mean  $\pm$  3 SD**; therefore, the 99.7% range is **0.03** ( $= \text{mean} - 3 \text{ SD} = 0.06 - 3 \times 0.01$ ) to **0.09** ( $= \text{mean} + 3 \text{ SD} = 0.06 + 3 \times 0.01$ ). Any result that falls outside this range (eg, a value exceeding this range) indicates that the value is different from what is seen in 99.7% of the reference population.

In laboratory measurements, although 95% is often used as a reference range, a 99% range is used in certain cases (eg, to determine cutoff for troponin in acute myocardial infarction). Other laboratory analysis methods involve performing more specific calculations when it is important to detect a difference in one direction (eg, for a cancer marker, knowing that the value is significantly higher than normal is more important than knowing that it is significantly different—either higher or lower—than normal). In some cases, high-sensitivity assays (eg, high-sensitivity C-reactive protein testing) allow the detection of values in the lower range of normal, which would not have been possible with standard assays.

#### **Educational objective:**

In a normal (bell-shaped) distribution, 68% of all values are within 1 standard deviation (SD) from the mean; 95% are within 2 SD from the mean; and 99.7% are within 3 SD from the mean.