

X

Public health officials involved in developing nutritional guidelines commission a study to determine how dietary eating patterns influence total body iron stores in children age 5-17. As part of the study, researchers want to assess how 2 independent variables, red meat consumption and egg consumption (both reported in units of ounces/week), affect serum ferritin concentrations while adjusting for age and gender. Which of the following statistical techniques is most helpful for determining the association between the study variables?

- A. Analysis of variance
- B. Meta-analysis
- C. Odds ratio
- D. Regression analysis
- E. Relative risk

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A geneticist is interested in the potential causes of a congenital abnormality. She hypothesizes that acetaminophen use during the first trimester of pregnancy might be associated with the abnormality. In her study, a sample of mothers of children with and without the abnormality are randomly selected from government birth records. Personal interviews are then conducted with the mothers to determine fetal exposure to acetaminophen. Results show that mothers of children who do not have the abnormality did not take acetaminophen as frequently during the first trimester. This type of study is most susceptible to which of the following types of bias?

- A. Allocation bias
- B. Detection bias
- C. Recall bias
- D. Referral bias
- E. Selection bias

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Item 10 of 40
Question Id: 1203

Mark

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

400 women aged 20-35 coming for routine check-up are asked about their smoking status. 40% of the women are smokers. Over the next ten years, 25 smokers and 24 non-smokers developed breast cancer. Which of the following best describes the study design?

- A. Prospective cohort study
- B. Retrospective cohort study
- C. Case-control study
- D. Cross-sectional study
- E. Randomized clinical trial

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Item 5 of 40
Question Id: 1189

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

Researchers are interested in the association between colorectal carcinoma and nonsteroidal anti-inflammatory drug use. They first interview a group of patients with biopsy-proven colorectal carcinoma and then interview a group consisting of the patients' neighbors who are of similar age and race. The analysis is based on comparing the results of pairs of individuals (one from each of the 2 groups) who have similar characteristics. This design technique best helps address which of the following potential problems with this study?

- A. Ascertainment bias
- B. Confounding
- C. Observer bias
- D. Recall bias
- E. Selection bias

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Item 3 of 40 Question Id: 1185 Mark Previous Next Full Screen Tutorial Lab Values Notes Calculator Reverse Color Text Zoom Settings

A 45-year-old man comes to the office for a routine visit. The patient has a first-degree relative with Alzheimer dementia and is concerned about his chances of developing the disease. He has read in the newspaper that decreased consumption of yellow and orange fruits and vegetables has been associated with Alzheimer disease and would like to know how likely he is to develop the disease. A medical literature review uncovers a recent cohort study that evaluated the association between blood carotene concentration and Alzheimer disease. The development of the disease was evaluated in a 20-year follow-up study of 200 middle-aged subjects who have a first-degree relative with Alzheimer disease. The results are as follows:

	Low carotene level	Normal carotene level	Total
Developed Alzheimer disease	18	42	60
Did not develop Alzheimer disease	27	113	140
Total	45	155	200

Assuming the patient has low carotene levels, what is his 20-year risk of developing Alzheimer disease?

- A. 0.19

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Item 3 of 40 Question Id: 1185 Mark Previous Next Full Screen Tutorial Lab Values Notes Calculator Reverse Color Text Zoom Settings

	Low carotene level	Normal carotene level	Total
Developed Alzheimer disease	18	42	60
Did not develop Alzheimer disease	27	113	140
Total	45	155	200

Assuming the patient has low carotene levels, what is his 20-year risk of developing Alzheimer disease?

- A. 0.19
- B. 0.23
- C. 0.27
- D. 0.30
- E. 0.40

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AA

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Question Id: 1184

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Calculator

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Settings

A case-control study was conducted to estimate the association between simvastatin therapy and serum levels of fibrinogen in patients who underwent percutaneous coronary intervention. Cases were identified as patients who underwent percutaneous coronary intervention and had high periprocedural levels of fibrinogen (>400 mg/dL), and controls were identified as patients who underwent percutaneous coronary interventions but had normal levels of fibrinogen (200-400 mg/dL). History of simvastatin therapy use was assessed through chart review for every patient. The number of patients corresponding to each classification criteria is given in the table below.

	Fibrinogen high (>400 mg/dL)	Fibrinogen normal (200-400 mg/dL)	Total
Simvastatin therapy	43	67	110
No simvastatin therapy	32	58	90
Total	75	125	200

Which of the following is the best statistical method to estimate the association between simvastatin use and high serum fibrinogen levels in this study?

- A. Analysis of variance
- B. Chi-square test
- C. Correlation analysis
- D. Meta-analysis
- E. Two-sample *t*-test

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Item 21 of 40
Question Id: 1202

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

Officials of a public health department report a higher than normal prevalence of acute myelogenous leukemia (AML) among children age 5-12 in their community. They observe that some households in the community are exposed to chemical waste from a nearby factory and worry that exposure to this waste is responsible for the increased prevalence of AML. A case-control study is designed to evaluate the health department officials' claim that exposure to chemical waste is associated with AML in childhood. Which of the following populations should be selected as the control group?

- A. Children who do not have AML and are exposed to chemical waste
- B. Children who do not have AML and are not exposed to chemical waste
- C. Children who do not have AML, regardless of exposure status to chemical waste
- D. Children who have AML and are exposed to chemical waste
- E. Children who have AML and are not exposed to chemical waste
- F. Children who have AML, regardless of exposure status to chemical waste

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Item 23 of 40
Question Id: 1188

Mark

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

A large prospective study evaluates the relationship between alcohol consumption and breast cancer. A total of 4000 middle-aged women are enrolled in the study through a random selection of residential addresses. Daily alcohol consumption and breast cancer incidence are assessed through the use of periodic questionnaires. On five-year follow-up, the investigators report the association between alcohol consumption and breast cancer as a relative risk of 1.32 (95% confidence interval = 0.90-1.85); 800 subjects were lost to follow-up by the end of the study, the majority of whom were moderate to heavy alcohol consumers. According to this information, which of the following biases is most likely to be present and may have affected the results?

- A. Lead-time bias
- B. Observer bias
- C. Random misclassification bias
- D. Recall bias
- E. Selection bias

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A large cohort study is conducted to assess the association between smoking and squamous cell carcinoma of the esophagus among middle-aged Chinese men. During 10 years of follow-up, smokers have 5 times the risk of esophageal carcinoma compared to non-smokers (relative risk = 5.0, 95% confidence interval = 2.9-7.1). According to the study results, what percentage of squamous cell carcinoma of the esophagus in smokers can be attributed to smoking?

- A. 25%
- B. 50%
- C. 70%
- D. 80%
- E. 90%

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Item 29 of 40 Question Id: 1231 Mark Previous Next Full Screen Tutorial Lab Values Notes Calculator Reverse Color Text Zoom Settings

Zeracizumab is an experimental angiogenesis inhibitor targeting vascular endothelial growth factor that is being tested for the treatment of advanced, chemotherapy-naive, non-squamous non-small cell lung cancer (NSCLC). Part of the drug company's evaluation process is to analyze the 1-year survival after treatment to determine the clinical efficacy of the experimental treatment. The results are given in the table below.

Zeracizumab-containing regimen	Standard chemotherapy
Alive at 1 year	40
Dead at 1 year	60

Which of the following best represents the number needed to harm for the zeracizumab-containing regimen?

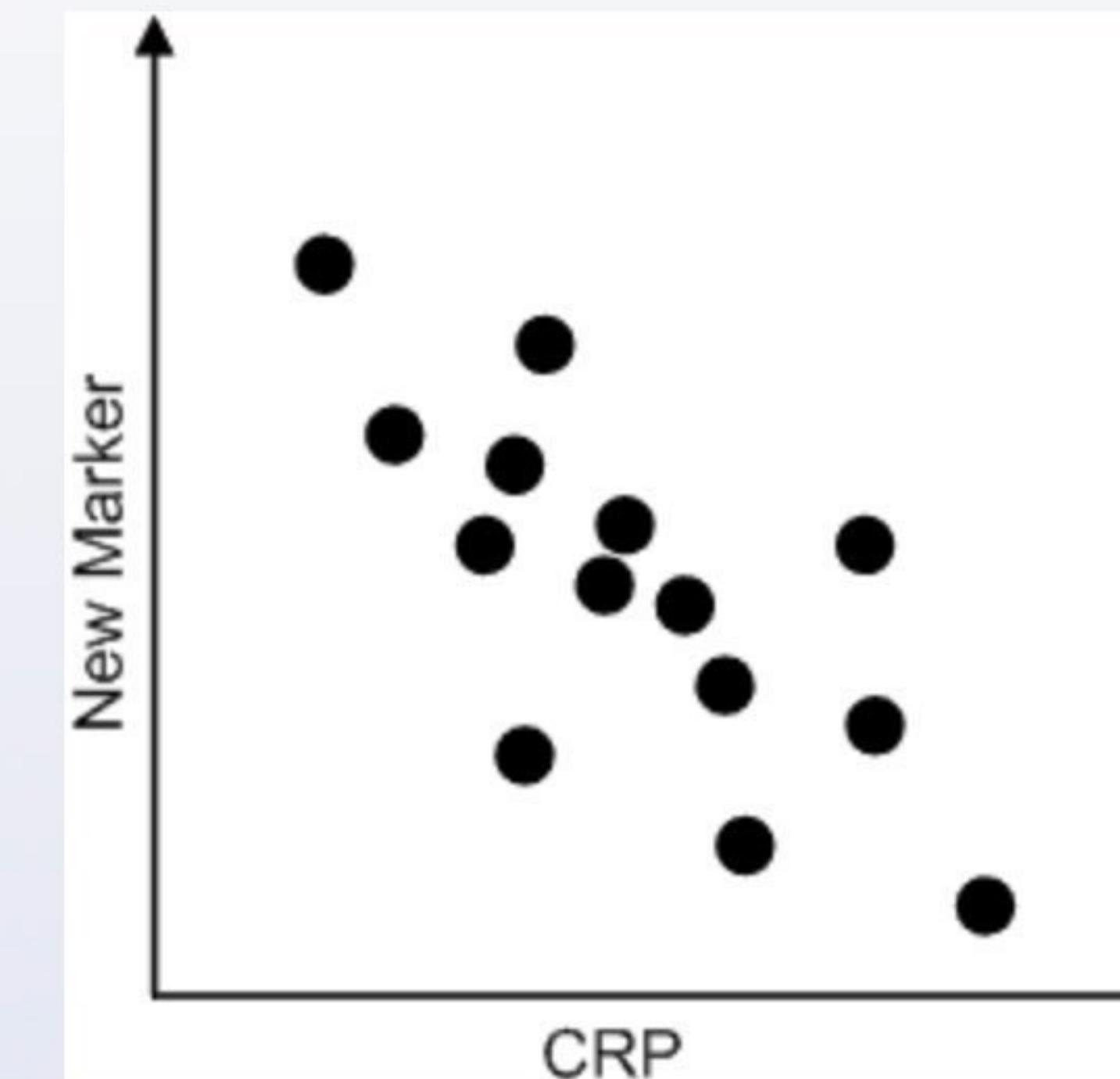
- A. 2
- B. 25
- C. 40
- D. 72
- E. 94

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Item 35 of 40 Question Id: 1210 Mark Previous Next Full Screen Tutorial Lab Values Notes Calculator Reverse Color Text Zoom Settings

Inflammatory biological markers are clinically useful in a number of different ways, one being the assessment of disease activity in conditions such as systemic lupus erythematosus (SLE). A new inflammatory marker is being investigated in patients with active SLE flares. When the blood level of the new marker (in mg/L) is plotted against the C-reactive protein (CRP) level (also in mg/L), the following plot is obtained:



Based on the plot, the correlation coefficient between the 2 variables is closest to which of the following values?

- A. +0.8
- B. +0.2
- C. 0
- D. -0.2
- E. -0.8



AA

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Item 36 of 40

Question Id: 1205

Previous NextFull Screen?Notes0.25A A A

A study is conducted to assess the effect of beta-blocker therapy in patients with acute myocardial infarction (MI). The study found that 20 patients out of 90 who took a beta-blocker during the week prior to developing an MI had a major arrhythmia event during hospitalization. The study also determined that 30 patients out of 70 who did not take any beta-blocker developed a major arrhythmia. What was the odds ratio of developing major arrhythmia in patients who took beta-blockers compared to those who did not take beta-blockers?

- A. $(20 \times 30) / (70 \times 40)$
- B. $(20 \times 40) / (70 \times 30)$
- C. $(20 \times 70) / (30 \times 40)$
- D. $(20 / 50) / (70 / 110)$
- E. $(20 / 90) / (30 / 70)$

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AA

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Item 37 of 40

Question Id: 1207

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Notes0.25
CalculatorReverse ColorA A A
Text ZoomSettings

A study evaluated the role of angiotensin-converting enzyme (ACE) inhibitors in the prevention of coronary events in patients with diabetes. During 5 years of follow-up, 120 out of 400 diabetic patients who had taken an ACE inhibitor developed an acute coronary event. Over the same time, 100 out of 300 diabetic patients who had not taken an ACE inhibitor experienced coronary events. What was the relative risk of developing a coronary event in diabetic patients who were taking ACE inhibitors compared to diabetic patients who were not taking ACE inhibitors?

- A. $(120 \times 100) / (280 \times 200)$
- B. $(120 \times 200) / (100 \times 280)$
- C. $(120 \times 280) / (100 \times 200)$
- D. $(120/220) / (280/480)$
- E. $(120/400) / (100/300)$

Proceed To Next Item



AA

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Item 38 of 40

Question Id: 1204

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A study determines that the mean blood cholesterol level is 195 mg/dL in 200 non-diabetic hospitalized patients and 210 mg/dL in 180 diabetic hospitalized patients. The probability that the observed difference is due to chance alone is reported to be 5%. There is also a 20% probability of concluding that there is no difference in blood cholesterol level when there is one in reality. What is the power of the study?

- A. 0.05
- B. 0.20
- C. 0.50
- D. 0.80
- E. 0.95

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Item 39 of 40

Question Id: 1272

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

A 62-year-old man with diabetes, hypertension, and hyperlipidemia comes to the emergency department of an academic medical center with chest pain, nausea, vomiting, and diaphoresis. An electrocardiogram demonstrates ST elevation in the anterior leads, and cardiac enzymes are markedly elevated. Investigators at the center are designing a randomized control trial to test the hypothesis that drug B will decrease the mortality associated with acute ST-elevation myocardial infarction compared to standard of care. To ensure that investigators will not miss a difference between drug B and standard of care (if a difference truly exists), which of the following would they want to maximize?

- A. α
- B. β
- C. Type I error
- D. Type II error
- E. $1 - \beta$

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Item 1 of 40 Question Id: 10570

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A large, multi-country study is conducted to determine the effect of economic development on cancer incidence and mortality. The study uses data obtained from the national cancer registries, along with information regarding per capita gross domestic product as reported by the International Monetary Fund and life expectancy as reported by the World Health Organization. Which of the following best describes the design of this study?

- A. Case-control study (4%)
- B. Cohort study (7%)
- C. Cross-sectional survey (28%)
- D. Ecological study (35%)
- E. Nested case-control study (1%)
- F. Qualitative study (4%)
- G. Randomized controlled trial (0%)
- H. Systematic review (18%)

Omitted

Correct answer

D



35%

Answered correctly



01 min, 35 secs
Time Spent



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Version

Explanation

This observational study is analyzing **population-level data** to evaluate the association between a potential

This observational study is analyzing **population-level data** to evaluate the association between a potential exposure (eg, low socioeconomic status population) and a given outcome (eg, increased cancer mortality). Using population-level (rather than individual-level) data as a unit of analysis in such a manner is consistent with an **ecological study**. Ecological studies are useful for generating hypotheses but should not be used to draw conclusions regarding individuals within these populations (**ecological fallacy**).

(Choices A and B) Case-control and cohort studies deal with *individuals* rather than populations. In case-control studies, the odds of exposure to a certain characteristic (eg, personal socioeconomic status) are compared between affected individuals (eg, patients with cancer) and unaffected individuals who serve as controls. In cohort studies, individuals with and without different exposures (eg, high or low personal socioeconomic status) are followed over time to determine the incidence of the disease of interest (eg, cancer).

(Choice C) Cross-sectional surveys evaluate the exposures and outcomes of interest in individuals (not populations) at a given point in time ("snapshot"). The overall design of this multi-country study relies on population-level data, not individual-level data.

(Choice E) Nested case-control studies start with cohort studies in which participants are followed over time; those participants who develop an outcome of interest become cases for a case-control study.

(Choice F) Qualitative studies use focus groups, interviews (structured and semi-structured), and other anthropologic techniques to obtain narrative information for explaining quantitative results.

(Choice G) Randomized controlled trials randomly assign subjects into a treatment group or a control group. The groups differ only in the intervention (treatment) of interest.

(Choice H) Systematic reviews and meta-analyses combine the results of several published studies (with an emphasis on high-quality, randomized controlled studies) to estimate the pooled effect.

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(Choice H) Systematic reviews and meta-analyses combine the results of several published studies (with an emphasis on high-quality, randomized controlled studies) to estimate the pooled effect.

Educational objective:

The unit of analysis in ecological studies is populations rather than individuals.

Biostatistics

Subject

Biostatistics & Epidemiology

System

Study designs

Topic



AA

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Item 2 of 40

Question Id: 19398

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A surveillance study is conducted to assess the long-term efficacy and safety of a drug currently being used to treat patients with heart failure. Researchers enroll 8,300 patients with heart failure. The patients receive the drug once daily for 6 months. The results show significant clinical improvement, but severe hypernatremia is observed in 23 patients. The study publication recommends a lower dose of the drug in patients with baseline normonatremia and hypokalemia to prevent hypernatremia. Which of the following best characterizes this type of study?

- A. Phase I clinical trial (4%)
- B. Phase II clinical trial (18%)
- C. Phase III clinical trial (29%)
- D. Phase IV clinical trial (47%)
- E. Preclinical study (0%)

Omitted

Correct answer

D



47%

Answered correctly



02 secs

Time Spent



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Version

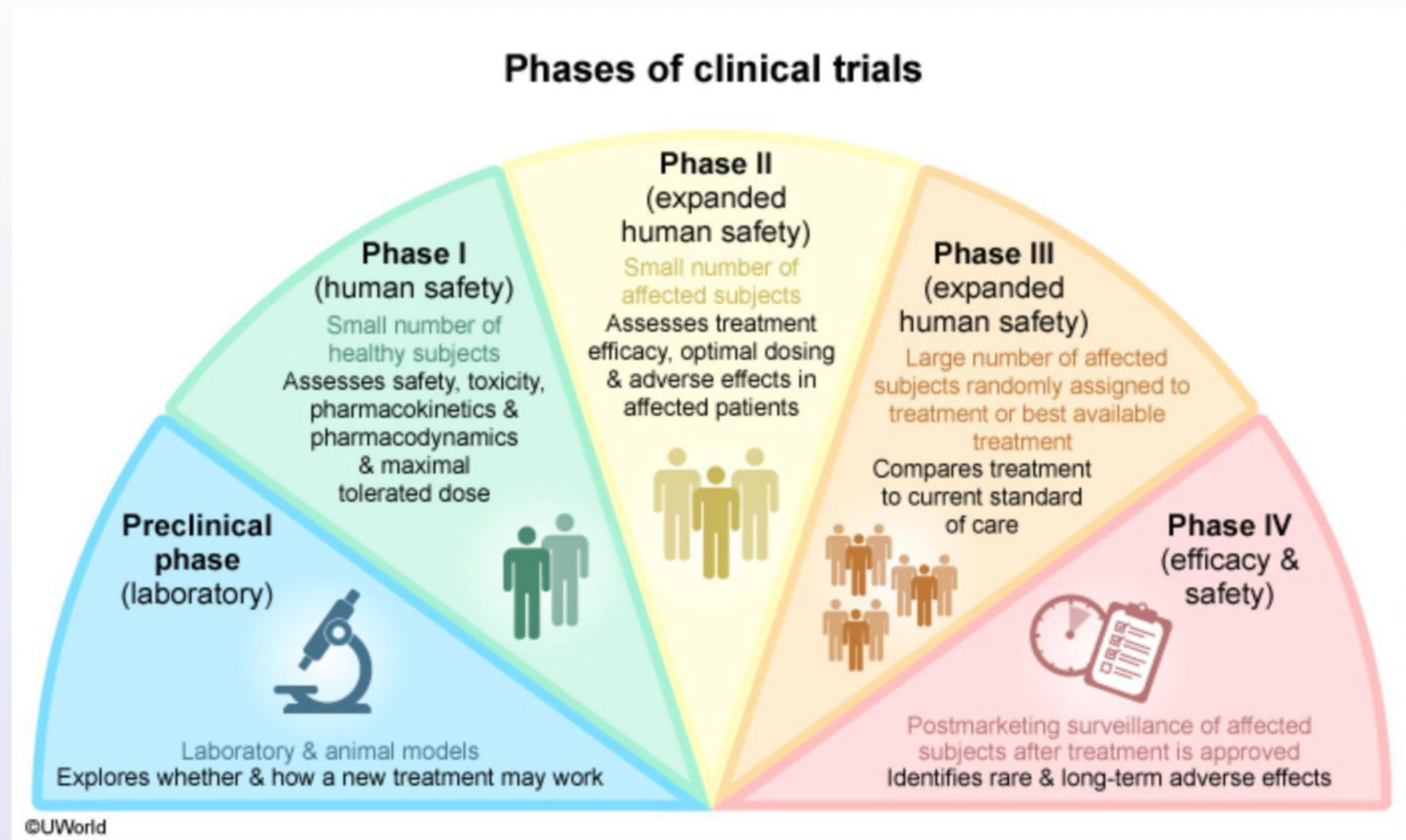
Explanation

Phases of clinical trials

Phase II
(expanded)

Item 2 of 40 Question Id: 19398

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Efficacy and safety of new drugs are established during the **clinical trials process**. New drugs are approved by a regulatory body (ie, Food and Drug Administration) following review of **phase I-III** trials. Phases differ in size, objective, and participant selection.

- **Phase I:** Assesses safety and pharmacokinetics. Phase I is usually conducted with a small number (eg, 20-80) of healthy participants. It often is performed in a strictly controlled environment with extensive biochemical and physiologic monitoring.
- **Phase II:** Assesses preliminary efficacy and optimal dosing. Phase II is conducted with a small number of

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objective, and participant selection.

- **Phase I:** Assesses safety and pharmacokinetics. Phase I is usually conducted with a small number (eg, 20-80) of healthy participants. It often is performed in a strictly controlled environment with extensive biochemical and physiologic monitoring.
- **Phase II:** Assesses preliminary efficacy and optimal dosing. Phase II is conducted with a small number of participants who have the condition of interest, and patient outcomes are often compared to historical controls. It sometimes is called a pilot study.
- **Phase III:** Compares treatment to standard of care. Phase III is conducted as a large, randomized, controlled trial (in contrast to this study, which is a surveillance study with no control group) to better assess treatment response and safety. It may include analysis of treatment effects in selected subsets of the target patient population.

The description of this study of a currently available drug is most consistent with a **phase IV (postmarketing) study**, which is conducted **after regulatory approval** of the drug. Phase IV assesses **long-term safety and effectiveness** and characterizes uncommon or **delayed adverse effects**. It typically involves surveillance of a large number of treated participants to detect small effects and variability in diverse patient populations. The results are often used to refine the use of the drug in clinical practice.

(Choice E) Preclinical studies are typically conducted without human subjects (ie, bench research) largely to determine the mechanism of action and/or make a preliminary estimation of safety and efficacy.

Educational objective:

Phase IV (postmarketing) trials are conducted with drugs that have already been approved for use in order to study long-term effectiveness and better characterize uncommon or delayed adverse effects. They are typically

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Question Id: 19398

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- **Phase III:** Compares treatment to standard of care. Phase III is conducted as a large, randomized, controlled trial (in contrast to this study, which is a surveillance study with no control group) to better assess treatment response and safety. It may include analysis of treatment effects in selected subsets of the target patient population.

The description of this study of a currently available drug is most consistent with a **phase IV (postmarketing) study**, which is conducted **after regulatory approval** of the drug. Phase IV assesses **long-term safety and effectiveness** and characterizes uncommon or **delayed adverse effects**. It typically involves surveillance of a large number of treated participants to detect small effects and variability in diverse patient populations. The results are often used to refine the use of the drug in clinical practice.

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Educational objective:

Phase IV (postmarketing) trials are conducted with drugs that have already been approved for use in order to study long-term effectiveness and better characterize uncommon or delayed adverse effects. They are typically designed to identify small treatment effects (ie, a high power study with large numbers of participants) in diverse patient populations, and the results may be used to refine the use of drugs in clinical practice.

References

- [Key concepts of clinical trials: a narrative review.](#)

Biostatistics
Subject

Biostatistics & Epidemiology
System

Clinical trials
Topic

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Item 3 of 40 Question Id: 19388

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A group of researchers conduct a study to evaluate the pharmacologic properties of oxfendazole, an anthelminthic agent. As part of the study, increasing oral doses of oxfendazole (0.5 to 60 mg/kg) are administered to healthy volunteers. Data is collected to form a pharmacokinetic profile of the drug and its metabolites, and the incidence of adverse effects is recorded for the various dosages. A total of 20 healthy male and female (nonchildbearing potential) volunteers participate in the study. Oxfendazole is found to be well tolerated throughout the dose range without any serious adverse effects or deaths. Which of the following best describes this type of study?

- A. Preclinical study (1%)
- B. Phase I clinical trial (79%)
- C. Phase II clinical trial (12%)
- D. Phase III clinical trial (4%)
- E. Phase IV clinical trial (2%)

Omitted
Correct answer
B

79%
Answered correctly

12 secs
Time Spent

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Version

Explanation

The **clinical trials process** addresses whether **new treatments** (eg, drugs, procedures) are **effective and safe** for their **intended use** (ie, treatment of a disease) in the **target population** (eg, subjects with the disease of

The screenshot shows a mobile application interface for a clinical trials question. At the top, there is a navigation bar with icons for back, forward, and search. The URL 'apps.uworld.com' is displayed in the address bar. Below the address bar is a toolbar with various icons: 'Item 3 of 40', 'Question Id: 19388', 'Mark', 'Previous', 'Next', 'Full Screen', 'Tutorial', 'Lab Values', 'Notes', 'Calculator', 'Reverse Color', 'Text Zoom', and 'Settings'. The main content area contains text about the clinical trials process, followed by a detailed description of a phase I trial, a note about cancer-related trials, and four choice options (A, C, D) for preclinical studies.

The **clinical trials process** addresses whether **new treatments** (eg, drugs, procedures) are **effective and safe** for their **intended use** (ie, treatment of a disease) in the **target population** (eg, subjects with the disease of interest). New treatments go through several research phases; some phases involve no human subjects (ie, preclinical studies) and some involve few (ie, phase I and II trials) or many (ie, phase III and IV trials) human subjects. Each of these phases has a different purpose.

A **phase I trial** is the first step in testing a new treatment in **humans**. Data is collected on the drug's **pharmacokinetic profile**, metabolism, and pharmacodynamic response (ie, how it affects the body). Different treatment routes (eg, orally, intravenously) may also be investigated. Human safety is assessed in terms of **adverse effects** and the maximum tolerated dose (MTD). **Gradually increasing doses** are typically administered to find the highest dose (ie, MTD) that does not cause unacceptable toxicity. Phase I trials usually include only a **small number of healthy subjects**.

Note: Cancer-related phase I trials may involve subjects with cancer (rather than healthy subjects) who have been unresponsive to other treatments.

(Choice A) Contrary to phase I, II, III, and IV trials, which include human subjects, preclinical studies do not involve human subjects.

(Choice C) A phase II trial assesses treatment efficacy in a small number of affected subjects (ie, those with the disease of interest), rather than in healthy subjects. For example, a phase II study would assess efficacy, optimal dosing, and adverse effects of oxfendazole among subjects with helminth infection. The study above evaluated the safety, pharmacokinetic profile, and metabolism of oxfendazole in a small number of *healthy subjects*.

(Choice D) A phase III trial assesses the safety and effectiveness of a new treatment compared to a standard treatment (or placebo); therefore, it involves ≥ 2 groups of affected subjects. For example, a phase III study

include only a small number of healthy subjects.

Note: Cancer-related phase I trials may involve subjects with cancer (rather than healthy subjects) who have been unresponsive to other treatments.

(Choice A) Contrary to phase I, II, III, and IV trials, which include human subjects, preclinical studies do not involve human subjects.

(Choice C) A phase II trial assesses treatment efficacy in a small number of affected subjects (ie, those with the disease of interest), rather than in healthy subjects. For example, a phase II study would assess efficacy, optimal dosing, and adverse effects of oxfendazole among subjects with helminth infection. The study above evaluated the safety, pharmacokinetic profile, and metabolism of oxfendazole in a small number of *healthy subjects*.

(Choice D) A phase III trial assesses the safety and effectiveness of a new treatment compared to a standard treatment (or placebo); therefore, it involves ≥ 2 groups of affected subjects. For example, a phase III study would evaluate the effectiveness of oxfendazole compared to placebo among subjects with helminth infection.

(Choice E) A phase IV trial studies the adverse effects caused over time by a new treatment after it has been approved and is on the market, as with a study to assess adverse effects related to oxfendazole use not seen in earlier trials.

Educational objective:

A phase I trial assesses the pharmacokinetics, pharmacodynamics, and safety profile (eg, adverse events, toxicity) of a new treatment in humans. It is usually conducted on a small number of healthy subjects.

Biostatistics

Subject

Biostatistics & Epidemiology

System

Clinical trials

Topic

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Item 4 of 40 Question Id: 1303

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Researchers studying the effects of hormone replacement therapy (HRT) on the risk of myocardial infarction (MI) among postmenopausal women calculate the relative risk (RR) of MI to be 1.30 ($p = 0.07$) among women who are taking HRT compared to those who are not. The researchers conclude that there is no statistically significant increased risk of MI with HRT (based on a cutoff of $\alpha = 0.05$). Subsequently, the results of a meta-analysis determine that there actually is an increased risk of MI, with an overall RR = 1.32 ($p = 0.03$) among postmenopausal women who are taking HRT compared to those who are not. Which of the following was the most likely problem in the first study?

- A. Berkson's bias (7%)
- B. Placebo effect (1%)
- C. Poor blinding (3%)
- D. Researcher expectancy (9%)
- E. Sample size (77%)

Omitted
Correct answer
E

77%
Answered correctly

24 secs
Time Spent

2023
Version

Explanation

Type I (α) and type II (β) errors

True status

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Item 4 of 40 Question Id: 1303

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Type I (α) and type II (β) errors

		True status	
		There is a true difference (ie, H_0 is false)	There is NO true difference (ie, H_0 is true)
Study result	Difference calculated as statistically significant (ie, reject H_0)	Correctly conclude there is a difference	Type I (α) error (Falsey conclude there is a difference)
	Difference calculated as NOT statistically significant (ie, fail to reject H_0)	Type II (β) error (Falsey conclude there is NO difference)	Correctly conclude there is NO difference

H_0 = null hypothesis of no difference.

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The first study and the meta-analysis (combined results of several studies) had similar outcomes in terms of relative risk (RR); however, they arrived at different conclusions because the p-value reached statistical significance ($p < \alpha = 0.05$) in the meta-analysis but not in the first study. The most probable reason behind this is that the **larger** meta-analysis reflects the true status (increased risk of myocardial infarction [MI] with hormone replacement therapy [HRT]), whereas the first study result represented a **type II (β) error (falsey concluded there was no increased risk of MI with HRT)**.

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(there was no increased risk of MI with HRT).

The probability of a type II (β) error is related to how much **power** a study has to detect a difference when a difference actually exists ($\text{power} = 1 - \beta$). **Sample size** and power are related in that studies with a larger sample size have greater power to detect differences if these exist. The small sample size of the first study made it underpowered to detect a difference in outcome between patients who were treated with HRT and those who were not.

The sample size did not change the value of α (typically set at 0.05). However, because the first study was underpowered, the p-value obtained was not statistically significant ($p = 0.07 > \alpha = 0.05$), leading to a false conclusion of no increased risk of MI with HRT.

(Choice A) Berkson's bias refers to selection bias that can be created by selecting hospitalized patients as the control group.

(Choice B) Placebo effect refers to patients' expectations affecting an outcome. However, in this case, the control group is taking neither HRT nor a placebo medication.

(Choices C and D) Given that the RR obtained in the first study was similar to the one obtained in the meta-analysis (1.32 versus 1.30), it is unlikely that design flaws (eg, poor blinding, researcher expectancy) were present in the study.

Educational objective:

A study's power increases as its sample size increases. Therefore, the larger the sample, the greater the ability of a study to detect a difference when one truly exists.

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Item 5 of 40 Question Id: 1170

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A new biomarker has been shown to allow for the early detection of non-small cell lung carcinoma. A preliminary analysis on a cohort study of this new test demonstrates that its use prolongs survival of lung cancer patients by 3 months when compared to the survival of patients diagnosed by conventional methods. A secondary analysis reveals no difference in 6-month mortality rates between the 2 groups. Which of the following factors most likely explains the study results?

- A. Confounding (1%)
- B. Lead-time bias (84%)
- C. Length-time bias (11%)
- D. Measurement bias (1%)
- E. Observer bias (0%)
- F. Rare disease assumption (0%)

Omitted
Correct answer
B

84%
Answered correctly

01 sec
Time Spent

2023
Version

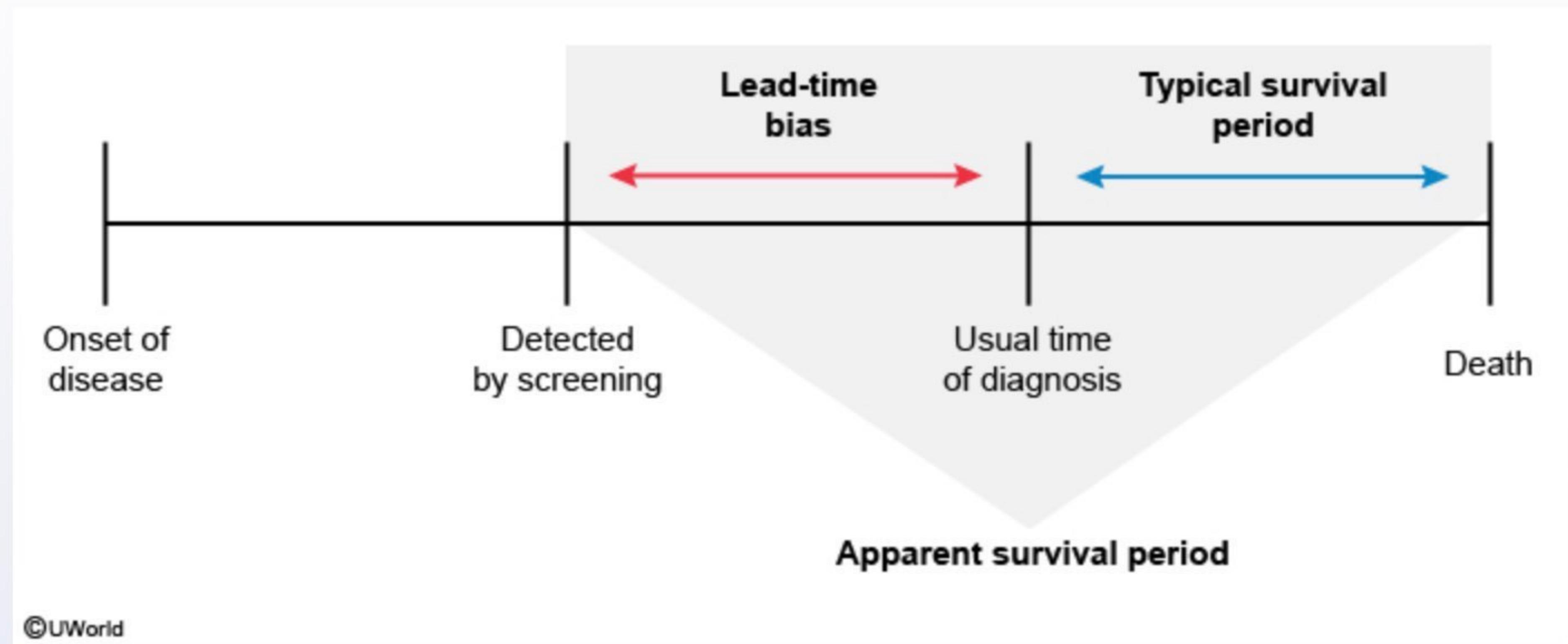
Explanation



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Item 5 of 40 Question Id: 1170

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Lead-time bias should always be considered when evaluating any screening test. Lead-time bias is an **apparent increase in survival time** among patients undergoing screening when they actually have an **unchanged prognosis**. Patients screened with more sensitive tests may appear to live longer only because the disease was detected earlier than had it been diagnosed clinically. The overall length of time from disease onset to death actually remains the same with or without the earlier screening. To determine the actual effectiveness of the screening program, it is necessary to follow up patients for periods that are **longer** than the apparent increase in survival time, and then to estimate and compare mortality rates among patients who have undergone the additional screening and those who have not.

In this case, patients screened by the new test appeared to have increased their survival time by 3 months when compared to those diagnosed by conventional methods. However, there was **no difference in 6-month mortality rate** between the 2 groups, which indicates that there is no actual benefit to the screening program.

(Choice A) Confounding distorts the relationship between risk factors and the disease of interest, and can

In this case, patients screened by the new test appeared to have increased their survival time by 3 months when compared to those diagnosed by conventional methods. However, there was **no difference in 6-month mortality** rate between the 2 groups, which indicates that there is no actual benefit to the screening program.

(Choice A) Confounding distorts the relationship between risk factors and the disease of interest, and can wholly or partially account for the observed effect. Although the results of this study could be potentially confounded, there is no information on how potential confounders were treated during the design or analysis stage of the study.

(Choice C) Length-time bias occurs when subjects with a rapidly progressive form of disease are less likely to be detected by screening compared to those with slowly progressive disease. This bias tends to overstate the beneficial effects of screening on length of survival and mortality. In this case, there is no indication that the patients identified by the new test have more benign forms of lung cancer.

(Choices D and E) Measurement bias and observer bias refer to the misclassification of outcome and/or exposure (eg, labeling diseased as non-diseased and vice versa) and are related to poor study design. The scenario described does not mention how the study was conducted.

(Choice F) Rare disease assumption refers to the practice of approximating the odds ratio and relative risk when conducting a case-control study for rare diseases. According to the assumption, the odds ratio approximates relative risk when disease incidence is low (eg, <10%).

Educational objective:

Lead-time bias occurs when a new test diagnoses a condition earlier than conventional studies, causing an apparent increase in survival time despite no improvement in overall mortality. Long-term mortality rates, not survival times, should be considered for measuring the effect of early screening and treatment.

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Item 6 of 40 Question Id: 1277

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A researcher is interested in studying whether there is an association between neural tube defects and use of acetaminophen during the first 3 months of pregnancy. He randomly chooses a group of women who have just delivered babies with neural tube defects, and a second group of women who delivered apparently healthy babies. These 2 groups were then asked about their use of acetaminophen during the first 3 months of pregnancy. Which of the following measures of association are the investigators most likely to report?

- A. Median survival (0%)
- B. Odds ratio (59%)
- C. Prevalence ratio (2%)
- D. Relative rate (2%)
- E. Relative risk (34%)

Omitted

Correct answer

B



59%

Answered correctly



02 secs

Time Spent



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Explanation

This scenario describes a typical **case-control study design**. People with the disease of interest (ie, **cases** [women who have just delivered babies with neural tube defects]) and people without this disease (ie, **controls** [women who delivered apparently healthy babies]) are asked about **previous exposure** to the risk factor being studied (eg, acetaminophen use during the first 3 months of pregnancy). The main measure of association is the

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Item 6 of 40
Question Id: 1277

Mark

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$$\text{OR} = (\text{odds of exposure in cases}) / (\text{odds of exposure in controls})$$

(Choice A) Median survival is calculated in cohort studies or clinical trials, and is usually used to compare the median survival times in ≥ 2 groups of patients (eg, those receiving a new treatment and those receiving a placebo).

(Choice C) Prevalence ratio is a ratio of 2 probabilities (ie, prevalence) commonly used in cross-sectional studies to compare the prevalence of disease among exposed and unexposed groups of people. In case-control studies, cases and controls are selected from a pool of potential cases and controls that do not represent the real frequency (ie, prevalence) of disease in the population. Therefore, estimating the prevalence of disease in case-control studies would be biased.

(Choices D and E) Incidence measures (eg, relative risk or relative rate) cannot be directly measured in case-control studies because cases, by definition, already have the disease (ie, the study does not follow a cohort for development of a disease). Relative risk and relative rate are calculated in prospective and retrospective cohort studies, where risk factor assessment occurs *first* and then exposed and unexposed groups are followed over time and assessed for development of disease.

Educational objective:

A case-control study is used to compare the exposure status of people with the disease (ie, cases) to the

~~exposure status of people without the disease (ie, controls). The main measure of association is the odds ratio.~~

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Educational objective:

A case-control study is used to compare the exposure status of people with the disease (ie, cases) to the exposure status of people without the disease (ie, controls). The main measure of association is the odds ratio.

Biostatistics

Subject

Biostatistics & Epidemiology

System

Odds ratio

Topic

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Item 7 of 40 Question Id: 1173

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Researchers conduct a prospective study that demonstrates an association between alcohol consumption and transitional bladder carcinoma, with a relative risk (RR) of 1.81 and a p-value of 0.03. They then divide the study subjects into 2 groups, smokers and non-smokers, and again examine the association between alcohol consumption and bladder cancer:

	RR	P-value
Smokers	0.95	0.87
Non-smokers	1.03	0.96

The discrepancy between the overall results and the stratified results is best explained by which of the following?

- A. Confounding (69%)
- B. Effect modification (17%)
- C. Measurement bias (5%)
- D. Meta-analysis (3%)
- E. Observer bias (2%)
- F. Recall bias (1%)

Omitted
Correct answer

69%
Answered correctly

05 secs
Time Spent

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Item 7 of 40 Question Id: 1173

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Initial crude analysis confounded by smoking status

		Bladder cancer	
		Yes	No
Alcohol use	Yes	23	207
	No	26	444

RR = 1.81

p-value = 0.03

Stratified analysis removes confounding effects of smoking

Smokers

		Bladder cancer	
		Yes	No
Alcohol use	Yes	19	81
	No	14	56

RR = 0.95

p-value = 0.87

Non-smokers

		Bladder cancer	
		Yes	No
Alcohol use	Yes	4	126
	No	12	388

RR = 1.03

p-value = 0.96

The screenshot shows a mobile application interface for a study. At the top, there is a header bar with icons for back, forward, and search. Below the header is a toolbar with various functions: Item 7 of 40, Question Id: 1173, Mark, Previous, Next, Full Screen, Tutorial, Lab Values, Notes, Calculator, Reverse Color, Text Zoom, and Settings. The main content area contains text about confounding in epidemiology, followed by text about effect modification and measurement bias.

Confounding occurs when the exposure-disease relationship is muddled by the effect of a confounding variable, an extraneous factor associated with both exposure and disease. An example is shown in the [exhibit](#). In a primary school, it may appear on crude analysis that students with bigger shoe sizes have a higher level of intelligence. However, this association is actually a result of age, not shoe size: Older students tend to have bigger shoe sizes and also to be more intelligent. Age is a confounder because it is associated with both shoe size and intelligence and muddles the association between them. When study subjects are grouped by age (**stratification**), the association between shoe size and intelligence is no longer significant.

Similarly, initial crude analysis suggested that alcohol use was associated with bladder carcinoma (similar to shoe size being associated with intelligence), with a relative risk (RR) of 1.81 and a p-value <0.05. However, smoking is associated with both bladder carcinoma and alcohol use. Therefore, **smoking** is a potential confounder that may explain the association observed between alcohol use and bladder cancer (similar to age in the school example). Stratified analysis by smoking status shows that both smokers and non-smokers have an RR ~1 with large p-values (>0.05). The RR of 1.81 found on crude analysis disappears and there is no true association between alcohol consumption and bladder cancer.

(Choice B) Effect modification results when an external variable positively or negatively impacts the observed effect of a risk factor on disease status. When analysis is performed based on stratification by this external variable, there will be a significant difference in risk between the stratified groups. For instance, aspirin use is associated with Reye syndrome in children but not adults; therefore, age modifies the effect of aspirin on Reye syndrome development. Effect modification can easily be confused with confounding; but stratified analysis can help distinguish between them. With confounding, there is usually no significant difference between the strata (as in this case with the smoker and non-smoker strata).

(Choices C and E) Measurement bias and observer bias distort the strength of association by misclassifying

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(Choices C and E) Measurement bias and observer bias distort the strength of association by misclassifying exposed/unexposed and/or diseased/nondiseased subjects. The scenario does not describe any issues that could affect the classification process.

(Choice D) Meta-analysis refers to compiling results from several studies to increase analysis power.

(Choice F) Recall bias results from inaccurate recall of past exposure by people in the study and applies mostly to retrospective (eg, case-control) studies.

Educational objective:

Confounding occurs when the exposure-disease relationship is muddled by the effect of an extraneous factor associated with both exposure and disease. Confounding bias can result in the false association of an exposure with a disease.