BIOSTATISTICS MCQS AND EXPLANATIONS

THESE MULTIPLE CHOICE QUESTIONS COVER THE IMPORTANT TOPICS FOR USMLE EXAMINATIONS.

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A group of researchers were examining the risk of Alzheimer's disease with Vaccine X. 300 subjects were given vaccine and 300 were given placebo. They were followed for 10 years. They got the following data:

	Alzheimer	No Alzheimer
Vaccine	100	200
Placebo	50	250

A review of literature revealed that hormone replacement therapy is also associated with Alzheimer disease. The researchers rearranged the data according to hormone replacement therapy as follows:

Subjects taking Hormone Replacement Therapy:

	Alzheimer	No Alzheimer
Vaccine	50	150
Placebo	50	150

Subjects who were not taking Hormone Replacement Therapy:

	Alzheimer	No Alzheimer
Vaccine	25	75
Placebo	25	75

The stratified result is explained by which of the following?

A. Selection bias
B. Recall bias
C. Measurement bias
D. Pygmalion effect
E. Confounding bias
F. Effect modification
G. Hawthorne effect

Explanation:

The correct answer is E.

In a cohort study, risk is quantified using Relative Risk.

	Alzheimer	No Alzheimer
Vaccine	100	200
Placebo	50	250

In the non-stratified data,

Risk of Alzheimer in those who got vaccine = 100/ (100 + 200) = 1/3

Risk of Alzheimer in those who got placebo = 50/ (50 + 250) = 1/6

Therefore, Relative risk (RR) of Alzheimer with vaccine

= (Risk of Alzheimer in those who got vaccine) / (Risk of Alzheimer in those who got placebo)

= (1/3) ÷ (1/6) = 6/3 = 2

Those who took vaccine were 2 times more likely to develop Alzheimer than those who took placebo.

Relative Risk for stratified data:

Subjects taking Hormone Replacement Therapy (HRT):

RR = (Risk of Alzheimer in those on HRT who got vaccine) / (Risk of Alzheimer in those on HRT who got placebo)

= (50/ (50+150)) ÷ (50/ (50+150)) = 1

Subjects not taking Hormone Replacement Therapy (HRT):

RR =   (Risk of Alzheimer in those not on HRT who got vaccine) / (Risk of Alzheimer in those not on HRT who got placebo)

= (25/(25+75)) ÷ (25/(25+75)) = 1

Thus, stratified analysis shows that relative risk of Alzheimer in HRT group and non HRT group is neutral that is 1. Therefore, the finding of RR of 2 in those who got vaccine in crude analysis was incorrect because of the confounding factor of Hormone Replacement Therapy.

Selection Bias (**Choice A**) occurs from nonrandom assignment of participants in study groups.

Recall Bias (**Choice B**) occurs when awareness of the disease and risk factors alters recall by the subject.

Measurement Bias (**Choice C**) occurs when groups who know they are being studied behave differently and thus it results in distortion of the data.

Pygmalion Effect (**Choice D**) occurs when investigators believe that certain treatment is effective and thus is more likely to report positive outcome.

Effect modification **(Choice F)**: If the relative risk had increased or decreased significantly in Hormone Replacement Therapy group then it would have been classified as effect modification.

Hawthorne effect **(Choice G)** is the tendency of study group to change their behavior when they know they are being studied.

Take Home Message

Know how to calculate relative risk and different types of bias and study errors.

A group of researchers were examining the risk of Alzheimer's disease with Vaccine X. 300 subjects were given vaccine and 300 were given placebo. They were followed for 10 years. They got the following data:

	Alzheimer	No Alzheimer
Vaccine	100	200
Placebo	50	250

A review of literature revealed that smoking is also associated with Alzheimer disease. The researchers rearranged the data according to smoking as follows:

Subjects who were currently smoking:

	Alzheimer	No Alzheimer
Vaccine	75	150
Placebo	25	150

Subjects who were not currently smoking:

	Alzheimer	No Alzheimer
Vaccine	25	75
Placebo	25	75

The stratified result is explained by which of the following?

    A. Selection bias
    B. Recall bias
    C. Measurement bias
    D. Pygmalion effect
    E. Confounding bias
    F. Effect modification
    G. Hawthorne effect

Explanation:

The correct answer is F.

In a cohort study, risk is quantified using Relative Risk.

	Alzheimer	No Alzheimer
Vaccine	100	200
Placebo	50	250

In the non-stratified data,

Risk of Alzheimer in those who got vaccine = 100/ (100 + 200) = 1/3

Risk of Alzheimer in those who got placebo = 50/ (50 + 250) = 1/6

Therefore, Relative risk (RR) of Alzheimer with vaccine

= (Risk of Alzheimer in those who got vaccine) / (Risk of Alzheimer in those who got placebo)

= (1/3) ÷ (1/6) = 6/3 = 2

Those who took vaccine were 2 times more likely to develop Alzheimer than those who took placebo.

Relative Risk for stratified data:

Subjects who were active smokers:

RR = (Risk of Alzheimer in active smokers who got vaccine) / (Risk of Alzheimer in active smokers who got placebo)

= (75/ (75+150)) ÷ (25/ (25+150)) = (75/225) / (25/175) = 0.33/0.14 = 2.35

Subjects who were not active smokers:

RR = (Risk of Alzheimer in those who were not active smokers who got vaccine) / (Risk of Alzheimer in those who were not active smokers who got placebo)

= (25/(25+75)) ÷ (25/(25+75)) = 1

Thus, stratified analysis shows that relative risk of Alzheimer in smokers is higher than crude analysis. This is effect modification.

Selection Bias (**Choice A**) occurs from nonrandom assignment of participants in study groups.

Recall Bias (**Choice B**) occurs when awareness of the disease and risk factors alters recall by the subject.

Measurement Bias (**Choice C**) occurs when groups who know they are being studied behave differently and thus it results in distortion of the data.

Pygmalion Effect (**Choice D**) occurs when investigators believe that certain treatment is effective and thus is more likely to report positive outcome.

The stratified analysis did not show relative risk of Alzheimer in active smoker and non-active smoker to be neutral that is 1. The sub-analysis showed an increase in relative risk (2.25). Thus smoking is an effect modifier and not a confounding factor (**Choice E**).

Hawthorne effect **(Choice G)** is the tendency of study group to change their behavior when they know they are being studied.
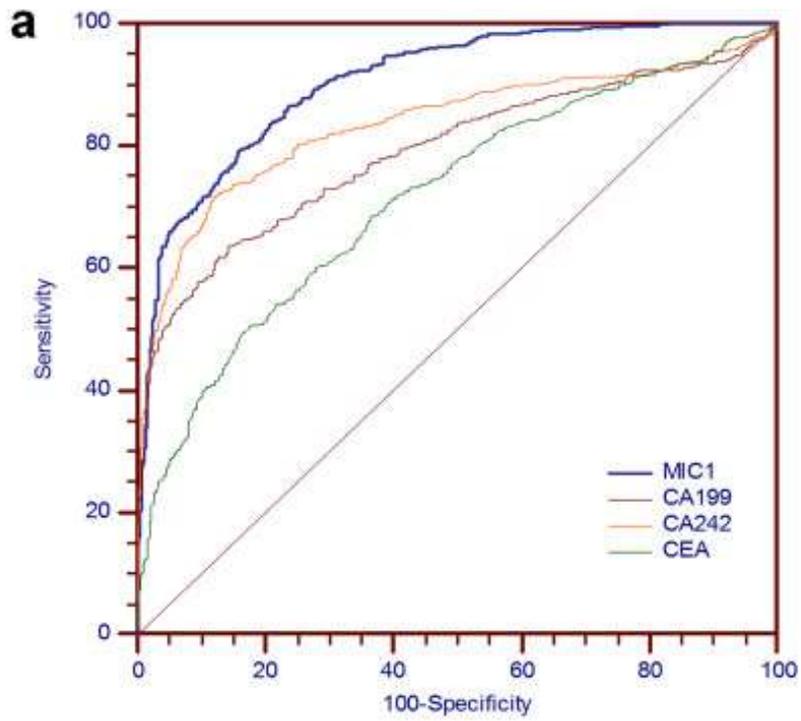
Take Home Message

Know how to calculate relative risk and different types of bias and study errors.

QUESTION 3.

In a research study, the diagnostic performance of Macrophage inhibitory cytokine 1 (MIC-1), CA19.9, CEA and CA242 was evaluated. The figure below shows the data analysis from the study.

a

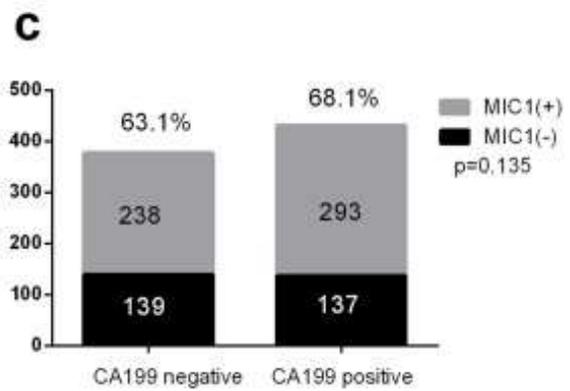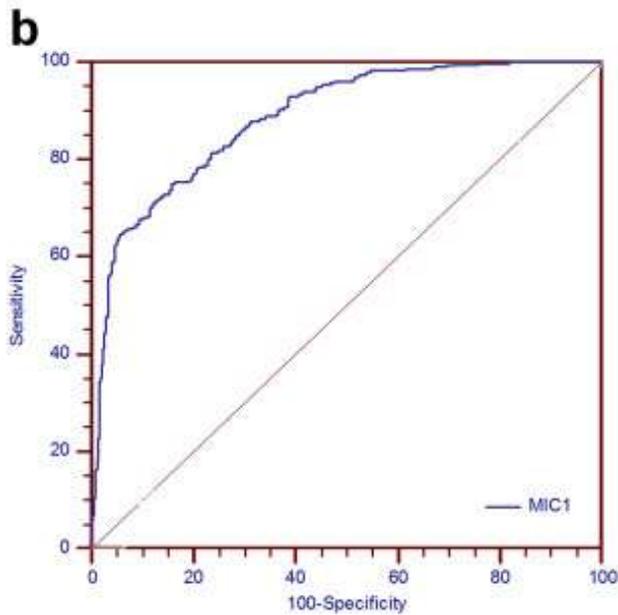| Area under receiver operating characteristic curve (AUROC)					
	AUC	SE	P value	95% CI	
				lower	up
MIC1	0.935	0.0065		0.920	0.948
CA199	0.803	0.0119	< 0.001	0.780	0.824
CA242	0.848	0.0107	< 0.001	0.828	0.867
CEA	0.725	0.0137	< 0.001	0.700	0.749

b

c

Figure. Comparison of the diagnostic performance of serum MIC-1, CA19.9, CEA and CA242 for PDAC. a. Sensitivities and specificities of MIC-1 , CA19.9, CEA and CA242 for the diagnosis of pancreatic ductal adenocarcinoma (PDAC) was compared through the analyses of ROC curves in the discovery group (n = 1307). AUROC curve of serum MIC-1 was much larger than that of CA19.9, CEA and CA242 (P < 0.001). **b**. The potential of serum MIC-1 for distinguishing CA19.9-negative pancreatic carcinomas from non–pancreatic carcinoma controls including benign pancreas tumors. **c**. A similar positive rate (present above the bar) of serum MIC-1 (using the cut off value 1000 pg/mL) was observed in patients with PDAC with different CA19.9 levels.(Ref: Ann R Coll Surg Engl. 2013 April; 95(3): 215–221.)

Based on the study, which one of the following is the most accurate diagnostic test for pancreatic ductal adenocarcinoma?

    A. MIC-1
    B. CA19.9
    C. CEA
    D. CA242

The correct answer is A.

Receiver Operating Characteristic curve (ROC curve) is used to compare the performance of different tests. The tests with the greatest area under the curve (AUC) is considered the most accurate.

ROC curve is a plot of true positive rate against the false positive rate for the different possible cut off level of a diagnostic test. True positive rate is the same as sensitivity and false positive rate is 100-specificity (in %age).

The closer the curve comes to the 45-degree diagonal of the ROC space, the less accurate the test.