Kaplan USMLE Step 1: Calculate the frequency of this disease

JUL 4, 2022

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If you’re preparing for the United States Medical Licensing Examination® (USMLE®) Step 1 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

This month’s stumper

An autosomal recessive disease has a carrier frequency of 1/25 in a specific population. Which of the following is the most likely frequency of individuals expressing the disease in this population?

A. 1/25.
B. 1/50.
C. 1/625.
D. 1/2,500.
E. 1/5,000.
The correct answer is D.

**Kaplan Medical explains why**

For an individual to express an autosomal recessive disease they would need to inherit one mutated allele from each parent, indicating that both their mother and father would be carriers for the disease. The probability that each parent is a carrier is 1/25. Each parent has a one in two chance of passing the defective allele to their child, such that there is a 1/50 probability that the child will inherit a defective allele from a carrier parent (1/2 x 1/25).

Since both parents have to transmit the mutant allele to the child, the overall probability of the child receiving a mutant allele from each parent is 1/2,500 (1/50 x 1/50). This is the carrier frequency for cystic fibrosis in the northern European population.

An alternative way to answer the question is to utilize the Hardy Weinberg equilibrium. The carrier frequency in the population for an autosomal recessive disorder is represented by 2pq, where p is the frequency of the wild-type allele (usually close to one), and q equals the frequency of the mutant allele. In this question 2pq equals 1/25, and if it is assumed that p is close to one, q would equal 1/50 (the frequency of the mutant allele). The term q^2 represents the frequency of individuals with the disease, which in this case would be 1/50 times 1/50, or 1/2,500.

**The Hardy-Weinberg Equation:**

- p^2 + 2pq + q^2 = 1
- p = frequency of allele 1 (conventionally the most common, normal allele)
- q = frequency of allele 2 (conventionally a minor, disease-producing allele)
p² = frequency of genotype 1-1 (conventionally homozygous normal)
2pq = frequency of genotype 1-2 (conventionally heterozygous)
q² = frequency of genotype 2-2 (conventionally homozygous affected)

Why the other answers are wrong

Choice A: The probability 1/25 is the carrier frequency, not the disease frequency.

Choice B: The probability 1/50 is the chance that a child will inherit one mutated allele from a parent in this population (1/25 x 1/2).

Choice C: 1/625 is (1/25)², but does not represent a value that could be obtained from the Hardy Weinberg equilibrium.

Choice E: 1/5,000 also does not represent a value that could be obtained from the Hardy Weinberg equilibrium.

Tips to remember

- Using the Hardy-Weinberg equilibrium 2pq equals 1/25, the frequency of individuals in the population who are carriers for the autosomal recessive disorder.
- Since p is close to one, q can be estimated at 1/50.
- q² represents the frequency of affected individuals in the population. In this case, 1/2,500.

For more prep questions on USMLE Steps 1, 2 and 3, view other posts in this series.

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