Deacon's Challenge

No 107 - Answer

Your paediatricians wish to screen a population for the presence of a rare disease which has a prevalence of 1 in 2000. However the preferred screening test, for which the sensitivity and specificity are both 99% is prohibitively expensive so you suggest a two step strategy employing a preliminary inexpensive screening test which has a sensitivity of 99% but a specificity of only 96%. The preferred (secondary) test will only be applied to those samples yielding a positive result in the preliminary test. The paediatricians have asked you to calculate:

a) The prevalence of disease in the population giving a positive result to the preliminary screening test.
b) The percentage of patients with disease who will be successfully identified using this strategy.
c) The percentage of patients identified as having the disease by this strategy which are false positives.

Abbreviations:

	Preliminary test	Secondary test
True positives	TP_1	TP_2
False positives	FP_1	FP_2
True negatives	TN_1	TN_2
False negatives	FN_1	FN_2

With these types of questions it is helpful to construct a 2 x 2 contingency table (although not all fields are needed to answer the question):

	Positives	**Negatives**	**Total**
With disease	TP Sensitivity x Prevalence	FN (1 – Sensitivity) x Prevalence	TP + FN Prevalence
Without disease	FP (1 - Specificity) x (1 - prevalence)	TN Specificity x (1 - prevalence)	FP + TN (1 - Prevalence)
Total	TP + FP	FN + TN	TP + FP + FN + TN

Prevalence, sensitivity and specificity are expressed as proportions i.e. prevalence of 1 in 2,000 becomes 1/2,000 = 0.0005, sensitivity of 99% = 0.99 and specificity of 96% = 0.96.

a) For the preliminary test (Test 1). Sensitivity = 0.99, specificity = 0.96, prevalence = 0.0005, (1 – prevalence) = 0.9995

	Positives	**Negatives**	**Total**
With disease	TP_1 0.99 x 0.0005 = 0.000495	FN_1 0.01 x 0.0005 = 0.000005	TP1 + FN_1 0.0005
Without disease	FP_1 0.04 x 0.9995 = 0.03998	TN_1 0.96 x 0.9995 = 0.95952	FP_1 + TN_1 0.9995
Total	TP_1 + FP_1 **0.040475**	FN_1 + TN_1 **0.959525**	TP_1 + FP_1 + FN_1 + TN_1 **1**

Prevalence of disease amongst group testing positive $= \frac{TP_1}{TP_1 + FP_1}$

$= \frac{0.000495}{0.040475}$

$=$ **0.0122** (to 3 sig figs)

Which can also be expressed as 1 in 1/0.0122 = **1 in 82**

b) The percentage of patients with disease which test positive by both the preliminary and secondary screening test is simply the product of the two sensitivities:

$$\% \text{ with disease identified by test strategy} = \frac{\text{Sensitivity}_{\text{Primary test}} \times \text{Sensitivity}_{\text{Secondary test}}}{100}$$

$$= \frac{99 \times 99}{100} = \mathbf{98\%}$$

c) Set up a similar table for the secondary test (test 2) – where sensitivity = 0.99, specificity = 0.99 prevalence = 0.0122 and (1 - prevalence) = 1 - 0.0122 = 0.9878:

	Positives	**Negatives**	**Total**
With disease	TP_2 0.99 x 0.0122 = 0.012078	FN_2 0.01 x 0.0122 = 0.000122	TP_2 + FN_2 0.0122
Without disease	FP_2 0.01 x 0.9878 = 0.009878	TN_2 0.99 x 0.9878 = 0.977922	FP_2 + TN_2 0.9878
Total	TP_2 + FP_2 **0.021956**	FN_2 + TN_2 **0.978044**	TP_2 + FP_2 + FN_2 + TN_2 **1**

$$\% \text{ of false positives in the secondary test} = \frac{FP_2 \times 100}{TP_2 + FP_2} = \frac{0.009878 \times 100}{0.021956} = \mathbf{45\%}$$

Question 108

Calculate the loading dose of intravenous aminophylline required to achieve a plasma theophylline concentration of 15 mg/L in a 55 kg man, given that aminophylline is 80% w/w theophylline and the volume of distribution of theophylline is 0.5 L/kg.
What infusion rate would be required to maintain this concentration if the half life is 8 hours?

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