Deacon's Challenge
No 173 - Answer

A screening programme for Down's Syndrome has a screen positive rate of 2.5% and a detection rate of 82%. Calculate the probability that a pregnancy judged to be at low risk will result in an affected child, given that the incidence of Down's Syndrome at term is 1.84/1000 live births in the absence of selective abortion. State any assumptions made.

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The screen positive rate is the proportion of all results which are positive and will consist of both true positives (TP) and false positives (FP):

$$\text{Screen positive rate} = \frac{(TP + FP) \times 100}{(TP + FP + TN + FN)} = 2.5\%$$

The detection rate is the same thing as sensitivity and is the proportion of all patients with Down's (TP + FN) which are detected by the test:

$$\text{Detection rate} = \frac{TP \times 100}{(TP + FN)} = 82\%$$

The calculation can be performed with absolute numbers, percentages or proportions. It is simplest to take an arbitrary population size so as to arrive at manageable numbers. Working with a total population of 1,000,000 the numbers become:

Total population	=	(TP + FP + TN + FN) = 1,000,000
Total with Downs	=	(TP + FN) = 1.84 x 1,000 = 1,840
Total without Downs	=	(TN + FP) = 1,000,000 - 1,840 = 998,160

Substitute (TP + FN) = 1840 into the expression for detection rate and solve for TP:

$$\frac{TP \times 100}{1{,}840} = 82$$

$$TP = \frac{82 \times 1840}{100} = 1{,}509$$

Subtraction of this value from the total with Down's gives FN:

FN = Total with Down's - TP

= 1,840 - 1,509 = 331

Substitution of TP = 1,509 into the expression for screen positive rate allows calculation of FP:

$$\frac{(1{,}509 + FP) \times 100}{1{,}000{,}000} = 2.5$$

$$1{,}509 + FP = \frac{2.5 \times 1{,}000{,}000}{100} = 25{,}000$$

$$FP = 25{,}000 - 1{,}509 = 23{,}491$$

Subtraction of this value from the total without Down's gives the value of TN:

TN = 998,160 - 23,491 = 974,669

The total classified at low risk is all the negative results (TN + FN) whereas the number in this group with Down's is FN, therefore

$$\text{Probability of Downs in low risk group} = \frac{FN}{(TN + FN)}$$

$$= \frac{331}{(974{,}669 + 331)}$$

$$= \frac{331}{975{,}000}$$

= **0.000339** (to 3 sig figs)

or 0.0339%

Therefore 1 in 1/0.000339 = 1 in 2,950 of those identified as low risk will be Down's pregnancies.

Question 174

Serum alkaline phosphatase activity is measured by monitoring the rate of hydrolysis of p-nitrophenyl phosphate to p-nitrophenol. p-nitrophenol has a molar absorption coefficient of 18,700 $L.mol^{-1}.cm^{-1}$. By convention, 1U alkaline phosphatase is defined as the amount of enzyme that results in the formation of p-nitrophenol at a rate of 16.67 nmol per second under standard conditions.

Your laboratory analyser uses 5 µL serum diluted with 250 µL reagent in a 0.5 cm light path cuvette. Absorbance is monitored over a period of 270 seconds during which a linear increase in absorbance is expected.

Calculate the serum alkaline phosphatase activity in a sample for which the absorbance change was 0.067 absorbance units over 270 seconds.

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