

Deacon's Challenge

No 178 - Answer

One definition of Acute Kidney Injury stage 1 is an increase in serum creatinine of $\geq 26 \mu\text{mol/L}$ within 48 hours. Assuming the within-individual biological variation of creatinine is 4.7%, calculate the maximal permissible analytical variation to allow $\geq 95\%$ confidence that an increase in measured creatinine from 150 to 176 $\mu\text{mol/L}$ is genuine. Table of z-distribution:

P (two sided)	0.10	0.05	0.02	0.01	0.002	0.001
z	1.65	1.96	2.33	2.58	3.09	3.29

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Since it is only an increase in creatinine we wish to detect, a single sided z-score is needed. Therefore select a z-score of 1.65 which will exclude 10% of results with half of these (5%) having an increase significantly higher than 26 $\mu\text{mol/L}$ i.e. an increase in creatinine greater than 26 $\mu\text{mol/L}$ will be detected with at least 95% certainty.

$$z = \frac{\text{Change in creatinine}}{\text{SD of the change}}$$

$$1.65 = \frac{176 - 150}{\text{SD of the difference}}$$

$$\text{SD of the difference} = \frac{176 - 150}{1.65} = \frac{26}{1.65} = 15.76 \mu\text{mol/L}$$

Converting to CV (%) at a mean value of 163 $\mu\text{mol/L}$:

$$\text{CV} (\%) = \frac{15.76 \times 100}{163} = 9.67\%$$

This is the CV of the difference between the two results. We need to find the CV of the individual measurements. When two values are subtracted (or added) the CV of the difference (or sum) is the square root of the sum of the squares of the individual measurements (CV_1 and CV_2):

$$\text{CV of the difference} = \sqrt{(\text{CV}_1^2 + \text{CV}_2^2)}$$

Assuming $\text{CV}_1 = \text{CV}_2$ (now becoming simply CV) this simplifies to:

$$\text{CV of the difference} = \sqrt{2 \times \text{CV}^2} = \sqrt{2} \times \text{CV} = 1.414 \text{ CV}$$

Therefore: $9.67 = 1.414 \text{ CV}$

$$\text{CV} = \frac{9.67}{1.414} = 6.84\%$$

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This is the total CV of each individual measurement which will be made up of biological ($\text{CV}_{\text{Biological}}$) and analytical ($\text{CV}_{\text{Analytical}}$) components:

$$\text{CV}_{\text{Total}}^2 = \text{CV}_{\text{Biological}}^2 + \text{CV}_{\text{Analytical}}^2$$

Substitute $\text{CV}_{\text{Biological}} = 4.7\%$ and $\text{CV}_{\text{Total}} = 6.84\%$ and solve for $\text{CV}_{\text{Analytical}}$:

$$6.84^2 = 4.72 + \text{CV}_{\text{Analytical}}^2$$

$$\text{CV}_{\text{Analytical}}^2 = 6.84^2 - 4.72 = 46.79 - 22.09 = 24.7$$

$$\text{CV}_{\text{Analytical}} = \sqrt{24.7} = 5.0\% \quad (2 \text{ sig figs})$$

Question 179

Recent work suggests that the incidence of Familial Hypercholesterolaemia (FH) in North-West Europe is approximately 1 in 200 live births. Using current techniques, the detection rate of disease-associated mutations in FH is approximately 50%.

Calculate (a) the incidence of homozygous FH, and (b) the probability that the child of a proband with genetically-confirmed FH has homozygous FH.

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- ⇒ **vedolizumab** (e.g. Entyvio®)


* ADA: anti-drug antibodies



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