Deacon's Challenge

No 178 - Answer

One definition of Acute Kidney Injury stage 1 is an increase in serum creatinine of ≥26 µmol/L within 48 hours. Assuming the within-individual biological variation of creatinine is 4.7%, calculate the maximal permissible analytical variation to allow ≥95% confidence that an increase in measured creatinine from 150 to 176 µmol/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 µmol/L i.e. an increase in creatinine greater than 26 µmol/L will be detected with at least 95% certainty.

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

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

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

Converting to *CV* (%) at a mean value of 163 µmol/L:

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

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):

$$CV \text{ of the difference} = \sqrt{(CV_1^2 + CV_2^2)}$$

Assuming $CV_1 = CV_2$ (now becoming simply *CV*) this simplifies to:

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

Therefore: $9.67 = 1.414\,CV$

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

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

$$CV_{Total}^2 = CV_{Biological}^2 + CV_{Analytical}^2$$

Substitute $CV_{Biological}$ = 4.7% and CV_{Total} = 6.84% and solve for $CV_{Analytical}$:

$$6.84^2 = 4.72 + CV_{Analytical}^2$$

$$CV_{Analytical}^2 = 6.842 - 4.72 = 46.79 - 22.09 = 24.7$$

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

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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