Agreement of diagnostic assay results within and between laboratories

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Rapid expansion in the inventory of laboratory assays available for detecting animal disease has stimulated interest in finding better ways of describing their performance. Guidelines for validation of assays now emphasise the need to assess agreement within laboratories (repeatability) and between laboratories (reproducibility). However, methodology suited to providingr robust inferences on agreement is poorly defined. For these reasons we aimed to assess repeatability and reproducibility for an ELISA used to detect antibody against bovine herpes virus 1. One thousand assays were performed on 20 sera in five laboratories in 10 weekly batches. Ten of the sera were negative for antibody by virus neutralisation test (VNT) and ten were VNT positive. Agreement of S/P ratio results was assessed graphically, using the coefficient of variation statistic and intraclass correlation coefficients (ICC) derived from variance components. Simulations evaluated the impact of sero prevalence on the estimates of reproducibility of S/P. Graphically, the S/P of VNT -ve sera had low repeatability due to low signal to noise ratio confirmed by the low values of ICC across all laboratories (range 0.01 to 0.27). S/P for VNT +ve sera showed a high signal to noise ratio, greater variation due to sera and higher estimates of repeatability (ICC range 0.63 to 0.92). Lab to lab variation caused the reproducibility of S/P ratio (agreement between laboratories) for VNT +ve sera (ICC 0.52) to be lower than repeatability estimates. Coefficients of variation were high for VNT -ve sera and unexpectedly low for VNT +ve sera. While measures of agreement do not replace measures of diagnostic accuracy, they are informative in many practical circumstances provided their limitations are acknowledged. Epidemiologists could encourage wider adoption of the measures illustrated here and so improve the development and validation of laboratory assays for animal disease.