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Comparison of ViraPap, Southern Hybridization, and Polymerase Chain Reaction Methods for Human Papillomavirus Identification in an Epidemiological Investigation of Cervical Cancer

In the paper by Guerrero et al. (1), 95% confidence intervals for sensitivity and specificity for the comparison of different methods of detection of human papillomavirus (HPV) are given. I should like to point out that the 95% confidence intervals given are based on large sample approximations and are therefore quite misleading when the numbers on which the estimates are based are small. For example, for all controls the sensitivity of ViraPap (VP) against Southern hybridization (SH) (Table 8 of Guerrero et al.) arises from 1 positive result from a total of 14, giving a value of 1/14 = 7% (Table 1).

TABLE 1. VP versus SH

Result by VP	No. of specimens with the following result by SH:		Total
	+	−	
+	1	8	9
−	13	225	238
Total	14	233	247

The 95% confidence interval is given as 0 to 21. However, by consulting the appropriate tables of reference 2, it can be seen that the correct confidence interval is 0.2, 33.9, rounded off to the first decimal place. It is not difficult to check that these values are correct.

Also, no confidence intervals are given for values of sensitivity and specificity when the estimated value is 0 or 100%. This may suggest to some readers that confidence intervals cannot be calculated in these situations. This is not so. For example, in the calculation of sensitivity and specificity of the SH method against PCR it can be deduced that the results given in Guerrero's Table 8 have arisen from the Table 2 of this letter. This shows a sensitivity for SH of 0/12 = 0% and a specificity for SH of 7/7 = 100%. From Geigy Scientific Tables (2) it follows that the 95% confidence interval for sensitivity is 0, 26.5 and that for specificity is 59.0, 100, rounded off to the first decimal place. Although these are effectively one-sided intervals, they are still useful as an indication of the variability of the measures considered.

TABLE 2. SH versus PCR

Result by SH	No. of specimens with the following result by PCR:		Total
	+	−	
+	0	0	0
−	12	7	19
Total	12	7	19

A second point concerns the measurement of agreement between type-specific diagnosis by SH and that by PCR. On p. 2951 of Guerrero et al., a concordance (percentage agreement) of 86% when HPVs were typed by both tests was found. It might be more appropriate in this circumstance to calculate Cohen's Kappa (κ) as a measure of chance-corrected agreement. This is a measure of agreement that ranges from 1, indicating perfect agreement, to a value of less than zero, with chance agreement corresponding to zero. If this is done, the resulting value for κ equals 0.48. Although this value can be shown to be significantly better than chance, it would usually be taken to indicate only fair agreement. Returning to the data in Guerrero's Table 5 on which the above results are based, note that a concordance between type-specific diagnosis for when HPVs were typed of 73.5% will arise on a chance basis alone.

On p. 2955 of Guerrero et al., the question of whether the presence of blood in the specimen will lead to false-negative results using VP is raised. Surely the right approach here would be to cross-tabulate the presence or absence of blood with a positive or negative result by the VP method. This could be repeated separately for results that were positive or negative according to the SH method. The comparison used on p. 2956 would appear to apply to examining the effect of the presence or absence of blood on finding a positive result by the SH method.

REFERENCES

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Ed. Note: *The author of the paper which this letter addresses has chosen not to respond.*