Comments on a paper about Zika detection by laboratories in Brazil

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Abstract

In a paper recently published it was reported about an external quality assessment for Zika virus testing, done in Brazil in 2017, with 15 participating laboratories. By considering the batch of laboratories either as a single unit or as a pool of independent laboratories, mean and standard deviation of sensitivity and specificity are derived.

Key-words

Zika virus, quality assessment, virus testing, sensitivity, specificity.

Introduction

This article comments on a paper (1) published in *Emerging Infectious Diseases*, which reports on quality of Zika virus diagnostic testing, an assessment conducted in Brazil during 2017.

The assessment was done by testing against a Gold Standard provided by German Centre for Infection Research, Berlin, Germany. Fifteen Brazilian laboratories received 4 samples of virus-positive (here simply called Z) specimens and 8 virus-negative (here simply called not-Z) specimens, tested them and reported their results. Although participant laboratories' names may be inferred from the 27 authors affiliations, in the paper the laboratories are only identified by a number (Lab ID1 to ID15). The authors of the paper concluded that 73% of participant laboratories showed suboptimal sensitivity and specificity for Zika virus detection. The paper was mentioned on the daily press in Brazil at time of publication.

The comments presented in this article arise from adopting two different points of view about the set of laboratories: one point of view is regarding the set as one aggregate, the other, as a pool of independent laboratories. It is thus possible to answer the question: if a laboratory is randomly chosen, what values of sensitivity and specificity may be expected from it? Moreover, is it possible to assign standard deviations to such properties?

Since one of the laboratories (ID8) did not complete all tests, its partial results are omitted here; only the remaining 14 laboratories will be considered in this article.

Results from original paper

The findings of the 14 laboratories are summarized Table 1 in a fashion more suitable to the purposes of this article. The laboratories tested 56 Z samples and 112 not-Z samples altogether, with a grand total of 168 samples. They detected 63 Z samples (43 correctly) and 105 not-Z samples (92 correctly).

Table 1 – Summary of results from paper (1)

Lab ID	Correctly detected Z samples	Correctly detected not-Z samples	Sensibility	Specificity
3	4	8	1	1
11	4	8	1	1
12	4	8	1	1
13	4	8	1	1
1	3	8	0.75	1
6	3	8	0.75	1
10	3	8	0.75	1
4	2	8	0.5	1
7	2	8	0.5	1
9	4	5	1	0.625
2	2	6	0.5	0.75
14	3	4	0.75	0.5
15	1	5	0.25	0.625
5	4	0	1	0

Sensitivity vs. specificity independence

By considering the set of 14 laboratories as an unity which processed the batch of 168 samples in a single experiment, the results of Table 1 may be written into a contingency table (Table 2) to check whether sensitivity and specificity are correlated.

Table 2 – Contingency Table pertaining to the aggregate

	Reported Z samples	Reported not-Z samples	Totals
Submitted Z samples	Correctly reported as containing Z (pertains to sensitivity) 43	Wrongly reported as containing not-Z (false negatives) 13	Total of submitted Z samples 56
Submitted not-Z samples	Wrongly reported as containing Z (false positives) 20	Correctly reported as containing not-Z (pertains to specificity) 92	Total of submitted not-Z samples 112
Totals	Total of samples reported as Z 63	Total of samples reported as not-Z 105	Grand total of samples 168

Chi-square test with $df=1$ gives $\chi^2 = 55$, therefore the hypothesis of independence may surely be abandoned.

The aggregate, considered as a single unit, has a sensitivity of $43/56 = 0.77$ and a specificity of $92/112 = 0.82$.

The bivariate distribution

This assessment indeed has double personality: it may be seen as performed by one laboratory (the aggregate), but also as a set of different laboratories, each one with its individual values of sensitivity and specificity.

In the second case, sensitivity and specificity may be treated as random variables with a bivariate distribution. This allows to compute distribution properties, like mean and standard deviation. Thus a person randomly choosing one of the 14 laboratories is informed not only about the values of sensitivity and specificity (the means of distributions) but also of their standard deviation, therefore getting an idea of the spread of possible values around the mean.

Table 2 shows the Lab ID of each laboratory in the cell at the intersection of its sensibility and specificity values. Table 3 shows the distribution proper. Blank cell must be interpreted as containing zeros. Marginal distributions are used to compute mean and standard deviation.

Table 2 – Auxiliary table to compute the distribution of sensitivity and specificity. The table collects the ID of laboratories having the values shown in first column and first row

Specificity → Lab ID ↘ Sensitivity ↓	0	0.25	0.5	0.625	0.75	1
0						
0.25				15		
0.5					2	4,7
0.625						
0.75			14			1,6,10
1	5			9		3,11, 12,13

Table 3 – Bivariate distribution $f_{xy}(x,y)$ of sensitivity (x) and specificity (y)

Specificity y →							
$f_{xy}(x,y)$ ↘	0	0.25	0.5	0.625	0.75	1	
Sensitivity x ↓							Marginal distribution of sensitivity $f_x(x)$
0							0
0.25				0.071			0.071
0.5					0.071	0.143	0.214
0.625							0
0.75			0.071			0.214	0.285
1	0.071			0.071		0.286	0.428
Marginal distribution of specificity $f_y(y)$	0.071	0	0.071	0.143	0.071	0.643	

The results are:

for sensitivity: mean = 0.77 (same as before); standard deviation = 0,24;

for specificity: mean = 0.82 (same as before); standard deviation = 0,29.

The correlation between sensitivity and specificity, as suggested by the contingency table, is confirmed by correlation coefficient $r = 0.70$.

It is obvious that ignoring the presence of faulty laboratories would result in a more favorable evaluation of the set of laboratories. In fact, ignoring the extremely bad LabID5 and LabID15 improves sensitivity (mean = 0.79; standard deviation = 0.20) and, more noticeably, specificity (mean = 0.91; standard deviation = 0.17).

References

1 – Fischer C, et al. External Quality Assessment for Zika Virus Molecular Diagnostic, Brazil, *Emerging Infectious Diseases*, Vol.24, No. 5, May 2018