Etest to detect drug-resistant *Neisseria gonorrhoeae* to contemporary treatment; methodological issues concerning accuracy and reproducibility

Siamak Sabour,1,2,*

I was interested to read the paper by Papp and colleagues published in the *Journal of Medical Microbiology* 2018. *Neisseria gonorrhoeae* is a sexually transmitted bacterial pathogen that continues to evolve to become resistant to known antibiotics. The authors aimed to examine the intra-laboratory variability of using the Etest method to provide consistent MIC values for *N. gonorrhoeae* and also compared the results of the Etest to known agar dilution MIC values [1]. Clinical *N. gonorrhoeae* isolates, 100 paired duplicates, were tested by 8 laboratories for antibiotic susceptibility to ceftriaxone, cefixime and azithromycin using Etest strips. The authors reported that, overall, >80% of the paired Etest MIC values were within one log2 dilution of the replicate. When compared to the agar dilution reference method, the cefixime Etest MIC values were consistently underreported by one dilution (seven laboratories) or two dilutions (one laboratory). The azithromycin Etest MIC values agreed 90.7% with the agar dilution MIC values, while the agreement with ceftriaxone was 90.9%.

However, these results are not the most appropriate estimates to assess accuracy (validity) and reproducibility (precision). First, reproducibility (precision, repeatability and reliability) is a completely different methodological issue compared to accuracy (validity). Reproducibility is the degree to which measures are free from error and therefore yield consistent results (i.e. the consistency of a measurement procedure). If a measurement device or procedure consistently assigns the same score to individuals or objects with equal values, the instrument is considered reliable. Validity (accuracy) has been defined by ‘the extent to which [a test] measures what it claims to measure’. A measure is valid if it measures what it is supposed to measure, and does so cleanly – without accidentally including other factors. It is crucial to know that, in reproducibility analysis, our approach should be individual-based; however, to assess accuracy, a global average approach is usually applied [2]. It is good to know that to assess reproducibility for quantitative variables, the intra-class correlation coefficient (ICCC) single measure or Bland–Altman plot can be applied. Regarding accuracy, depending on the type of the variable (qualitative or quantitative), well-known statistical tests can be considered. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), positive likelihood ratio, negative likelihood ratio and the diagnostic odds ratio (the ratio of true to false results) are the most appropriate estimates to evaluate the validity of a test compared to a gold standard. In the case of quantitative variables, depending on the distribution of the variable, the Pearson r or Spearman rho can be applied. Therefore, to assess reproducibility and accuracy, appropriate tests as well as correct interpretations should be considered [2–5].

In this letter, I emphasized methodological and statistical issues in reproducibility and accuracy analysis. Papp and colleagues concluded that the Etest method yielded reproducible MIC values within each laboratory, with the azithromycin and ceftriaxone MIC results being consistent with the reference agar dilution method. Any conclusion should be supported by the above-mentioned methodological and statistical issues.

**Funding information**
The authors received no specific grant from any funding agency.

**Conflicts of interest**
The authors declare that there are no conflicts of interest.

**References**
2. Szkoł M, Nieto FJ. Epidemiology Beyond the Basics, 2nd ed. Manhattan, New York, United State: Jones and Bartlett Publisher; 2007.