SEROLOGICAL FALSE REACTIVITY - IMPLICATIONS FOR HIV TESTING ALGORITHMS

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BACKGROUND

World Health Organization (WHO), in collaboration with the Institute of Tropical Medicine, Belgium, conducts independent performance evaluations of in vitro diagnostics (IVDs) as part of WHO prequalification assessment of safety, quality and performance.

These assessments provide data on sensitivity and specificity of commercially available IVDs that are used in low and middle income countries. WHO also issues recommendations about how HIV IVDs should be used within testing strategies* for HIV diagnosis, see figures 1 and 2.

For the testing strategies described above, the correctness of the final HIV status is not solely dependent on the specificities (false positive rate) of assays used but also the positive predictive value of the overall testing strategy - this is the probability an individual who was assigned a HIV-positive status truly has HIV infection.

However, for testing strategies that use more than one assay, the correctness of the final HIV status is also dependent on the probability that any specimen that is false-reactive on the first assay (A1) will also not be false-reactive on the second assay (A2) and third assay (A3).

Therefore, it is important to know the level of common false-reactivity between assays that selected for use (the testing algorithm). WHO prequalification assessment uses a single clinical specimen panel so that these patterns of false reactivity can be observed.

*A testing strategy is generically describes a testing sequence for a specific objective, taking into consideration the presumed HIV prevalence in the population being tested. Whereas, a testing algorithm is the combination and sequence of specific assays (brand names) used within HIV testing strategies.

METHODS

WHO and ITM collected a panel of serum/plasma specimens collected worldwide that comprises of:
1. HIV positive (n=462) specimens
2. HIV-negative (n=658) specimens

These specimens were characterized by the following assays:
1. 3rd generation anti-HIV-1/2 enzyme immunoassay
2. 4th generation anti-HIV-1/2 combined with p24 antigen enzyme immunoassay
3. anti-HIV-1/2 line immunoassay and
4. HIV-1 p24 antigen enzyme immunoassay.

Between 2011 and 2016, a total of 27 rapid diagnostic tests and 7 enzyme immunoassays were tested on the same panel. The common false reactive specimens were tabulated.

RESULTS

Of the 658 HIV-negative specimens tested, 15 specimens showed false reactive results for at least two of 34 IVDs tested. A further 7 specimens were false reactive on four or more IVDs.

IVDs that are WHO prequalified or have been approved by regulatory authorities of Australia, Canada, European Union, Japan, and United States are assessed to determine if there is adequate data for validation and verification to support claims made for performance (e.g. sensitivity and specificity).

Therefore, when selecting IVDs that have already been assessed, there is little added value to repeat these diagnostic accuracy studies. Instead, WHO recommends a smaller scale verification study to determine if the testing algorithm(s) selected works well and that common false reactivity between assays chosen is minimal to avoid HIV misdiagnosis (WHO, 2017).

REFERENCES