Can we reduce HIV confirmation testing based on the HIV screen semi-quantitative test result?

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Introduction

HIV confirmation testing is time-consuming, assays are expensive and often batched which delays result reporting. For other serology assays (e.g., HCV) confirmation testing is no longer required when the result of the screening assay is above a certain cut-off.

Data from **six Belgian Aids Reference Laboratories (ARL) (ULB, UGent, STP, ULiège, KUL and ITM)** covering various **4th and 5th generation HIV Enzyme Immunoassay (EIA)** were compiled.

The aim was to investigate whether **we can set a cutoff for these different HIV screening assays above which the HIV infection can be confirmed without further testing**. Additionally, for 5th generation assays, it was verified if the separate Ag result could reliably indicate an HIV seroconversion at a certain cut-off.

Methods

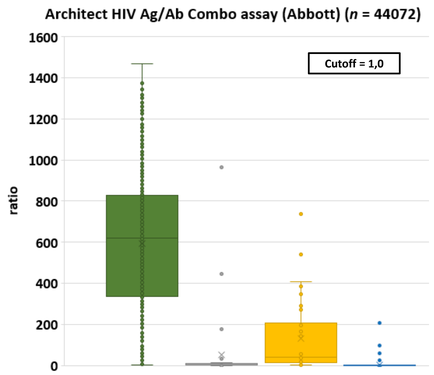
All assays used in the ARLs are categorized in 2 different groups (**4th generation** assay detecting antigen and antibodies (Ag/Ab) at the same time and **5th generation** assay detecting Ag and Ab separately).

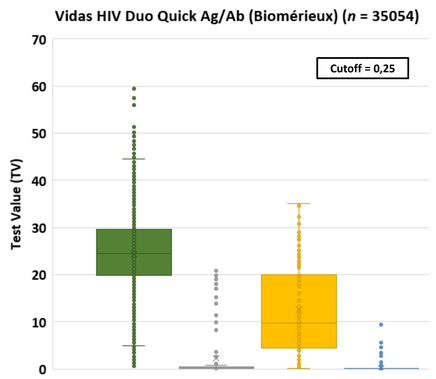
All samples sent to ARLs for screening and/or confirmation testing from 2016 to 2020 were assigned to 4 different groups:

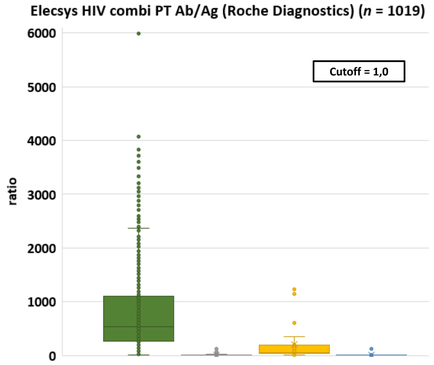
- **HIV-1 or HIV-2 positive infected patient** : reactive Ag/Ab screening test and **HIV-1 positive Ab or HIV-2 positive Ab confirmation** test
- **HIV indeterminate** : **reactive or negative screening Ag/Ab** test and **indeterminate Ab confirmation or blot** test
- **HIV seroconverter** : reactive Ag/Ab screening test, **positive p24 antigen** test and **negative Ab confirmation**
- **HIV negative patient** : negative or reactive screening Ag/Ab test and **negative Ab confirmation**

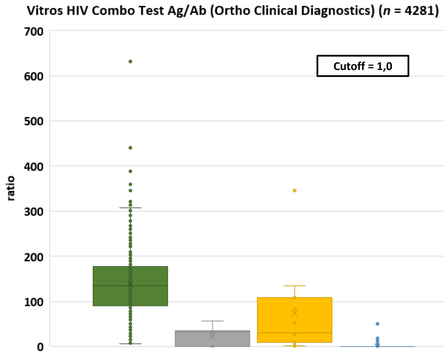
Ratios and **test values** (Ab, Ag, Ab/Ag) for all samples per test were analyzed in a **boxplot for comparison between groups**.

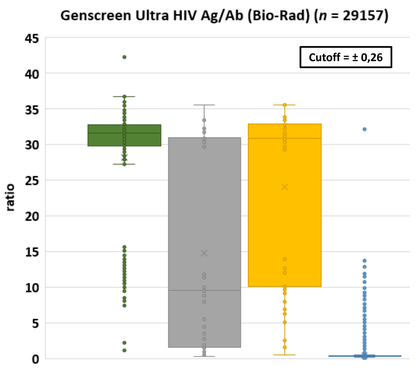
Results 4th generation test



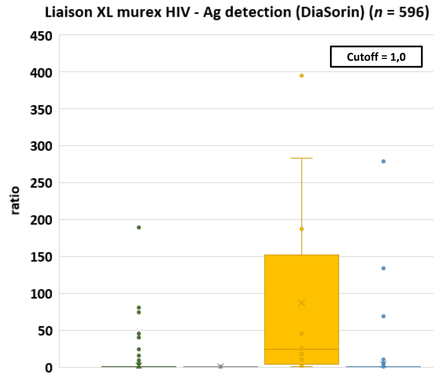


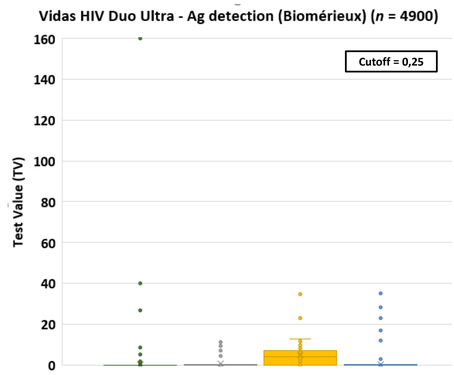


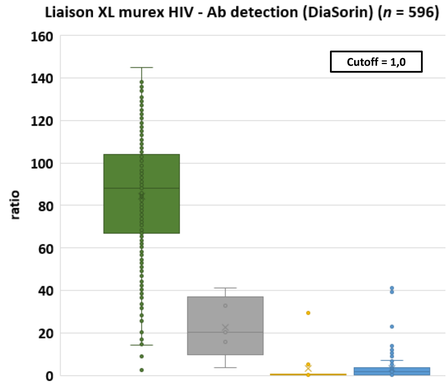


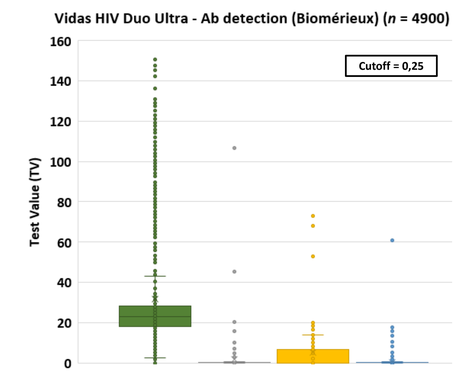


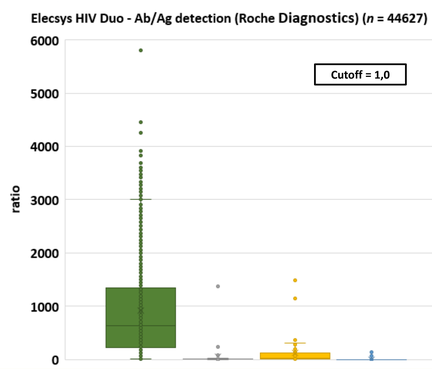
Results 5th generation test











Conclusion

The risk of mis-diagnosing a person as HIV positive can undermine the public's trust in HIV test results. Due to the appearance of undeniable outliers and the many indeterminate results with high test values, HIV confirmation testing remains necessary as infection can never be reliably confirmed based on the screening result. Also, differentiation between HIV-1 and HIV-2 cannot be established without confirmation testing. The separate p24 Ag result in 5th generation tests does not allow to conclude acute HIV infection and additional tests (e.g., viral load, other p24 Ag assays) are needed due to aspecific cross-reactivity with high Ag values. This data analysis provides insight into the semi-quantitative screening assay results and can be of aid for the ARLs to interpret complicated confirmation patterns. An EIA screening test alone cannot be used for a diagnostic conclusion without additional tests. The cut-offs set by the commercial kit cannot be set higher as low values are observed for HIV infected patients.

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