Routine HIV Testing Results in 6 U.S. Clinical Laboratories Using the CDC/APHL Laboratory HIV Testing Algorithm with Geenius HIV 1/2 Supplemental Assay

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Potential conflicts of interest

- Dr. Valsamakis is now employed by Roche Molecular Systems, Inc.
- Dr. Yao received clinical research grants from and serves as a member of scientific advisory boards for Roche Molecular Systems, Inc., and Bio-Rad Laboratories, Inc., whose assays were investigated in this multi-center study.

Background

Geenius is an HIV-1/HIV-2 antibody differentiation test used for the 2nd step in the CDC/APHL HIV lab testing algorithm.

- **Most published evaluations of algorithm outcomes used Multispot HIV-1/HIV-2 Rapid Test.**
  - Geenius reports 3 additional test results: HIV indeterminate, HIV-2 indeterminate and HIV-2 positive with HIV-1 cross reactivity
- **Quantifying true HIV-2 reactivity relative to false reactivity may help to determine the value of differentiating HIV-1 from HIV-2 at the 2nd step.**

Objectives

- To examine routine HIV testing outcomes at six U.S. clinical laboratories using Geenius as the differentiation test in the laboratory testing algorithm
- To characterize the occurrence of true HIV-1 and HIV-2 infections and false-positive results
- To describe algorithm implementation and laboratory test result reporting challenges

Methods

Routine HIV testing data were retrospectively collected from the date each laboratory began to use the algorithm with Geenius through 9/30/2017.

- **ARUP Institute for Clinical, Experimental Pathology**
- **Children's Hospital of Philadelphia**
- **Grady Health System**
- **Johns Hopkins**
- **Laboratory Corporation of America**
- **Mayo Clinic Laboratories**

Methods

- **Initial antigen/antibody tests**
  - ARCHITECT HIV Ag/Ab Combo (4 laboratories)
  - ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay (2 laboratories)
- **HIV-1/HIV-2 antibody differentiation test**
  - All labs used Geenius (before gp140 HIV-2 envelope band cut-off was increased).
- **Nucleic acid test**
  - APTIMA HIV-1 RNA Qualitative Assay (3 laboratories)
  - Abbott RealTi*me* HIV-1 assay (1 laboratory)
  - Roche Cobas AmpliPrep / Cobas TaqMan HIV-1 Test, version 2.0 (2 laboratories)

Methods

- **Positive predictive value of HIV-1 and HIV-2 reactivity with Geenius**
- **Interpreting results**
  - We collected information on how laboratories report test results that are HIV-1 positive with an HIV-2 indeterminate band pattern to providers.

Results

Final Algorithm Results	*n*	%
Total Specimens	5,046,684	
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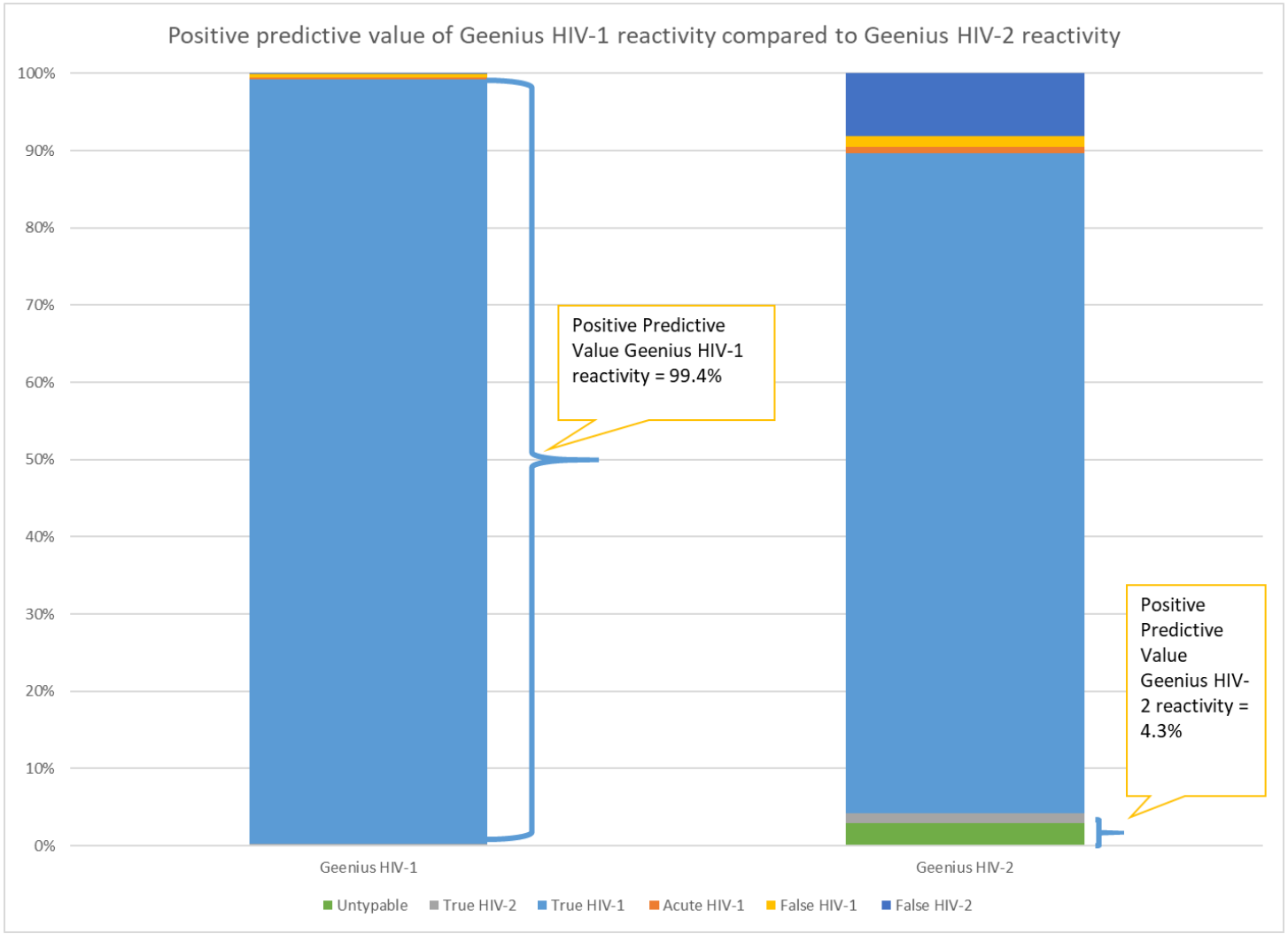
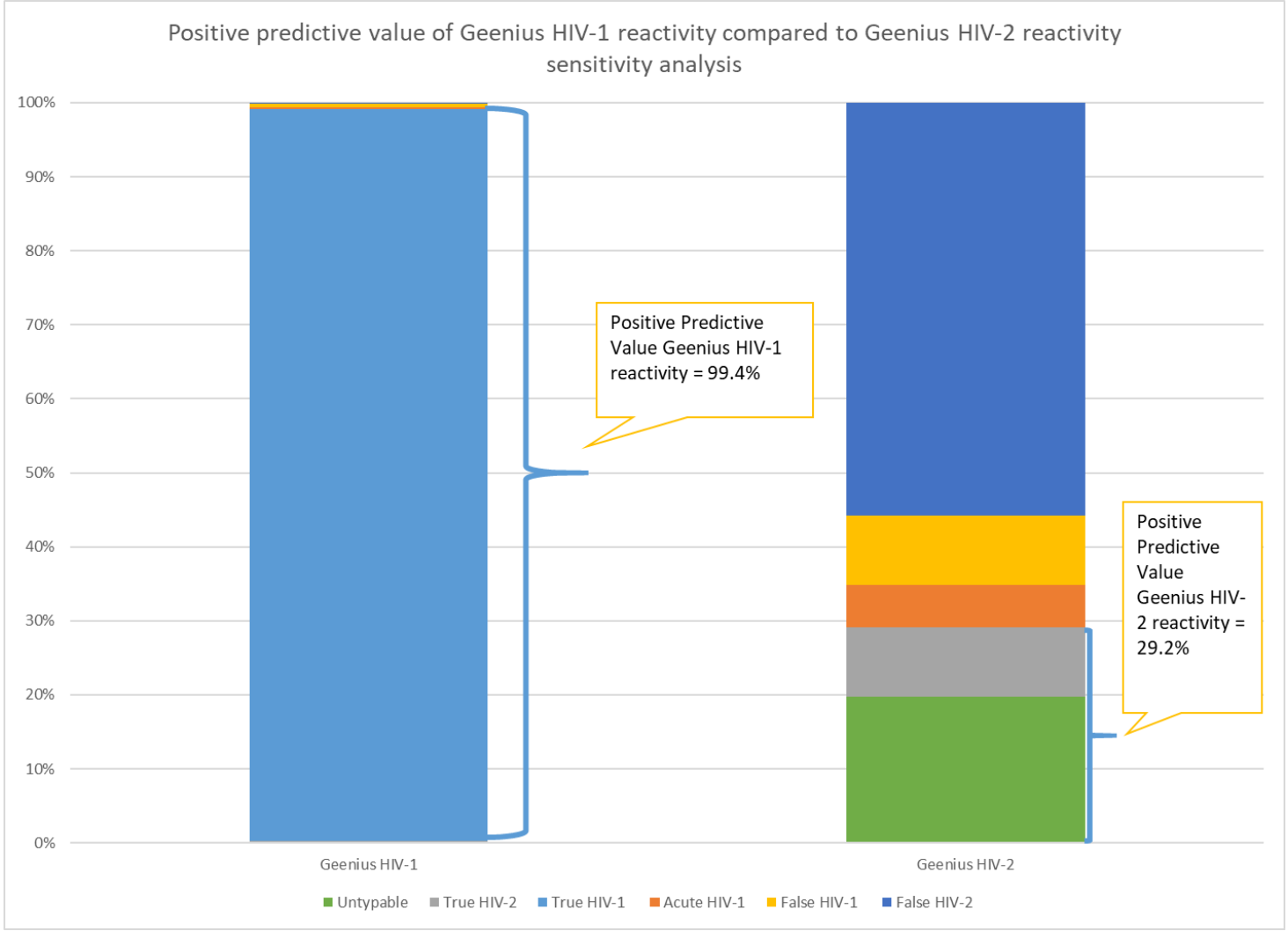
Ag/Ab test false positive	7,505	0.15
False Ag/Ab positive, Geenius indeterminate results	363	0.01


Positive predictive value of Geenius HIV-1 reactivity compared to Geenius HIV-2 reactivity
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Positive Predictive Value Geenius HIV-1 reactivity = 99.4%
Positive Predictive Value Geenius HIV-2 reactivity = 4.3%
Geenius HIV-1
Geenius HIV-2
Untypable
True HIV-2
True HIV-1
Acute HIV-1
False HIV-1
False HIV-2


Positive predictive value of Geenius HIV-1 reactivity compared to Geenius HIV-2 reactivity sensitivity analysis
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Positive Predictive Value Geenius HIV-1 reactivity = 99.4%
Positive Predictive Value Geenius HIV-2 reactivity = 29.2%
Geenius HIV-1
Geenius HIV-2
Untypable
True HIV-2
True HIV-1
Acute HIV-1
False HIV-1
False HIV-2

Results

- **Reporting results to the provider**
  - Geenius final assay interpretation of HIV-1 positive (with HIV-2 indeterminate band)
    - 4 laboratories reported the result as HIV-1 positive.
    - 2 laboratories reported it as HIV-1 positive and HIV-2 indeterminate.
      - 1 indicated HIV-1 RNA testing was not needed.
      - 1 indicated HIV-2 RNA or DNA testing is needed if the person was at risk for HIV-2.

Discussion

- HIV-1/HIV-2 antibody differentiation testing resulted in few HIV-2 antibody-positive results (<0.01%).
- Differentiating HIV-1 and HIV-2 at the 2nd step complicates the algorithm and result interpretation, given the number of Geenius results and ambiguous test results that require additional testing.
- HIV-2 indeterminate bands in specimens with a final Geenius assay interpretation of HIV-1 positive were more common than true HIV-2.
- If HIV-1 and HIV-2 results are reported without a final assay interpretation, it may cause confusion and lead to unnecessary testing for HIV-2.

Discussion

- **Almost 900 specimens lacked the NAT to determine if they were acute.**
  - Two labs with greatest occurrence required separate plasma specimen for NAT.
- **One lab changed from APTIMA to a quantitative NAT.**
  - Dual qualitative and quantitative-use HIV NATs are needed, like Hepatitis C.

Limitations

- Follow-up HIV test results were not available.
- The analysis was conducted by specimen, not person.
- We were not able to de-duplicate by person; would still expect a low rate of HIV-2 infections.
- We were not able to reanalyze the rate of false HIV2 results using the new gp140 cutoff.

Conclusions

- The laboratory testing algorithm was implemented successfully with Geenius.
- Few HIV-2 infections were identified as a result of HIV-1 and HIV-2 differentiation occurring at the 2nd step in the algorithm.
- Numerous testing algorithm outcomes may cause provider confusion.
- Differentiating HIV-1 from HIV-2 at algorithm's 2nd step should be reconsidered.
- Alternative strategies are needed to expeditiously identify HIV-1 infections (e.g., HIV-1 NAT at 2nd step).

Disclaimer

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Questions?

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