Evaluation of the Alternative Algorithm for HIV Diagnostics among Men who have Sex with Men (MSM) in five US cities - 2011

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The views expressed in this presentation are those of the authors and do not necessarily represent those of the Centers for Disease Control and Prevention.
New FDA-approved assay that detect HIV infection earlier than WB raised the need for alternative algorithms to improve accuracy of HIV diagnosis.

A1: Sensitivity HIV-1/2 immunoassay
(eg. 4th generation Ag/Ab Assay)

A1 (+)

A1 (-) Negative for HIV-1 and HIV-2 Ab (and p24 Ag)

HIV-1/HIV-2 differentiation IA (IgG)

HIV-1 Ab+
Initiate care
Viral Load

HIV-2 Ab+
Initiate care

HIV-1 & -2 Ab -
NAT

NAT (+) Acute HIV-1 infection
initiate care

NAT (-) Negative for HIV-1

HIV-2 NAT
Improved sensitivity of alternative algorithms (AA) for acute HIV infections (AHI)

- 3rd/4th gen immuno assays (IAs) +6 rapid tests (RT)+ Nucleic Acid testing (NAT): 103-134 vs. WB: 56 ($p<0.0001$)
- Use of RT decrease turn around time -> faster initiation to care

AA correctly classifies established infections

- Comparable results to Western blot (WB)-based algorithm
- Sensitivity 99.3 - 100.0% (3rd/4th gen IAs+4 RTs+ NAT)
- Specificity 100.0%

AA in established infections and blood donors

- Sensitivity of algorithm 99.95% (NAT)
- Specificity of 100.00%

¹Masciotra S et al; ²Wesolowski L et al
Update on HIV Diagnostic Testing Algorithms II

- Evaluation of FDA-approved 4th generation assays\(^3,4\)
  - reduced diagnosis window -> greater number of HIV detected
- Regardless of the screening test and RT used the AA correctly classified the infection status in a high-risk population\(^5\)
- AA decreases the number of indeterminate results and detects HIV-2 infections\(^6,7\)

\(^3\)Bentsen C. et al; \(^4\)Chavez P. et al; \(^5\)Delaney K et al; \(^6\)Styer L. et al; \(^7\)Torian L. et al
Objectives

- To evaluate the performance of the alternative algorithm with plasma specimens collected among MSM in 5 US cities in 2011
- To compare the alternative algorithm with the different site-specific testing algorithms
Materials and Methods

- **NHBS pilot study in 5 cities in the US-2011**
  - National HIV Behavioral Surveillance Survey (NHBS)
  - MSM enrolled using venue-based, time-space sampling
  - **HIV screening** by RT in 4 sites
  - 309 whole blood tubes within 48 hs to CDC lab -> “fresh plasma”
  - 836 Frozen plasma (4 sites)
  - NHBS database
    - HIV results from field, self-reported HIV and ARV status

- **At CDC 992 plasma specimens were tested**
  - Screening **GSHIV-1/2 Combo Ag/Ab IA**
  - RR specimens tested with **Multispot**
  - 4th gen- non reactive and discordant specimens tested by **APTIMA**
## Site WB-based testing algorithms

<table>
<thead>
<tr>
<th>Site</th>
<th>Screening RT</th>
<th>Confirmatory Specimen</th>
<th>Screening test in lab</th>
<th>Confirmatory test in lab</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OraQuick Advance (OF)</td>
<td>Blood</td>
<td>GS HIV-1/HIV-2 Plus O (Bio-Rad)</td>
<td>HIV-1 WB (Bio-Rad)</td>
</tr>
<tr>
<td>2</td>
<td>OraQuick Advance (OF)</td>
<td>OF</td>
<td>Not performed</td>
<td>HIV-1 WB (OraSure)</td>
</tr>
<tr>
<td>3</td>
<td>OraQuick Advance (fingerstick)</td>
<td>DBS</td>
<td>GS HIV-1/HIV-2 Plus O (Bio-Rad) Validated protocol</td>
<td>HIV-1 WB (Bio-Rad)</td>
</tr>
<tr>
<td>4</td>
<td>OraQuick Advance (OF)</td>
<td>OF</td>
<td>GS HIV-1/HIV-2 Plus O (Bio-Rad) Validated protocol</td>
<td>HIV-1 WB (OraSure)</td>
</tr>
<tr>
<td>5</td>
<td>Not performed</td>
<td>Blood</td>
<td>GS HIV-1/HIV-2 Plus O (Bio-Rad)</td>
<td>HIV-1 WB (Bio-Rad)</td>
</tr>
</tbody>
</table>

*OF: oral fluid; DBS: dried blood spot*
Results
Alternative algorithm results – CDC
26% HIV overall prevalence among MSM

- 992 plasma
- GSHIV Combo Ag/Ab IA
- 255 RR
- Multispot
- 1 NR
- APTIMA

- 737 NR
- APTIMA
- 736 neg
- 1 Positive AHI

- 1 Positive AHI
- 255 HIV-1 infections were detected
- No HIV-2 infections were detected by Multispot
- One AHI was identified by NAT only

RR: repeatedly reactive
R: reactive
NR: non reactive
Comparing algorithms results

- No significant differences between CDC and sites algorithms
- Specimens were missed at screening by OF testing with Oraquick Advance (OF-OQ)
- One acute HIV infection was missed by Ag/Ab testing
Specimens were misclassified by supplemental testing with WB

One acute HIV-1 infection was missed by a WB-based algorithm
Summary of missed specimens by site-specific algorithms

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of specimens missed at</th>
<th>Specimen type</th>
<th>Self-reported HIV status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RT screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>OF</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>OF</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>OF</td>
<td>2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>blood</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>WB confirmation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>OF</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>10 IND</td>
<td>OF</td>
<td>10&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>2 NEG</td>
<td>blood</td>
<td></td>
</tr>
</tbody>
</table>

- Overall 19 infections were missed by site-specific algorithms
  - significant difference ($p<0.0001; McNemar's Test$)
- <sup>a</sup> 2 WB IND
- <sup>b</sup> 8 WB IND and 2 WB NEG on anti-retroviral therapy
Conclusions

Proposed alternative algorithm:

- **performs well in high-risk population (MSM)**
- overall significantly detected more infections than site-specific algorithms
- most discrepancies with site-specific algorithms associated with initial or supplemental OF testing
- increased the number of individuals with reactive results during early infection
- should reduce turn-around time and facilitate linkage to care
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