Efficacy of 4th generation HIV screening algorithm in detecting acute HIV infection and the utility of Abbott Architect signal-to-cutoff ratio in that regard

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Session D: CDC/APHL Laboratory Testing Algorithm (Part 2)
Presentation D1, 3:00 PM – 3:15 PM
PART 1:

Efficacy of 4th generation HIV screening algorithm in detecting acute HIV infection
Background

• Harris Health System: the publicly funded healthcare system in the Houston area consisting of 3 hospitals and 29 outpatient primary care and same day clinics

• Routine Universal Screening for HIV (RUSH) program in place since 2008

• Patients ≥16 receiving blood draw for other reasons are tested for HIV unless they opt out

• Over 585,000 tests have been performed yielding 1316 new diagnoses (0.22%)

• Transition to revised CDC HIV testing algorithm:
  • In February 2014, switched to Abbott Architect 4th generation screening, with Western blot as confirmatory test
  • In October 2014, switched confirmatory assay to BioRad Multispot, with reflex to Roche HIV-1 viral load (VL) when screen positive and Multispot negative
Methods

• Retrospective cohort study of all results of HIV tests performed between February 2014 and October 2015
• Evaluated the yield in detecting acute infections
• Testing data extracted from lab reports and the Electronic Medical Records (EMR)
• “New” diagnoses confirmed in collaboration with the City of Houston Department of Health
• “Acute” diagnoses defined as screen positive, confirmatory negative, HIV VL positive >10,000 copies/mL within 30 days of the initial test
• “False Positive” defined as screen positive, confirmatory negative, undetectable HIV VL within 30 days of the initial test
**4th Generation HIV Tests Performed**
(February 2014 – October 2015; N = 198,726)

- **Tests With a Positive Initial Screening Result** (N = 3073)
  - Positive Confirmatory (chronic infection) *: 1869 (61%)
  - Negative Confirmatory **: 3343 (1.5%)
  - Indeterminate Western Blot: 883 (29%)
  - No Confirmatory (known positive): 301 (10%)

**Tests With a Discordant Confirmatory Result** (Positive Screening, Negative Confirmatory; N = 301)

- Undetectable VL (False Positive): 102 (34%)
- VL>10,000 (Acute Infection): 155 (52%)
- VL<=10,000 but detectable (Further tests needed*): 43 (14%)
- No VL Available within 30 days: 1

*Upon further tests this case was confirmed acute*
Yield of the Algorithm for positive screens not known to be positive in our system

• Following the revised algorithm, 44 tests were consistent with acute HIV infection:

  ✓ 22.1% of discordant cases (with a VL)
  ✓ 2.01% of positive tests*
  ✓ 0.022% of all tests

• There were also 155 tests consistent with a false positive screening result:

  ✓ 77.9% of discordant cases (with a VL)
  ✓ 7.08% of positive tests*
  ✓ 0.078% of all tests

*Denominator includes positive screens not known to be positive in our system
Summary of Part 1

• The 4th generation HIV screening test with antibody confirmatory testing and HIV VL for discordant results was successful in identifying acute HIV infections.

• The diagnosis of acute HIV infection in a universal screening program is rare, and false positive screening results are more common than diagnoses of acute HIV infection (4:1).

• Procedures need to be revised so that samples for viral load testing are readily available to discriminate false positive results from acute HIV infection.
PART 2:

Can Abbott Architect signal-to-cutoff ratio predict acute HIV infection?
Background and Methods

- Literature suggests that the signal-to-cutoff ratio (SCR) reported by Abbott Architect could predict subsequently confirmed HIV infection*
  - Cut-point of 151 has been suggested as 100% positive predictive value and 67% sensitivity for detecting HIV infection; SCR data not reported for detecting acute HIV infection.
  - We evaluated whether SCR could predict acute infection
  - We extracted signal-to-cutoff ratio via manual data collection from logbooks for a subset of tests performed on the Architect machine in one of the hospitals (967 of the positive screening tests)
  - Per Abbott Architect manual:
    - ✓ Specimens with SCR values < 1.00 are considered nonreactive (therefore not in the logs)
    - ✓ Specimens with SCR values ≥ 1.00 are considered reactive (included in this study)

*Kim et al. 2010; Jensen et al. 2015
Distribution of the SCR values

Number of Cases

Signal Cutoff Ratio (Abbott Value)

False Positive  Chronic Previously Diagnosed  Chronic New Dx  Acute
SCR by Diagnosis Type

Signal-to-Cutoff Ratio

Acute
N=23

False Positive
N=99

Chronic New Dx
N=300

Chronic Prev Dx VL < 200
N=78

Chronic Prev Dx VL ≥ 200
N=209

Chronic Prev Dx No VL
N=238
Positive Predictive Value Vs. SCR

- Acute
- Chronic+Acute
Suggested cut off values miss acute infections

• In a recent study\(^1\), an SCR of ~151 was shown to have a 100% positive predictive value (PPV) and 67.4% sensitivity for detection of subsequently confirmed HIV infections.

• Our data confirms those findings for chronic cases; in fact in our data, an SCR of 37 had a 100% PPV and 95.8% sensitivity for chronic cases.

• However, either of those thresholds would miss all or most of acute infection cases.

Summary of Part 2

• SCR for positive screens ranged between 1.05 to 1313

• Confirmed chronic HIV infection produced markedly higher SCR compared to acute infection

• No significant difference in SCR between chronic infections that were new diagnoses and those that had a prior diagnosis regardless of VL

• Significant overlap in SCR between cases of acute HIV infection and false positive screens

• A high SCR result (>37 in this dataset) for the Abbott Architect screening test predicts HIV infection but a low value does not rule-out acute HIV infection, and nucleic acid-based testing is required.
Thank you!

• Project RUSH is a collaborative effort between various parts of Harris Health System and the City of Houston Department of Health and Human Services.

• The project has received funding among other sources from the CDC, Texas Department of State Health Services, and Gilead’s HIV FOCUS program.
Extras
Revised CDC HIV Screening Algorithm*

**HIV-1/2 antigen/antibody combination immunoassay**

- **(+)**: Negative for HIV-1 and HIV-2 antibodies and p24 Ag
- **(-)**: HIV-1/2 antibody differentiation immunoassay

- **HIV-1 (+)**: HIV-1 antibodies detected
- **HIV-2 (-)**: HIV-2 antibodies detected
- **HIV-1 (-)**: HIV-1 antibodies detected
- **HIV-2 (+)**: HIV-2 antibodies detected
- **HIV-1 (+)**: HIV antibodies detected
- **HIV-2 (+)**: HIV antibodies detected

**HIV-1 (-) or indeterminate HIV-2 (-)**

**HIV-1 NAT**

- **HIV-1 NAT (+)**: Acute HIV-1 infection
- **HIV-1 NAT (-)**: Negative for HIV-1

*Branson et al., 2014*
## Indeterminate Western Blot tests (N = 20)

<table>
<thead>
<tr>
<th>Test #</th>
<th>VL</th>
<th>Signal-to-Cutoff Ratio</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>20</td>
<td>Likely False Positive</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>151</td>
<td>Chronic, on ARV and virally suppressed</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>1.91</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.91</td>
<td>148</td>
<td>Chronic, on ARV and virally suppressed</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>5.21</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>358000</td>
<td>12.3</td>
<td>Likely Acute</td>
</tr>
<tr>
<td>7</td>
<td>981000</td>
<td>132</td>
<td>Likely Acute</td>
</tr>
<tr>
<td>8</td>
<td>35100</td>
<td>29</td>
<td>Likely Acute</td>
</tr>
<tr>
<td>9</td>
<td>379000</td>
<td>28</td>
<td>Likely Acute</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>11.6</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>72</td>
<td>Chronic, on ARV and virally suppressed</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>8.7</td>
<td>Likely False Positive</td>
</tr>
<tr>
<td>14</td>
<td>20</td>
<td>58</td>
<td>Not sure since a followup Multispot &lt; year later was positive</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
<td>54</td>
<td>Not sure since a followup Multispot &lt; year later was positive</td>
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<tr>
<td>16</td>
<td></td>
<td>1.71</td>
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<tr>
<td>17</td>
<td></td>
<td>8.3</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td></td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>10000000</td>
<td>177</td>
<td>Likely Acute</td>
</tr>
</tbody>
</table>
SCR Ranges

- SCR values for cases of acute HIV infection are overlapping with the False Positive cases making it difficult to separate the two solely by the SCR

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>stdev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>23</td>
<td>1.4</td>
<td>95.7</td>
<td>27.6</td>
<td>31.8</td>
</tr>
<tr>
<td>Chronic (New Dx)</td>
<td>300</td>
<td>6</td>
<td>1256</td>
<td>552.9</td>
<td>281.4</td>
</tr>
<tr>
<td>Chronic (previously diagnosed)</td>
<td>525</td>
<td>4</td>
<td>1313</td>
<td>649.8</td>
<td>260.4</td>
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<tr>
<td>False Positive</td>
<td>99</td>
<td>1.05</td>
<td>36.7</td>
<td>4.03</td>
<td>6.1</td>
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<tr>
<td>Indeterminate Western Blot</td>
<td>20</td>
<td>1.3</td>
<td>177</td>
<td>48.3</td>
<td>57.3</td>
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<tr>
<td><strong>OVERALL</strong></td>
<td>967</td>
<td>1.05</td>
<td>1313</td>
<td>526.4</td>
<td>329.4</td>
</tr>
</tbody>
</table>
Time since Original Dx Vs. SCR
Viral Load Vs. SCR

![Graph showing the relationship between Abbott Value and Average Viral Load](image-url)
ROC Curves

**ACUTE**

Area under the curve: 0.845

**ACUTE + CHRONIC**

Area under the curve: 0.995