Performance of the NJ Rapid 4th Generation POC Testing Algorithm - New Jersey -

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Why an RTA?

1. In low prevalence areas, false positive HIV screens are common and adversely impact effective use of clinic time, physician and laboratory resources.
2. In NJ, clients not linked to care rapidly (within the first 3 months, commonly do not enter system for YEARS!)
3. Prior to the use of an RTA in NJ >7% would refused a confirmatory Western blot & simply drop off the radar.
4. An RTA is not the same as a confirmatory assay.
5. A ‘presumptive positive’ assumes there will be a physician follow-up and additional testing will occur.
The Value of an RTA

1. Credibility
   - False Positive referrals are reduced in number
   - Clients see their tests turn positive twice and usually directly in front of them –
   - Clinicians can better trust referrals and benefit from the reduced number of false positive screens they end up working up
   - Linkage to care is expedited!
   - It is cost effective!

2. Presumptive Positives are reportable. CDC Surveillance - 2011
2008 – The first NJ RTA – 24 sites

- Not new or novel  - WHO recommended this approach years ago for countries in which the prevalence of HIV exceeds 10% for a number of years
- In 2008 sites, we validated this approach for sites with a 2% or lower prevalence
  
  - Introduced RTA screening at 24 sites in NJ
  - Did not eliminate Western blot confirmation BUT the RTA did provide the basis for expedited linkage into care!

HIV-1/2 Rapid HIV Test (Blood) STAT-Pak  
Or  
HIV-1/2 Rapid HIV Test (Oral) Oraquick

Second Rapid  
(Trinity Unigold HIV-1 Fingerstick)

A1+  

A1-  
Negative for HIV-1/2 Ags

A2+  
Presumptive positive for HIV-1 or HIV-2 antibodies:  
Requires medical follow-up → LINKAGE TO CARE  
Requires definitive western blot testing

A2-  
Inconclusive rapid test result:  
Requires additional testing
Predictive Value as a Function of Return for Results

HIV Prevalence

New Jersey HIV Prevalence at CTS centers

Positive Predictive Value

HIV Prevalence

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%

NJ - 70% get results
Standard PPV
Evolution of the RTA and the Introduction of 4th gen. screening in New Jersey

- HIV Antibody with Confirmatory Western Blot (2004-2011)
- Presumptive Confirmation 2012-2015 - (Rapid-Rapid) - 2 test RTA

- 2004
  - Rapid HIV testing with REQUIRED Western Blot Confirmation

- 2008
  - A two-test RTA implemented at 24 NJ sites beginning in Dec 2008.
  - Confirmed by Western Blot

- 2012
  - January 12, 2012 Letter from CDC eliminating Western blot at existing NJ RTA locations
  - Approval of R2R testing at two licensed NJ DHSTS sites

- 2014
  - December 2014 - CLIA waiver approved for a 4th generation rapid HIV1/2 screening test: (Determine Combo (DC)) -

- Dec 2015
  - Determine Combo implemented @ 166 sites
  - Orthogonal testing available on site or at a nearby clinical site (Rapid-Rapid or Rapid-2-Rapid)

2011-2015 – A Focus on Linkage

- Address issues identified as barriers to linkage:
  1. We needed to: Identify-refer-enroll and retain clients
     - Added sites to improve HIV screening access
  2. Allow use with a 4th generation rapid test
     - Modified our NJ RTA to facilitate linkage
  3. With the help of specially trained Patient Navigators we link screen positive clients rapidly into care within 2 days!
Optimistic Hopes

1. An expedited referral system that might lay the groundwork for rapid entry into care
2. Use a modified Rapid Testing Algorithm to avoid saturating limited clinician availability with falsely positive referrals from a screening assay
3. Employ a more sensitive HIV rapid test with an ability (?) to screen for acute HIV infections from a fingerstick
A Long Way... But Not Enough...

Rapid Followed by Western Blot 2004

- Confirmed W blot POS: 326
- Results Reach Client: 244
- Did NOT Receive Results: 82
- NAP notified: 47
- Results Reach Client thru NAP: 11

Rapid Test Algorithm (2009-2014)

- Prelim. Pos.: 2057
- Unigold Confirm: 1925
- Unigold Refusal: 1047
- Same Day Connect Care: 1555
- 30 Day Linkage: 30 Day
Expanded HIV Screening Locations - NJ

- 102 RWJ Licensed sites (includes 87 stationary sites and 14 mobile vans)
- 64 Non RWJ sites - Hospitals, etc.

166 Total sites

- 83 are Rapid-Rapid Testing sites (incl. Mobile Vans)
- 83 sites perform a single Rapid test and verify by a Rapid-2-Rapid (Confirmation & Linkage) strategy

- COMMUNITY BASED ORGANIZATIONS: 18
  - MOBILE VANS: 11
- CORRECTIONS: 4
- FQHC: 24
  - MOBILE VANS: 1
- HEALTH DEPARTMENTS: 18
  - MOBILE VANS: 4
- UNIVERSITY: 4
- HOSPITALS: 8
- FAMILY PLANNING: 17 - not under RWJMS licensure

- ADDICTIONS: 21 Sites: 20 + 1 mobile counselor serving 6 sites
Alere Determine Ag/Ab Combo

- Tests for the simultaneous and separate qualitative detection free HIV-1 p24 antigen and antibodies to both HIV-1 and HIV-2.
The Range of HIV Sensitivity – Screening to Diagnosis

Sequence of Assay Reactivity Plasma

Single NAT: Aptima ~9-11 Days after infection

Implementation: Determine Combo

<table>
<thead>
<tr>
<th>Product</th>
<th>Volume (2015)</th>
<th>POS</th>
<th>Seroprevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>StatPak</td>
<td>47,091</td>
<td>366</td>
<td>0.75%</td>
</tr>
<tr>
<td>Determine</td>
<td>40,391</td>
<td>352</td>
<td>0.78%</td>
</tr>
</tbody>
</table>
The NJ Rapid Test Algorithm - 2015

MODIFIED FOR USE WITH A 4TH GEN. RAPID HIV TEST
Determine Combo HIV1/2 EIA

NEG

PRELIM POS

DC p24 Ag +

Can we confirm the presence of HIV Ab?

DC Antibodies +

Trinity UniGold

HIV-1 +/ HIV-2 -
HIV-1 antibodies detected and confirmed

NEG

To a DISCORDANT workup

Link to Care with CD4 and Viral Load at Point of Care

DISCORDANT WORKUP

• Immediate quant. RNA viral load
• 4th Gen. lab based with reflex to MS and/or Aptima if necessary

PRELIM POSITIVE FORM submitted characterizing whether p24Ag+/HIV1/2 Abs and lot numbers for both rapid tests.
Determine Combo - 2015 - NJ Rollout:
Volume - Prelim. Pos. - Discordant Frequency
IS SUES W ITH IM PLEM EN TAT I ON

DEVIL IS ALWAYS IN THE DETAILS!

- OPERATORS – Learning Curve.. How fast do operators move through it? Importance of our technical liaisons!
- Small details can be very important...e.g. transfer pipets!
- TEST DEVICES – How are they functioning?
- NEW PROCEDURES – How are we adapting?

EXPER TATTIONS:

1. **SHORT TERM** increase in the number of discordant results observed
2. Modest Increase in the number of identified HIV Ab+ specimens
3. Uncertain whether we would see HIV p24Ag+ fingerstick specimens
SUMMARY DATA – RTA 2015 DC

- DC Ab+/UG + Reported by clinic
  - POS: 0
  - NEG: 1

- DC Ab+/UG -
  - POS: 6
  - NEG: 25

- DC Ag+
  - POS: 1
  - NEG: 11

- DC Ag+/Ab+/UG -
  - POS: 0
  - NEG: 5

DISCORDANT WORKUP

1. Immediate Quantitative RNA viral load
2. 4th Gen. HIV Comb Immunoassay
   - Auto reflex to MultiSpot if POS
   - and/or Aptima if MS NEG

WHY?

- Our reference facility – Quest performs a quantitative RNA viral load with a 20 copy/mL detection limit on an original plasma specimen
- The Aptima is a ‘pour off’ specimen sent to another state – (Chantilly, VA).
- Delays & mislabeling occur
# Discordant Analysis - 2015 - New Jersey

## Clearview StatPak 2015

<table>
<thead>
<tr>
<th>StatPak</th>
<th>47,091</th>
<th>366 POS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Marker</strong></td>
<td><strong>Frequency</strong></td>
<td><strong>Notes</strong></td>
</tr>
<tr>
<td>True POS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP/FN UG</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>True POS</strong></td>
<td><strong>TOTAL: 1</strong></td>
<td></td>
</tr>
<tr>
<td>False POS</td>
<td>FP Ab</td>
<td>10</td>
</tr>
<tr>
<td>False POS</td>
<td>FP Both Rapids</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>12</strong></td>
</tr>
</tbody>
</table>

## Determine Combo 2015

<table>
<thead>
<tr>
<th>Determine</th>
<th>40,391</th>
<th>352 POS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Marker</strong></td>
<td><strong>Frequency</strong></td>
<td><strong>Notes</strong></td>
</tr>
<tr>
<td>True POS</td>
<td>P24 Ag +</td>
<td>1</td>
</tr>
<tr>
<td>True POS</td>
<td>TP/FN UG</td>
<td>6</td>
</tr>
<tr>
<td><strong>True POS</strong></td>
<td><strong>TOTAL: 7</strong></td>
<td></td>
</tr>
<tr>
<td>False POS</td>
<td>FP Ab</td>
<td>25</td>
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<tr>
<td>False POS</td>
<td>FP Ag</td>
<td>11</td>
</tr>
<tr>
<td>False POS</td>
<td>FP Ag/Ab</td>
<td>5</td>
</tr>
<tr>
<td>False POS</td>
<td>FP Both Rapids</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>41</strong></td>
</tr>
</tbody>
</table>
Determine Combo

DISCORDANT SUMMARY: New Jersey

<table>
<thead>
<tr>
<th>2015</th>
<th>HIV INFECTED</th>
<th>NON INFECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITIVE</td>
<td>311</td>
<td>41</td>
</tr>
<tr>
<td>NEGATIVE</td>
<td>Est.¹ (14-24¹)</td>
<td>(40,025-40015¹)</td>
</tr>
<tr>
<td></td>
<td>Est. (325-335¹)</td>
<td>(40,066-40,056¹)</td>
</tr>
</tbody>
</table>

**NJ PERFORMANCE** - Determine HIV 1/2 Ag/Ab Combo

Based Upon Estimates of False Negative Rapids From previous Newark Pooled NAAT estimates ¹

- Positive Predictive Value: 88.35%
- Negative Predictive Value: 99.94%-99.97%
- Prevalence of Disease: 0.80% - 0.83%
- Sensitivity: 92.84%-95.69%
- Specificity: 99.90%


Gold Standard: Pooled NAAT
Not yet available for Determ. Combo.

Depends upon the number of false negatives which, in turn, depends on the selected ‘gold standard’.
So far, the performance of p24 Ag marker has been disappointing

- A single, truly positive DC p24Ag+ in 40,391 tests (>10 Million copies/mL)
- Eleven (11) false positive DC p24Ag+

The presence of 6 truly positive discordant, DC Ab+/UG- speaks to the higher sensitivity of the antibody marker which would express itself through False Positive Ab Discordants that would later be found to be truly positive. The True Pos yield of the 4th gene RTA compared with the performance of the 2nd gen RTA supports this observation.

Still needed… A determination of how many positives are actually being missed – and whether this is tied to the failure to disassociate bound Ag+
Summary:

1. We expanded our statewide RTA allowing virtually anyone screened by a single rapid to receive verification and linkage within 2 business days.

2. By verifying false positive screens, we’ve reduced screening ‘noise’ and the unnecessary waste of clinic and physician time to resolve falsely positive screens.

3. We implemented a 4th generation rapid HIV device statewide and characterized the performance of that device relative to the 2nd generation device in use for the past decade in NJ.

4. We conclude that the Determine Combo 4th gen. rapid has:
   - Limited value in identifying the majority of AH1 present in our community.
   - But, the improved antibody sensitivity of the screening device may improve screening yield.
A REMINDER TO US ALL!

IT’S NOT ONLY A QUESTION OF TEST SENSITIVITY, IT’S ALSO QUESTION OF HOW FREQUENTLY WE TEST, HOW EFFECTIVELY WE LINK THOSE WHO ARE AFFECTED INTO CARE, HOW WELL WE RETAIN THOSE IN CARE AND HOW EFFECTIVELY WE RE-ENGAGE CLIENTS LOST TO CARE!