NJ HIV: Status Update

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Professor of Pathology and Laboratory Medicine
Co-Director, NJ HIV
Objectives

1. NJ HIV – An Overview
2. A little bit of history and how much more remains!
3. Some of the themes from the past decade
4. Why and How we’re focusing on earlier stages of an HIV infection
5. Outcomes:
   – Statewide Implementation of 4th Generation Screening
   – Performance of the NJ Rapid Testing Algorithm in 2015 – what did they mean?
6. Next Year:
   – Pooled NAAT availability in Newark
   – Syphilis screening (limited)
7. On the Horizon
A Ten Year Partnership

- In 2004, the Department of Pathology at Rutgers – RWJMS was asked by the Department of Health, to assist with implementation of rapid HIV testing in conjunction with a number of CDC-driven HIV initiatives.
- NJ requires NJ Clinical Laboratory Licensure (CLIS) for many tests which are federally CLIA-waived – including HIV.
- HIV was declared a NJ healthcare emergency allowing us to provide oversight to rapid HIV testing in multiple venues across the state.
- This statewide, centralized approach is important – and unique:
  - Publications
  - Requests for technical assistance by other states,
  - Opportunities to serve on CDC committees and taskforces
  - Requests by manufacturers to assist w/ licensing of new products.
NJ HIV - Rapid Testing Support

RUTGERS - RWJMS

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Co-Director NJ HIV, PI - DHSTS grant

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Co-Director NJ HIV PI - DMHAS MOA

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Aida Gilanchi, BS, MT
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Administration:
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• Karen Williams

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Medical Director, DHSTS

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Assistant Commissioner, DHSTS

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Aye Maung Maung

NJ DHS/DMHAS

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Assistant Commissioner, DMHAS

Adam Bucon, LSW
Office of the Medical Director
ASTHO “VISION” AWARDS – 1\textsuperscript{st} Place

RAPID HIV TESTING PROGRAM
- 2006 -

PATIENT NAVIGATOR PROGRAM
-2013-
RAPID HIV SITES THROUGHOUT NEW JERSEY

- 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

ADDITIONS: 21 Sites: 20 + 1 mobile counselor serving 6 sites
Themes from the decade

1. Making HIV screening broadly available in NJ
2. Linkage and how effectively we link HIV+ into care
3. Credibility in the screening process – RTA(s)
4. How often rapid screening misses early (AHI) infections
5. Implementation of a – 4th gen. rapid statewide
6. Performance of the 4th gen. rapid
7. HIV – HCV Screening
8. COMING 2016-7:
   - HIV – Syphilis Screening
   - Implementation of a Pooled NAAT follow-up of high risk individuals
It's not just a question of how sensitive a test is... it's also a question of how often we test, how effectively we link the affected into care, and how well we retain clients in care...

BACKGROUND & PERSPECTIVE
Optimal Testing, Early Treatment & Improved Adherence.

Annual number of new HIV infections over 20 years for MSM in New York City

Test-and-treat interventions may increase the numbers of patients initiating ART early, BUT without stabilizing the back end of the treatment continuum (i.e., care retention and ART adherence), test-and-treat strategies will fall short of their potential!

Sorenson et al. 2012
http://dx.doi.org/10.1371/journal.pone.0029098
The Range of HIV Sensitivity – Screening to Diagnosis

Why is this Important? Why earlier?

HIV RNA in Semen (Log$_{10}$ copies/ml)

Risk of Transmission Male to Female - Blue
Reflects Genital Viral Burden – Yellow
Effect of ART – Theoretical - Red

(1/30-1/200)

(1/500 - 1/2000)

(1/1000 - 1/10,000)

(1/100 - 1/1000)

Acute Infection  Asymptomatic Infection  HIV Progression  AIDS

Cohen and Pilcher, *Amplified HIV transmission and new approaches to HIV prevention* JID 191:1391, 2005
4th generation – Point of Care

Claims for the Alere Determine™ HIV-1/2 Ag/Ab Combo indicate a higher sensitivity, but a lower specificity than the second generation, rapid HIV tests (StatPak) in use since 2006.

SENSITIVITY: Probability that a test result will be positive when the disease is present = true positive/(true positive + false negative)

SPECIFICITY: Probability that a test result will be negative when the disease is not present = true negative/(false positive + true negative).

-PROBABILITY OF A FALSE POSITIVE-

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Specificity Claim</th>
<th>Expected False Positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLEARIVEW STATPAK</td>
<td>99.9%</td>
<td>3 FALSE POS/10,000 screens</td>
</tr>
<tr>
<td>NJ PERFORMANCE YTD</td>
<td>99.97%</td>
<td></td>
</tr>
<tr>
<td>DETERMINE COMBO</td>
<td>99.8%</td>
<td>20 FALSE POS/10,000 or 80 PER/40,000</td>
</tr>
<tr>
<td>NJ PERFORMANCE YTD</td>
<td>99.92%</td>
<td>8 FALSE POS/10,000 screens</td>
</tr>
</tbody>
</table>
Effective screening IS NOT definitive diagnosis

**DIAGNOSIS**

- **GOAL:** Definitively determine who is affected and who is not
  - Sensitivity of the assay
  - Specificity of the assay
- **No limits**
  - Take however long it takes to arrive at the correct diagnosis.
  - Spare no expense

**SCREENING**

- **GOAL:** Identify who is likely affected and rapidly link them to care for follow-up
  - Minimize unnecessary referrals
  - Maximize the rate of linkage into care
  - Personalize the linkage to keep folks connected
- **Orthogonal confirmation (RTA)**
  - Presumptive diagnosis
  - Minimize missed calls
  - Likely diagnosis (<1:200 are wrong)
NJ Statewide Implementation

4TH GEN. POCT HIV SCREENING
Determine Combo – 2015 – NJ Rollout:
Volume – Prelim. Pos. – Discordant Frequency

- Monthly Test Volume
- Number Positives or Discordants

Legend:
- Test VOL
- Prel. POS
- Disc Freq
Determine Combo HIV1/2 EIA

Can we confirm the presence of HIV Ab?

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

RNA Testing
Implementation: Determine Combo

Rapid HIV Screen Device

<table>
<thead>
<tr>
<th>Month</th>
<th>Stat-Pak (2nd Gen)</th>
<th>Determine Combo (4th Gen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-15</td>
<td>6700</td>
<td>2800</td>
</tr>
<tr>
<td>Feb-15</td>
<td>6500</td>
<td>2600</td>
</tr>
<tr>
<td>Mar-15</td>
<td>6800</td>
<td>2700</td>
</tr>
<tr>
<td>Apr-15</td>
<td>6600</td>
<td>2900</td>
</tr>
<tr>
<td>May-15</td>
<td>6900</td>
<td>2800</td>
</tr>
<tr>
<td>Jun-15</td>
<td>7600</td>
<td>3000</td>
</tr>
<tr>
<td>Jul-15</td>
<td>7500</td>
<td>3000</td>
</tr>
<tr>
<td>Aug-15</td>
<td>7400</td>
<td>2900</td>
</tr>
<tr>
<td>Sep-15</td>
<td>7300</td>
<td>2800</td>
</tr>
<tr>
<td>Oct-15</td>
<td>7200</td>
<td>2700</td>
</tr>
<tr>
<td>Nov-15</td>
<td>7100</td>
<td>2600</td>
</tr>
<tr>
<td>Dec-15</td>
<td>7000</td>
<td>2500</td>
</tr>
</tbody>
</table>

<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>
### DISCORDANT (RTA) 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>Marker</td>
<td>Frequency</td>
<td>Notes</td>
</tr>
<tr>
<td>True POS</td>
<td>TP/FN UG</td>
<td>1</td>
</tr>
<tr>
<td>True POS</td>
<td>TP/FN UG</td>
<td>TOTAL: 1</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>False POS</td>
<td>TOTAL: 12</td>
<td></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>Marker</td>
<td>Frequency</td>
<td>Notes</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>True POS</td>
<td>TOTAL: 7</td>
<td></td>
</tr>
<tr>
<td>False POS</td>
<td>FP Ab</td>
<td>25</td>
</tr>
<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>False POS</td>
<td>TOTAL: 41</td>
<td></td>
</tr>
</tbody>
</table>

**Expected False Pos = 40**

**Expected False Pos = 80**
## Summary: Discordant Workups - 2015

### Summary Data – RTA 2015 DC

<table>
<thead>
<tr>
<th></th>
<th>POS</th>
<th>NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC Ab+/UG+</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>DC Ab+/UG -</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>DC Ag+</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>DC Ag+ Ab+/UG -</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>41</td>
</tr>
</tbody>
</table>

### 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
HOW MANY ARE WE MISSING?

Risk of Transmission Male to Female - Blue
Reflects Genital Viral Burden – Yellow
Effect of ART – Theoretical - Red

HIV RNA in Semen
(Log10 copies/ml)

1/30-1/200

(1/100 - 1/1000)

(1/1000 – 1/10,000)

(1/500 - 1/2000)

Acute Infection
Asymptomatic Infection
HIV Progression
AIDS

Cohen and Pilcher, Amplified HIV transmission and new approaches to HIV prevention JID 191:1391, 2005
# NAAT Testing of Antibody Negative Blood

<table>
<thead>
<tr>
<th>Program</th>
<th>Dates</th>
<th>Description</th>
<th>Rapid Tested</th>
<th>NAAT Tested</th>
<th>AHI</th>
<th>HIV Ab+</th>
<th>% HIV Ab+</th>
<th>% Inc in Yield</th>
<th>% Yield AHI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maryland</strong></td>
<td>6/06-3/08</td>
<td>HIV Ab neg adults seen at two STD clinics (6/06-3/08); multiple venues 7/07-3/08)</td>
<td>58,925</td>
<td>7</td>
<td>1,709</td>
<td>2.90%</td>
<td>0.41%</td>
<td>0.01%</td>
<td></td>
</tr>
<tr>
<td><strong>North Carolina</strong></td>
<td>11/02-10/03</td>
<td>HIV Ab neg persons in North Carolina seeking HIV testing at 110 publicly funded sites (n = 109,250)</td>
<td>108,667</td>
<td>23</td>
<td>583</td>
<td>0.54%</td>
<td>3.95%</td>
<td>0.02%</td>
<td></td>
</tr>
<tr>
<td><strong>Los Angeles</strong></td>
<td>2/04-4/04</td>
<td>HIV Ab neg men seeking HIV testing at three STD clinics (n = 1712)</td>
<td>1,698</td>
<td>1</td>
<td>14</td>
<td>0.82%</td>
<td>7.14%</td>
<td>0.06%</td>
<td></td>
</tr>
<tr>
<td><strong>NEWARK, NJ</strong></td>
<td>2/10 to 1/12</td>
<td>HIV Ab neg adults receiving testing and counseling at two high risk urban hospitals in Newark, NJ</td>
<td>12,390</td>
<td>6,785</td>
<td>116</td>
<td>0.94%</td>
<td>6.90%</td>
<td>0.12%</td>
<td></td>
</tr>
<tr>
<td><strong>Seattle King County</strong></td>
<td>9/03-1/05</td>
<td>HIV Ab neg MSM seeking HIV testing through Seattle-King County (n = 3525)</td>
<td>3,439</td>
<td>5</td>
<td>81</td>
<td>2.36%</td>
<td>6.17%</td>
<td>0.15%</td>
<td></td>
</tr>
<tr>
<td><strong>Atlanta</strong></td>
<td>10/02-1/04</td>
<td>2202 adults receiving HIV testing and counseling at three high risk urban sites in Atlanta, Georgia</td>
<td>2,136</td>
<td>4</td>
<td>66</td>
<td>3.09%</td>
<td>6.06%</td>
<td>0.19%</td>
<td></td>
</tr>
<tr>
<td><strong>San Francisco</strong></td>
<td>10/03-7/04</td>
<td>HIV Ab neg persons seeking HIV testing at San Francisco Municipal STD clinic (n = 3075)</td>
<td>2,722</td>
<td>11</td>
<td>105</td>
<td>3.86%</td>
<td>10.48%</td>
<td>0.40%</td>
<td></td>
</tr>
</tbody>
</table>

*Translation: Anticipate missing 48 in 40,000 screens*
Next Year’s Effort

• Pooled NAAT for HIGH RISK individuals who are Negative by POCT is the Standard of Care in Seattle and San Francisco.
• We will pilot this approach in Newark & Paterson
• Why? Transmission…. Transmission. Transmission!

• What do we anticipate:
  – We hope to pick up fewer AHI’s then in our 2010 study using 2nd gen. screening affirming the improved sensitivity of the Determine Combo
  – Expect that we will not eliminate AHI’s missed by rapid screening
## 2015 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) (14-24)(^1)</td>
<td>(40,025-40015(^1))</td>
</tr>
<tr>
<td></td>
<td>Est. (325-335(^1))</td>
<td>(40,066-40,056(^1))</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 \(^1\)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Positive Predictive Value:</td>
<td>88.35%</td>
</tr>
<tr>
<td>Negative Predictive Value:</td>
<td>99.94%-99.97%</td>
</tr>
<tr>
<td>Prevalence of Disease:</td>
<td>0.80% - 0.83%</td>
</tr>
<tr>
<td>Sensitivity:</td>
<td>92.84%-95.69%</td>
</tr>
<tr>
<td>Specificity:</td>
<td>99.90%</td>
</tr>
</tbody>
</table>


Depends upon the number of false negatives which, in turn, depends on the selected ‘gold standard’.

Gold Standard: Pooled NAAT

Not yet available for Determine Combo.
The Value of a Rapid Testing Algorithm and NJ HIV

1. Credibility.
   - False Positive screenings are reduced in number.
   - Clients see their tests turn positive **twice** and usually directly in front of them.
   - Clinicians can trust our referrals.
   - Linkage to care is expedited!

2. Presumptive Positives are reportable. *CDC Surveillance - 2011*

3. Teamwork.
   - Expertise is available and freely shared.
   - [http://www.njhiv1.org](http://www.njhiv1.org)

   - Technologists are on-site.
   - We check … and we follow-up monthly!

5. Scale Matters.
   - By centralizing our program, we gained serious pricing leverage with our suppliers and multiply our ability to screen (~$7.00 to verify a result).
Reminder!

HIV SCREENING IS NOT A CONFIRMED DIAGNOSIS AND THERE ARE CONFIRMATORY CHANGES COMING IN JULY
Lab Confirmation Changes: Biorad Geenius

- Supplemental Assay: differentiate ANTIBODIES to Human Immunodeficiency Virus Types 1 and 2 in WB, PLASMA OR S
- Analyze results:
  - HIV-1
    - p31 HIV-1 polymerase peptide,
    - gp160 HIV-1 recombinant protein envelope,
    - p24 HIV-1 recombinant protein core, and
    - gp41 Group M and O HIV-1 peptide envelope)
  - HIV-2
    - gp 36 and
    - gp 140 HIV-2 peptide envelope).
- WILL REPLACE THE BIORAD MULTISPOT IN THE CDC LABORATORY TESTING ALGORITHM
- CLIA; MODERATE COMPLEXITY
LABORATORY DIAGNOSTICS

BIORAD GEENIUS SYSTEM – JUNE/JULY 2016

Geenius™ HIV 1/2 Confirm
A Game Changer

Band 4
gp160 (HIV-1, recombinant protein envelope)
HIV-1 ENV

Band 6
gp41 (Group M and O)
(HIV-1, peptide envelope)
GEENIUS CASETTE:
Simultaneous Detection and Identification of Multiple HIV for each sample.

FIFTH GENERATION TESTING
BioPlex® HIV Ag-Ab Assay – Fully Automated Screening: HIV-1 p24 Ag, HIV-1 Ab & HIV-2 Ab

Antibody Mike Leos, William Link, Alfredo Villarreal, Roger Walker
Bio-Rad Laboratories, Inc., 5500 East 2nd Street, Benicia, CA 94510 USA
At San Francisco General they have figured out a way to start Anti-Retroviral Therapy on DAY 1!

ART IN A DAY
Linkage to medical care in ≤ 30 and ≤ 90 days, 2007-2014

Percentage Linked to Care

<table>
<thead>
<tr>
<th>Year</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤90</td>
<td>47.0</td>
<td>63.8</td>
<td>69.4</td>
<td>75.6</td>
<td>74.5</td>
<td>72.5</td>
<td>79.3</td>
<td>84.0</td>
</tr>
<tr>
<td>≤30</td>
<td>35.2</td>
<td>50.1</td>
<td>56.8</td>
<td>63.0</td>
<td>62.2</td>
<td>59.8</td>
<td>66.7</td>
<td>74.0</td>
</tr>
</tbody>
</table>

Median time to linkage

<table>
<thead>
<tr>
<th>Year</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
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<tbody>
<tr>
<td>25th Percentile</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Median</td>
<td>132</td>
<td>30</td>
<td>21</td>
<td>15</td>
<td>16</td>
<td>17</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>75th Percentile</td>
<td>437</td>
<td>166</td>
<td>85</td>
<td>107</td>
<td>116</td>
<td>57</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>
2013 San Francisco General RAPID Protocol

**HIV+ Diagnosis**
- Disclosure
- HIV education
- Counseling
- Referral
- Scheduling

**1st Clinic Visit**
- Registered
- Insurance
- Assess housing, substance use, mental health needs
- HIV education
- Counseling
- Labs

**1st Primary Care Provider Visit**
- Medical evaluation
- Assess preparedness

**ART Start**
- Prescription
- Pharmacy pick-up

**ART Management**
- Viral load monitoring
- Adherence
- Retention

**RAPID Visit: ART Start**
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up

**Primary Care Provider Visits: ART Management**
- Viral load monitoring
- ART management
- Adherence
- Retention
Same Day Medical Visit

- Baseline Lab tests ordered but NOT typically available prior to ART start:

- Pre-approved regimens:
  - Local expert committee decide upon ART regimens that could be used without the results of genotyping or lab testing pre-approved
  - committee reviews local patterns of transmitted drug resistance and drug in light of the low prevalence of transmitted resistane to tenofovir and dolutegravir in SF).
Overview

• Roughly half of their patients end up eligible for RAPID Protocol
• Virtually all began observed ART within 24 hours.
• Toxicity is a minor problem

OUTCOMES

– Loss to Follow-up is similar to delayed treatment
– Time to virologic suppression (<200 copies HIV RNA/mL) is significantly faster compared to patients treated under existing approaches (2 months)

• CONCLUSION: Same Day ART may shorten the time to virologic suppression
THE END