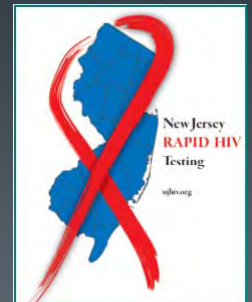


# Newer Technologies and HIV Screening in NJ


Eugene Martin, Ph.D.  
Professor of Pathology & Laboratory Medicine  
UMDNJ - Robert Wood Johnson Medical School

New Jersey HIV/AIDS Planning Group  
Rutgers University - Busch Campus  
Thursday, September 15, 2011



# Key Questions

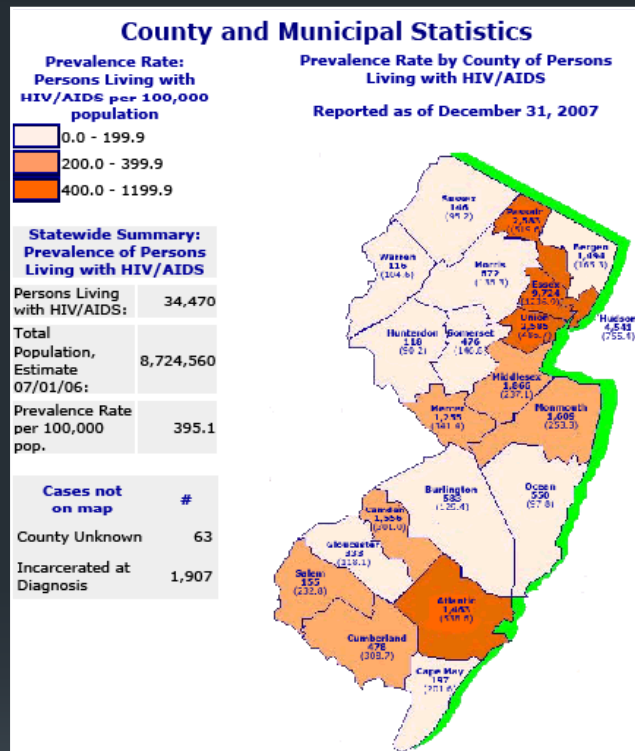
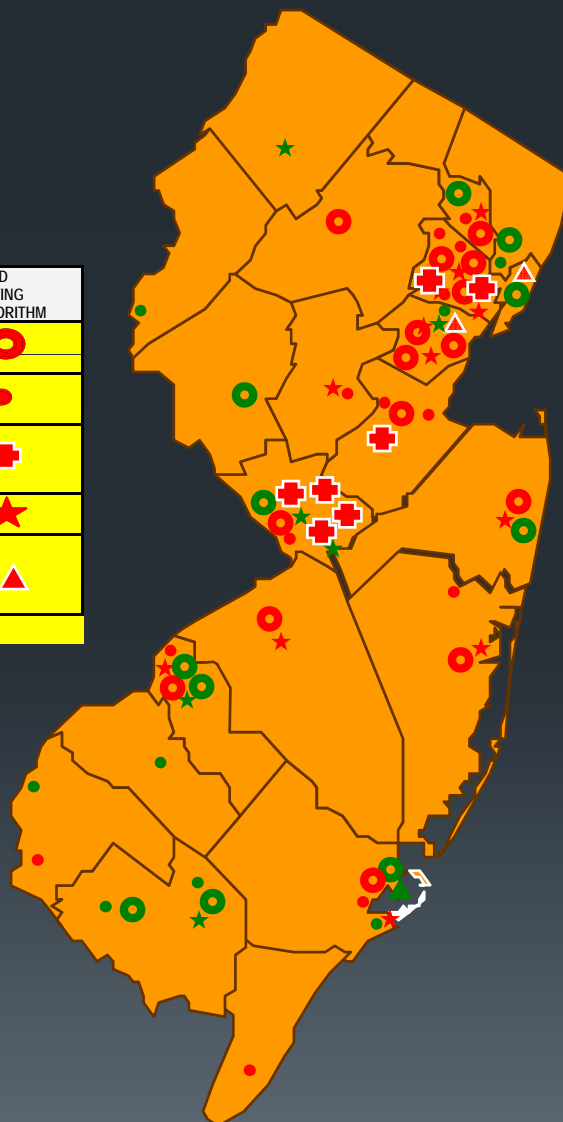
1. What strategies will get more people to learn their HIV status?
2. How do we get more infected individuals into care AND encourage treatment earlier?
3. How does improved ART impact our efforts to reduce transmission?
4. How can we eventually stop the cycle of transmission?



HIV Screening and the Technology  
of Screening is  
**ONLY** part of the answer!

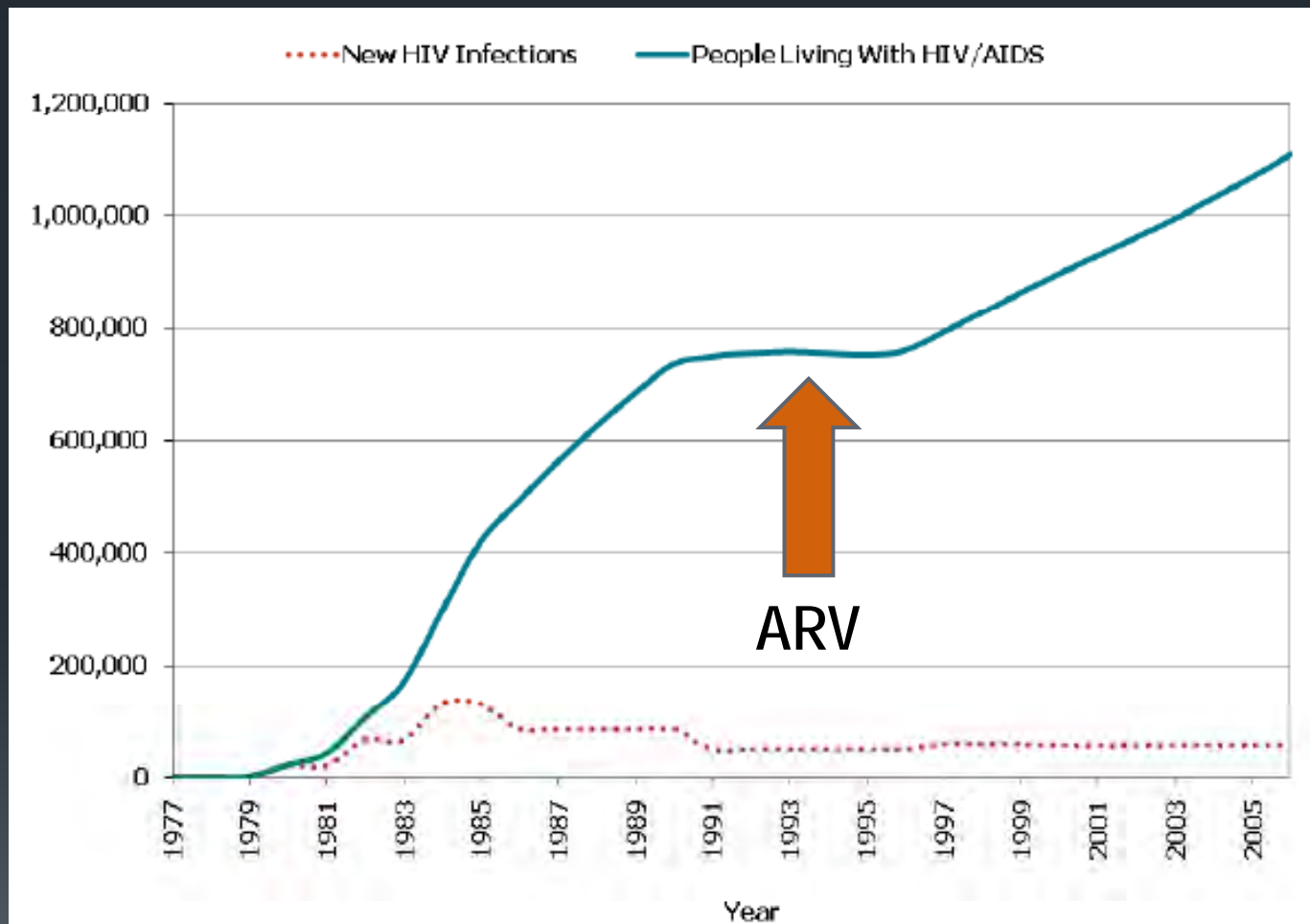
# Placement of Screening Sites – Diversity of Approach

| LEGEND                     | TRADITIONAL | RAPID TESTING ALGORITHM |
|----------------------------|-------------|-------------------------|
| RAPID TESTING PRIMARY SITE |             |                         |
| COMMUNITY BASED ORG. (CBO) |             |                         |
| MEDICAL CTR. ER            |             |                         |
| MOBILE VAN                 |             |                         |
| PRISONS                    |             |                         |



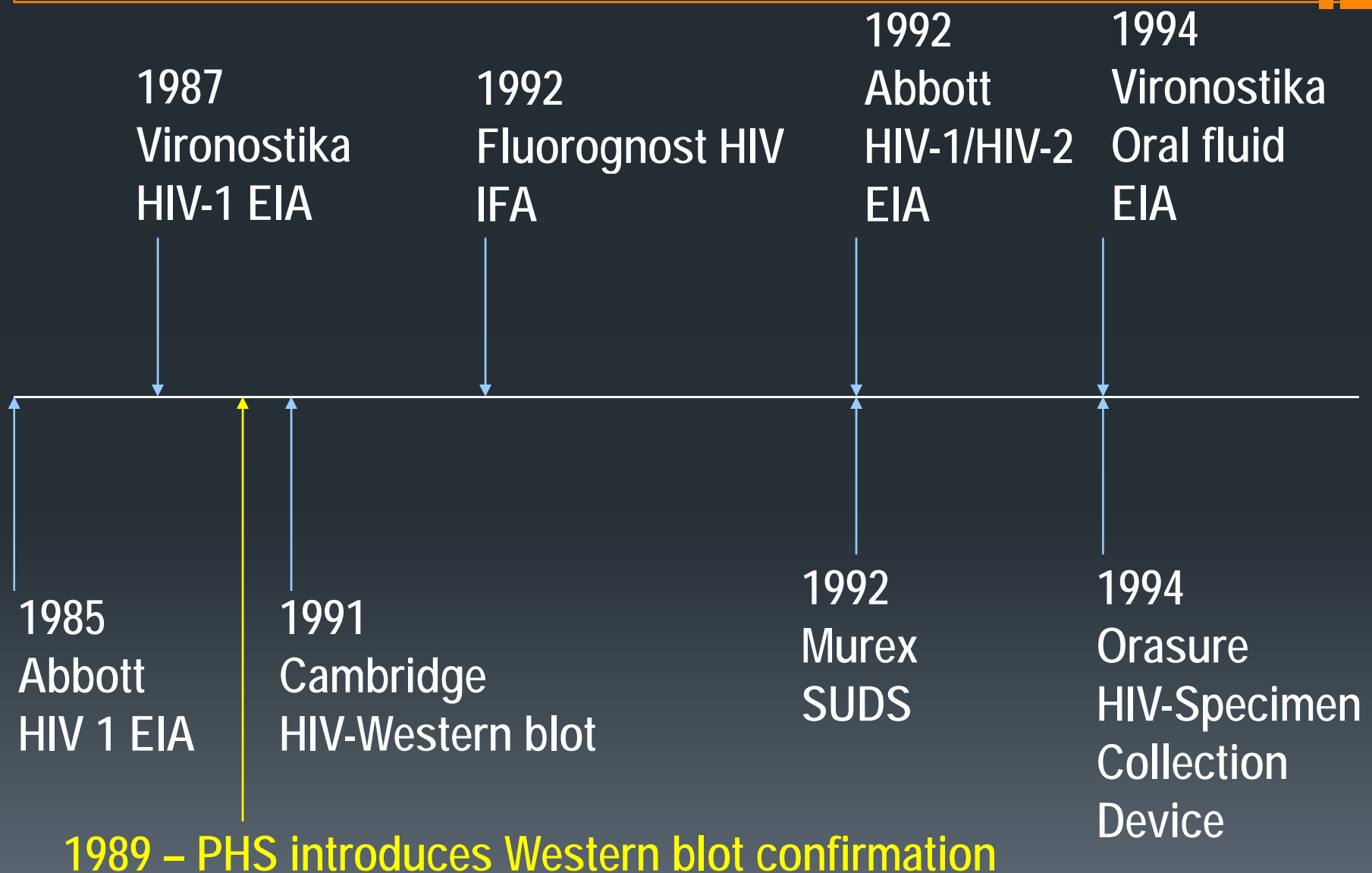
**Note:** Top number indicates number of persons living with HIV/AIDS (HIV Positive Infection or AIDS) as of as of 12/31/2007. Not Included in this number are cases of Perinatal HIV Exposure that are not confirmed HIV Positive. Bottom number in parentheses indicates prevalence rate of persons living with HIV/AIDS per 100,000 population (July 1, 2006 estimate)

# Numbers of Infected Increase



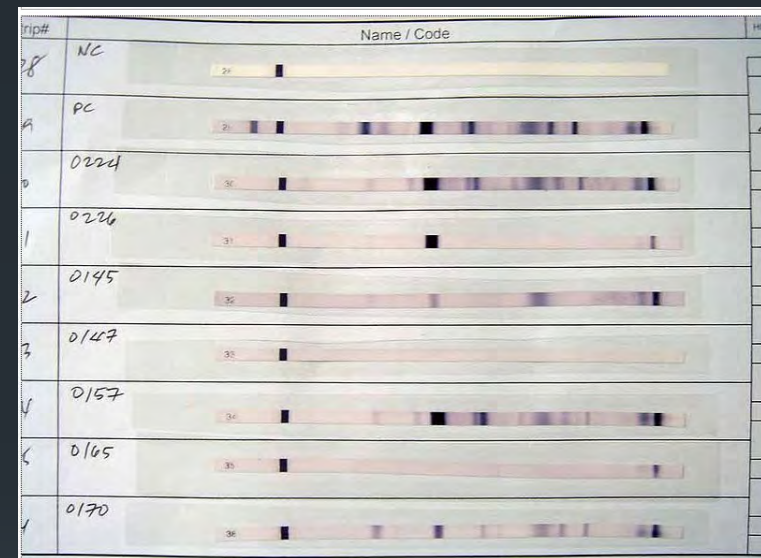
**Transmission is a function of Viral Load!**

# Early Generation HIV Assays

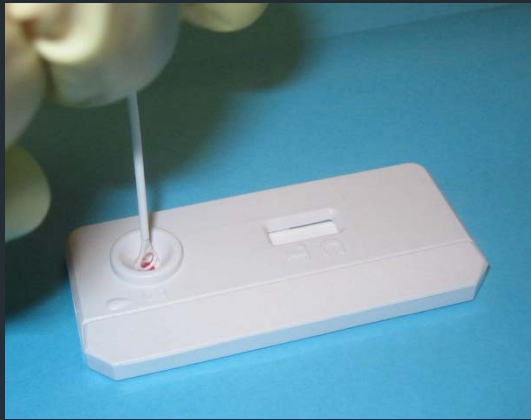


# An HIV Western Blot

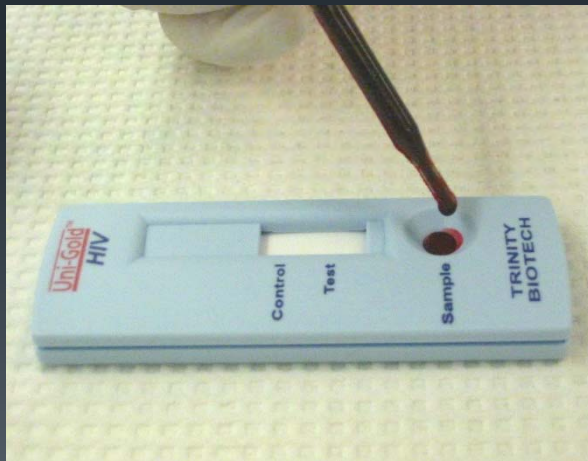
- High complexity, labor intensive assay that CONFIRMS an HIV infection.
- Introduced in the mid-80's to improve the **specificity** of the HIV testing process
- Not very sensitive and potentially problematic but it does improve the performance of the testing algorithm. **Less likely to have falsely positive results.**



# HIV Rapid Test Formats



Clearview StatPak



Trinity Uni-Gold

CLIA-waived Complexity



Clearview HIV1/2 Complete



Oraquick Rapid



# Specimen Types



Fingerstick



Wholeblood

## RAPID HIV ASSAYS—

- Many formats:
  - Whole blood
  - Fingerstick
  - Serum
  - Plasma
  - OMT
- From 1-40 minutes



Oral Mucosal Transudate

# Rapid Testing Has Unanticipated Consequences

- In the US, the first **reliable** CLIA-waived rapid HIV test (Oraquick) was approved in June 2004.

- **OBVIOUS ADVANTAGES:**

- No transportation expense or delay
- Minimal equipment requirements
- Whole blood, finger-stick or oral specimens
- Easy to interpret
- No additional laboratory personnel expense
- Negative results can be reported immediately

UNANTICIPATED:

- Increased HIV+ enter care earlier



# FDA-Approved Rapid HIV Tests

| FDA Approved  | Manufacturer  | Product                        | Method | Sensitivity % | Specificity % | HIV2 | Waived formats |
|---------------|---|--------------------------------|--------|---------------|---------------|------|----------------|
| November 2002 | Orasure Technologies Inc.,<br>Bethlehem, PA   | Oraquick Rapid<br>HIV1/2       | LF     | 99.6          | 100           | Yes  | OF<br>WB       |
| December 2003 | Trinity Biotech plc, Bray, Ireland<br><a href="http://www.unigoldhiv.com">www.unigoldhiv.com</a>                            | UniGold<br>Recombinant<br>HIV1 | LF     | 100           | 100           | No   | WB             |
| May 2006      | Inverness Medical Professional<br>Diagnostics<br><a href="http://www.invernessmedicalpd.com">www.invernessmedicalpd.com</a> | Clearview HIV1/2<br>StatPak    | LF     | 99.7          | 99.9          | Yes  | WB             |
| May 2006      | Inverness Medical Professional<br>Diagnostics<br><a href="http://www.invernessmedicalpd.com">www.invernessmedicalpd.com</a> | Clearview HIV1/2<br>Complete   | LF     | 99.7          | 99.9          | Yes  | WB             |

• *SENSITIVITY*– i.e. the ability to call a true positive, positive

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- *SPECIFICITY – i.e. the ability to call a true negative, negative*

# Limitations of Rapid Testing

- Currently, rapid HIV Tests require a CONFIRMATORY TEST – Western blot
- The Rapid HIV Test Measures
  - **Antibodies** to HIV
  - **DOES NOT Measure**
    - **HIV virus/RNA or DNA**
- How Sensitive Is It?
  - At least as sensitive as some of the older EIA used in some hospitals and laboratories.
  - In some cases they are more sensitive than the Western blot, the 'Gold Standard'

# Unanticipated Consequences - Wblot

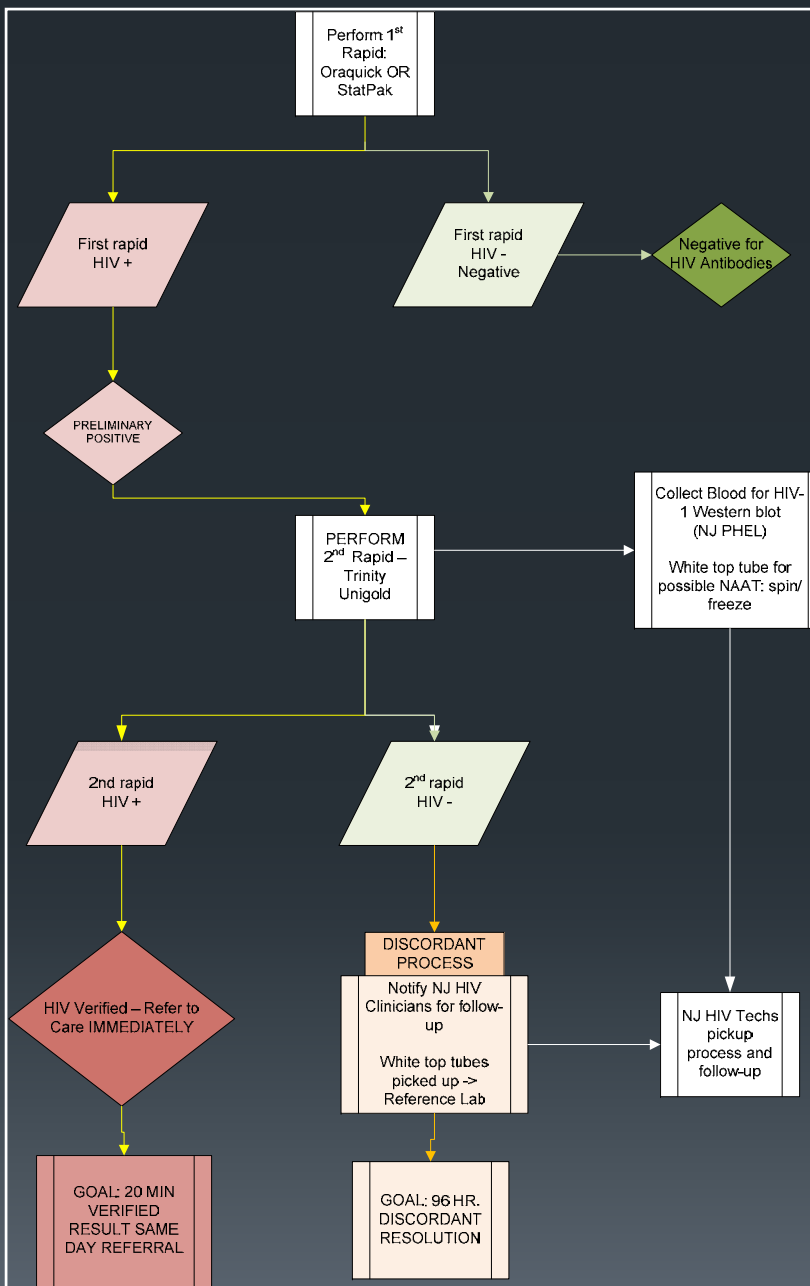
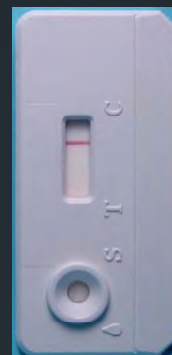
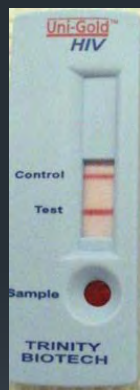
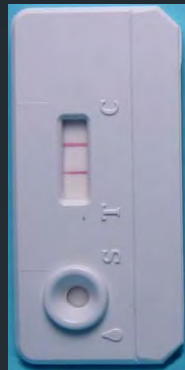
- **People refuse confirmatory tests**
  - In NJ, 7.1% of positives could not be confirmed because specimens are not collected
- **Many don't return to get their final results**
  - New Jersey: 25 – 30% fail to return for a second testing-related visit
  - Los Angeles: 35-40% fail to return
  - Other urban environments – similar story, sometimes even worse
- **Bottom line:**
  - **ONLY ~ 70 % actually get their confirmed + result!!**
- Impact → Linkage to Care is →
  - Delayed – Sometimes for years!



# Can We Increase the Entry to Care?

## The RAPID – RAPID ALGORITHM

# NJ RAPID TESTING ALGORITHM



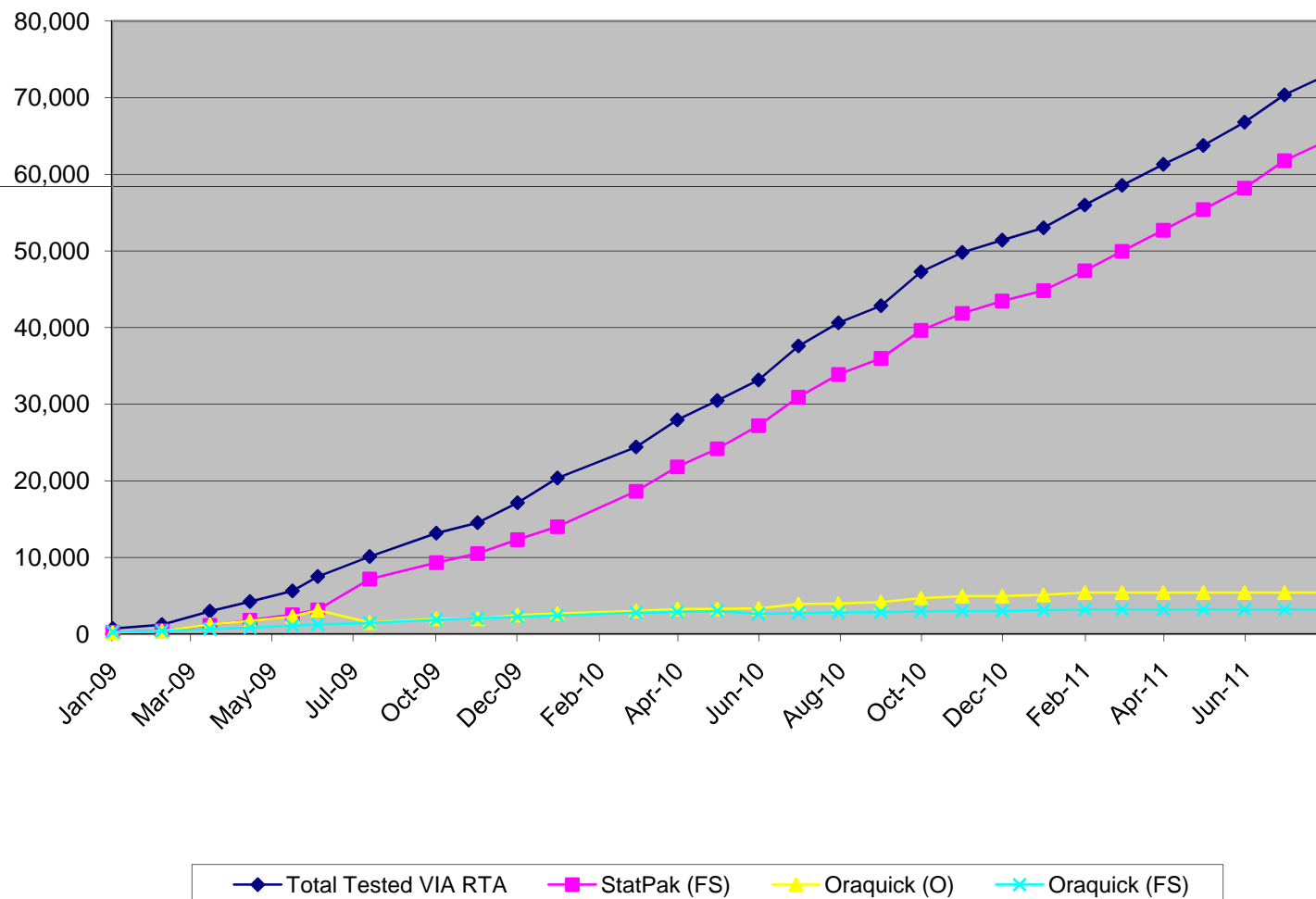


# The Two-Test Rapid Testing Algorithm (RTA)

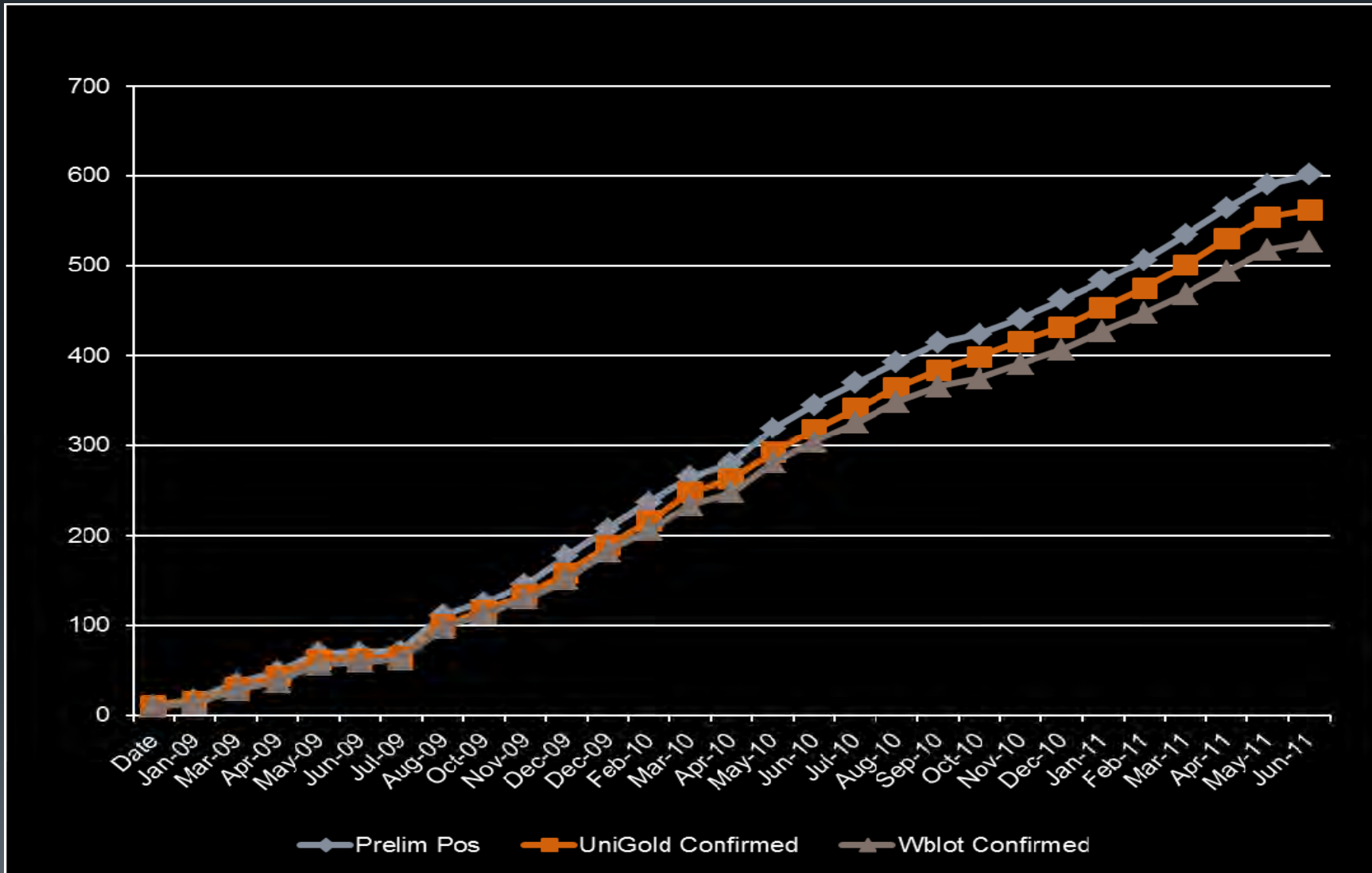
- **Concept:** If we identify 98% of infected clients in a single visit, and successfully connect them to healthcare → way ahead
- Less to remember, less to forget in a two-test algorithm
- **Downside:** A small number will not be resolvable at the time of initial testing
- **Key:** What happens to the problem cases – NJ is centralized → laboratorian/physician interaction early.

# Implementation of Rapid-Rapid

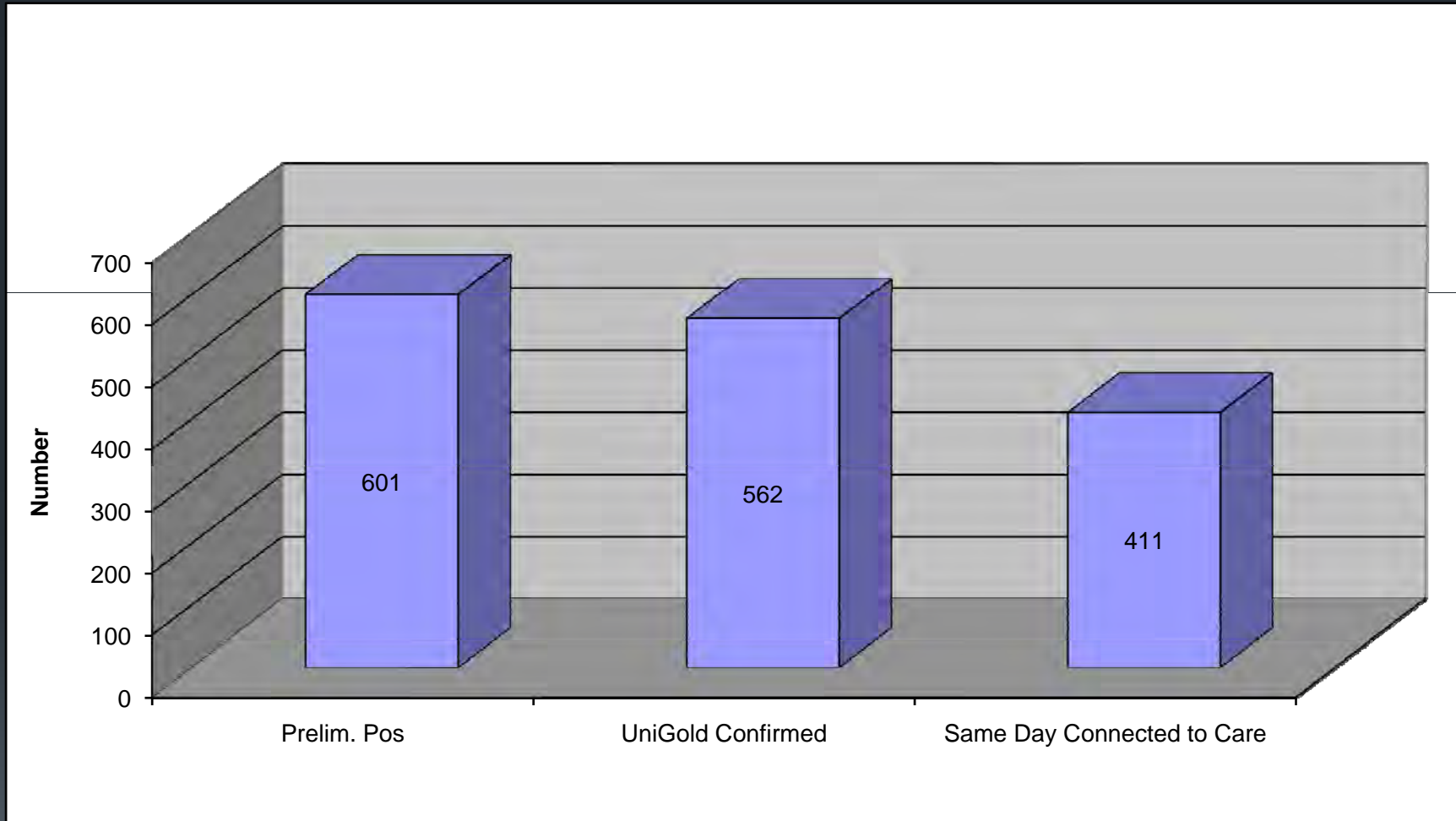
## Rapid-Rapid Testing NJ



# Faster....Verifies More Results!



# Outcomes – Linkage to Care



■ July 2011 Data

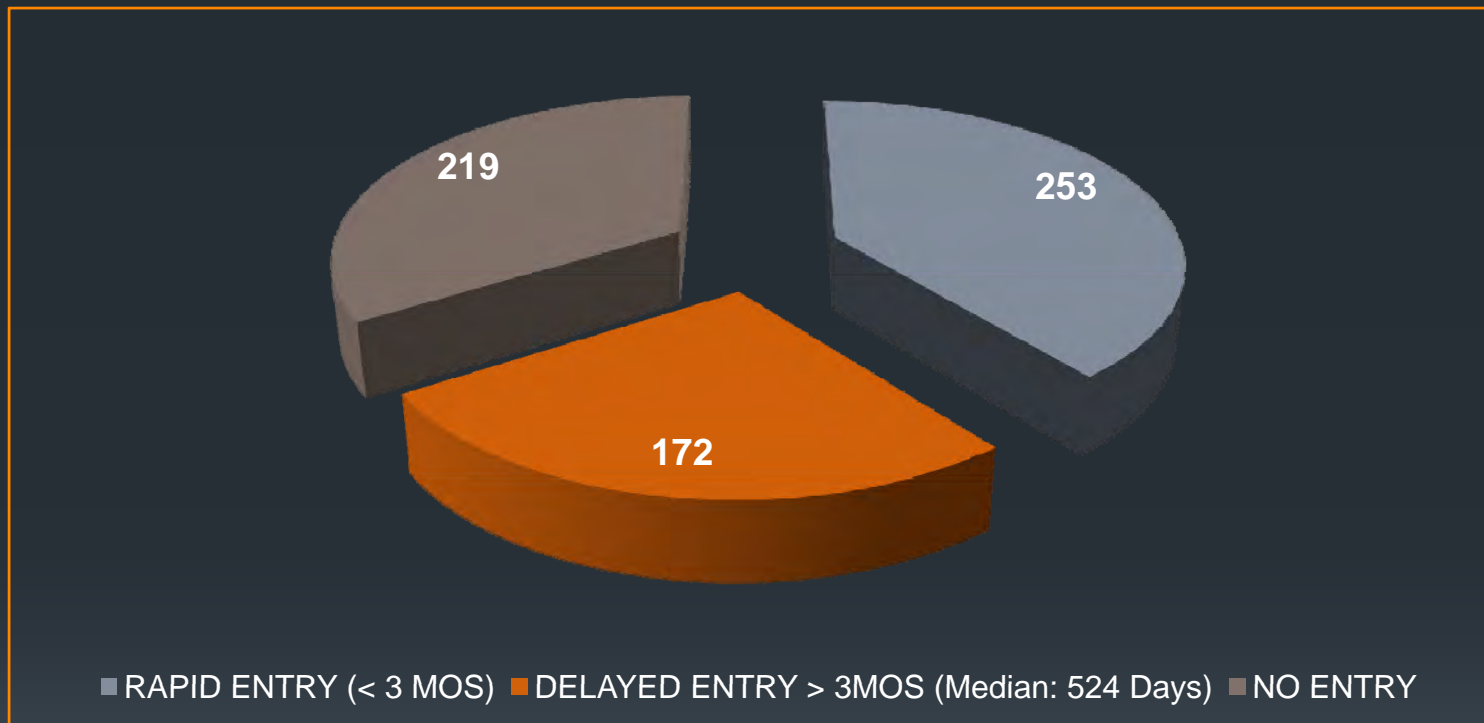
# Rapid-Rapid Summary – July, 2011

|                                       |               |
|---------------------------------------|---------------|
| <b>Tested via RTA</b>                 | <b>72,884</b> |
|                                       |               |
| <b>Prelim. Pos.</b>                   | <b>601</b>    |
|                                       |               |
| <b>Unigold Verified</b>               | <b>562</b>    |
|                                       |               |
| <b>Same-Day Connect to Care</b>       | <b>411</b>    |
|                                       |               |
| <b>Verified &amp; Linked Same Day</b> | <b>73.1%</b>  |

# Rapid-Rapid Summary - February, 2010

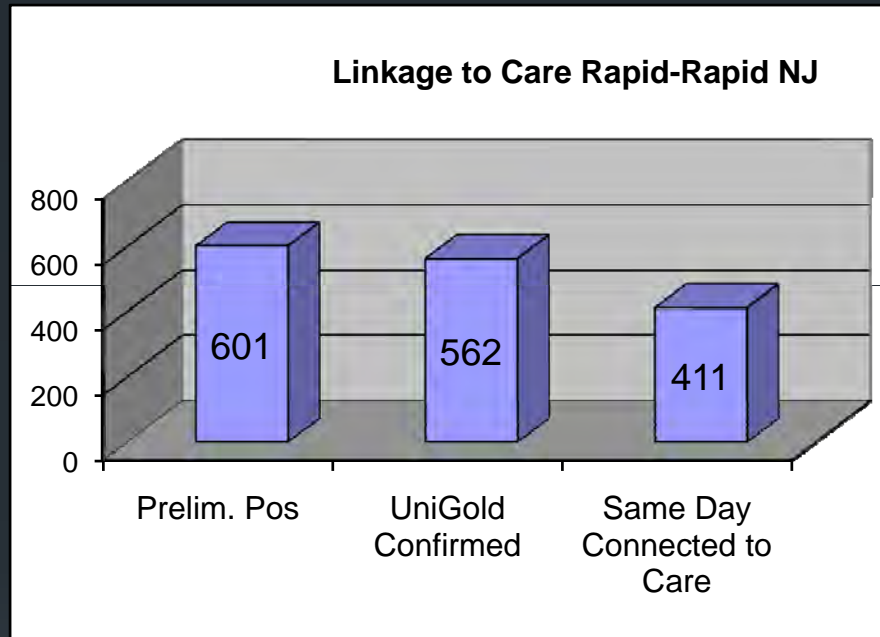
| WB Results       | 1st Rapid Positive | 2nd Rapid Positive | 2nd Rapid Negative | Notes:<br><i>Percentages calculated excluding those who refused WB</i> |
|------------------|--------------------|--------------------|--------------------|--|
| Total WB results | 197                | 186                | 11                 |  |
| Pct WB POS       | 95.4%              | 99.5%              | 27.3%              |  |
| Pct WB Ind       | 0.0%               | 0.0%               | 9.1%               |  |
| Pct WB Neg       | 4.1%               | 0.5%               | 80.0%              |  |
| Pct Refused WB   | 7.0%               |                    |                    |  |

# Linkage to Care: Rapid Test and a Wblot



**NOT GREAT, BUT**  
Compared to conventional testing (EIA + Wblot – 2 visits) Rapid Testing represents a 3.6 X improvement!

# Who Gets Linked to Care - RTA



- 75% of 'verified' HIV positives receive appts on the same day
- 26% DID NOT receive appts on the same day!!
- Site Specific Issues - Ongoing

If you link immediately after verification with a second rapid, it improves linkage to healthcare by 21% more than traditional testing!!

QUESTION: Will this hold? Will clients remain in care?



# Linkage to Care - Where matters!

- 62 RTA positives identified in the first six months of RTA program: 76.7 % - same day appointments for treatment
  - Academic medical centers (1) and FQHCs (4) identified 33 HIV positive individuals using an RTA
  - 82% received immediate appts
  - **97% were in care at six months, 1 lost to care**
- Health Departments (2) and CBOs identified 29 infections
  - 16 (55%) appts were made on same day
  - **19 (47%) were in care at 6 months, 10 (34.4%) lost to care**
- **Efforts to better connect and retain infected clients is needed particularly in non-traditional settings**

# Rapid-Rapid Facts:

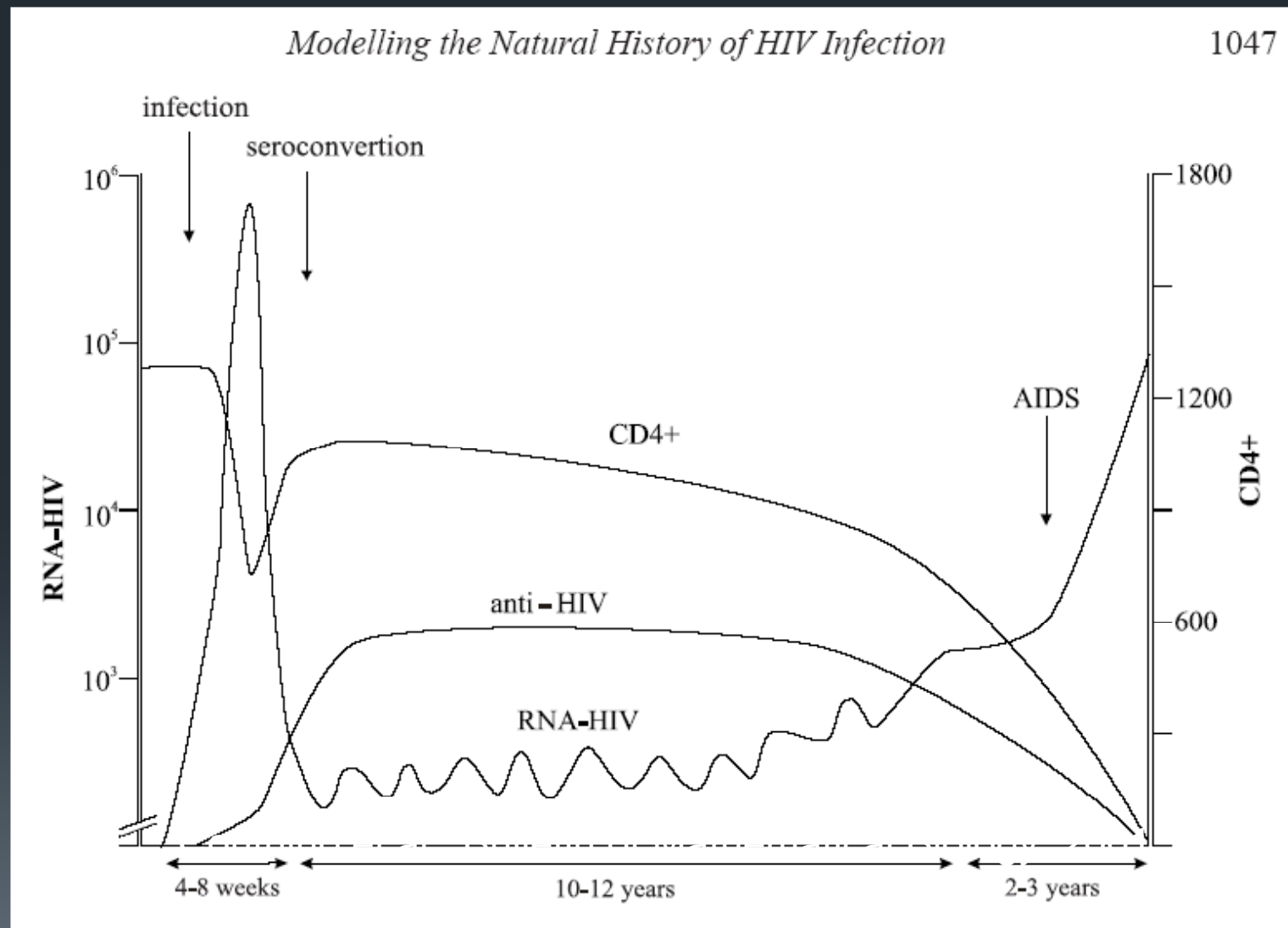
1. The result of the second rapid is “**credible verification.**”
2. With the results of the second rapid available, there is little reason to procrastinate entry to care.
3. The cost of a second rapid is between \$7-15. The cost of a Western blot is between \$70 - \$250.
4. CDC Surveillance Taskforce is likely to propose acceptance of a second rapid.

# Can We Improve the Process!

1. “Pooled Screening” - Testing for very early infection in antibody negative blood – Newark ER’s
2. Impending licensure of 4<sup>th</sup> generation POC and laboratory-based tests



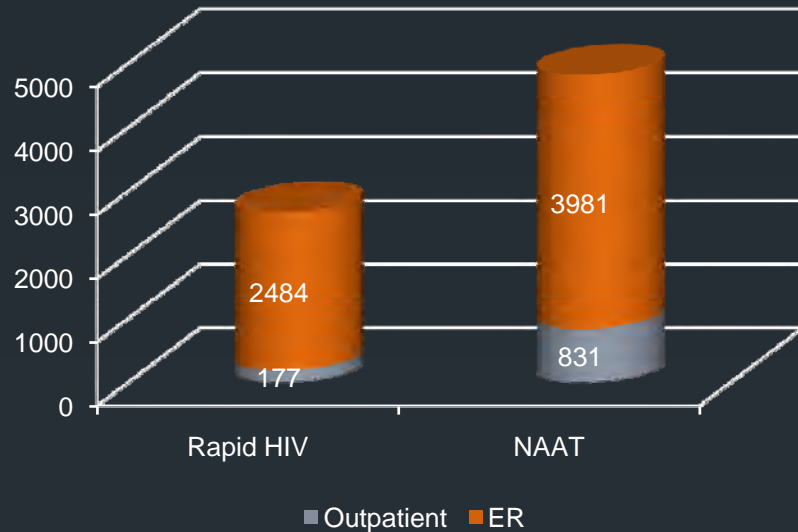
# Natural History - HIV Infection



# AHI Study in Emergency Rooms

- Begun in a High Prevalence, possibly High Incidence Area → central ward of Newark
  - University Hospital
- How frequently do individuals present in the ER with evidence of acute HIV infection?
  - AHI: Appearance of HIV virus associated with burst of infectivity. No antibody present. Possibly p24 Ag is present.

# NAAT Program - Newark



## NAAT Testing Program at University Hospital

|            | Rapid HIV | NAAT | All patients | Pct Getting NAAT |
|------------|-----------|------|--------------|------------------|
| Outpatient | 177       | 831  | 1008         | 82%              |
| ER         | 2484      | 3981 | 6465         | 62%              |
| Overall    | 2661      | 4812 | 7473         | 64%              |

Estimated that we missed 3 NAAT + patients from the number who refused to be tested!

# NAAT AND AHI DETECTION

| Program                    | Dates       | Description   | NAAT Tested | AHI | HIV Ab+ | % HIV Ab + | % Inc in Yield | % Yield AHI |
|----------------------------|-------------|---|-------------|-----|---------|------------|----------------|-------------|
| <b>Maryland</b>            | 6/06-3/08   | HIV Ab neg adults seen at two STD clinics (6/06--3/08); multiple venues 7/07-3/08)                  | 58,925      | 7   | 1,709   | 2.90%      | 0.41%          | 0.01%       |
| <b>North Carolina</b>      | 11/02-10/03 | HIV Ab neg persons in North Carolina seeking HIV testing at 110 publicly funded sites (n = 109,250) | 108,667     | 23  | 583     | 0.54%      | 3.95%          | 0.02%       |
| <b>Los Angeles</b>         | 2/04-4/04   | HIV Ab neg men seeking HIV testing at three STD clinics (n = 1712)                                  | 1,698       | 1   | 14      | 0.82%      | 7.14%          | 0.06%       |
| <b>NEWARK, NJ</b>          | 3/10-8/11   | HIV Ab neg adults receiving testing and counseling at two high risk urban hospitals in Newark, NJ   | 5,130       | 7   | 96      | 1.28%      | 7.29%          | 0.14%       |
| <b>Seattle King County</b> | 9/03-1/05   | HIV Ab neg MSM seeking HIV testing through Seattle-King County (n = 3525)                           | 3,439       | 5   | 81      | 2.36%      | 6.17%          | 0.15%       |
| <b>Atlanta</b>             | 10/02-1/04  | 2202 adults receiving HIV testing and counseling at three high risk urban sites in Atlanta, Georgia | 2,136       | 4   | 66      | 3.09%      | 6.06%          | 0.19%       |
| <b>San Francisco</b>       | 10/03-7/04  | HIV Ab neg persons seeking HIV testing at San Francisco Municipal STD clinic (n = 3075)             | 2,722       | 11  | 105     | 3.86%      | 10.48%         | 0.40%       |

# Is a NAAT Program Worth it?

## POSITIVES

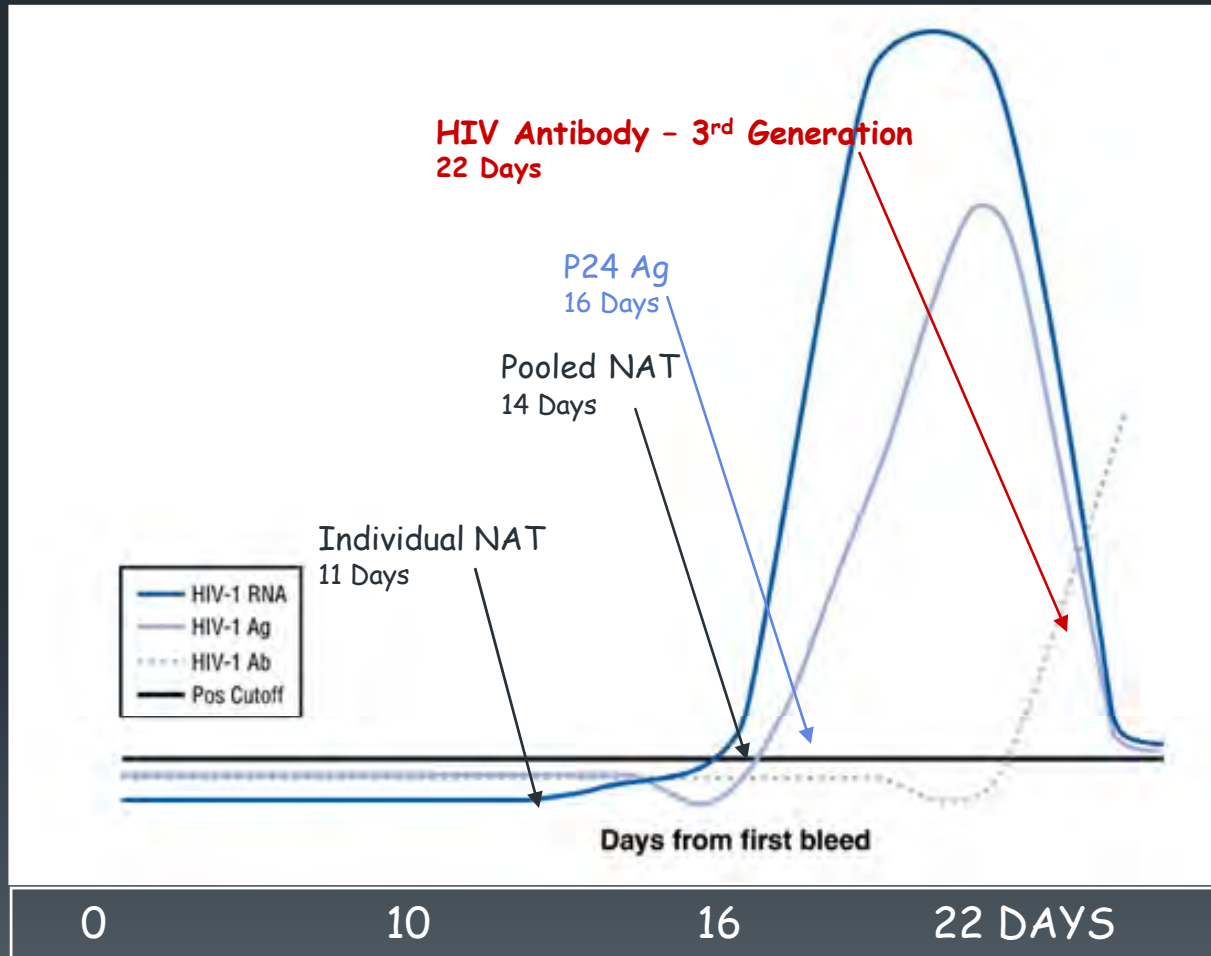
- INCREASES HIV DETECTION RATE BY 5-10%!
- THOSE IDENTIFIED ARE MORE INFECTIOUS!
- TREATMENT AS PREVENTION – the lower the viral load, the lower the risk an individual has to infect others. The sooner you enter treatment, the less likely you are to transmit.

## NEGATIVES

- EXPENSIVE – Cost of NAAT Program ~ \$100,000 without labor!
- LOW YIELD, but ....
- *Are there better alternatives?!*



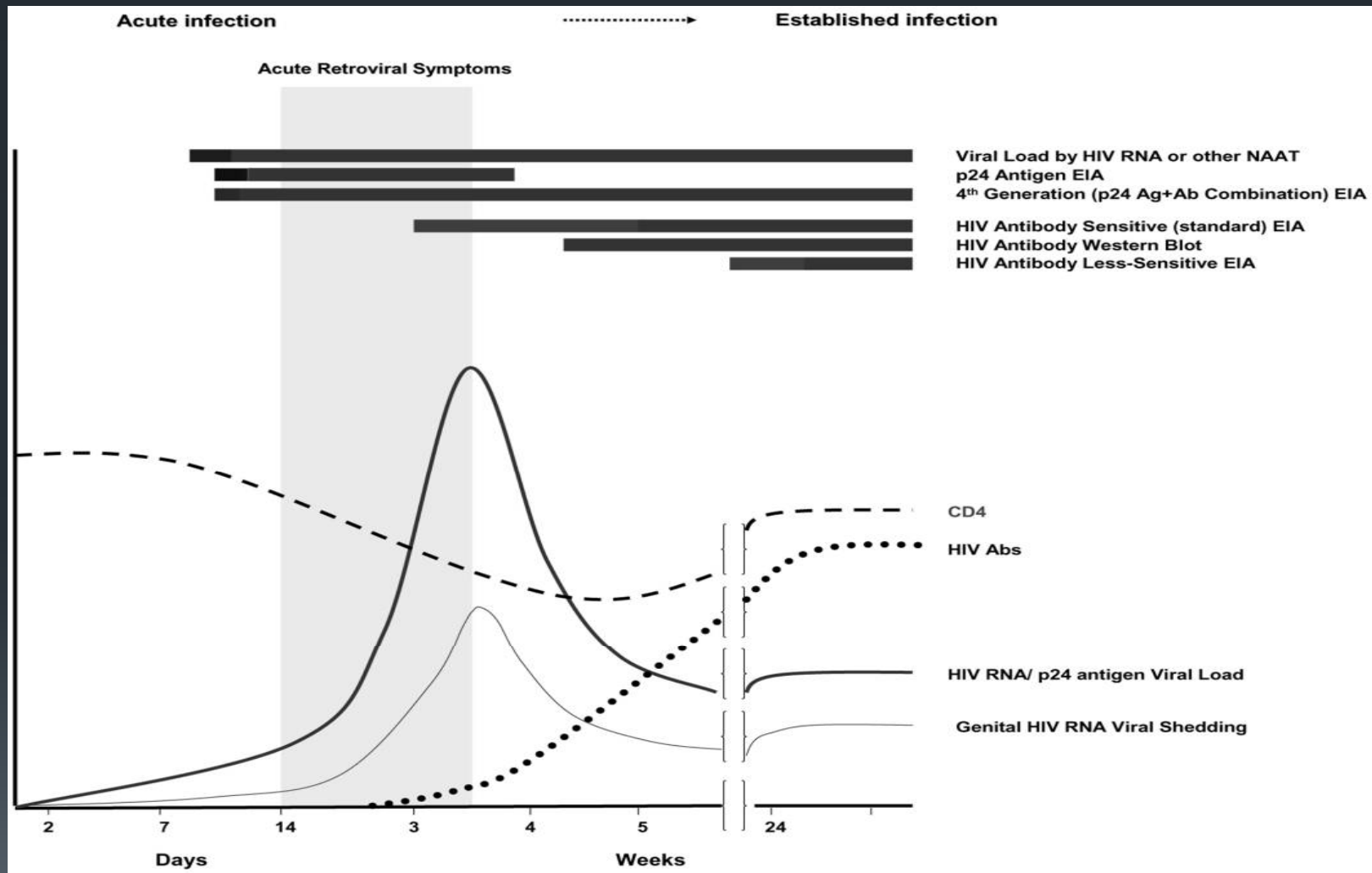
# Viremia During Early HIV Infection



- Ramp-up Viremia  
Doubling Time = 21.5 hrs
- Peak Viremia  
 $10^6 - 10^8$  gEq/mL
- Viral set-point  
 $10^2 - 10^5$  gEq/mL
- WINDOW
  - Antibody – 22 Days
  - Antigen – 16 Days
  - Pooled NAT – 14 Days
  - Individual NAT – 11 Days

ANTIBODY WINDOW

# P24 Antigen Tests for HIV

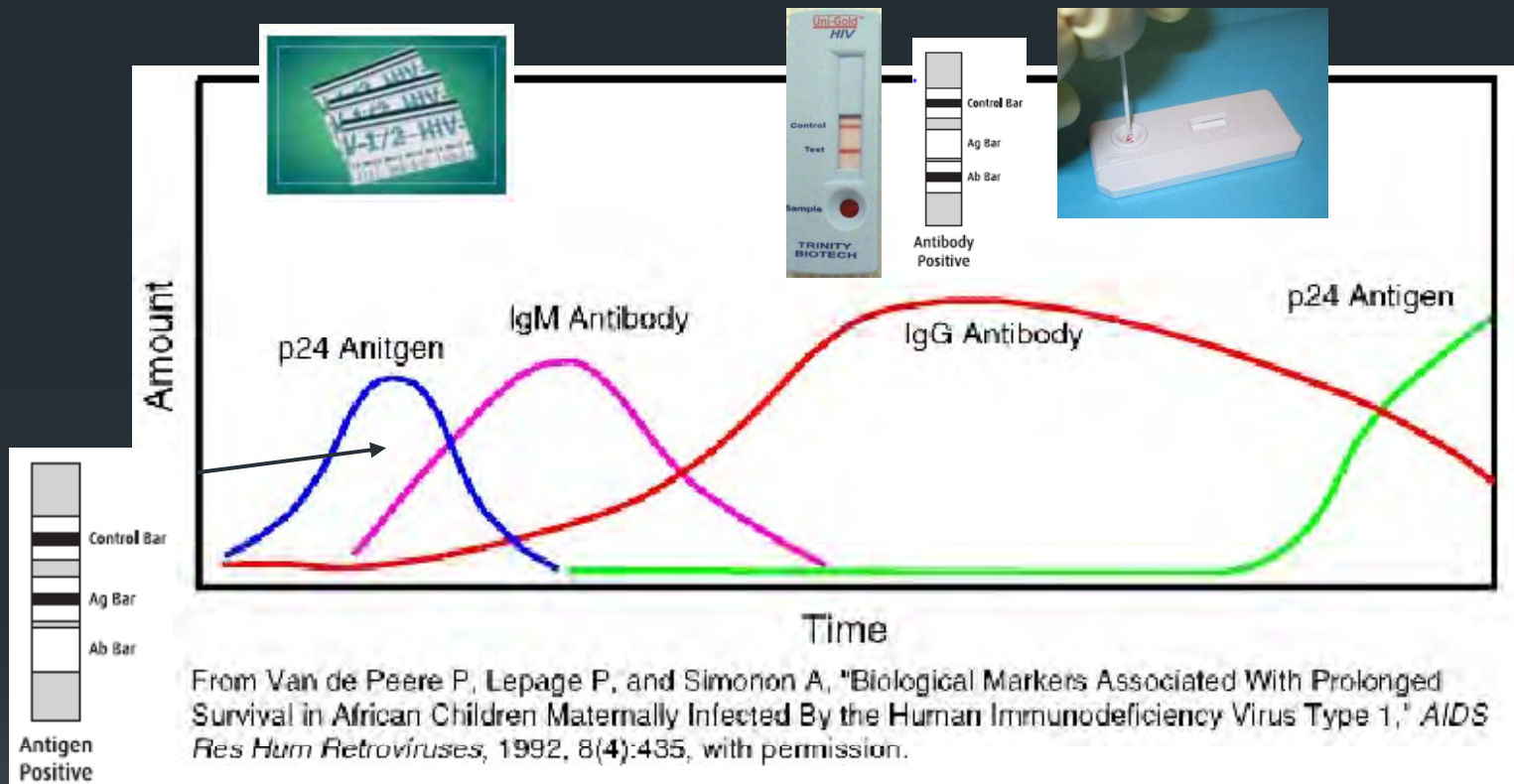


Christopher D. Pilcher,<sup>1</sup> Katerina A. Christopoulos,<sup>1</sup> and Matthew Golden<sup>2</sup>

# Why Worry about the '30 day window'?

- HIV transmission
  - 50% occurs PRIOR to the appearance of antibodies!
- How do we *EFFECTIVELY* narrow the 'HIV window?'
  - Implement alternative technologies to identify:
    - Other serologic markers that appear earlier
    - Utilize nucleic amplification technologies to look for the virus

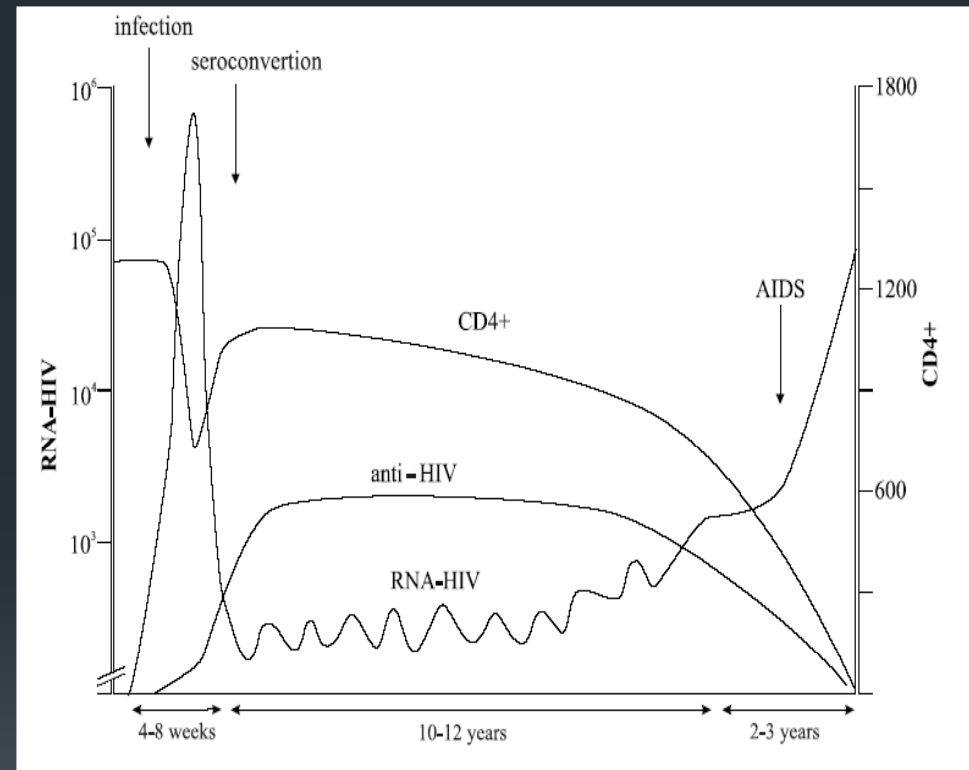
# Determine Combo



*Just completed a trial at Henry J. Austin and Neighborhood Health testing a low risk population (408). Performed exactly as described. High degree of specificity in a low risk population. FDA submission is anticipated shortly.*

# Acute HIV Infection

- HIV virus is associated with burst of infectivity
- No detectable antibody present for ~ 22 days
- Possibly p24 Ag present
- **?: If we screen with a POCT product detecting p24 Ag can we:**
  - Detect most or all of the AHI episodes?
  - Is that good enough?
  - Does the immediate result offset the delay issues?



# Technology Trade-Offs

## POOLED NAT

- ~ 14 days
  - Sensitive
  - Labor intensive
  - Expensive
  - Often referred
  - Reporting delays:  
Days → Weeks

## P24 Ag Detect

- ~ 16 days
- Originally a lab-based technology
- Approaching licensure is a POCT like rapid HIV
  - ? Pricing
  - ? How to utilize

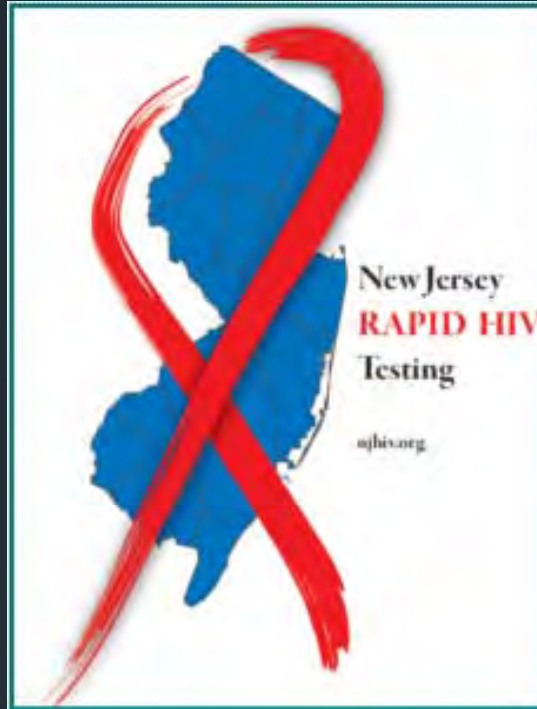
# Ongoing Efforts:

- Will p24 Ag detection be an acceptable alternative to NAAT in a screening environment?
- PLAN 2011-12
  - Continue to set the stage w/ NAAT Testing
  - Follow-up w/ Determine Combo when it is FDA approved
  - UNANTICIPATED : The 'Great Recession!'
    - Affordability – cost of reagents, cost of QA
- Focus on 'linkage to care?'
  - Put in place methods to identify successful linkage
- Treatment as Prevention



## RWJMS

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# THANKS!

