

RUTGERS

Robert Wood Johnson Medical School

## NJ HIV: Status Update

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# 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 4<sup>th</sup> 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

## RUTGERS - RWJMS

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## NJ DHS/DMHAS

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*Office of the Medical Director*

# ASTHO "VISION" AWARDS – 1<sup>st</sup> Place

## RAPID HIV TESTING PROGRAM

- 2006 -



## PATIENT NAVIGATOR PROGRAM

-2013-





## RAPID HIV SITES THROUGHOUT NEW JERSEY

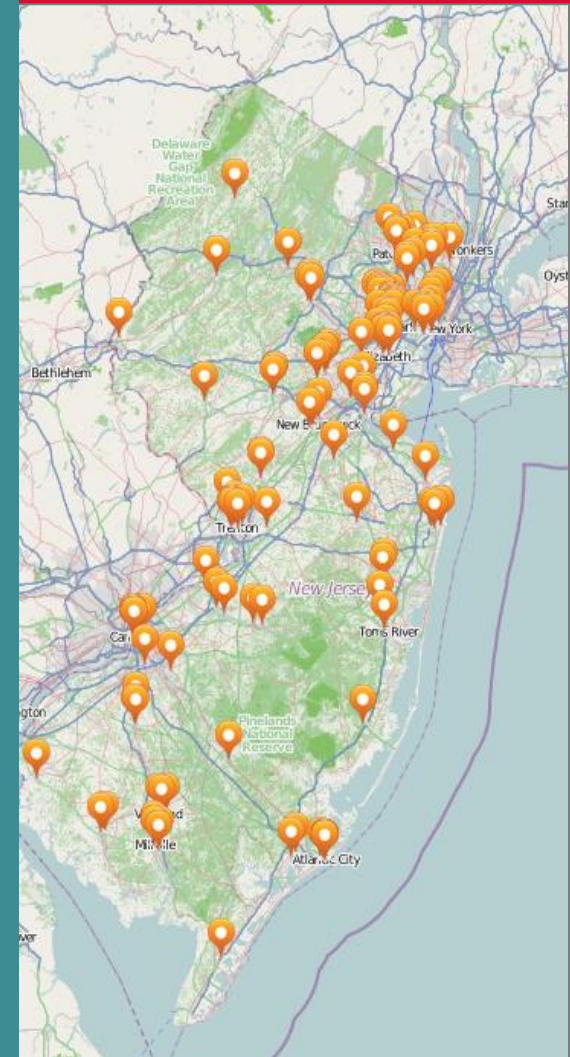
- 102 RWJ Licensed sites (includes 87 stationary sites and 14 mobile vans)
- 64 Non RWJ sites – Hospitals, etc.

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
- 
- ADDICTIONS: 21 Sites: 20 + 1 mobile counselor serving 6 sites

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## Themes from the decade

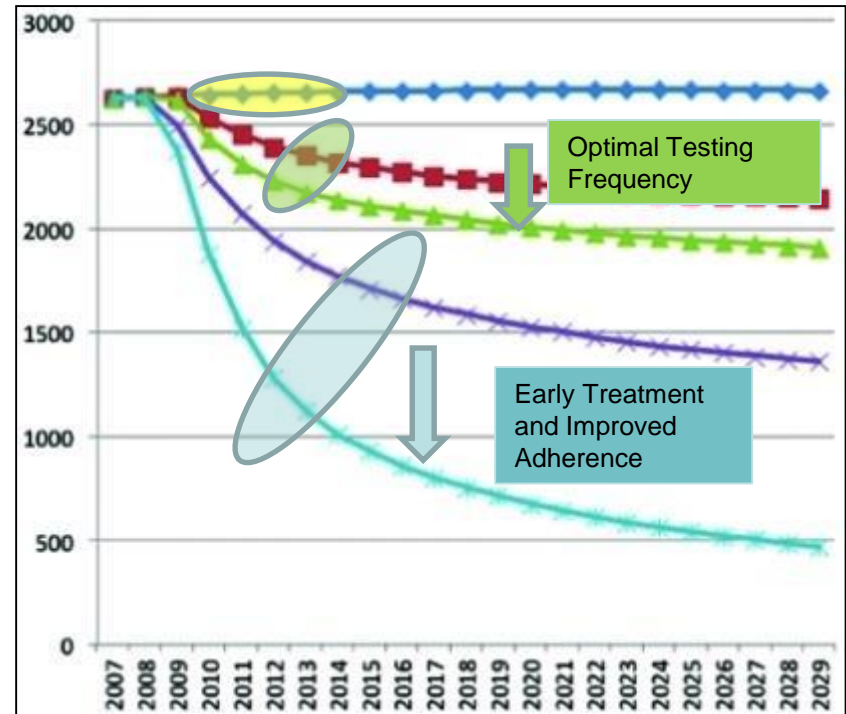
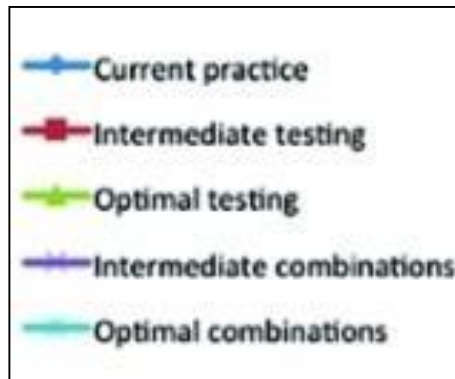
1. Making HIV screening broadly available in NJ
2. Linkage and how effectively we link HIV+ into care
3. Credibility in the screening process – RTA(s)
4. How often rapid screening misses early (AHI) infections
5. Implementation of a – 4<sup>th</sup> gen. rapid statewide
6. Performance of the 4<sup>th</sup> 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.

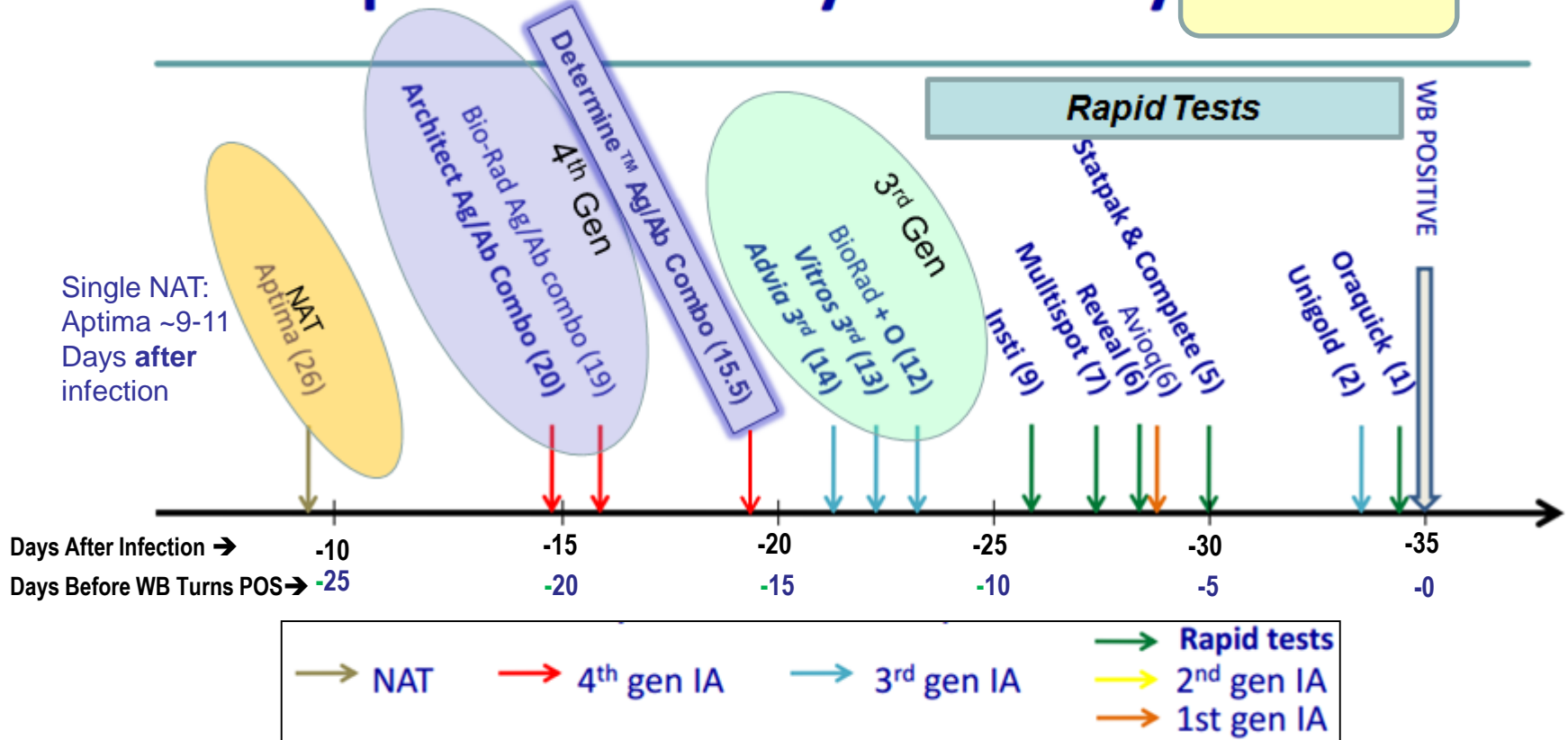
## Annual number of new HIV infections over 20 years for MSM in New York City



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!

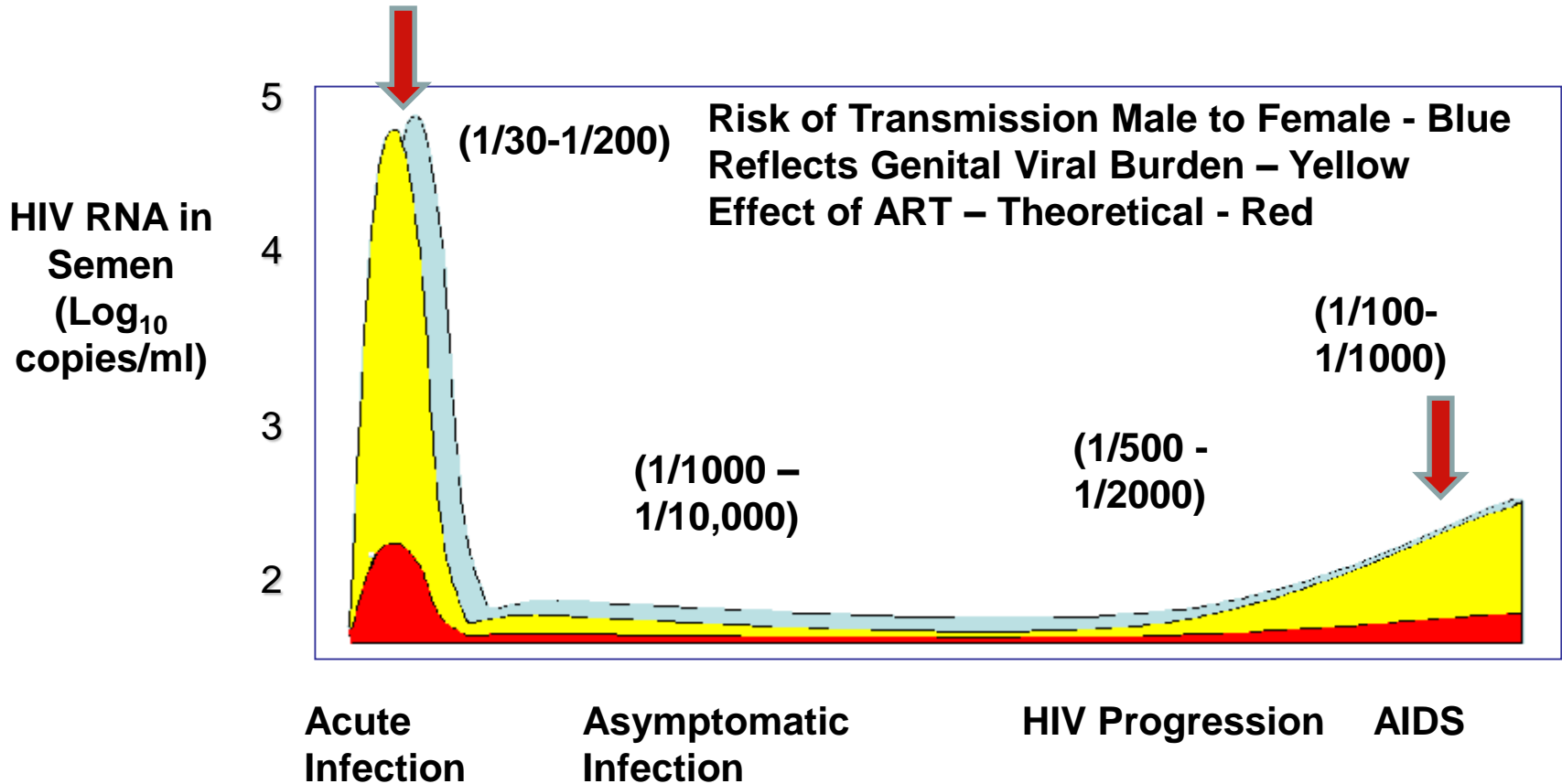
# The Range of HIV Sensitivity – Screening to Diagnosis

## Sequence of Assay Reactivity **Plasma**



Adapted from Owen et al J Clin Micro 2008 and Masciotra et al J Clin Virol 2011

# Why is this Important? Why earlier?

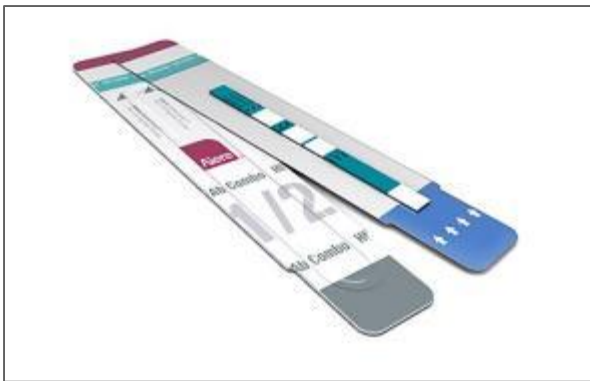


# 4<sup>th</sup> generation – Point of Care

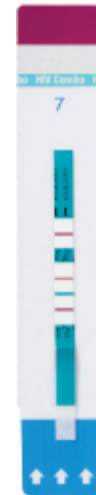
Claims for the Alere Determine™ HIV-1/2 Ag/Ab Combo indicate a higher sensitivity, but a lower specificity than the second generation, rapid HIV tests (StatPak) in use since 2006.

**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). ← PROTECTION (RTA)



<b>-PROBABILITY OF A FALSE POSITIVE-</b>
<b>CLEARVIEW STATPAK</b> Package Insert Specificity Claim: 99.9%
<b>NJ PERFORMANCE YTD</b> 99.97% = 3 FALSE POS/10,000 screens
<b>DETERMINE COMBO</b> Package Insert Specificity Claim: 99.8% EXPECTED = 20 FALSE POS/ 10,000 or 80 PER/ 40,000
<b>NJ PERFORMANCE YTD</b> 99.92% = 8 FALSE POS/10,000 screens



# 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

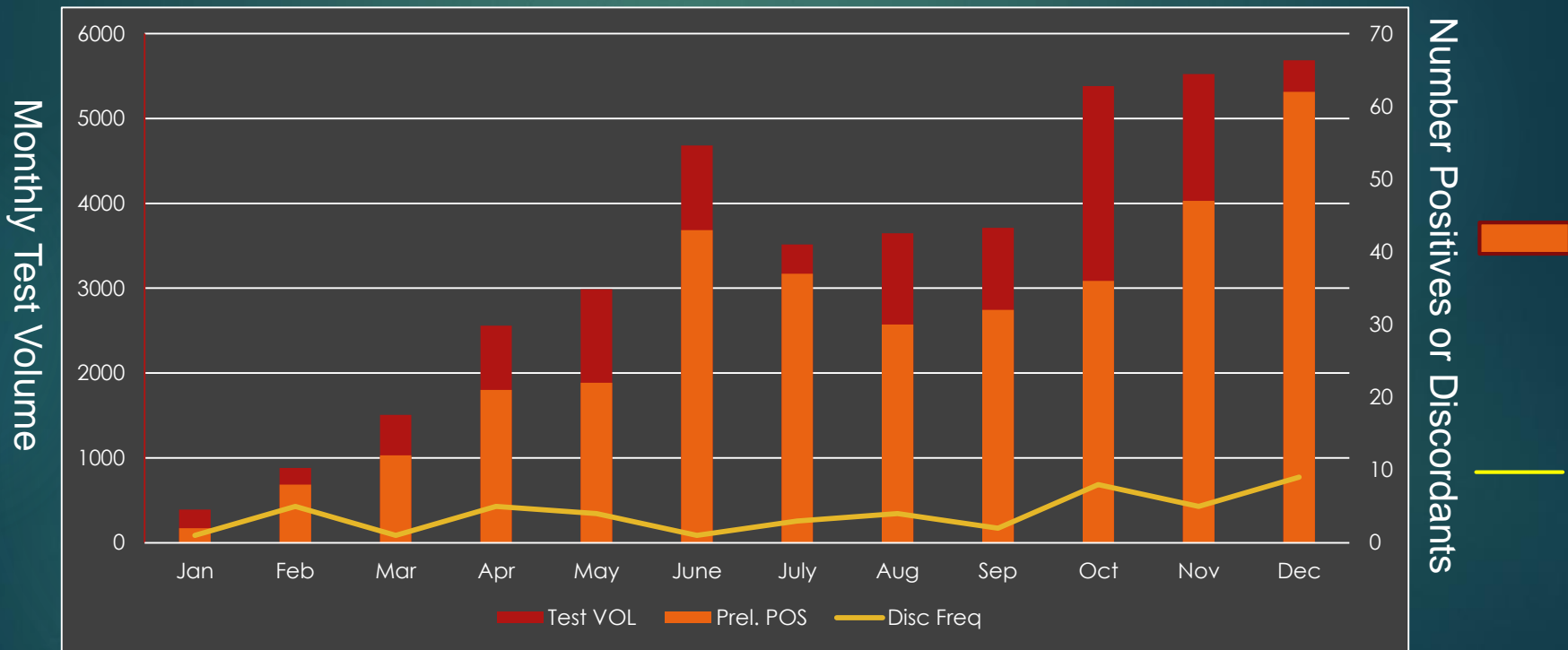
## SCREENING

- 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)

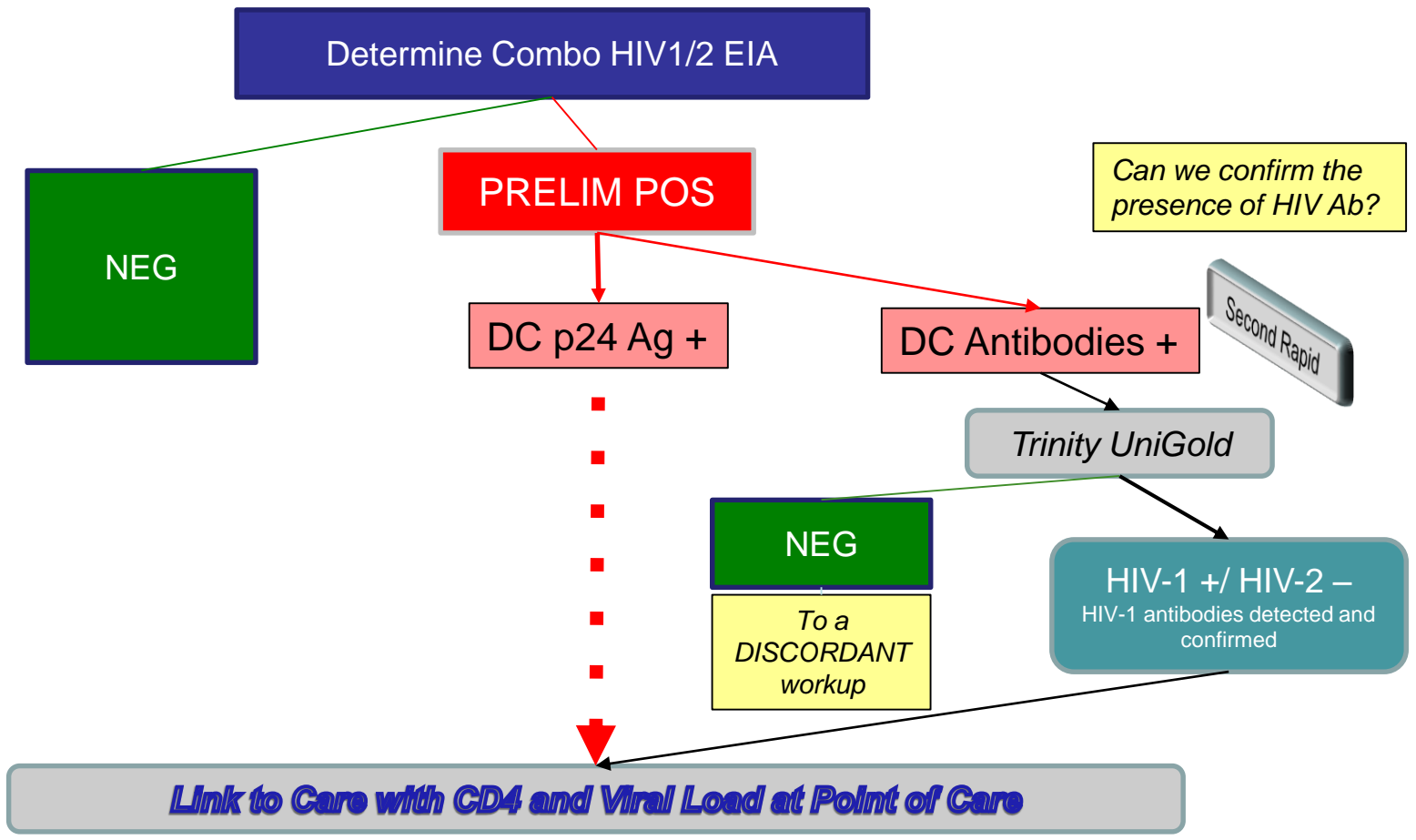
NJ Statewide Implementation

# **4<sup>TH</sup> GEN. POCT HIV SCREENING**

# Determine Combo – 2015 – NJ Rollout: Volume – Prelim. Pos. – Discordant Frequency



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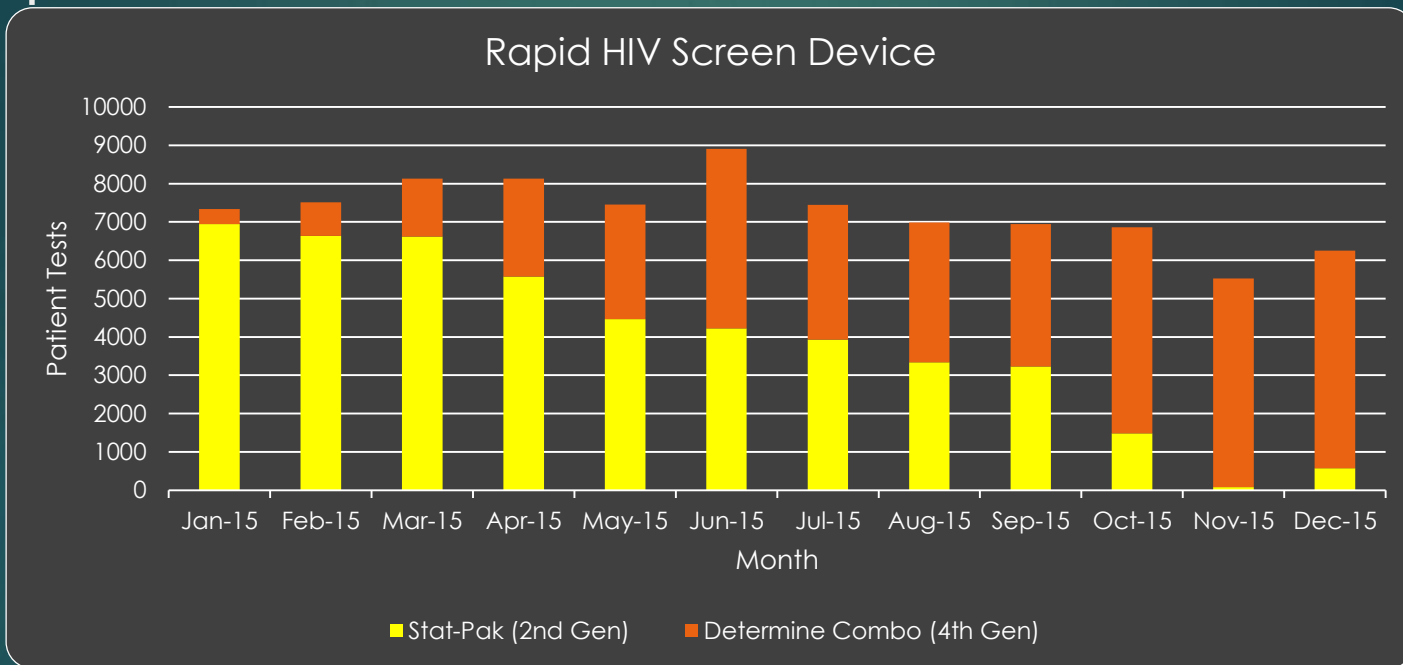


DISCORDANT WORKUP

RNA Testing



# Implementation: Determine Combo



PRODUCT	Volume (2015)	POS	Seroprevalence
StatPak	47,091	366	0.75%
Determine	40,391	352	0.78%

# DISCORDANT (RTA) ANALYSIS – 2015: New Jersey

## CLEARVIEW STATPAK 2015

StatPak	47,091	366 POS
Marker	Frequency	Notes
True POS		
	TP/FN UG	1
<b>True POS</b>		<b>TOTAL: 1</b>
False POS	FP Ab	10
	FP Both Rapids	2
<b>False POS</b>		<b>TOTAL: 12</b>

Expected False Pos = 40

## DETERMINE COMBO 2015

Determine	40,391	352 POS
Marker	Frequency	Notes
True POS	P24 Ag +	1
	TP/FN UG	6
<b>True POS</b>		<b>TOTAL: 7</b>
False POS	FP Ab	25
	FP Ag	11
	FP Ag/Ab	5
	FP Both Rapids	1
<b>False POS</b>		<b>TOTAL: 41</b>

Expected False Pos = 80

# Summary: Discordant Workups - 2015

## SUMMARY DATA – RTA 2015 DC

POS 0	DC Ab+/UG+ Reported by clinic	NEG 1
POS 6	DC Ab+/UG -	NEG 25
POS 1	DC Ag+	NEG 11
POS 0	DC Ag+ Ab+/UG -	NEG 5
7		41

False Neg

False Pos

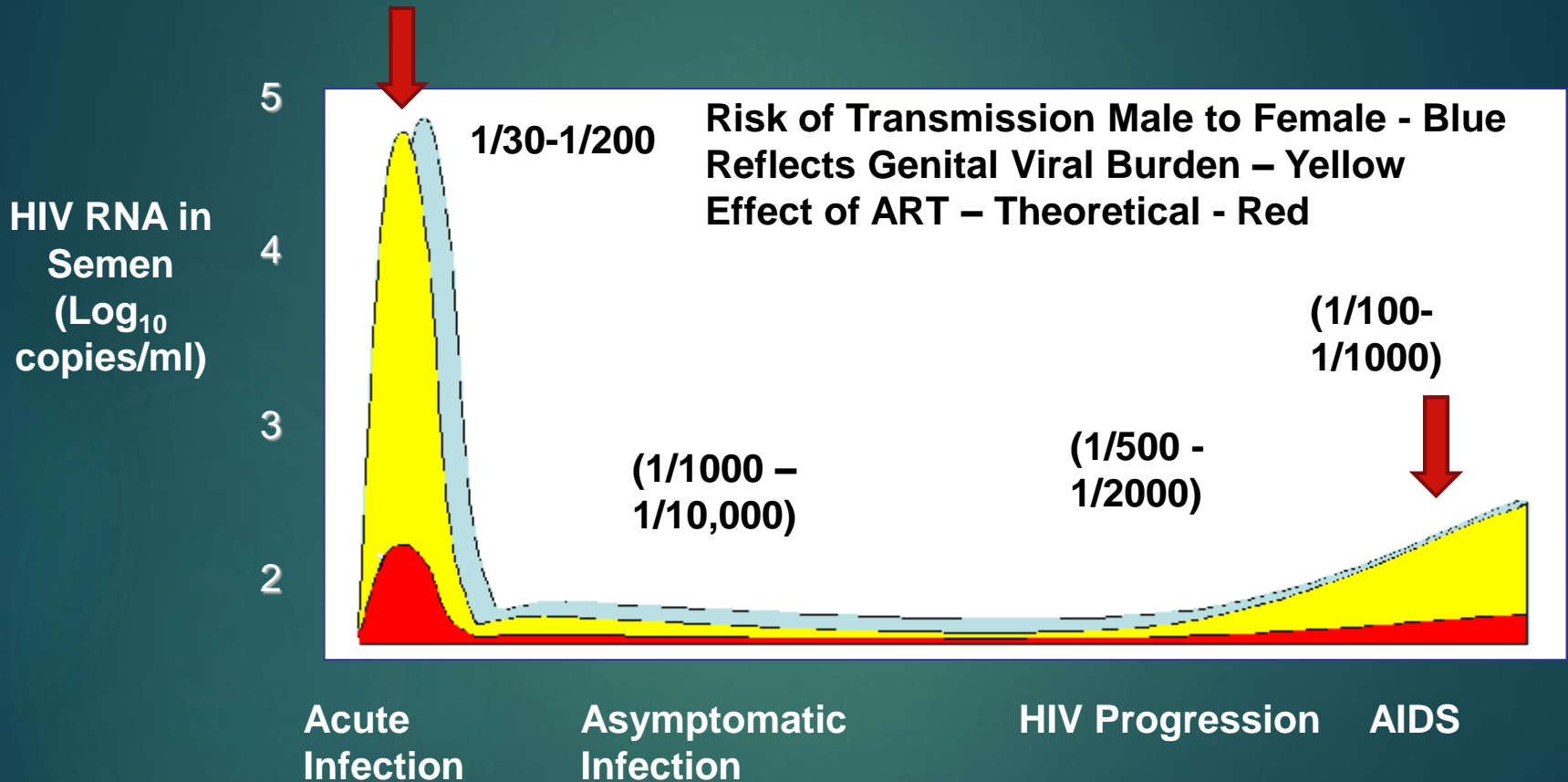
## DISCORDANT WORKUP

1. Immediate Quantitative RNA viral load
2. 4<sup>th</sup> 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?



Cohen and Pilcher, *Amplified HIV transmission and new approaches to HIV prevention* JID 191:1391, 2005

# NAAT Testing of Antibody Negative Blood

Program	Dates	Description	Rapid Tested	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%
North Carolina	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>	2/10 to 1/12	HIV Ab neg adults receiving testing and counseling at two high risk urban hospitals in Newark, NJ	12,390	6,785	<b>8</b>	116	0.94%	6.90%	0.12%
<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%

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.... Tranmission. Tranmission!
- What do we anticipate:
  - We hope to pick up fewer AHI's then in our 2010 study using 2<sup>nd</sup> 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

2015	HIV INFECTED	NON INFECTED	
<b>POSITIVE</b>	311	41	352
<b>NEGATIVE</b>	Est. <sup>1</sup> (14-24 <sup>1</sup> )	(40,025-40015 <sup>1</sup> )	40,039
	Est. (325-335 <sup>1</sup> )	(40,066-40,056 <sup>1</sup> )	

NJ PERFORMANCE - Determine HIV 1/2 Ag/Ab Combo	Based Upon <b>Estimates</b> of False Negative Rapids From previous Newark Pooled NAAT estimates <sup>1</sup>
<b>Positive Predictive Value:</b>	88.35%
<b>Negative Predictive Value:</b>	99.94%-99.97%
<b>Prevalence of Disease:</b>	0.80% - 0.83%
<b>Sensitivity:</b>	92.84% <sup>1</sup> -95.69%
<b>Specificity:</b>	99.90%

<sup>1</sup> E.G. Martin et al. "Finding those at risk: Acute HIV infection in Newark, NJ" Journal of Clinical Virology 58S (2013) e24-e28

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

Gold Standard:  
Pooled NAAT

Not yet available for  
Determ. 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>
4. Quality Assurance.
  - 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!

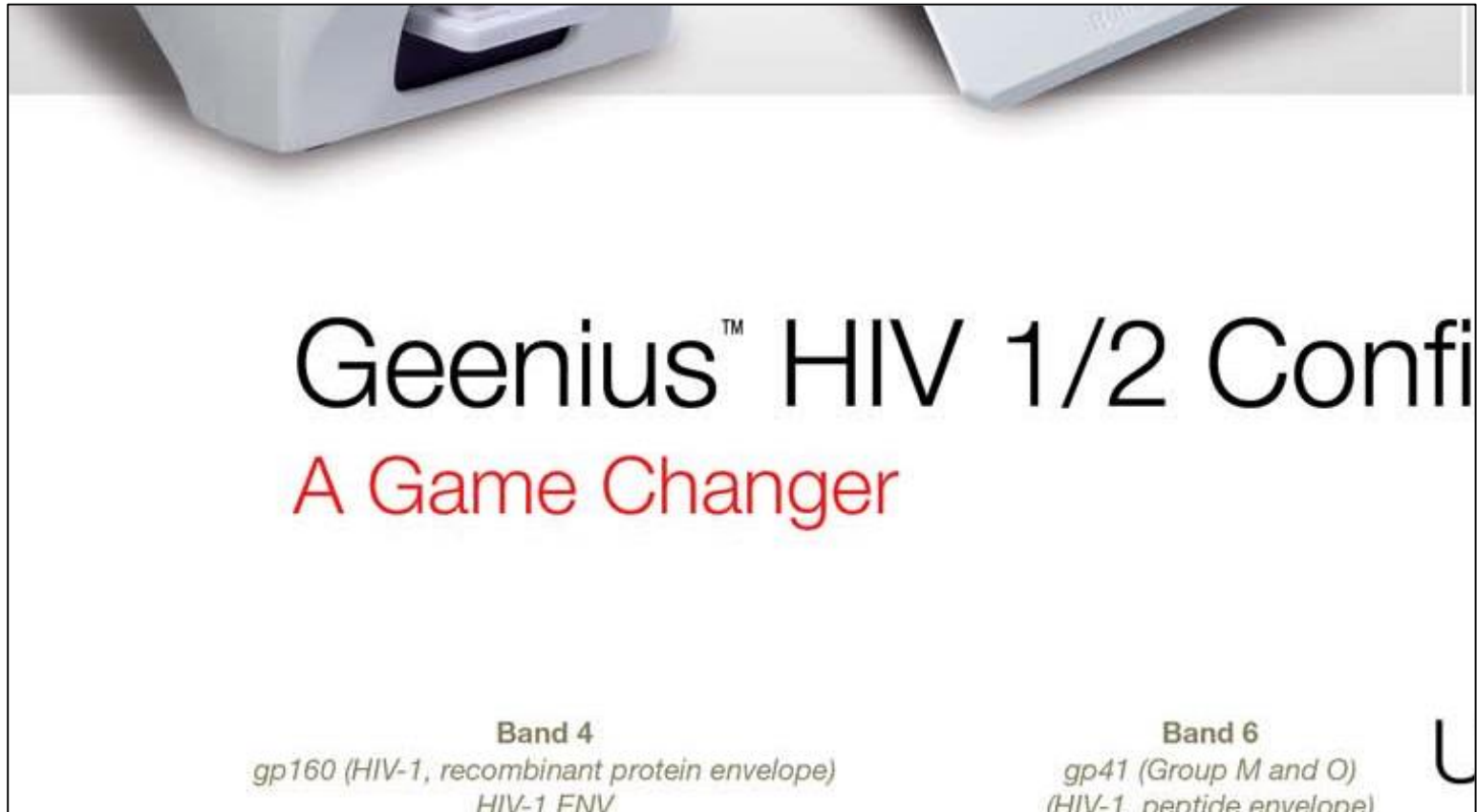
**HIV SCREENING IS NOT A CONFIRMED  
DIAGNOSIS AND THERE ARE  
CONFIRMATORY CHANGES COMING IN  
JULY**

# 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 CASSETTE:



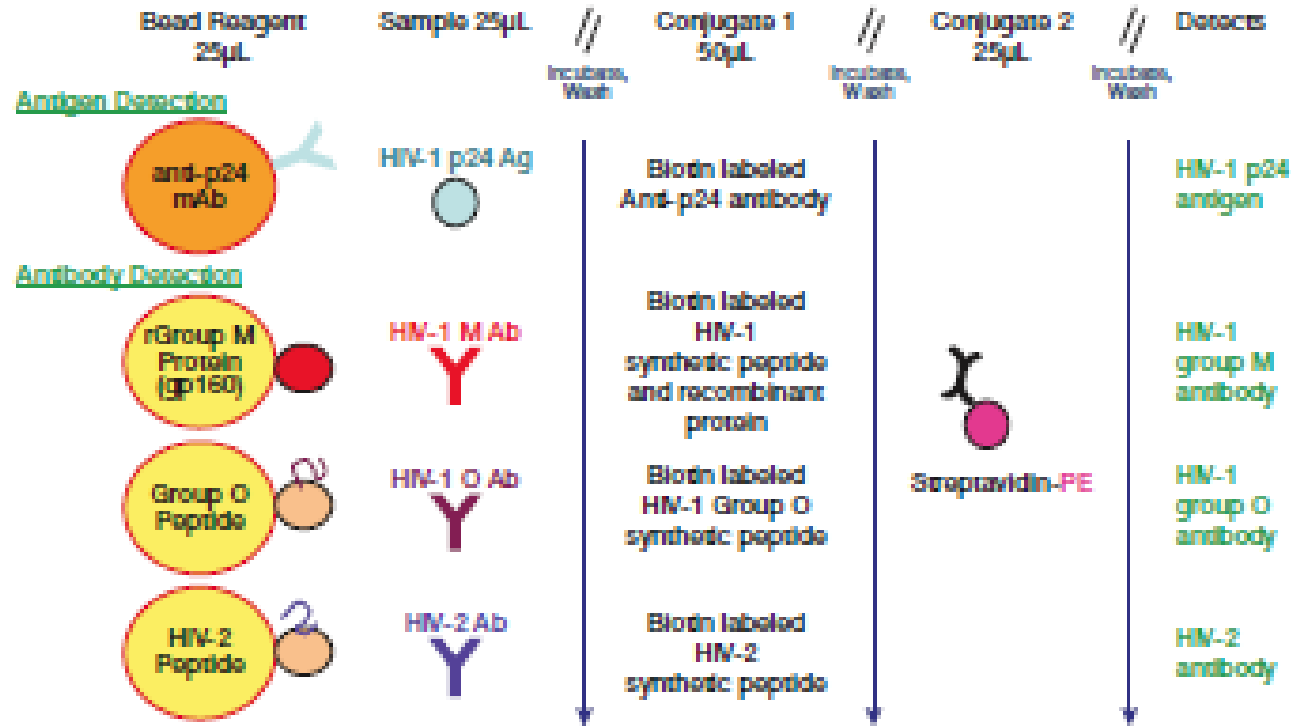
# LABORATORY DIAGNOSTICS

Simultaneous Detection and Identification of Multiple HIV for each sample.

## FIFTH GENERATION TESTING

# BioPlex<sup>®</sup> HIV Ag-Ab Assay – Fully Automated Screening: HIV-1 p24 Ag, HIV-1 Ab & HIV-2 Ab

Figure 1: The 5th generation assay design allows for the simultaneous detection and identification of multiple HIV analytes for each sample processed



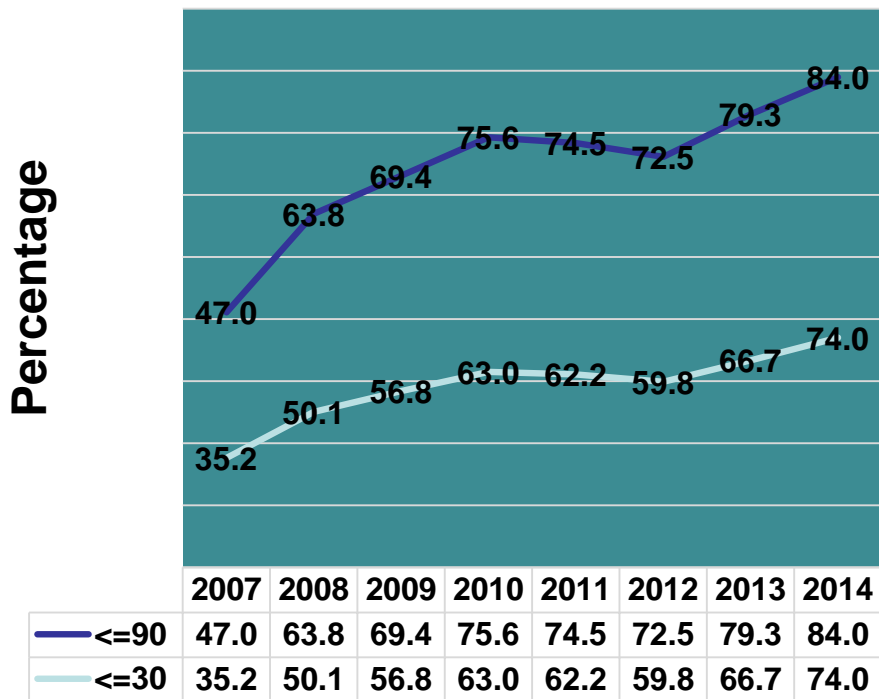
# WHERE IS ALL HEADED?

At San Francisco General they have figured out a way to start Anti-Retroviral Therapy on DAY 1!

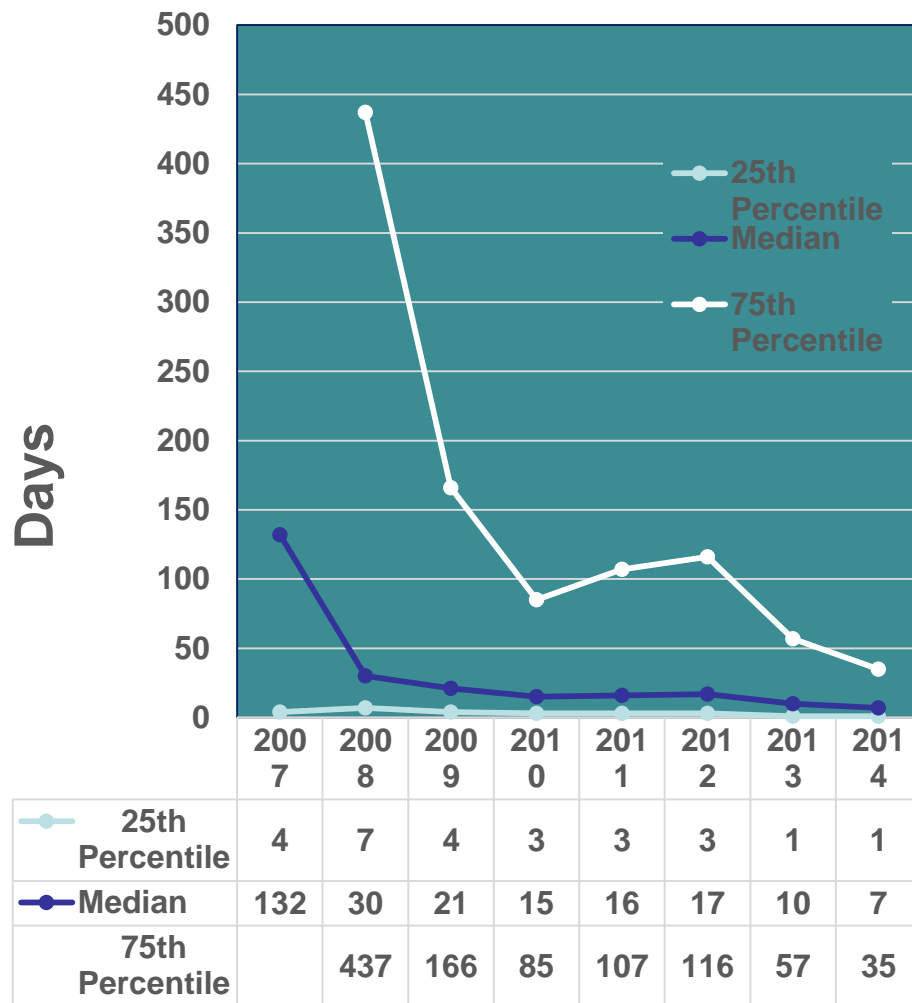
## ART IN A DAY

# Linkage to medical care in $\leq 30$ and $\leq 90$ days, 2007-2014

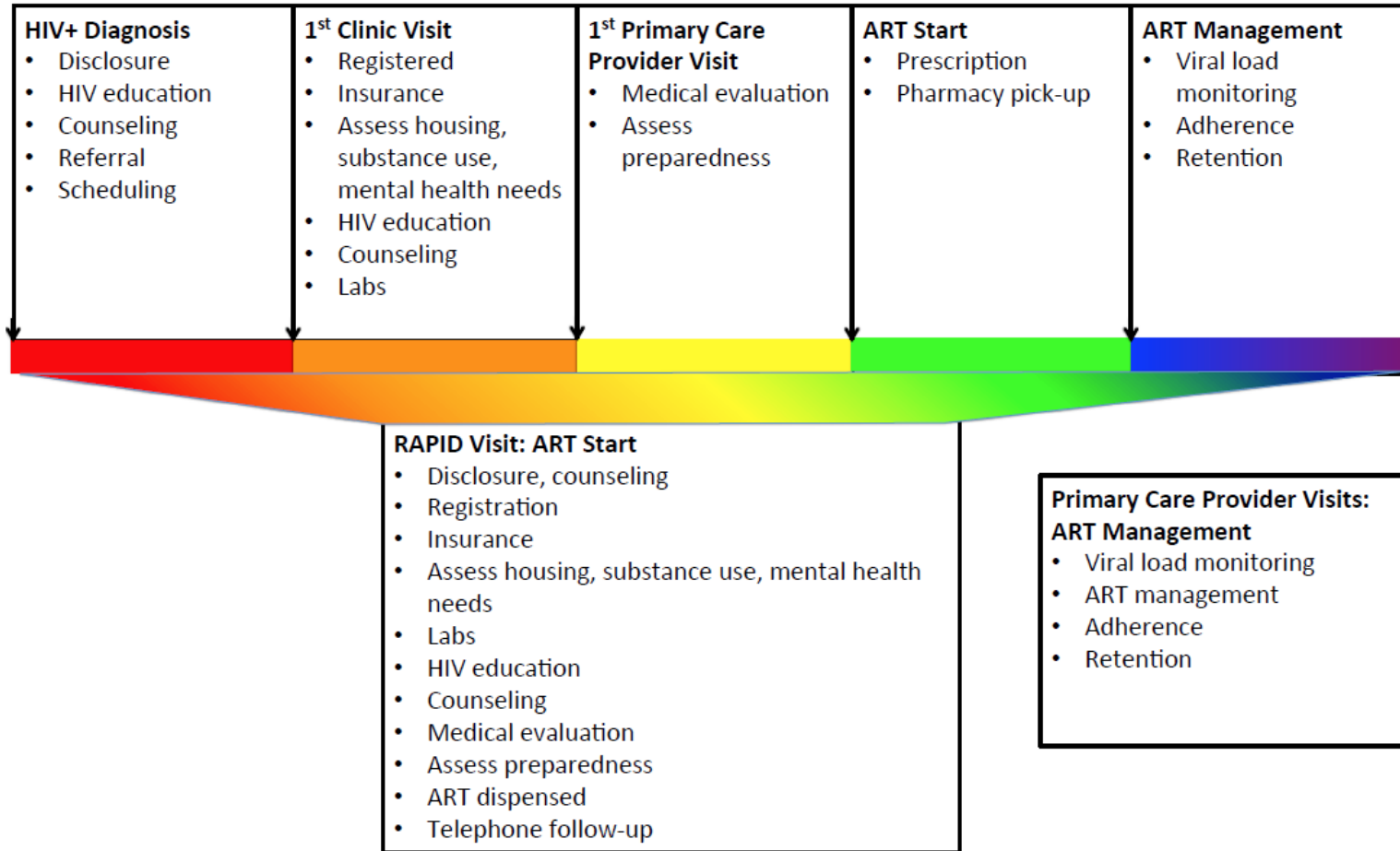
## Percentage Linked to Care



## Median time to linkage



# 2013 San Francisco General RAPID Protocol



# 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 resistance 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**