

# Introduction to Communicable Disease Surveillance and Investigation in North Carolina



# Human Immunodeficiency Virus

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**and**

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# Learning Objectives

## Participants

- Know HIV Screening Guidelines
- List barriers to HIV screening
- Identify Four Prevention Opportunities
- List advantages to 4<sup>th</sup> Generation Testing
- Describe the HIV Cascade and implications for NC Public Health



# North Carolina Public Health & Centers for Disease Control and Prevention Recommendations

## In health care settings:

HIV screening is recommended in all health care settings. You must inform the patient that HIV testing may be done unless the patient specifically declines (known as opt-out screening).

Separate written consent for HIV testing is not required. General consent for evaluation and treatment is sufficient to encompass consent for HIV testing

Persons at risk for HIV infection should be screened for HIV at least annually. High risk and/or MSM should be screened every 3 months

Prevention counseling need not be conducted in conjunction with HIV testing

# Rationale for Revising Recommendations

- Many HIV-infected persons access health care but are not tested for HIV until symptomatic
- Treatment will prevent progression and transmission
- Awareness of HIV infection leads to substantial reductions in high-risk sexual behavior
- Inconclusive evidence about prevention benefits from typical counseling for persons who test negative

# North Carolina Administrative Code (NCAC)

Opt-out HIV screening in medical settings and for prenatal and STD visits

Pre-test counseling not required

Post-test counseling required only for positives

HIV tests at first prenatal visit and 3<sup>rd</sup> trimester

Mandatory HIV test at L&D for all women for whom HIV status is unknown and in infant if test not obtained from mother

## North Carolina Integrated Response to HIV Prevention and Treatment

*“...the objective of improving HIV care provision in North Carolina through the transformation of the current, disjointed, HIV testing and care delivery system into a single structure where testing and care are linked.*

*The coupling of testing and provision of care is necessary in order for patients to benefit from treatment and prevention messages...”*

# Barriers to Initiation of Testing: Patients

The lack of perceived vulnerability to HIV acquisition could be broadly divided into three themes:

- people who did not recognize their behavior as risky
- people who viewed their behavior as very low risk
- people who felt like exposure to HIV was unlikely, regardless of behavior

Few identified benefits of seeking an HIV test

# Barriers to Initiation of Testing: Access to Health Care

- Most participants accepted testing when it was offered, suggesting that routine screening may increase the numbers of people tested and de-stigmatize the testing process.
- For expanded HIV testing programs to have impact, people living with unrecognized HIV infection must have contact with the healthcare system.
- In the Southeast, HIV infection is often a disease of the rural and poor; new strategies to improve health care access will be a necessary precursor for any increased screening to reach the groups most in need.

# Summary: HIV Testing

A large proportion of patients who suspect that they have been infected with HIV delay testing for several years.

Increased awareness of the importance of HIV testing among high risk populations and their providers is essential.

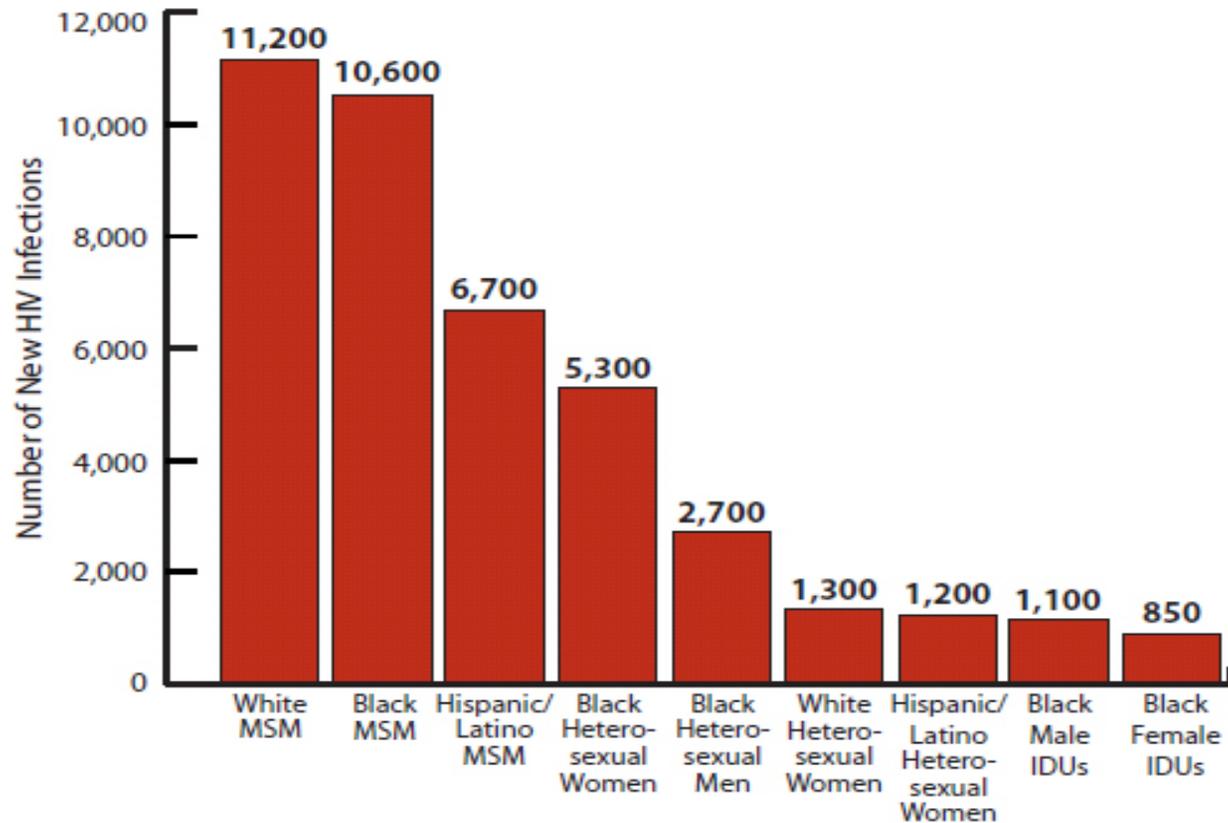
Find the intersection!

Opt-out testing can increase testing.

**We need to make systems of care that reduce time from *infection to care initiation* a priority.**

# Getting to Zero

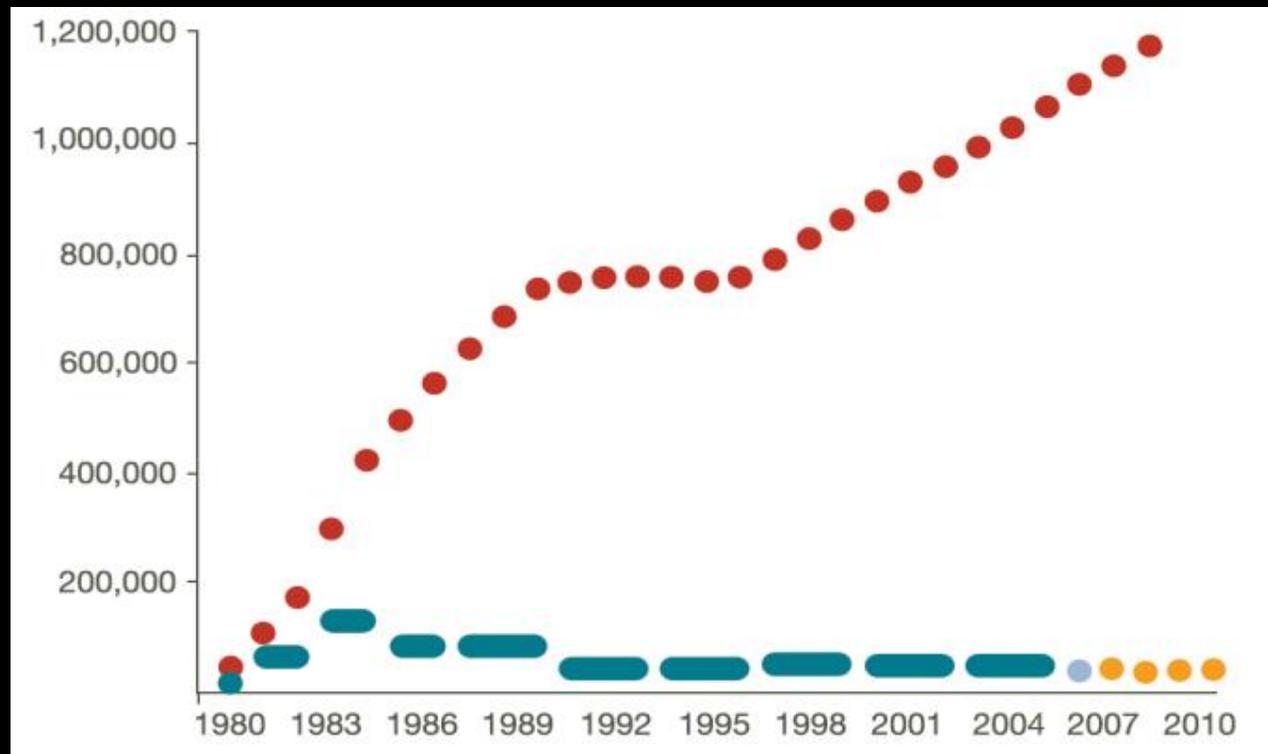
# Estimated New HIV Infections in the United States, 2010, for the Most Affected Subpopulations



Subpopulations representing 2% or less of the overall US epidemic are not reflected in this chart.

Source: CDC Website

# HIV Prevalence and New Infections, 1980-2010



● People living with HIV

● New HIV infections using back-calculation methodology

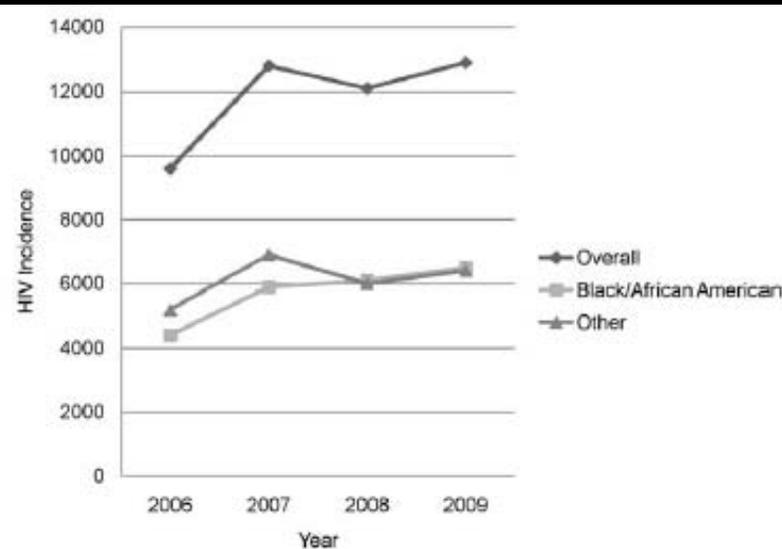
● New HIV infections using original incidence surveillance methodology

● New HIV infections using updated incidence surveillance methodology

Reference: United States Centers for Disease Control and Prevention.

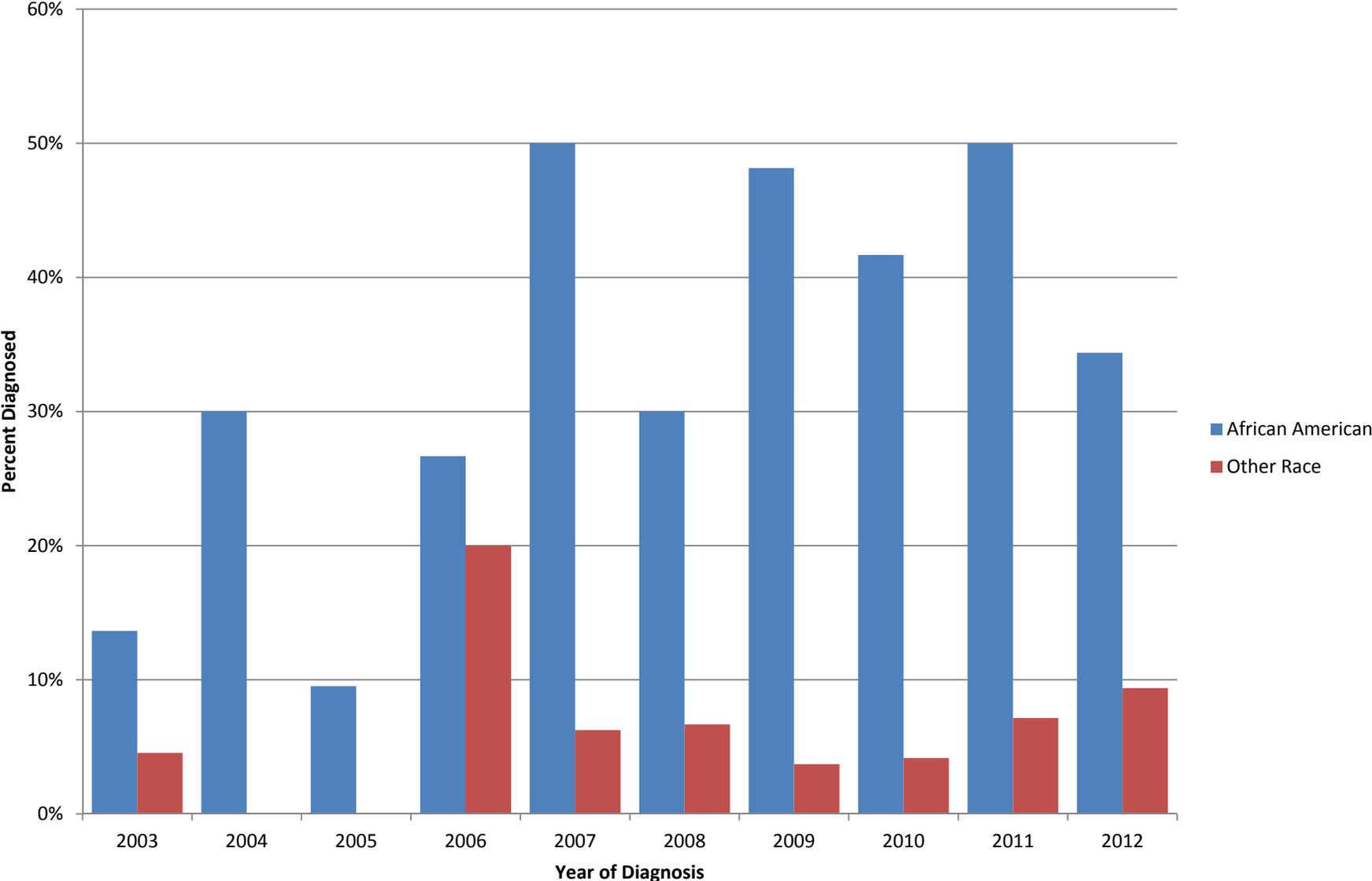
<http://www.cdc.gov/nchstp/newsroom/docs/HIVFactSheets/TodaysEpidemic-508.pdf>

# Rising Incidence Young MSM



**Figure 2. HIV incidence among 13–29 year old men who have sex with men (MSM) overall and by race/ethnicity – United States, 2006–2009.** HIV incidence in all MSM 13–29 demonstrated a statistically significant estimated annual percentage change (EAPC) of 8.1% (95% CI: 1.9%–14.9%;  $p = 0.01$ ). The EAPC for young black/African American MSM was 12.2% (95% CI: 4.2%–20.9%;  $p = 0.002$ ) but was not significant for other young MSM.  
doi:10.1371/journal.pone.0017502.g002

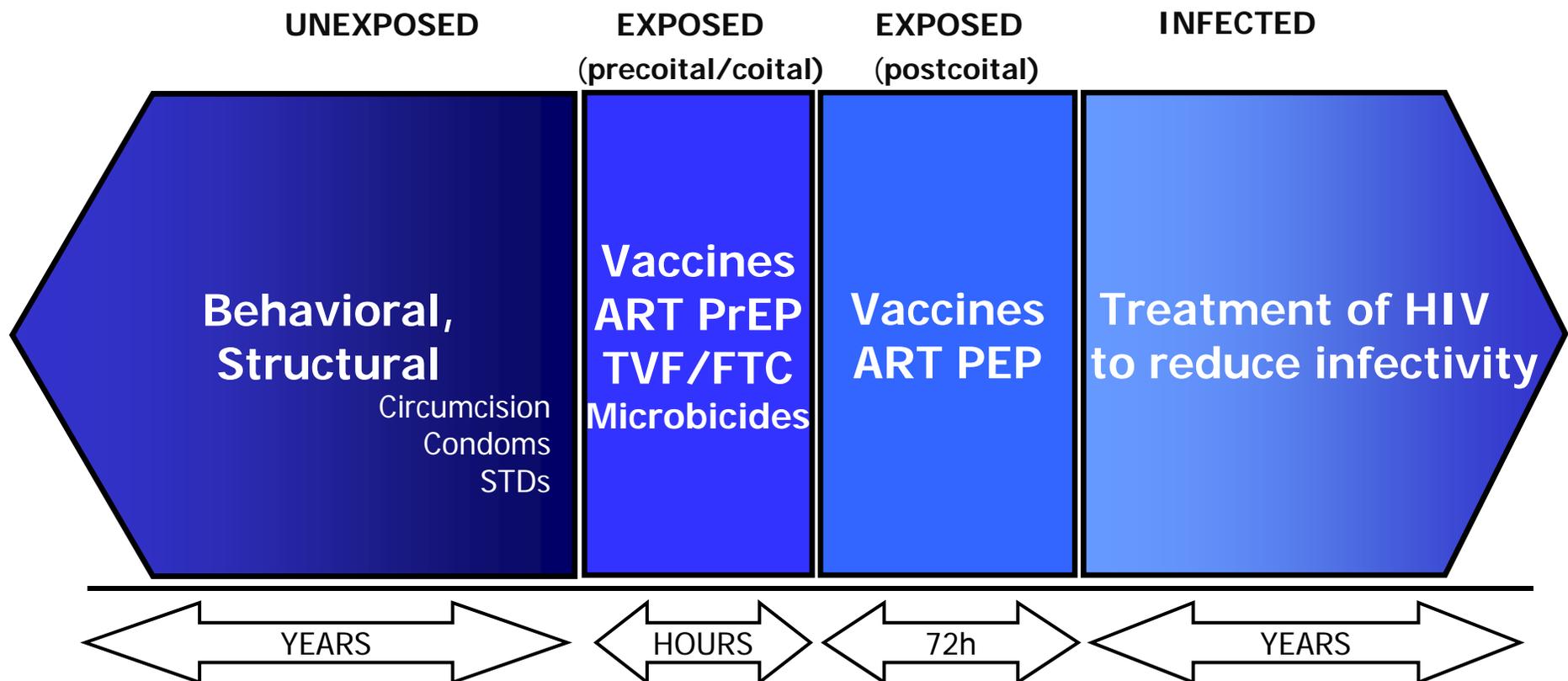
# Proportion MSM $\leq$ 24 years Diagnosed per Year by Race (2003-2012)



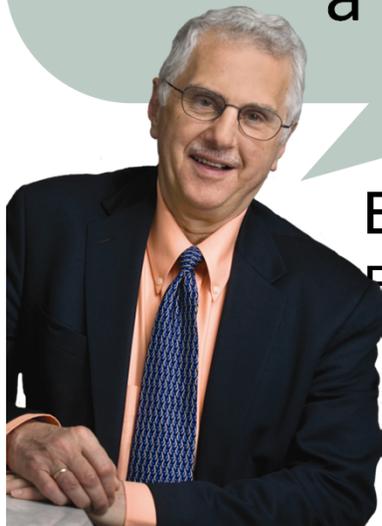
# Four Prevention Opportunities

*Cohen et al. JCI, 2008*

*Cohen et al. JIAS, 2008*



“The results have galvanized efforts to end the world’s AIDS epidemic in a way that would have been inconceivable even a year ago”

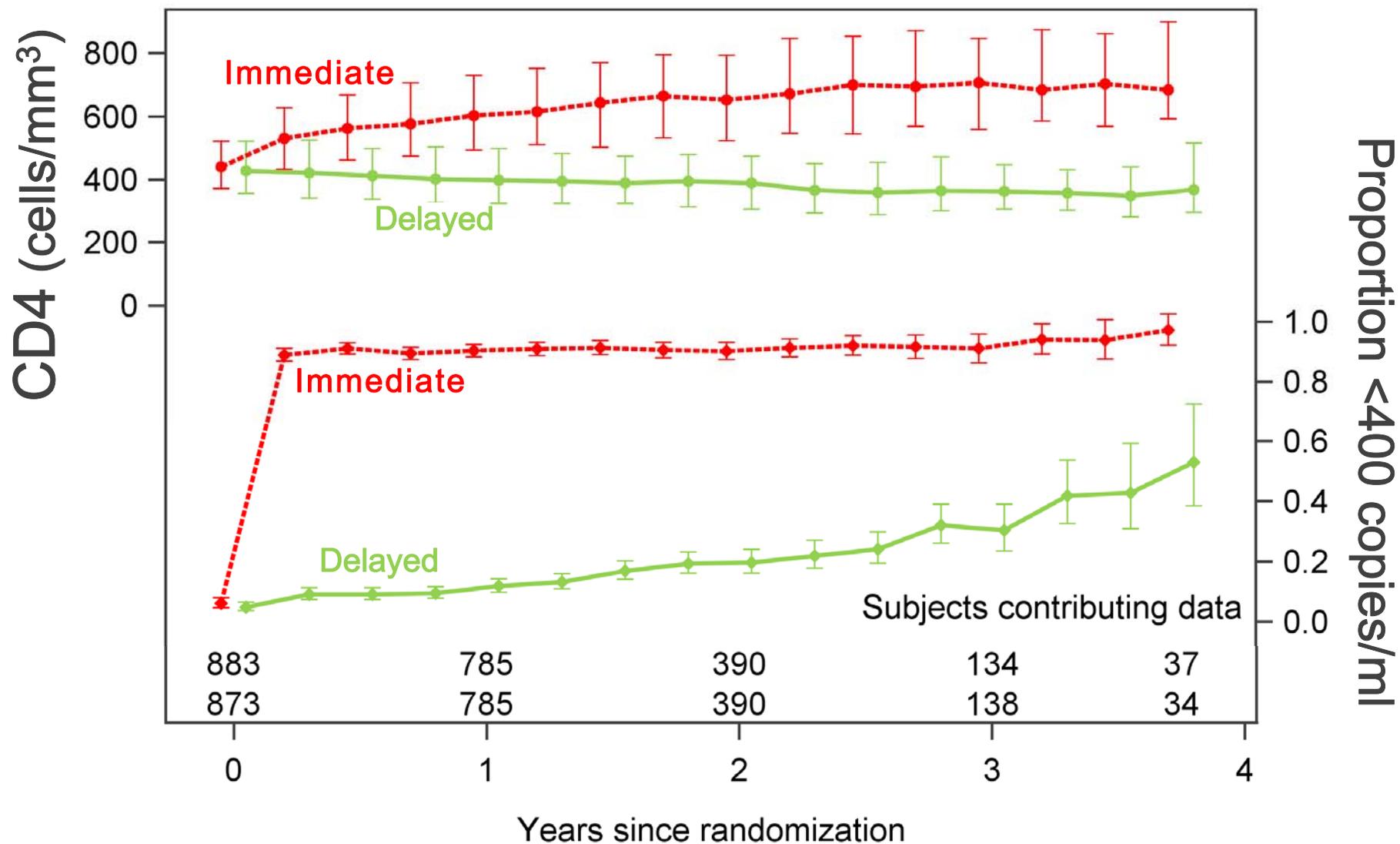


Bruce Alberts  
Editor of *Science*

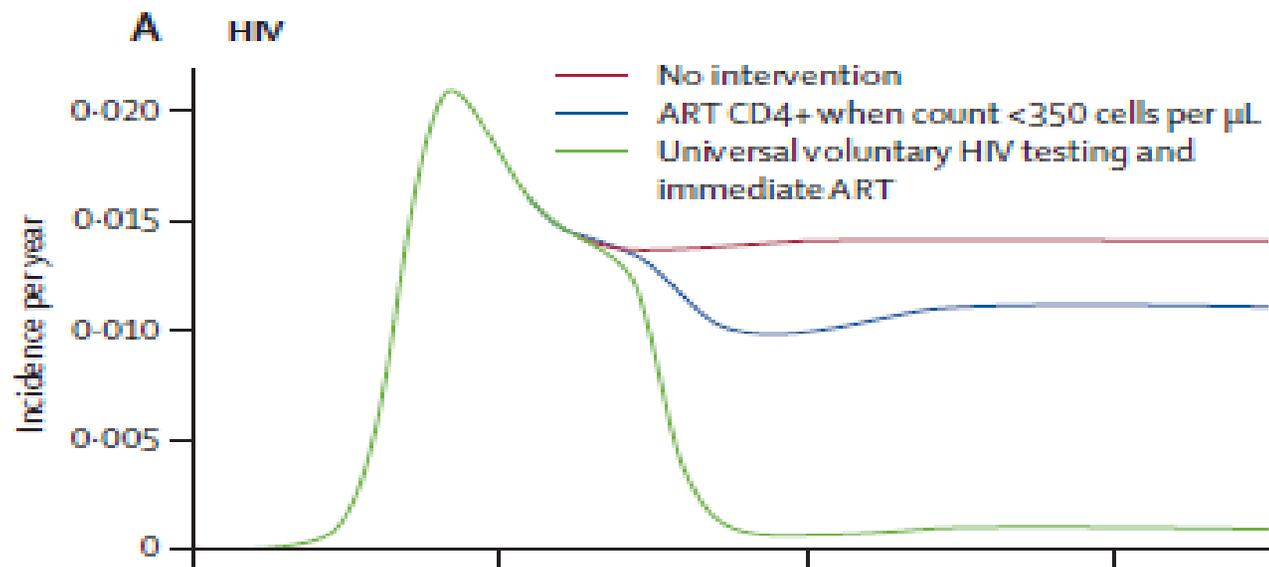


# HIV-1 RNA and CD4 Over Time (ITT)

*Grinsztejn et al. (Lancet ID in press)*



# Test and Treat Model



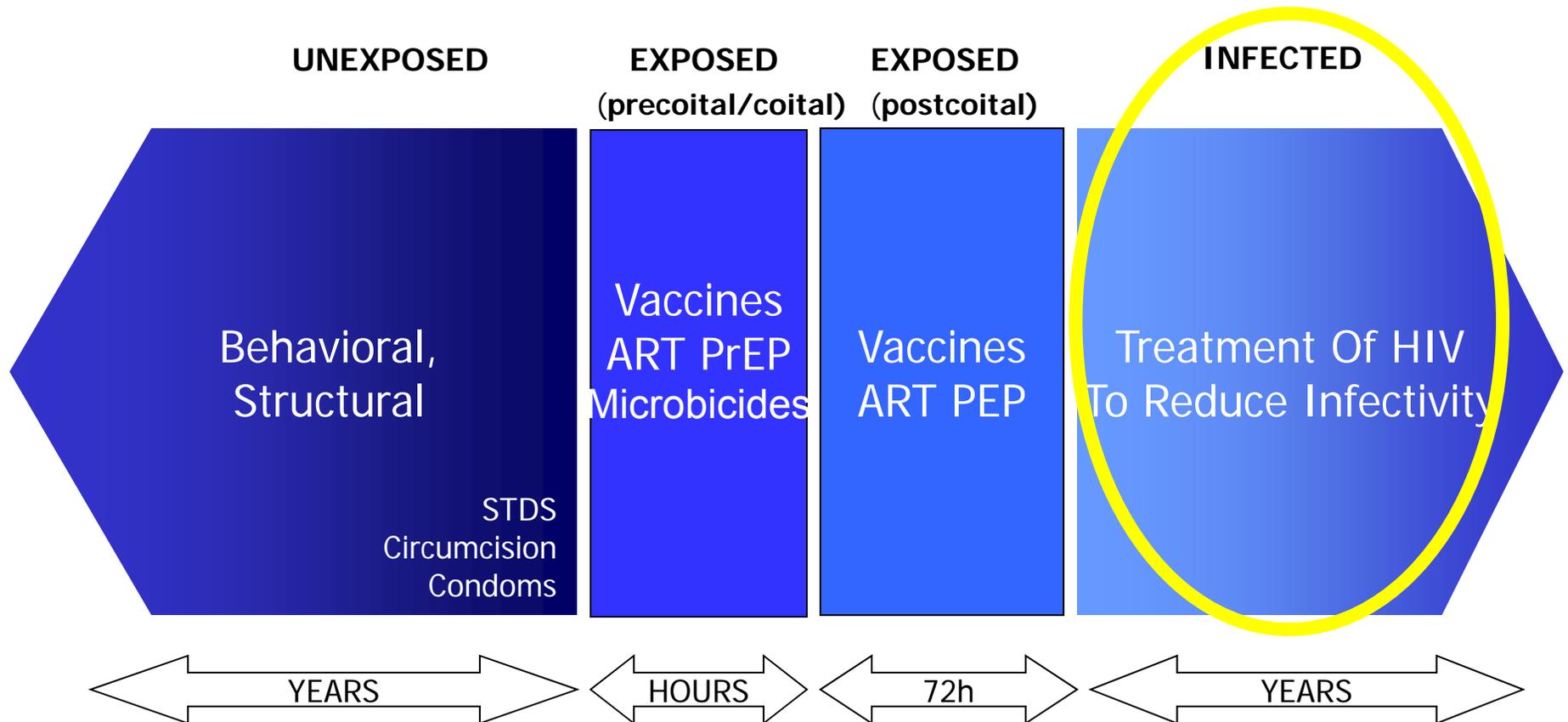
Granich RM, et al Lancet 2009

SPECIAL ARTICLE

## Cost-Effectiveness of HIV Treatment as Prevention in Serodiscordant Couples

Rochelle P. Walensky, M.D., M.P.H., Eric L. Ross, B.A.,  
Nagalingeswaran Kumarasamy, M.B., B.S., Ph.D., Robin Wood, D.Sc.,  
Farzad Noubary, Ph.D., A. David Paltiel, Ph.D., M.B.A., Yoriko M. Nakamura, B.A.,  
Sheela V. Godbole, M.D., Ravindre Panchia, M.B., B.Ch.,  
Ian Sanne, M.B., B.Ch., D.T.M.&H., Milton C. Weinstein, Ph.D., Elena Losina, Ph.D.,  
Kenneth H. Mayer, M.D., Ying Q. Chen, Ph.D., Lei Wang, Ph.D.,  
Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D.,  
George R. Seage III, D.Sc., M.P.H., Myron S. Cohen, M.D.,  
and Kenneth A. Freedberg, M.D.

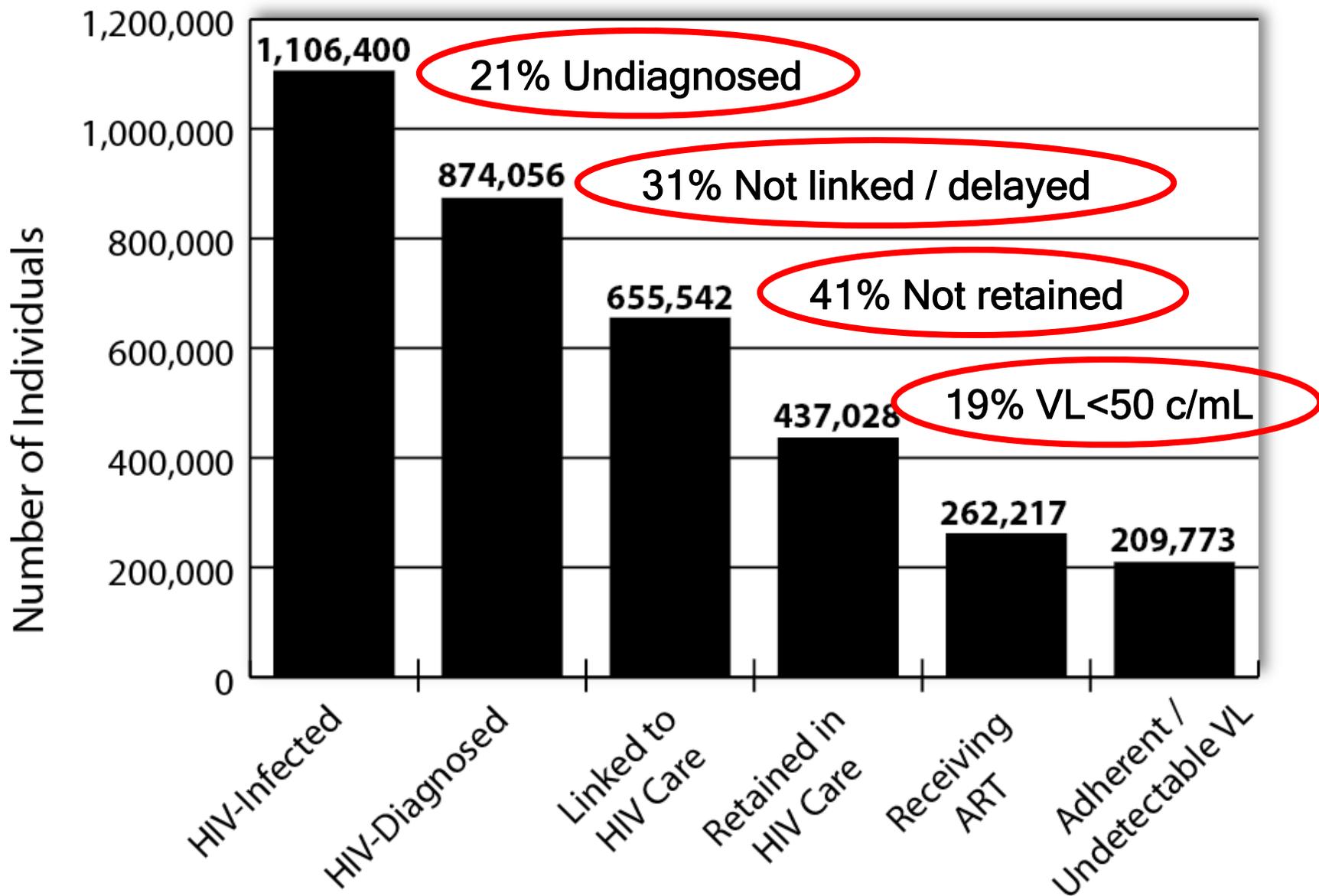
# Four Prevention Opportunities



# Why Everyone Should Start ART?

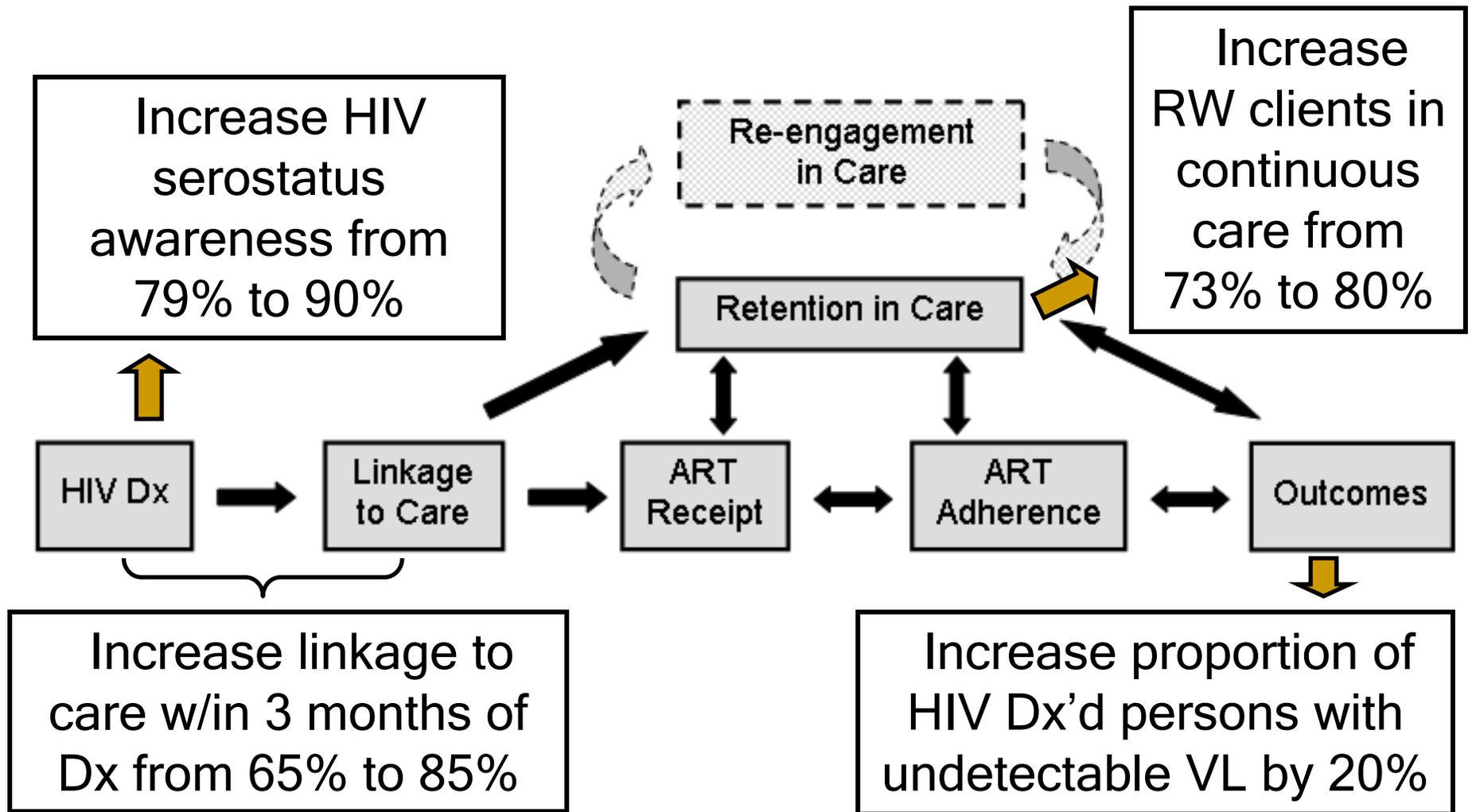
## IAS-USA, DHHS Guidelines

- The consequences of replication (+)
- Reduced long-term survival (?)
- Ongoing HIV transmission (+++)
- Micro and macroeconomic analysis (+)
- *The arguments for delay include*
  - Anticipated detection of novel “harm” (?)
  - Ongoing search for “benefit” (?)
  - Intense focus on logistical challenges
  - Individual needs to prove “readiness”



Adapted from: Gardner et al. *Clin Infect Dis* 2011;52:793, Greenberg et al. *Health Affairs* 2009;28:1677, Marks et al. *AIDS* 2010;24:2665

# National HIV/AIDS Strategy



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Goal

Zero HIV  
Transmission

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# HIV Transmission

Those unaware of infection

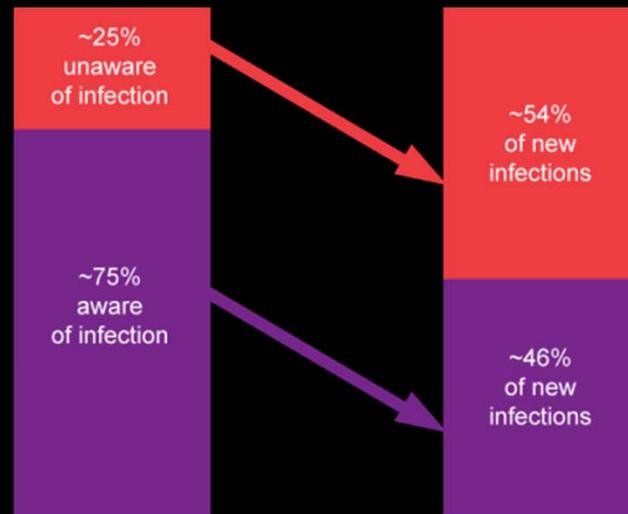
Those aware and not viral suppressed (VS)

Bottom Line Transmission:

- Prevalent Undiagnosed
- Acute HIV Infection
- Diagnosed, but not in care and not VS
- STI/HIV co-infection

# More than Half of New Infections Caused by Those Unaware of Their HIV Infection?

We  
don't  
know  
what  
we  
don't  
know



## Acute HIV: New sexual infections

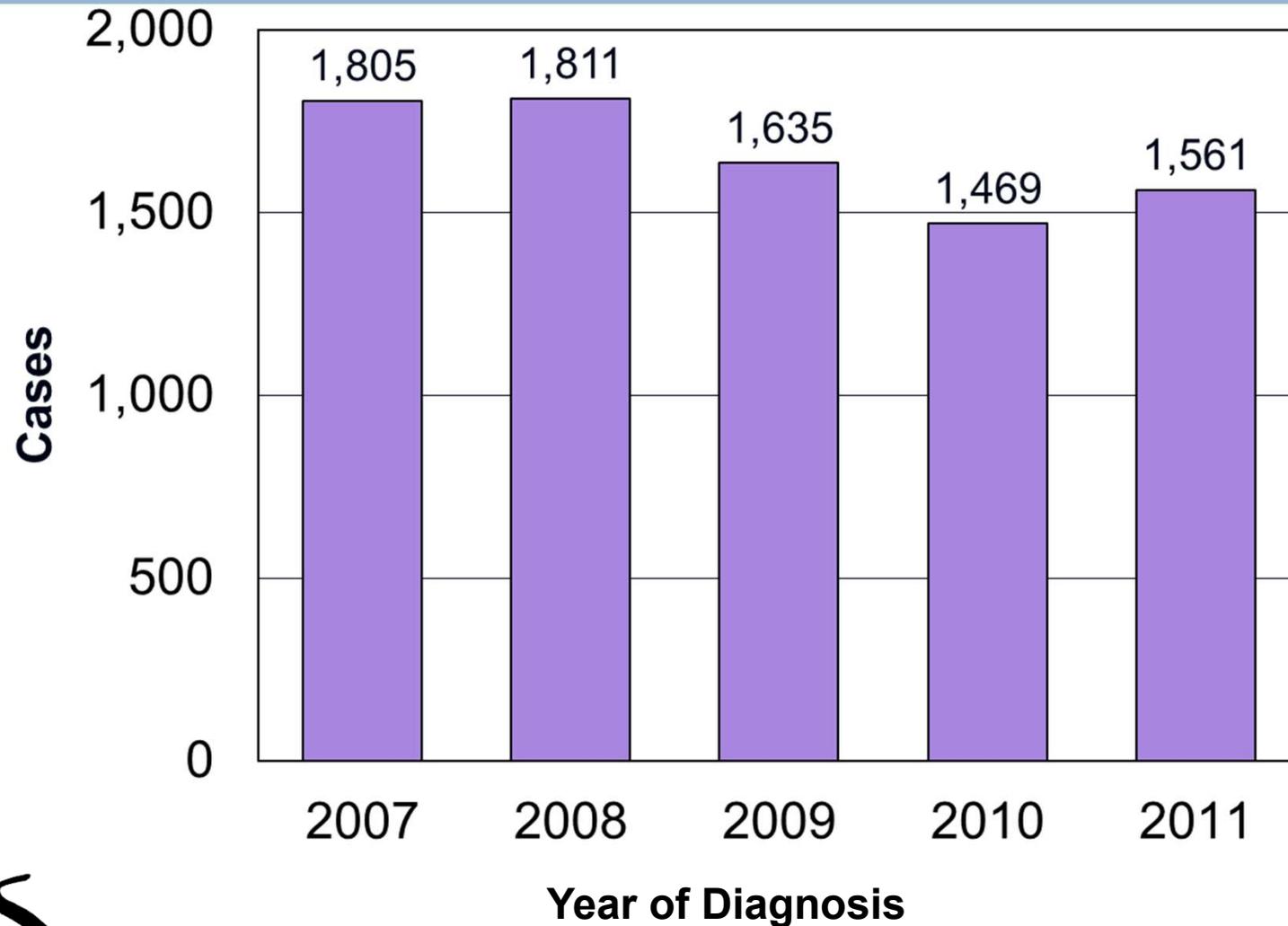
Awareness of serostatus among people with HIV and estimates of transmission

Reference: Marks, et al *AIDS* 2006;20:1447-50.

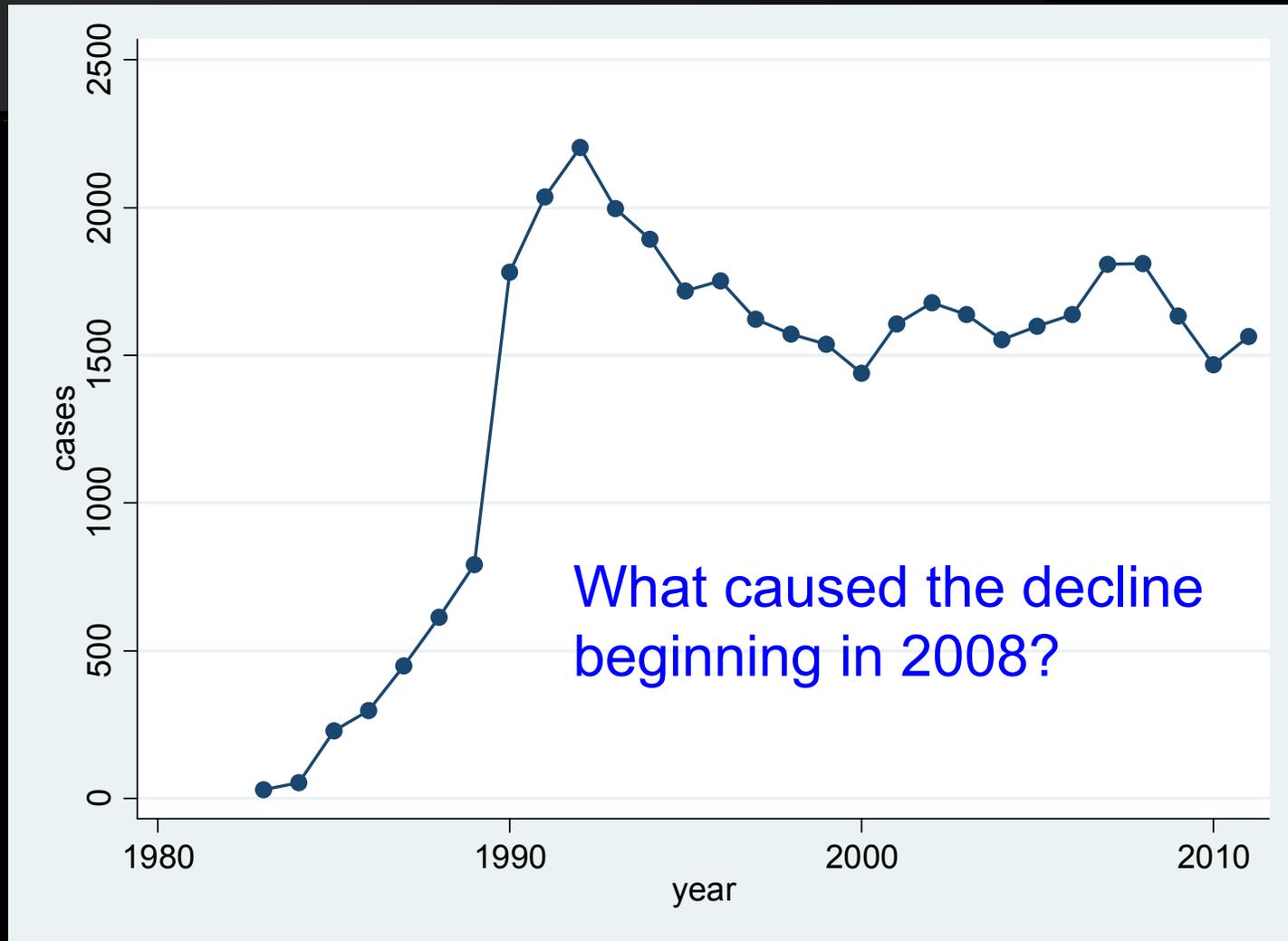
Adapted from Branson, Benard, MD. "Revised Recommendations for HIV Testing in Healthcare.

Settings in the U.S." PowerPoint presentation, February 2007, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Atlanta, GA.

# Number of New HIV Disease Cases in N.C. 2007-2011 (*preliminary*)

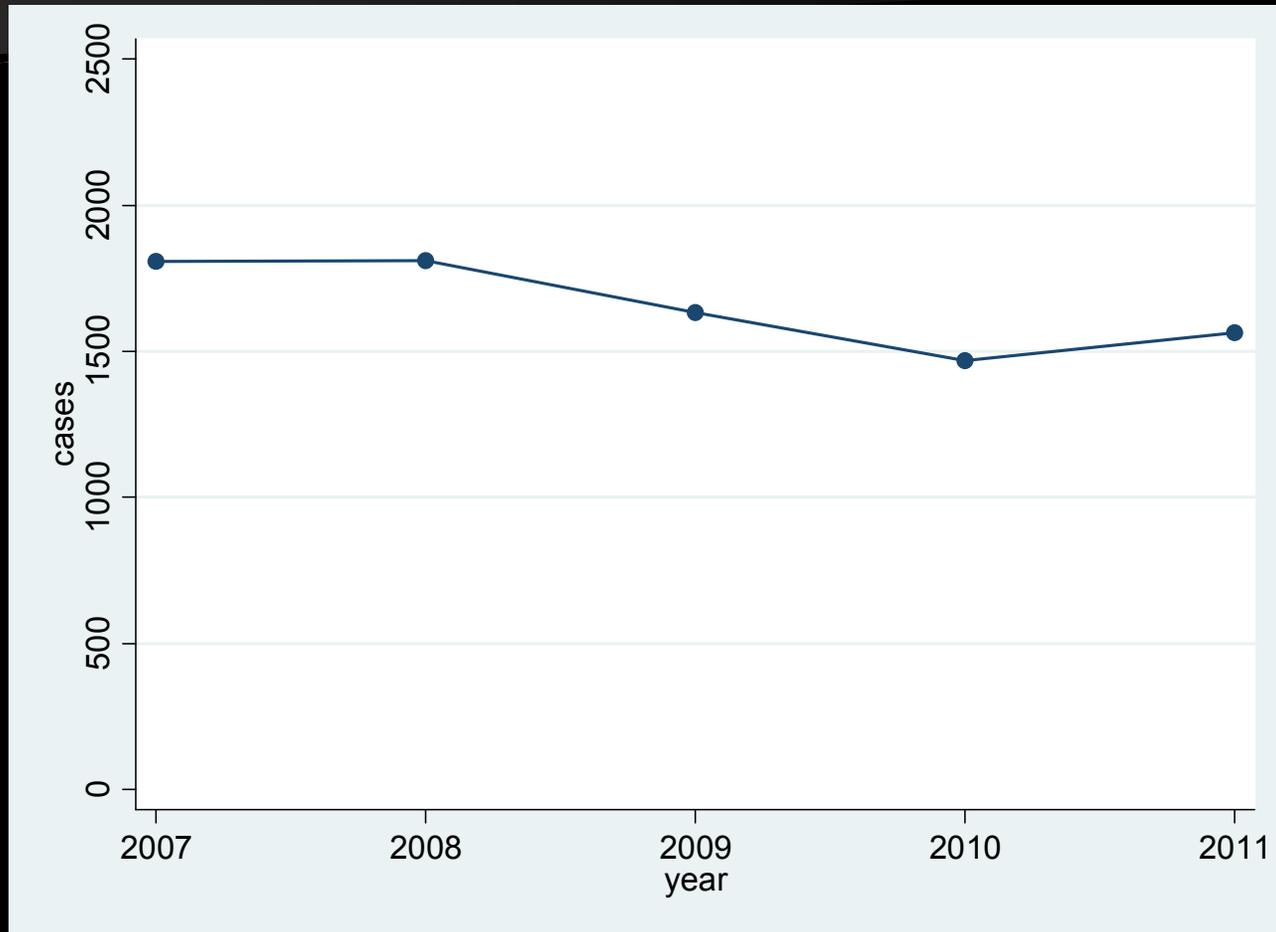


# Newly Diagnosed Cases HIV NC

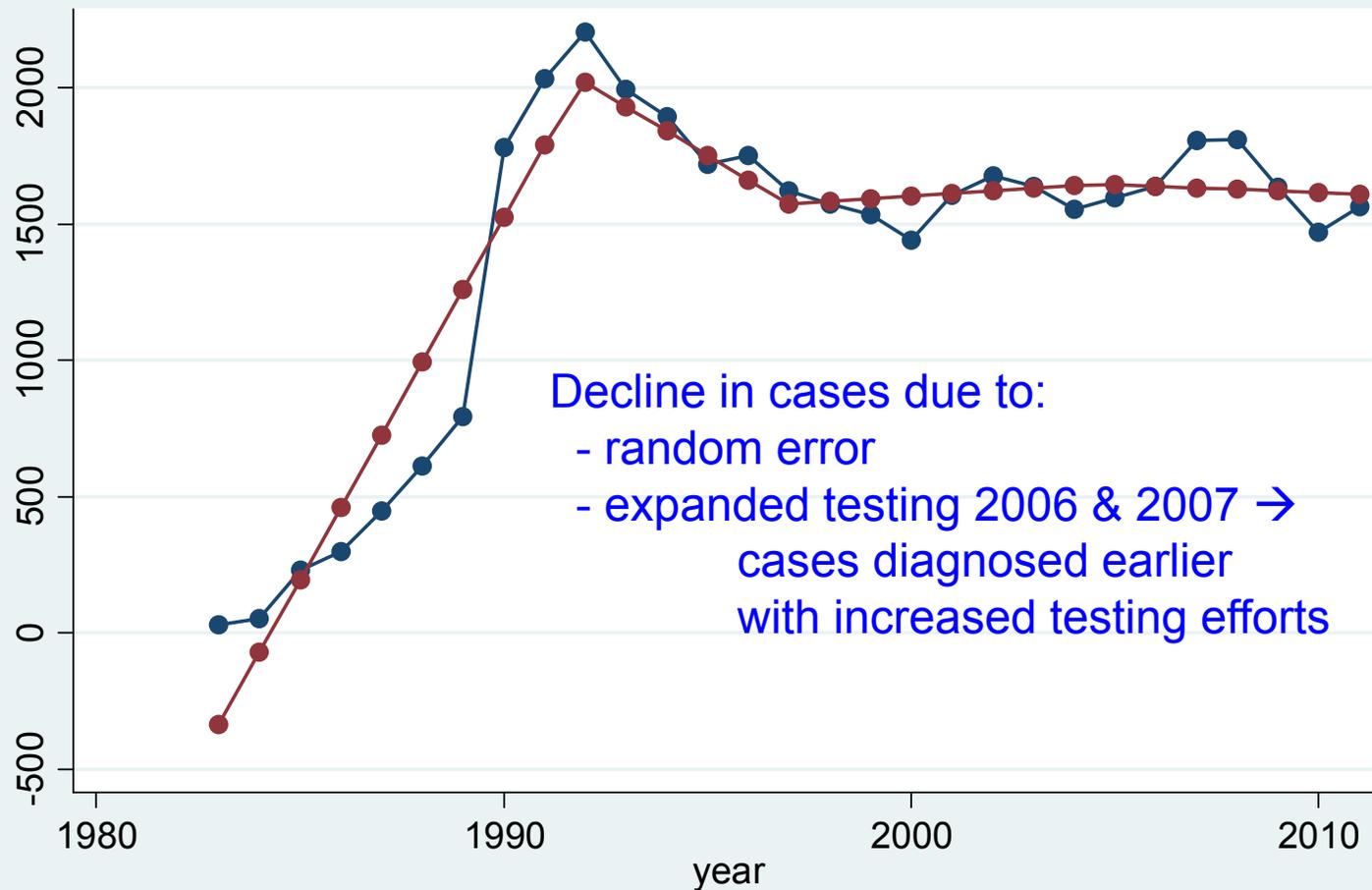


# North Carolina

## New cases $\neq$ Incidence



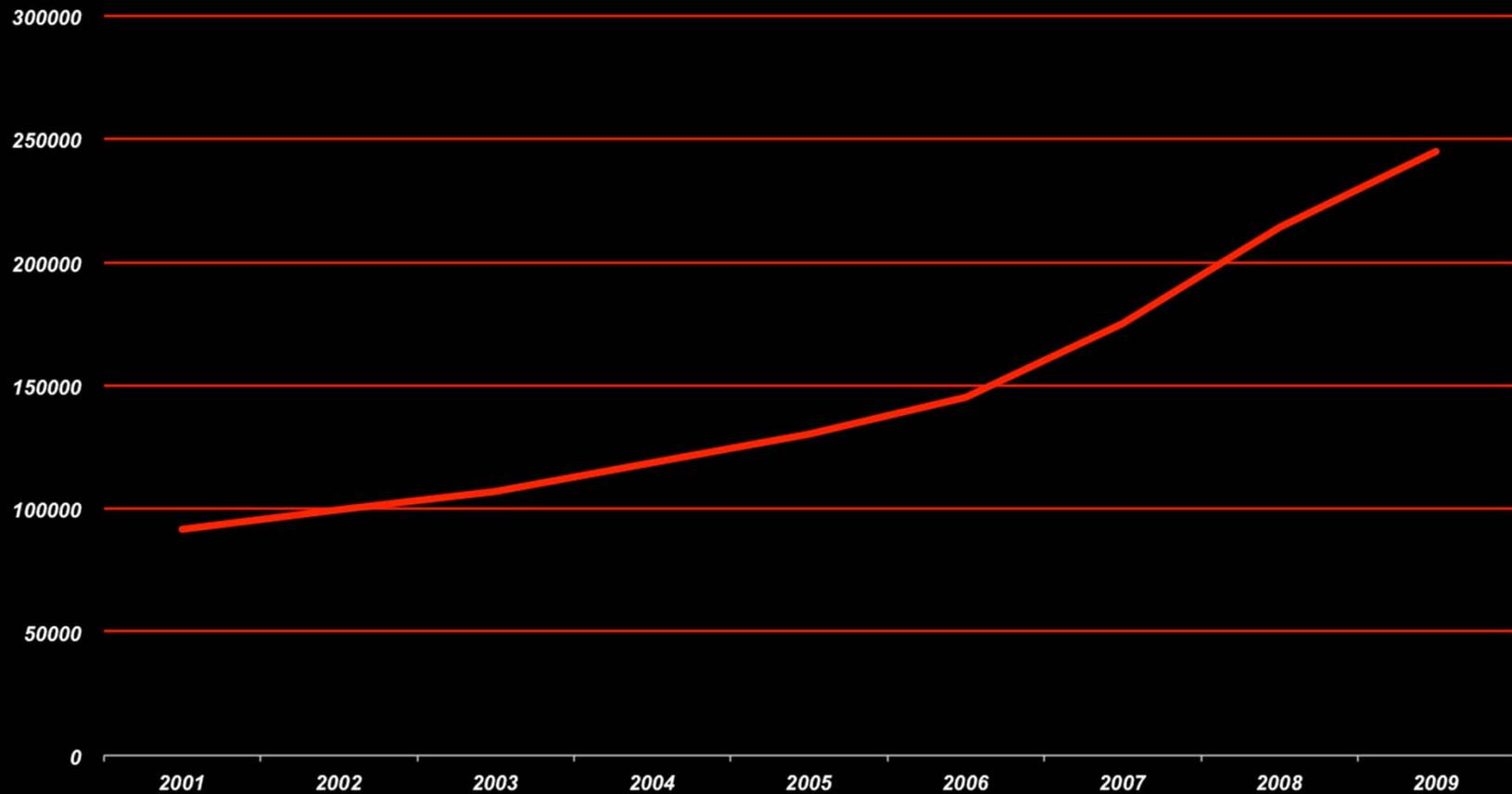
# New cases – possible explanations



—●— cases    —●— Fitted values

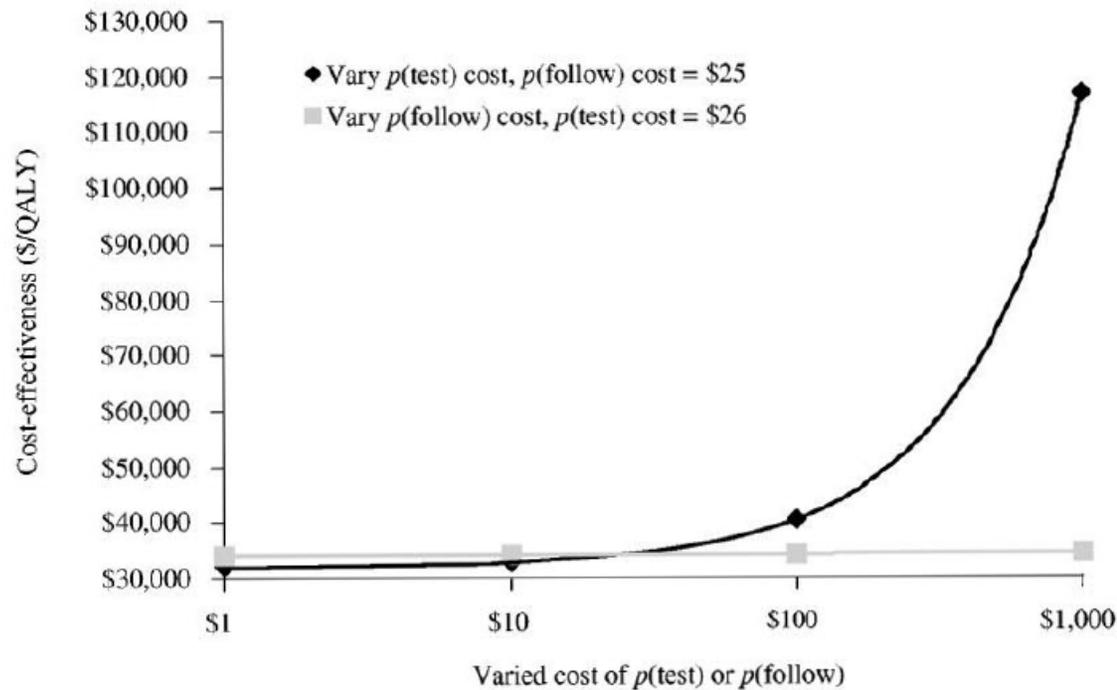
# HIV Tests

## NC Public Health Laboratory

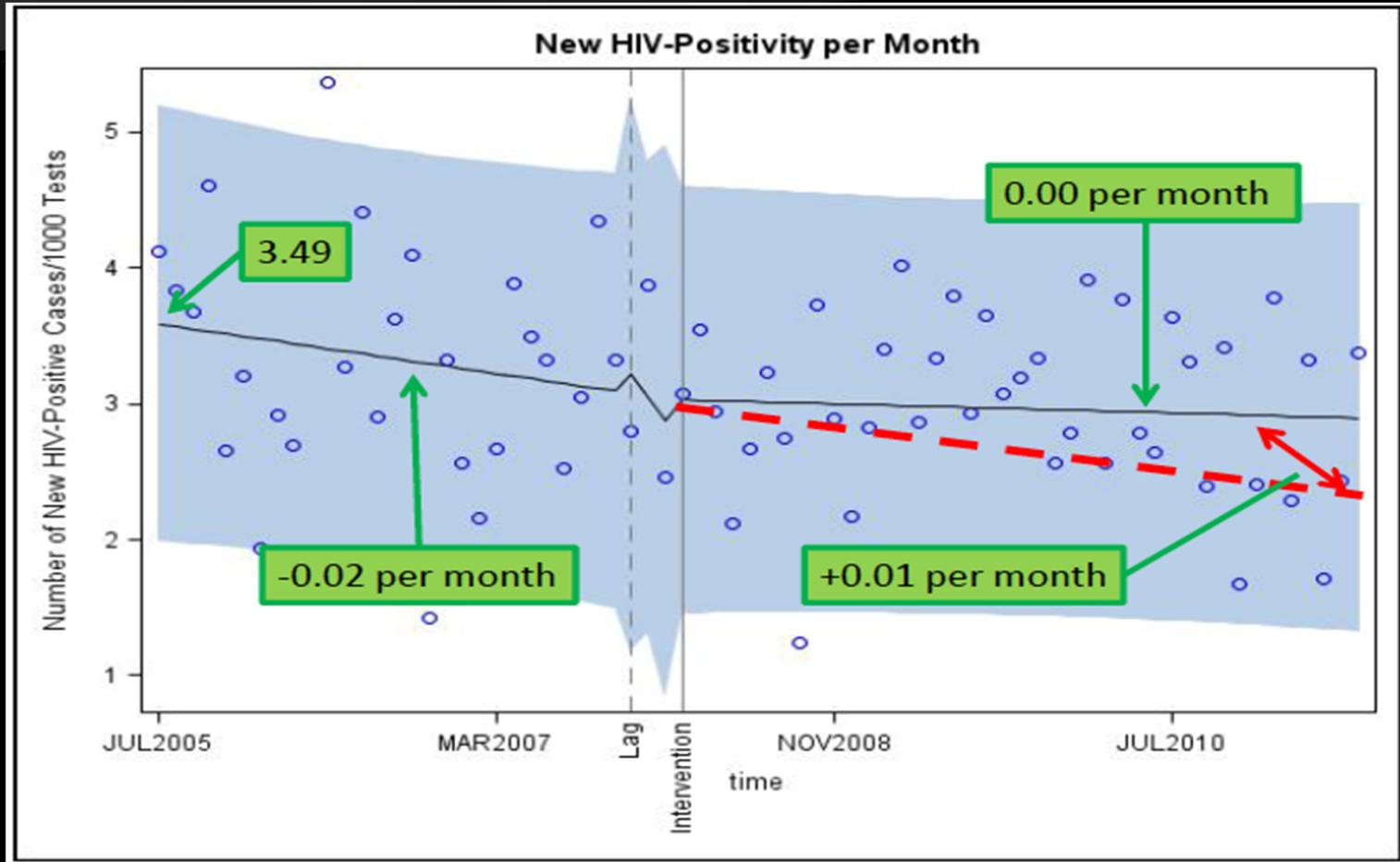


With switch to 4<sup>th</sup> gen may be able to offer 400,000 tests

# Optimal Allocation of Testing Dollars



# Diminishing Return of Expanded Testing NC STD Clinics



Klein 2013 in press

# Minimal Overall Impact of Intervention

Overall, little evidence of intervention impact.

HIV Testing: Pre-intervention increase  
Slowed with intervention

Case Detection: Pre-intervention decrease  
mitigated to zero with intervention

Progression to AIDS: no change

Greatest impact among low-risk persons (women)

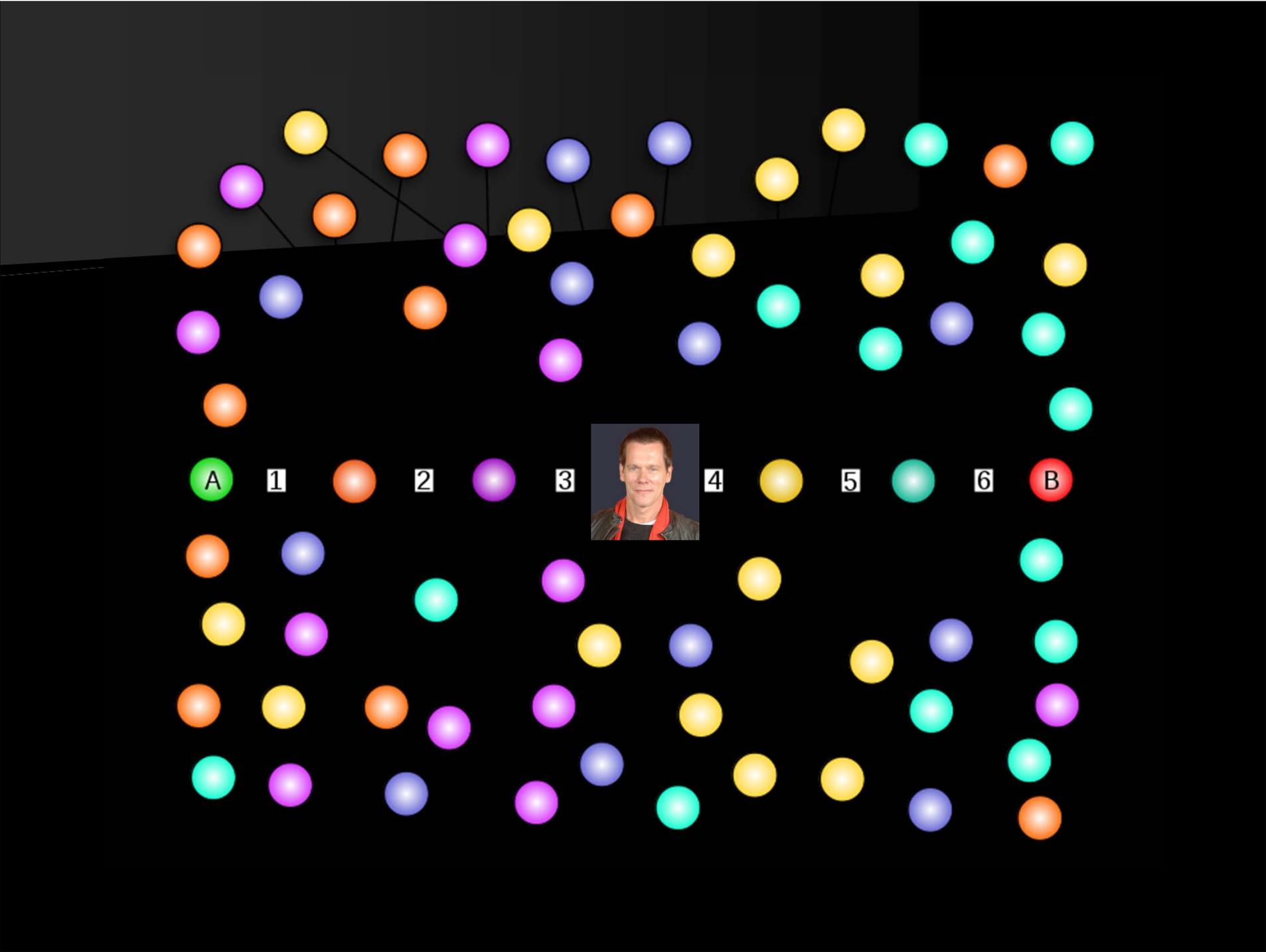
# Cost effectiveness of Test and Treat Depends on Phase of Epidemic

- Homogeneous distribution of risk
- Heterogeneous distribution of risk with random mixing
- Heterogeneous distribution of risk with assortative mixing

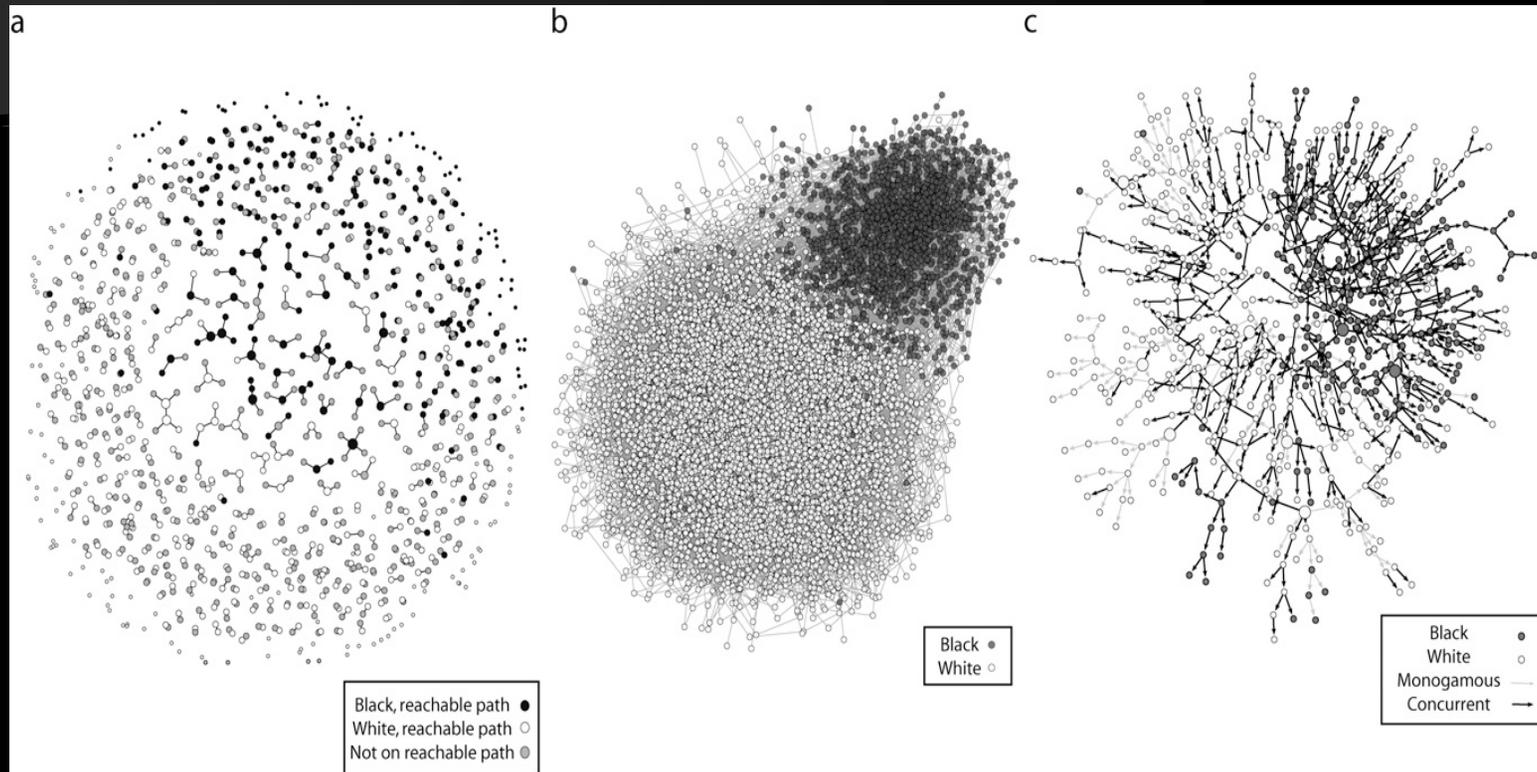
# Not all are the same: Super Spreaders and the 20/80 rule



Galvani and May Nature 2005

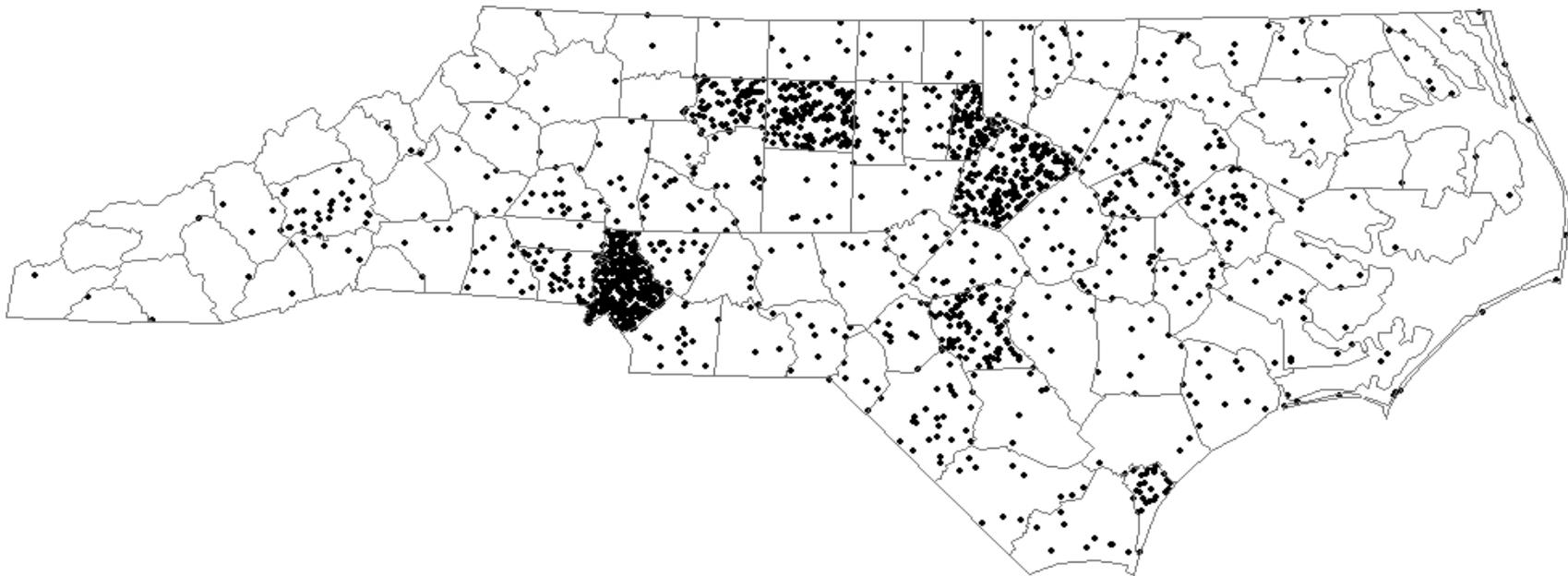


# Concurrency modeling



Simulations based on data from a representative simulation showing (a) contact network from day 1, (b) cumulative contact network (10-year total), and (c) reachable paths from the 10 initially infected seeds. Morris AJPH 2009

## North Carolina HIV diagnoses, all cases, 2007-2011

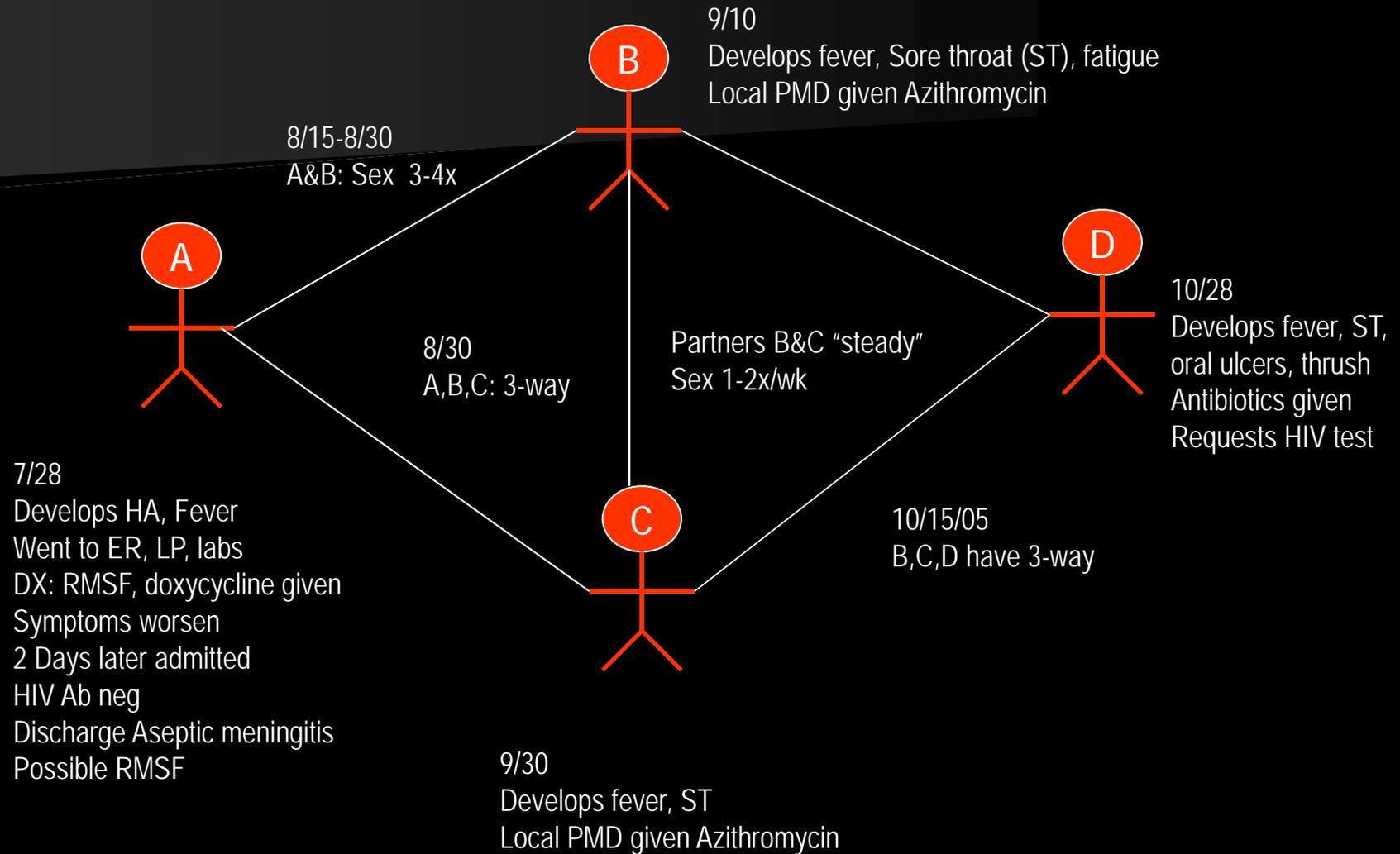


1 dot represents 5 Cases

Note that dots do not represent actual locations of HIV cases,  
but reflect the number of diagnoses in each county.

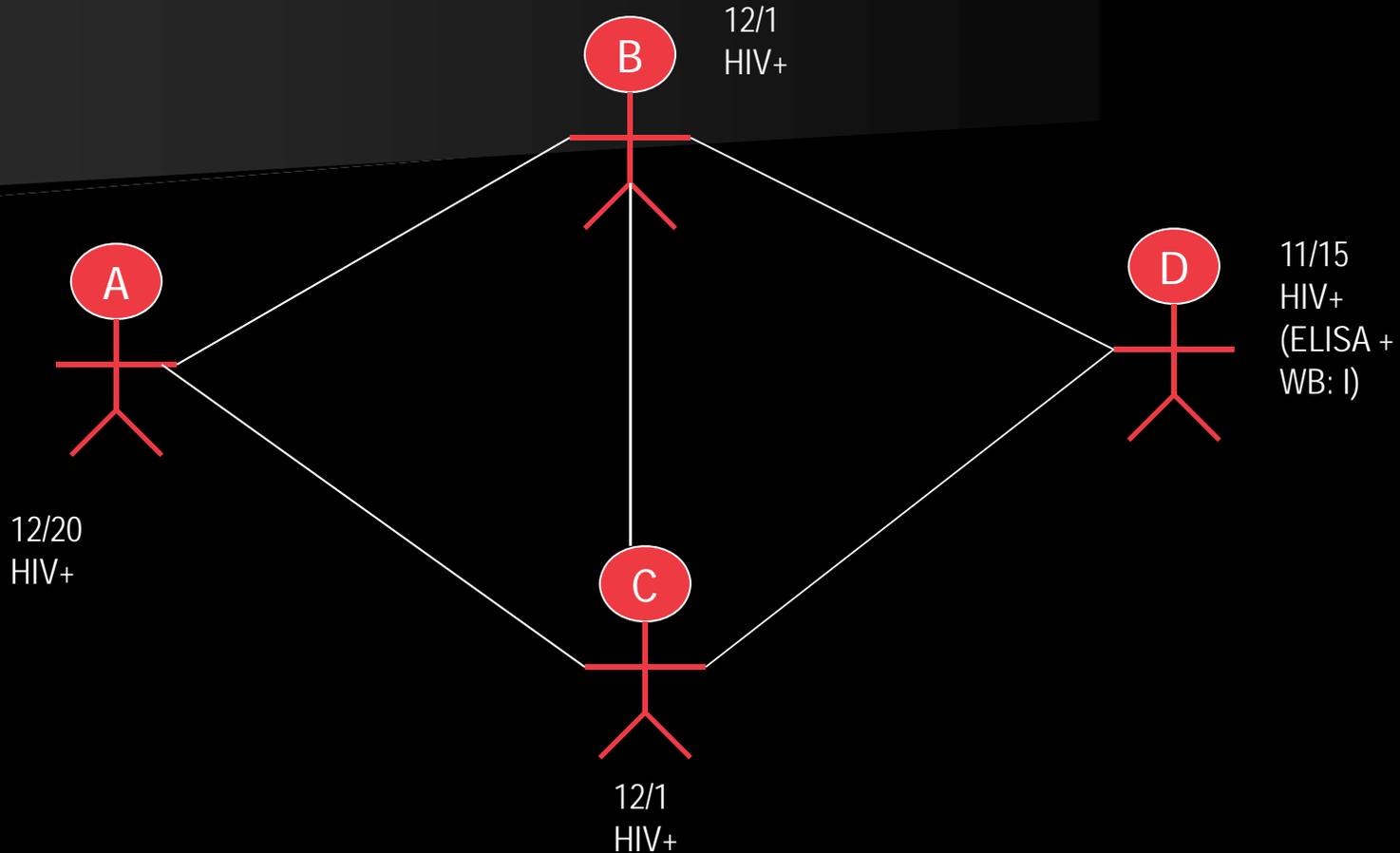


# Case Study



Reference: Leone, Peter, MD. "Acute HIV and the North Carolina STAT Program." PowerPoint presentation, March 18, 2011 Grand Rounds, Akron, Ohio.

# Case Study (cont'd)



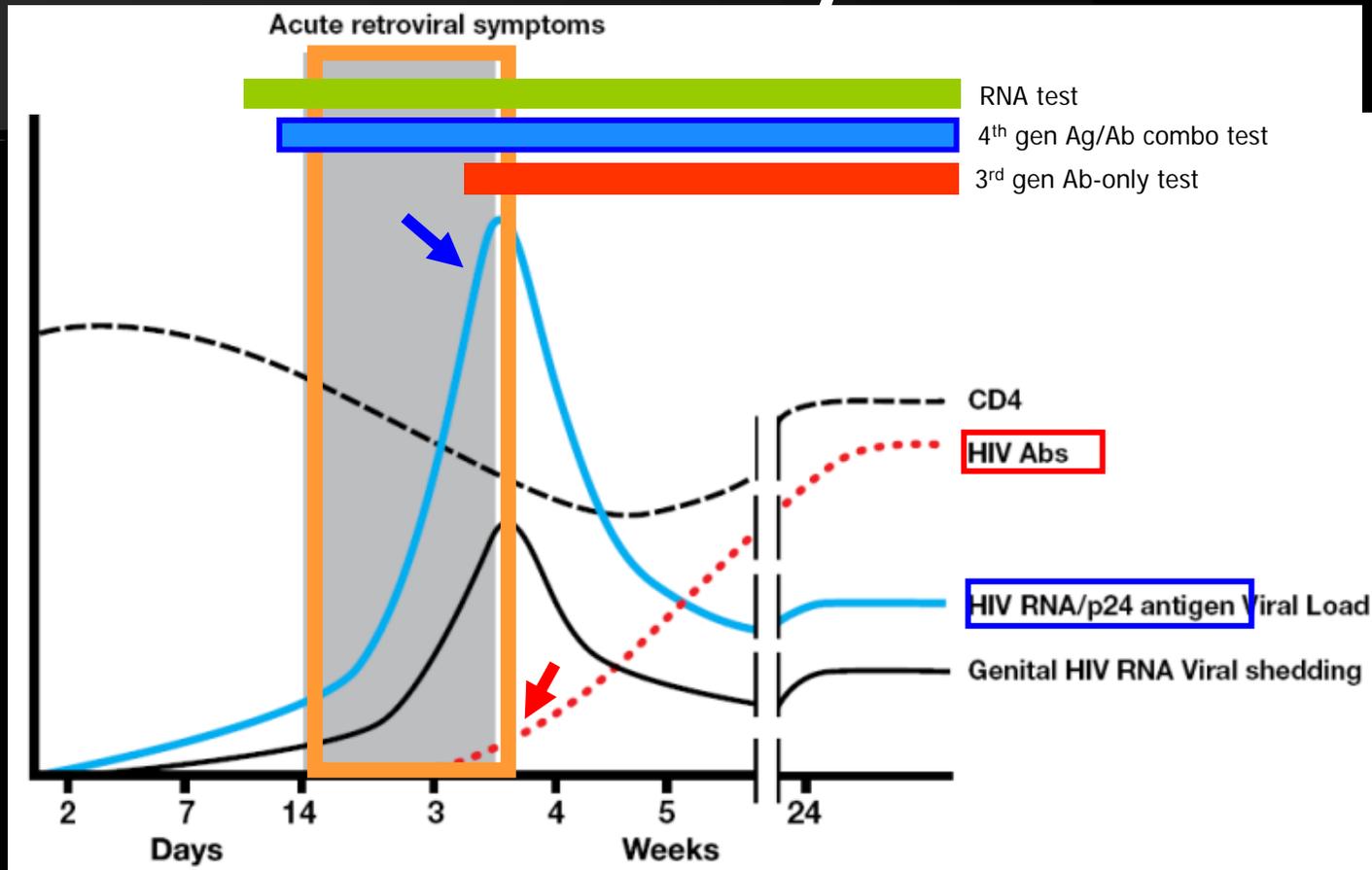
*4 infections could have been avoided*  
if acute HIV infection considered at first presentation

Reference: Leone, Peter, MD. "Acute HIV and the North Carolina STAT Program." PowerPoint presentation, March 18, 2011 Grand Rounds, Akron, Ohio.

# Change in HIV Testing

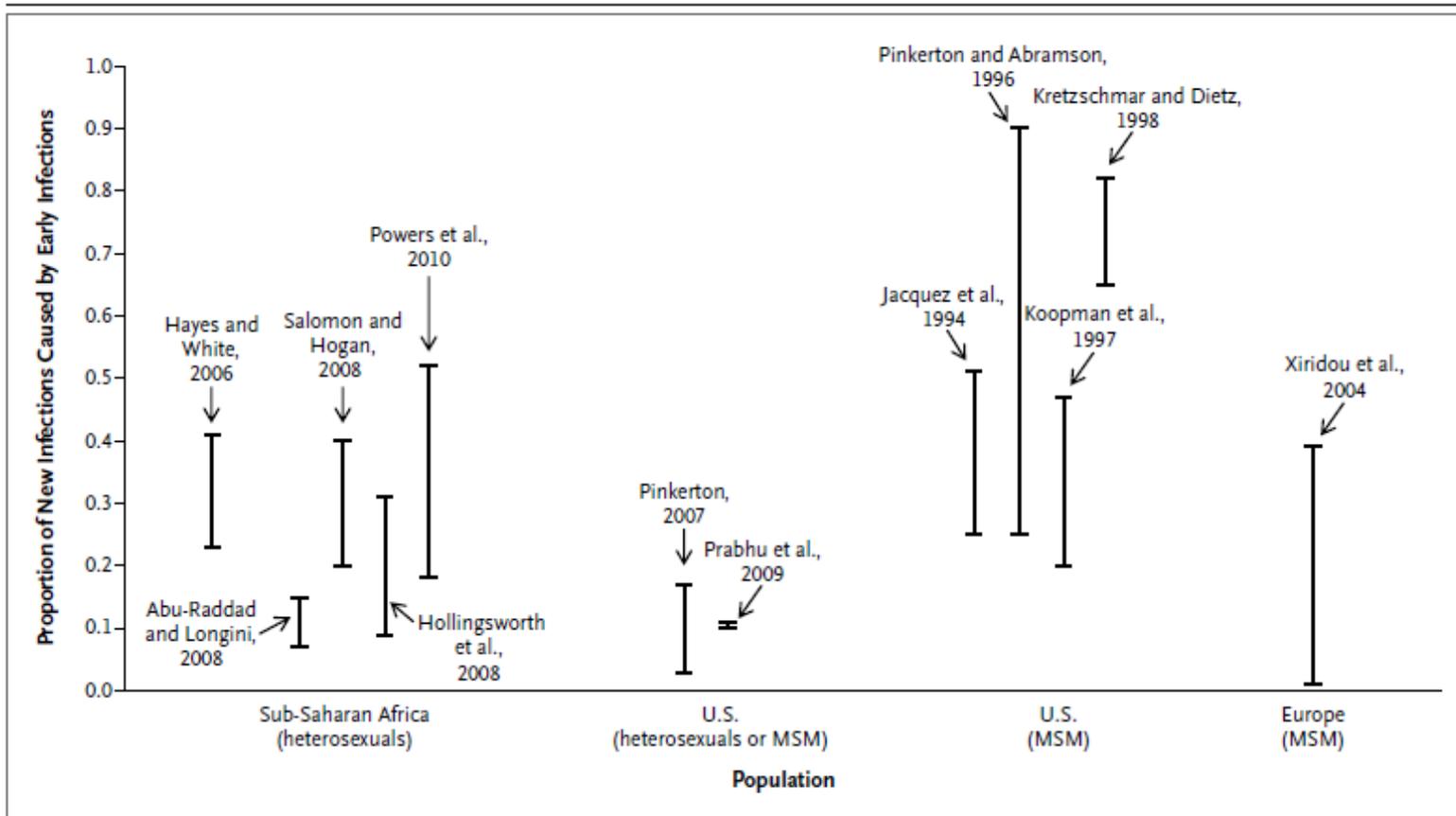
**MIND THE GAP**

# Phases of HIV and Diagnostic HIV Assays



Adapted from: Marquez, *MLO* February 2008. "HIV Testing: An Update."

# Find AHI



**Figure 4.** Role of Acute and Early HIV-1 Infection in the Spread of HIV-1, According to Population Studies in Sub-Saharan Africa, the United States, and Europe.

# Window Periods for HIV Tests

HIV test	Assay method	"Window period" estimates, weeks <sup>a</sup>	"Window period" reduction, days <sup>b</sup>
First-generation EIA	Viral particles used to bind patient HIV Ab, detected by marker conjugated to anti-human Ab	~6	...
Second-generation EIA	Same as first-generation EIA except uses purified HIV Ag or recombinant virus	~4-6	10
Third-generation EIA	"Antigen sandwich": synthetic peptide used to bind patient HIV Ab followed by marker conjugated to additional HIV Ag; able to detect IgM	~3-4	6
Fourth-generation EIA	Uses third-generation EIA methodology plus monoclonal Ab to p24 Ag to detect patient p24 Ag	~2	5
Pooled HIV NAT	First combines multiple individual samples into one common pool, then uses PCR or other amplification techniques to detect patient viral nucleic acids	<1-2	3
Individual HIV NAT	As above, except that samples are tested individually rather than diluted by pooling	<1-2	3

# Detecting Acute HIV Infections

Symptoms



p24 Antigen



HIV RNA

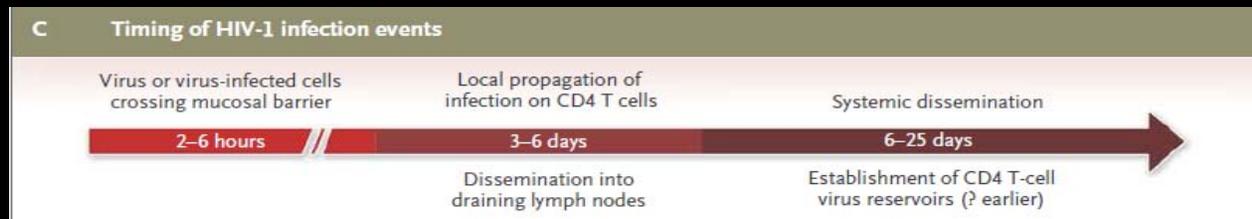


HIV Ab Tests



0 1 2 3 4 5 6 7 8 9 10

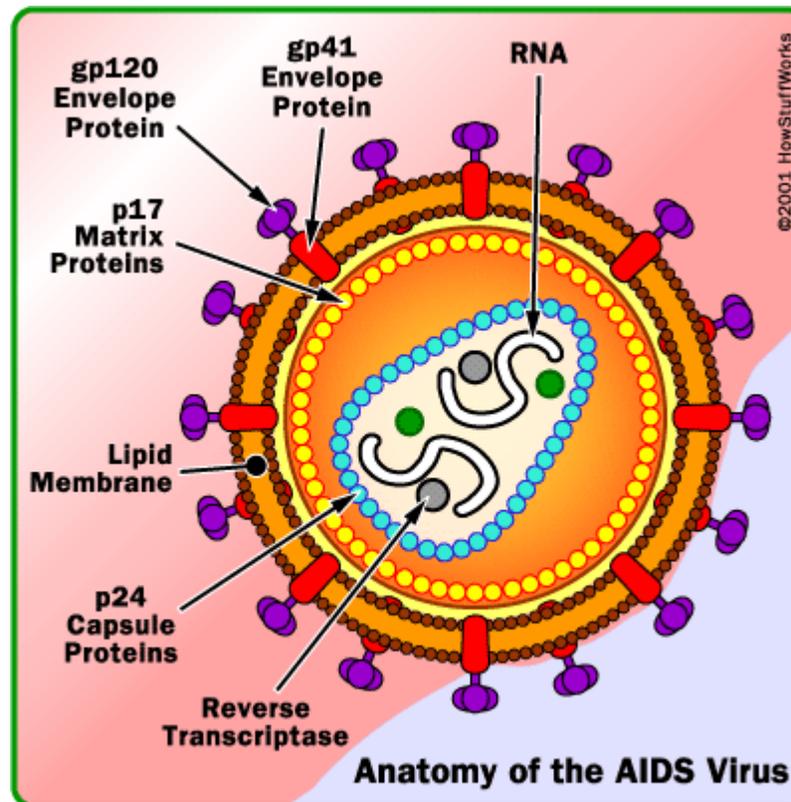
Weeks Since Infection



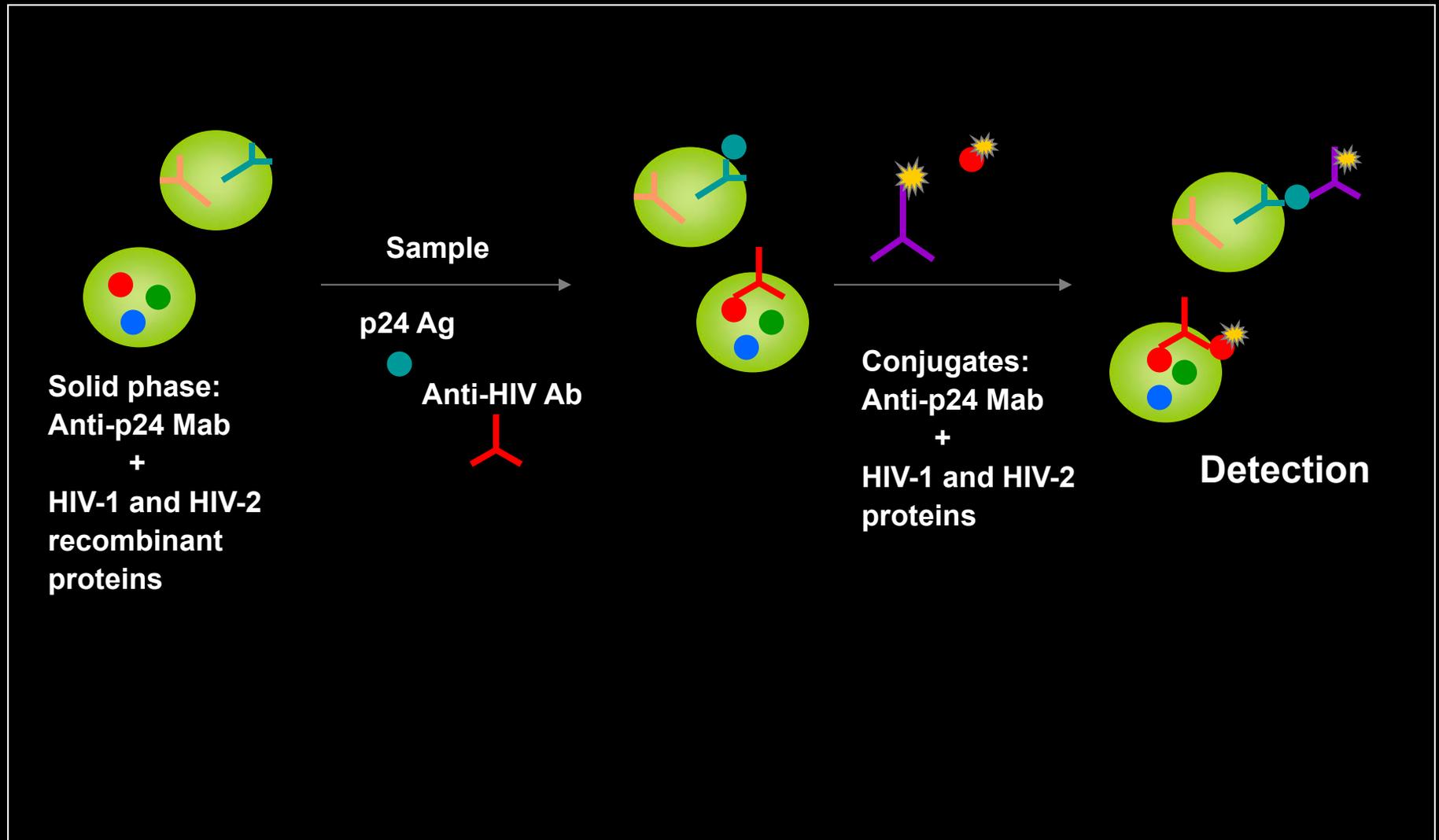
# Direct detection of virion

## Using IA:

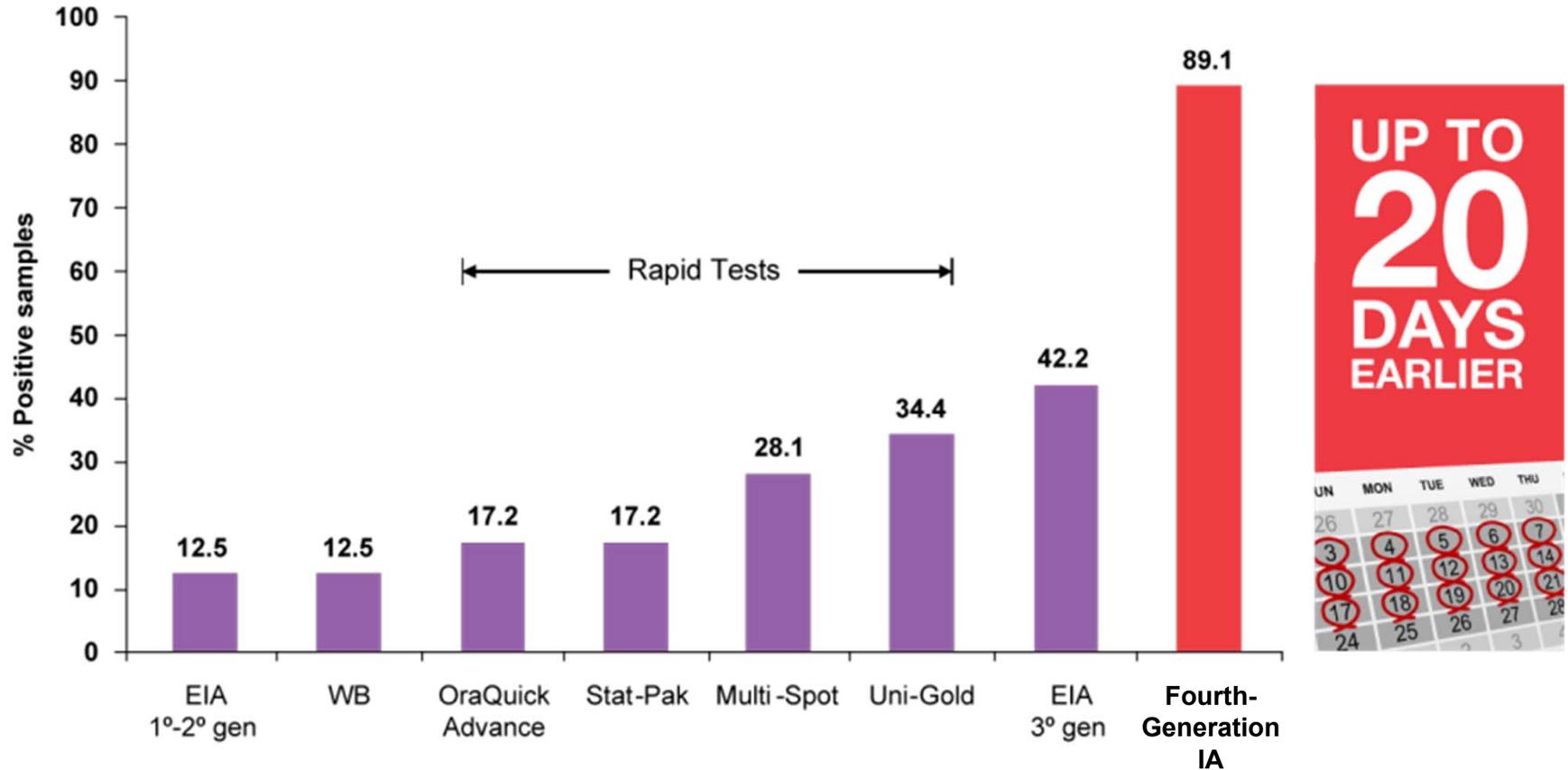
p24 antigen detection (core of virus; most numerous protein—1200 protein copies per virion)



# 4th Generation HIV Ag/Ab Assay



# Choosing a Diagnostic HIV Assay

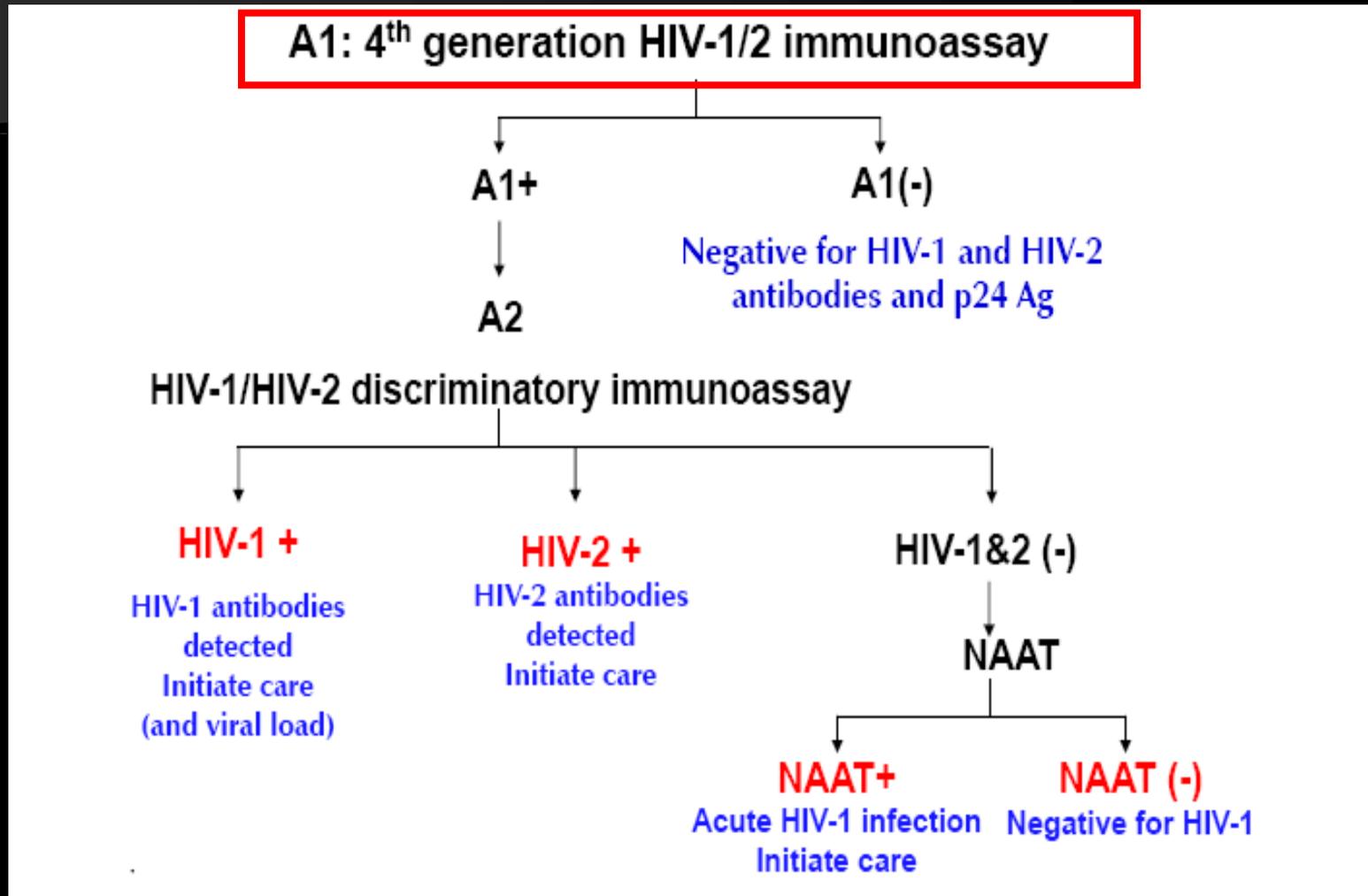


Sensitivity on acute/recent infections ( $n=64$ )

Reference: Architect HIV Ag/Ab Regent Package Insert, Approved by FDA June 2010, pg16,

<http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm216291.htm>

# HIV Confirmation Algorithm



# HIV Test Interpretation

## REPORT #1

### Laboratory Results

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#### *Serology Laboratory*

**HIV Ag/Ab Combo**

Method: **CMLA**

Result: **Nonreactive**

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### Additional Information

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#### **Clinical Interpretation:**

HIV-1 p24 Antigen and HIV-1/HIV-2 Antibodies were not detected. Patient negative for HIV.

#### **Recommended Follow-Up Action:**

HIV-1 p24 Antigen may be negative for 14 days after acquisition of HIV infection. Recommend repeat HIV testing as per state and CDC guidelines. Repeat HIV testing recommended in 3 months for men who have sex with men (MSM).

# HIV Test Interpretation

## REPORT #2

### Laboratory Results

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#### *Serology Laboratory*

**HIV Ag/Ab Combo**

Method: **CMIA**

Result: **Reactive\_**

**Rapid HIV-1/HIV-2 Antibody**

Method: **Rapid EIA**

Result: **HIV-1 Positive**

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### Additional Information

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#### **Clinical Interpretation:**

HIV-1 Antibody was detected. Patient HIV infected.

#### **Recommended Follow-Up Action:**

Please consult with Disease Intervention Specialist to arrange for linkage to care [and partner notification](#).

# HIV Test Interpretation

## REPORT #6

### Laboratory Results

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#### *Serology Laboratory*

<b>HIV Ag/Ab Combo</b>	Method: <b>CMLA</b>	Result: <b>Reactive_</b>
<b>Rapid HIV-1/HIV-2 Antibody</b>	Method: <b>Rapid EIA</b>	Result: <b>Nonreactive</b>
<b>HIV-1 RNA *</b>	Method: <b>NAAT</b>	Result: <b>Not Detected</b>

#### **Comments:**

- \* This test was developed and its performance characteristics determined by the NCSLPH. It has not been cleared by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

### Additional Information

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#### **Clinical Interpretation:**

HIV-1/HIV-2 infection status considered negative.

#### **Recommended Follow-Up Action:**

If no risk factors for HIV in prior 14 days, recommend repeat HIV testing as per state and CDC guidelines. Repeat HIV testing recommended in 3 months for men who have sex with men (MSM).

# HIV Test Interpretation

## REPORT #7

### Laboratory Results

#### *Serology Laboratory*

HIV Ag/Ab Combo	Method: CMIA	Result: <b>Reactive</b>
Rapid HIV-1/HIV-2 Antibody	Method: Rapid EIA	Result: <b>Nonreactive</b>
HIV-1 RNA *	Method: NAAT	Result: <b>Detected</b>

#### **Comments:**

\* This test was developed and its performance characteristics determined by the NCSLPH. It has not been cleared by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

### Additional Information

#### **Clinical Interpretation:**

HIV-1 RNA detected. Acute HIV Infection.

#### **Recommended Follow-Up Action:**

Please immediately consult with Disease Intervention Specialist and the North Carolina STAT program to arrange for further HIV-1 testing and immediate linkage to care. Recommend clinical evaluation with Infectious Disease Specialist for evaluation and care of Acute HIV Infection.

# HIV Test Interpretation

## REPORT #9

### Laboratory Results

#### *Serology Laboratory*

HIV Ag/Ab Combo	Method: CMIA	Result: Reactive
Rapid HIV-1/HIV-2 Antibody	Method: Rapid EIA	Result: HIV-1 Indeterminate
HIV-1 RNA *	Method: NAAT	Result: Detected

#### **Comments:**

\* This test was developed and its performance characteristics determined by the NCSLPH. It has not been cleared by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

### Additional Information

#### **Clinical Interpretation:**

HIV-1 RNA detected. Patient HIV infected and this likely represents Acute HIV infection.

#### **Recommended Follow-Up Action:**

Please immediately consult with Disease Intervention Specialist and the North Carolina STAT program to arrange for further HIV-1 testing, linkage to care and partner notification. Recommend clinical evaluation with Infectious Disease Specialist for evaluation and care of Acute HIV Infection.

## Remember

- 4<sup>th</sup> gen positive with either negative or Indeterminate WB ~~=~~ False Positive
- Assume AHI and follow up with HIV RNA
- 4<sup>th</sup> gen + with ELISA and/or WB -/I and RNA + is diagnostic for AHI

# **HIV RAPID TESTING EARLY REFERRAL TO CARE**

**dual rapid testing protocol**

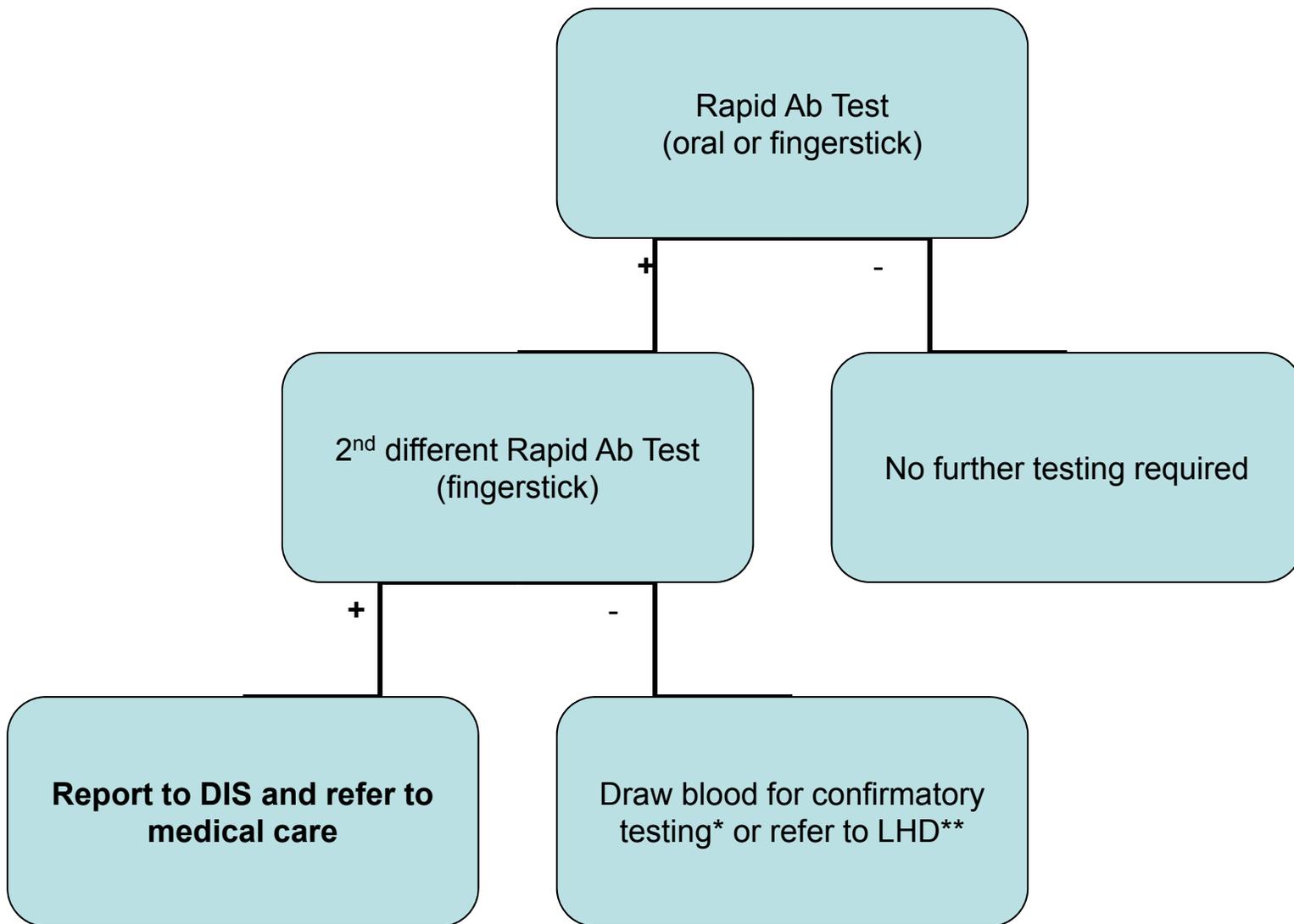
# EARLY REFERRAL TO CARE FOR RAPID POSITIVE

Repeatedly positive HIV antibody tests meets case definitions for HIV infection

Patients who test positive by more than one rapid HIV test should be:

referred to medical care

reported to the regional DIS office



**\*If the confirmatory blood work is positive, patients should be reported to DIS and referred to care.**

**\*\*Consider also referring patient to a HIV medical provider for confirmatory testing.**

# WHEN YOU GET A POSITIVE

Follow protocol for dual rapid testing

Provide counseling and referral (to DIS and to care)

Notify HIV and STD prevention office of all positives

# **WHAT TO SAY WHEN YOU GET A POSITIVE? 2 POSITIVE RAPID TESTS ON SAME DAY**

- Make sure client matches name and other info on test result log and labeled test kit.
- Give the test results immediately. Say clearly, “Your tests were positive. This means that you have HIV infection. Further evaluation for treatment is needed with referral to care.”
- Allow silence. Don’t rush the client.
- Assess the clients understanding of the results .

# WHAT TO SAY WHEN YOU GET A POSITIVE?

## 2 POSITIVE RAPID TESTS ON SAME DAY

- Ask “ who have you told about getting HIV testing today?” This may be a clue to a person who will provide support
- Inform them of disease control measures
- Tell them that a DIS will be in contact with them (to help with follow-up counseling and to help notify their partners)
- Refer to care and to HIV case manager who can assist with access and coordination of services and resources

## **FOLLOW-UP FOR NEGATIVES**

The window period for rapid tests is 4-8 weeks.

Repeat HIV testing is recommended for all MSM and high risk individuals every 3 months.

A negative HIV test does not reduce your risk for HIV, take steps to reduce your risk.

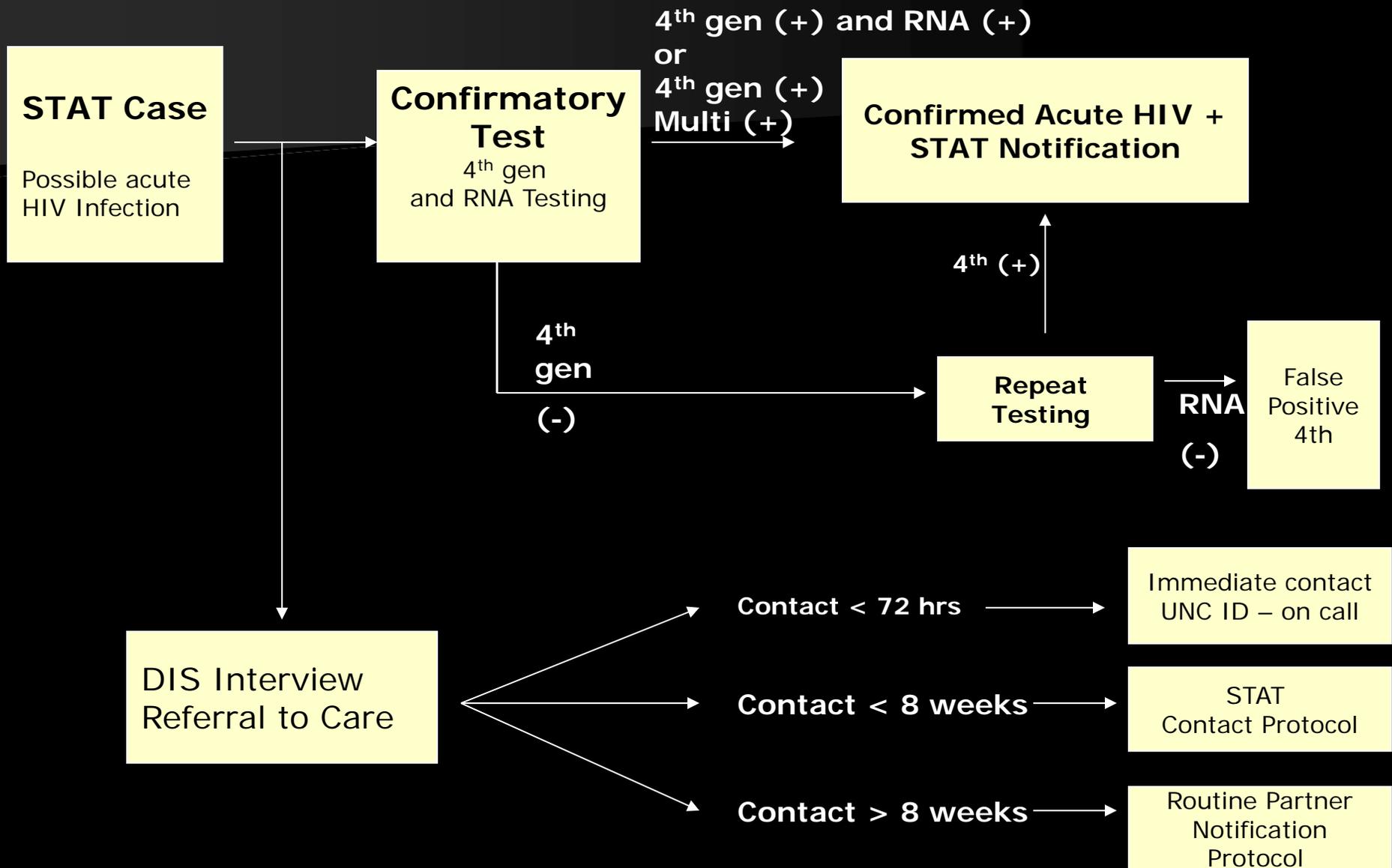
Anyone with signs or symptoms consistent with Acute HIV (2 Or more of the following signs, symptoms: fever of more than 48-72 hours, rash and/or diffuse lymphadenopathy) should be referred for further medical evaluation and to DIS.

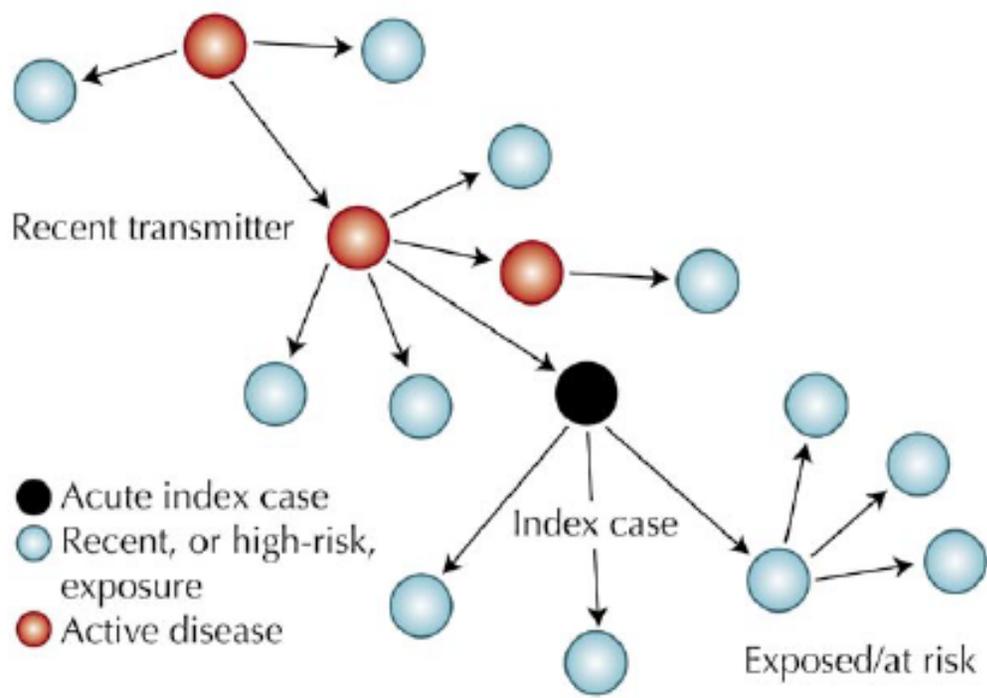
## Performance of Ab tests on total Panel

- 3<sup>rd</sup> gen EIA: detected **42% of panel**
- Uni-Gold Rapid: detected **34% of panel,**
- R: Stat-Pak and OraQuick: **17%**
- 1<sup>st</sup> gen EIA and Western Blot: **0%**



# STAT Index Case Protocol

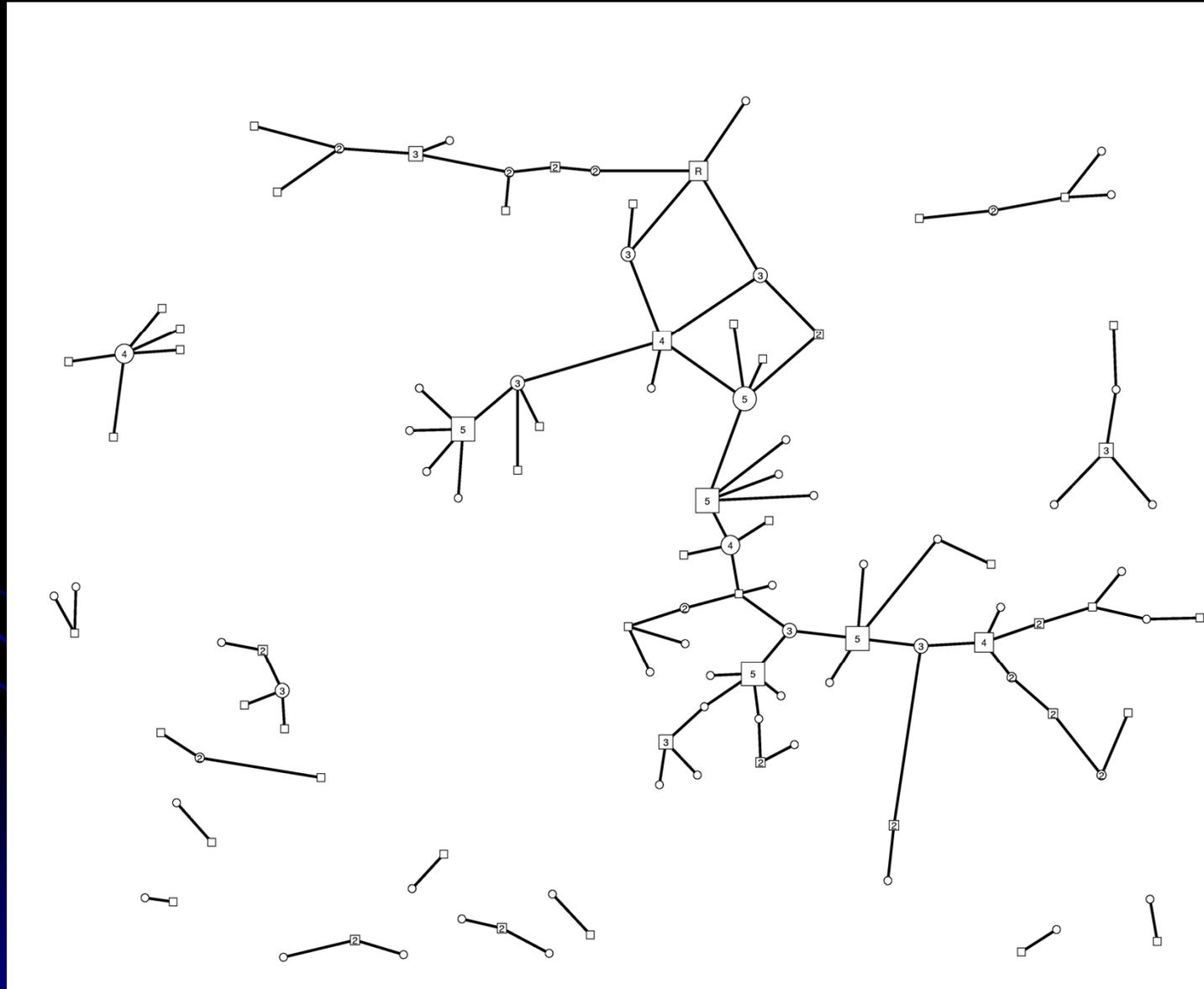




# Comparison of Named Partners Identified by Persons with AHI versus EHI (2002-2007)

- Higher median number of named partners identified by persons with AHI
  - 3 versus 1,  $P < 0.01$
- Ratio of named partners identified by persons with AHI to named partners identified by persons with EHI  $> 1$  for most age, race/ethnicity categories

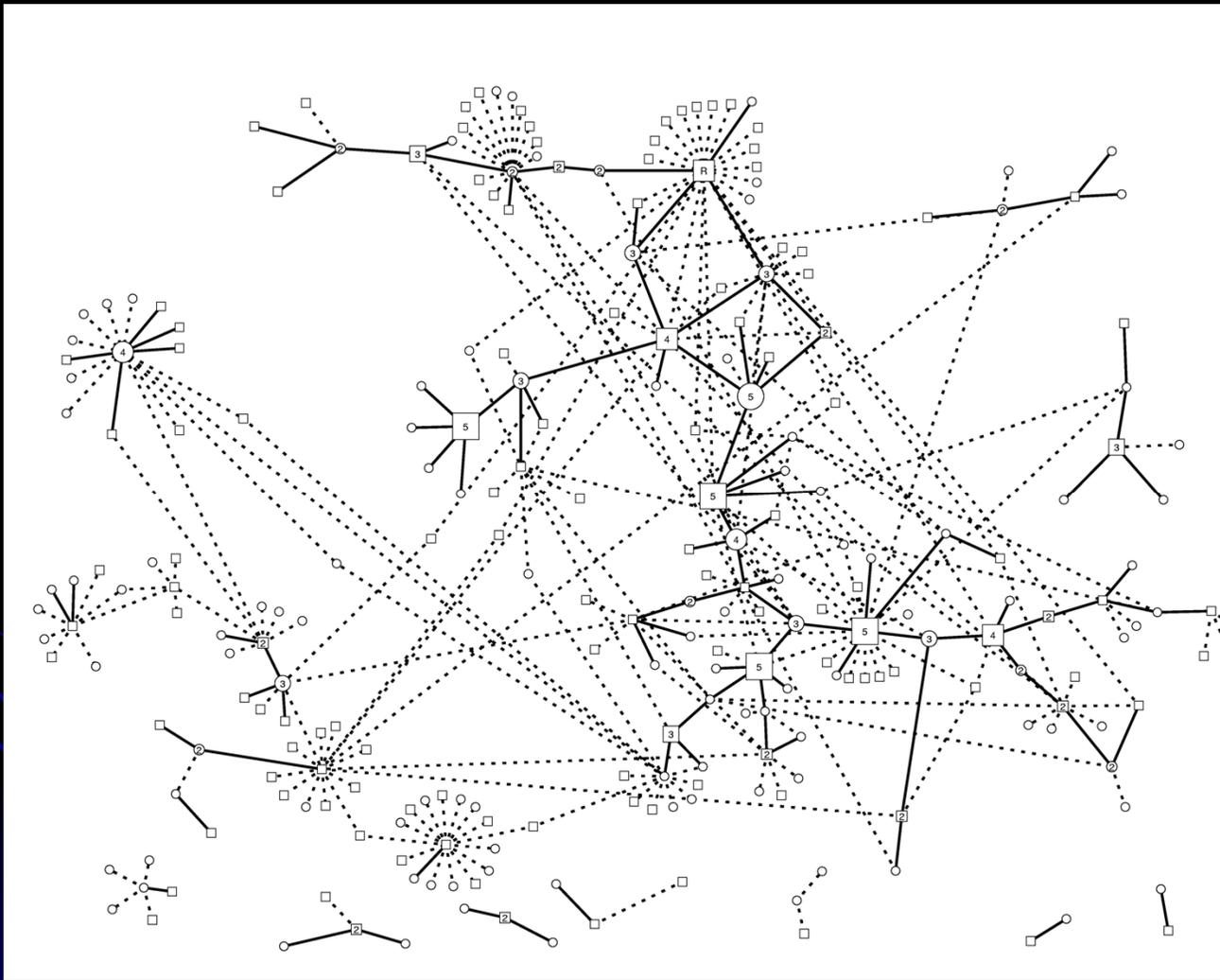
# Sexual contact tracing network (N=116) during the early syphilis outbreak in Columbus County, 2001-Feb 2002



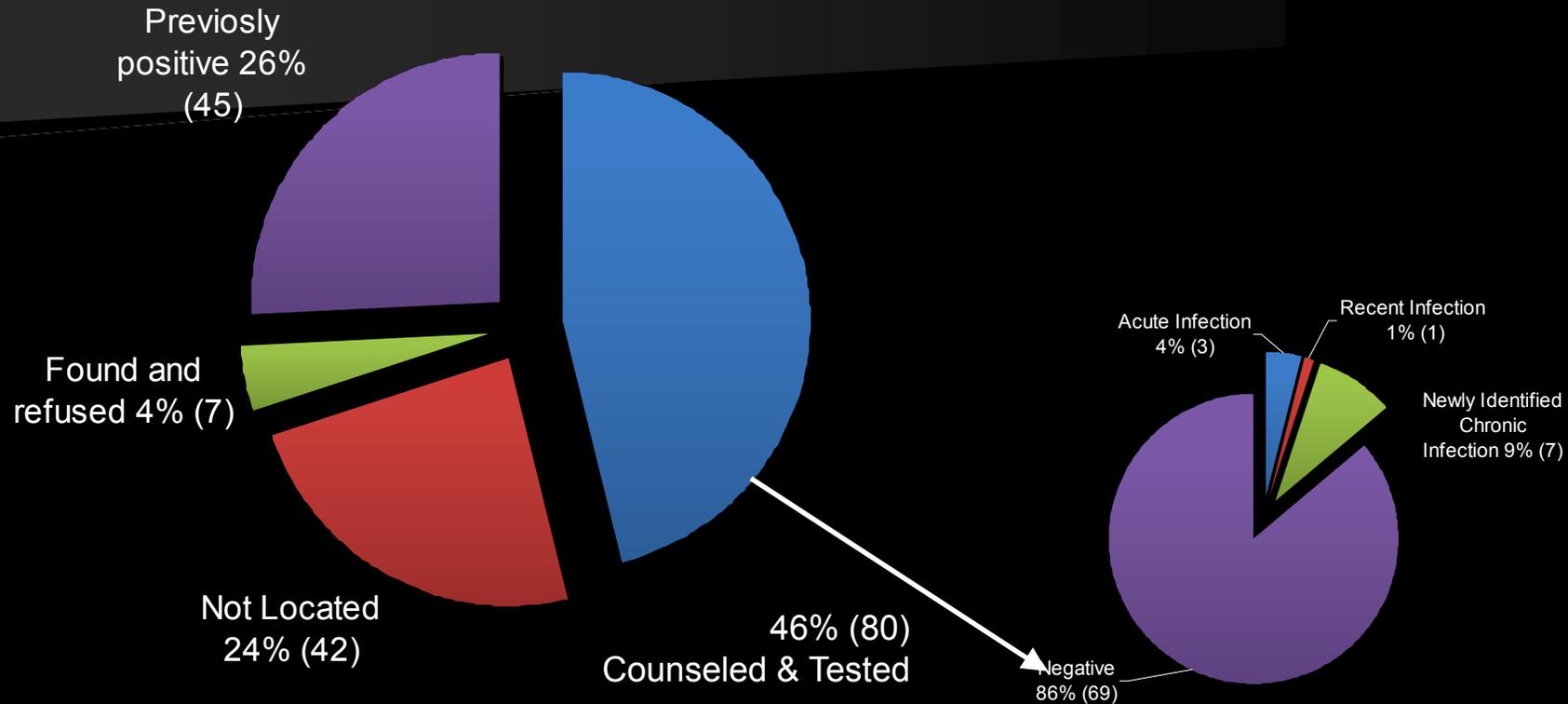
# Cluster Interviews

- **Partners:** sexual or needle sharing contacts from possible infectious period until the time of index case interview
- **Suspects:** sex or needle sharing partners prior to infectious period, or other individuals named by the index as being at high risk
- **Associates:** members of the index case's social or sexual network felt by DIS to be at high risk of HIV/Syphilis
- Also includes locations/venues where individuals meet partners

**Same network (N=250), showing additional social contacts elicited through cluster interviewing, Columbus County, 2001-Feb 2002.**

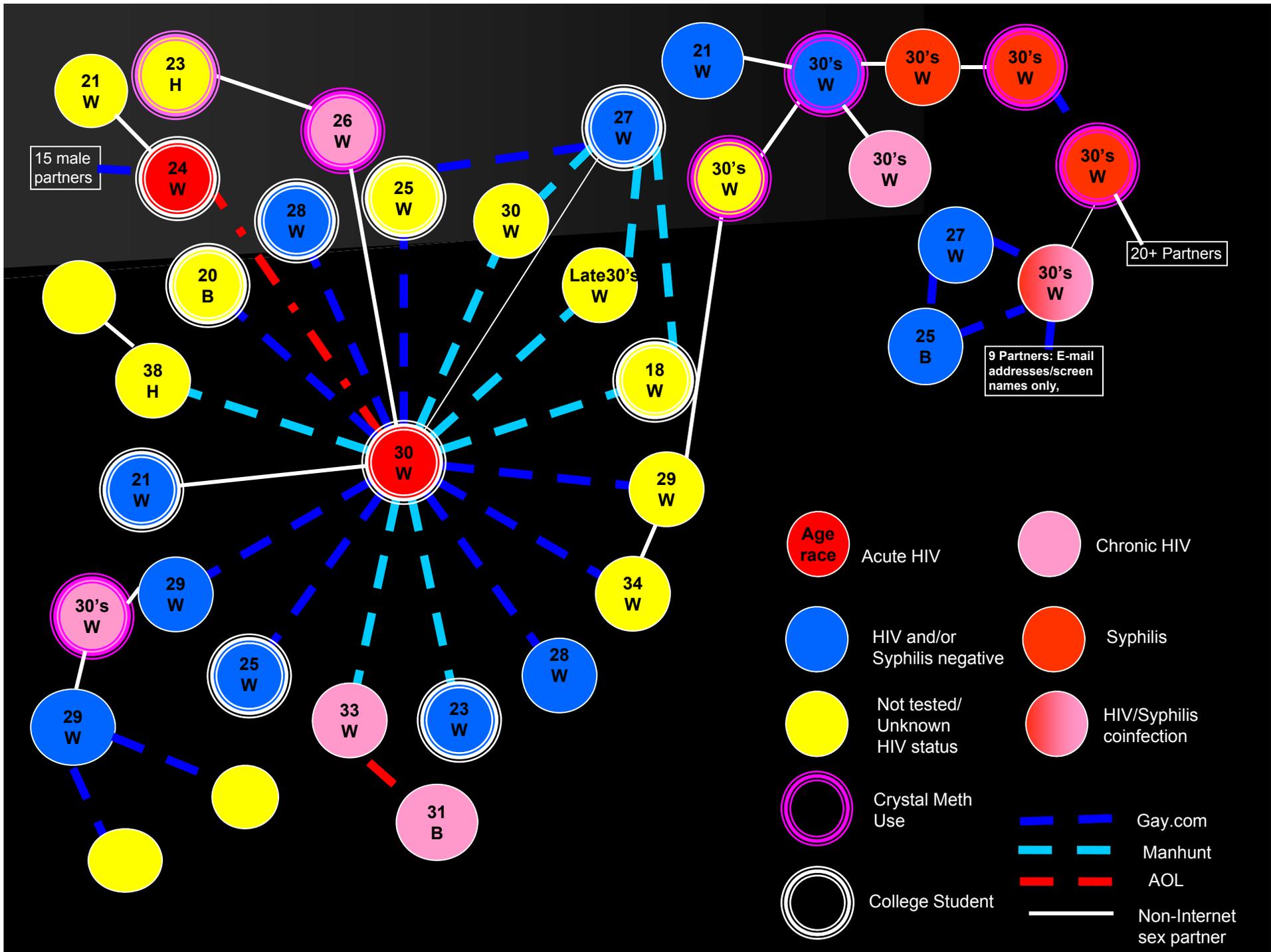


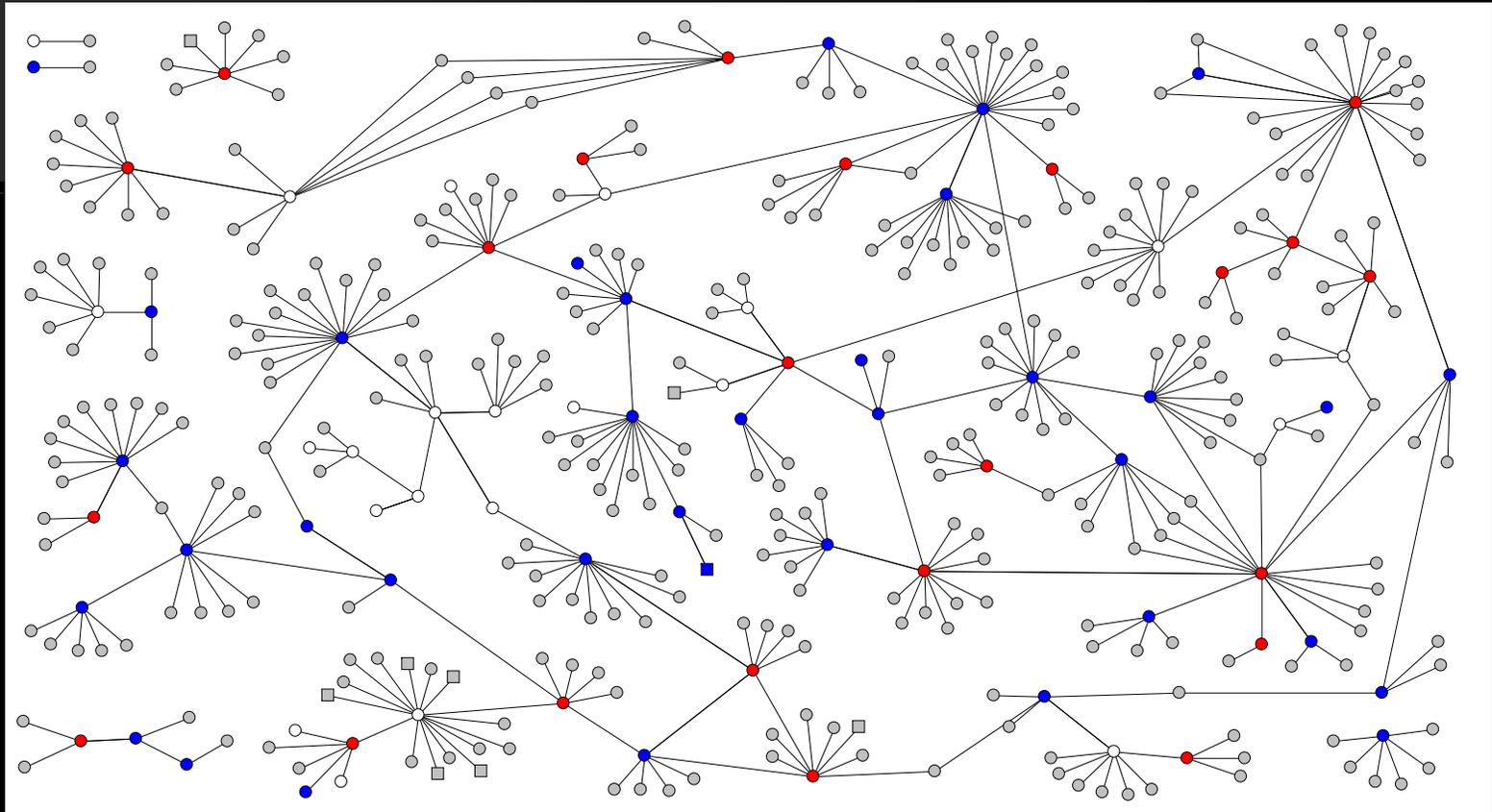
# STAT PCRS Outcomes (2003-2006)



# Network Opportunities

- Venues and individuals for screening
- Treatment for newly Dx HIV
- Repeat screening for HIV negative
- Screen for other STDs
- PrEP, PEP and High Intensity Behavioral Counseling for HIV negative
- Apply to Syphilis and GC MSM networks

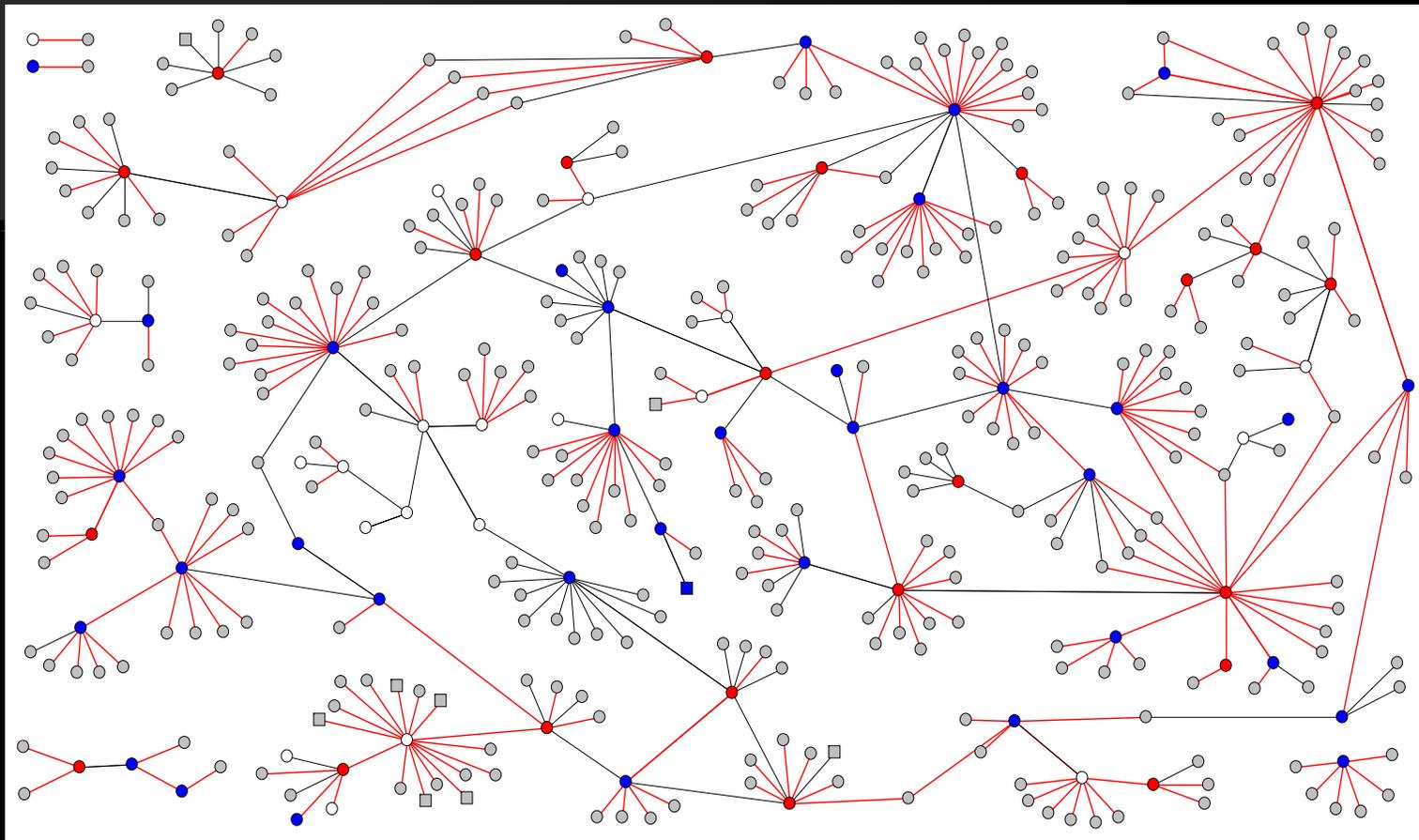




## Network Map

14 March 2011

- Acutely or recently HIV-infected
- Chronically HIV-infected
- Confirmed HIV-uninfected
- HIV status unknown



## Network Map

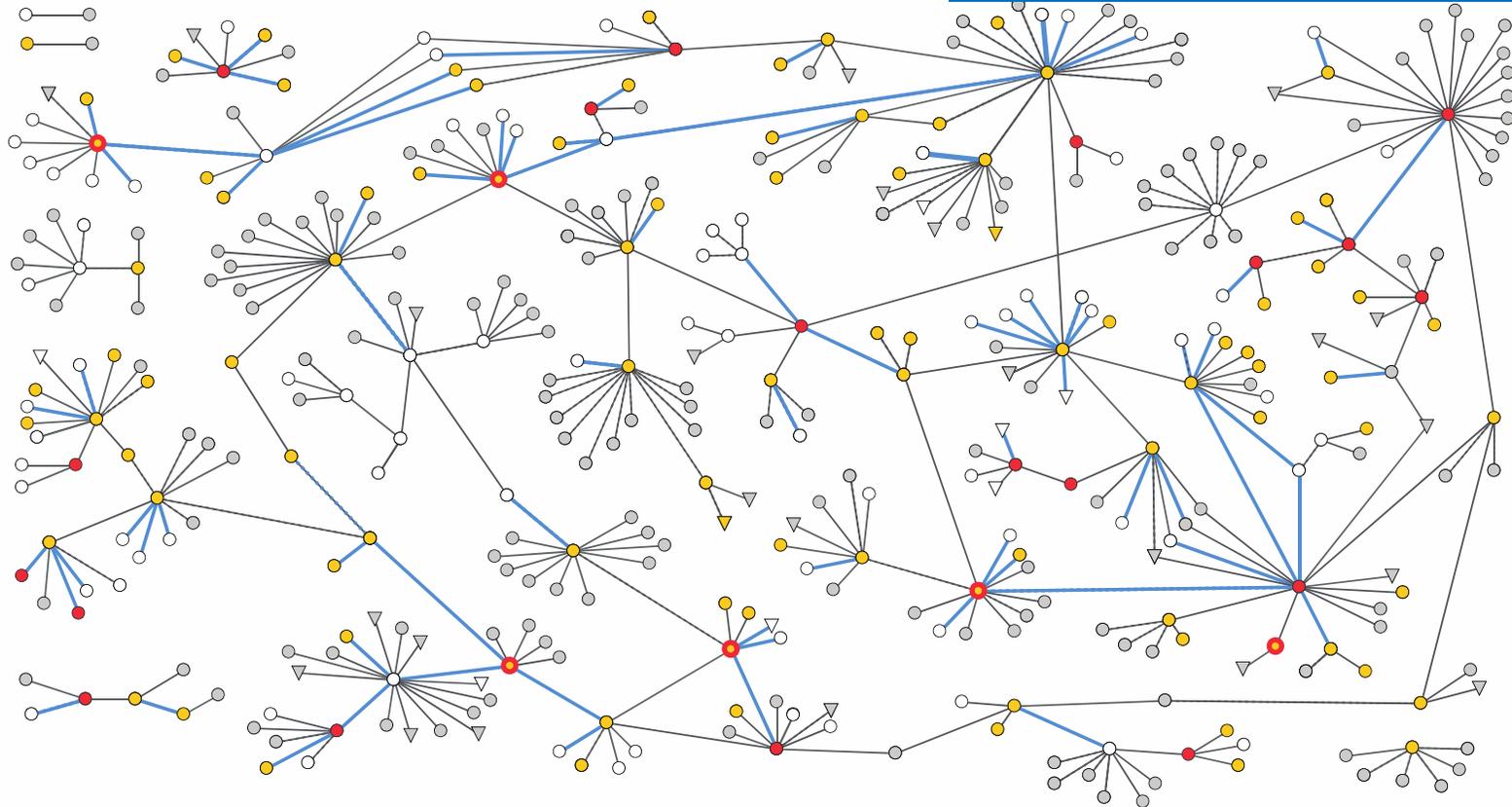
14 March 2011

- Acutely or recently HIV-infected
- Chronically HIV-infected
- Confirmed HIV-uninfected
- HIV status unknown

- Met online
- Did not meet online

# All relationships, 1989-2010

- 398 Individuals
- $\frac{3}{4}$  black, 94% MSM
- 117 HIV + (29%)
- 47% UNKNOWN sero status
- 150 Untraceable
- Acutely infected patients 4x MORE LIKELY to have traceable partners.



○ Uninfected male    ▽ Uninfected female    ● HIV-infected, chronic    ● HIV-infected, acute    ● HIV-infected, previously acute    ● HIV status unknown  
— Sexual relationship, new    - - - Sexual relationship, ongoing    — Serodiscordant relationship, new    - - - Serodiscordant relationship, ongoing    ► Seroconverter

# DETERMINANTS OF THE RATE OF TRANSMISSION: Goal Drop $R_0 < 1$

➤  $R_0 = \beta DC$ , where:

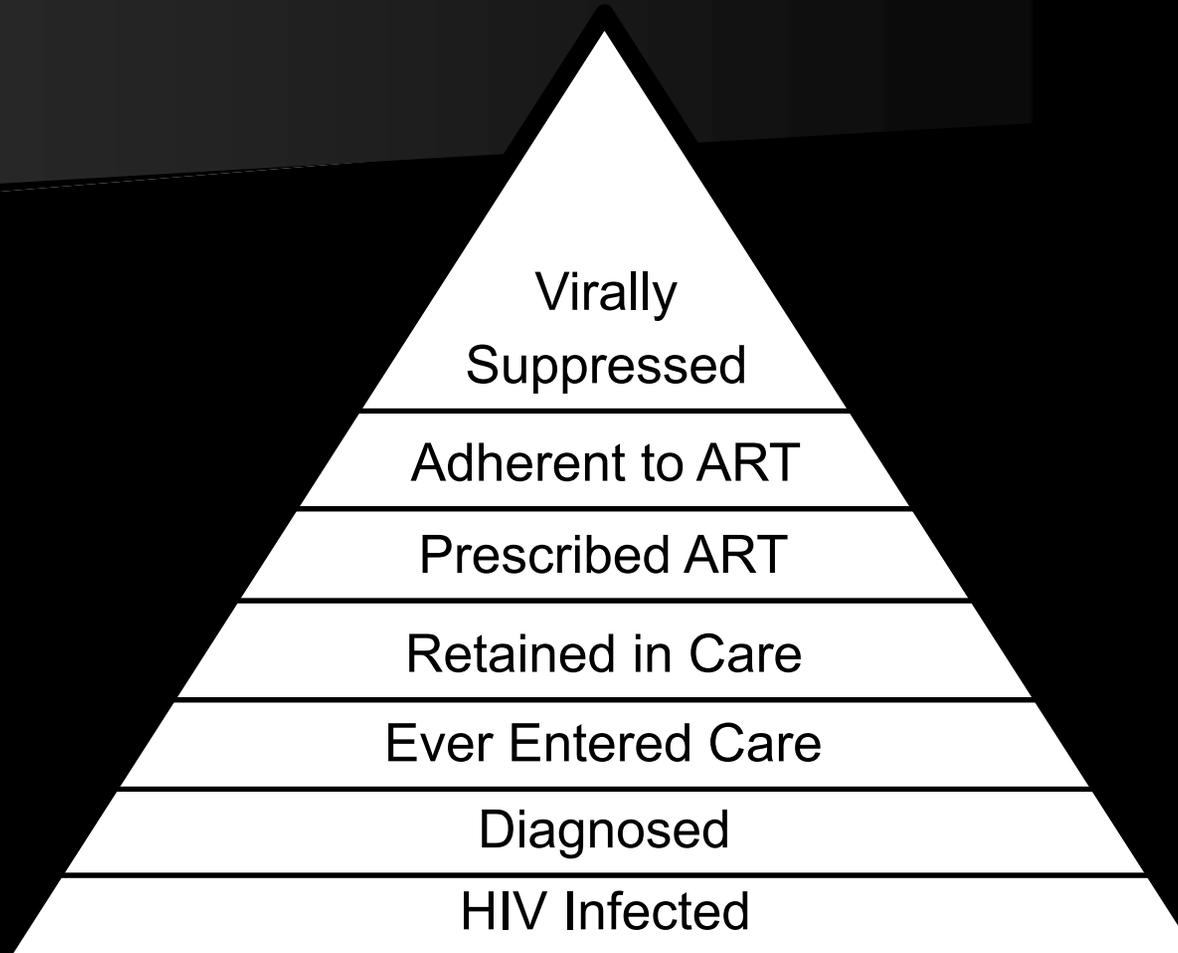
$R_0$  = average number of secondary cases generated by one primary case

$\beta$  = the average probability of transmission per partner sexual contact

$D$  = the average duration of infectiousness of an infected person

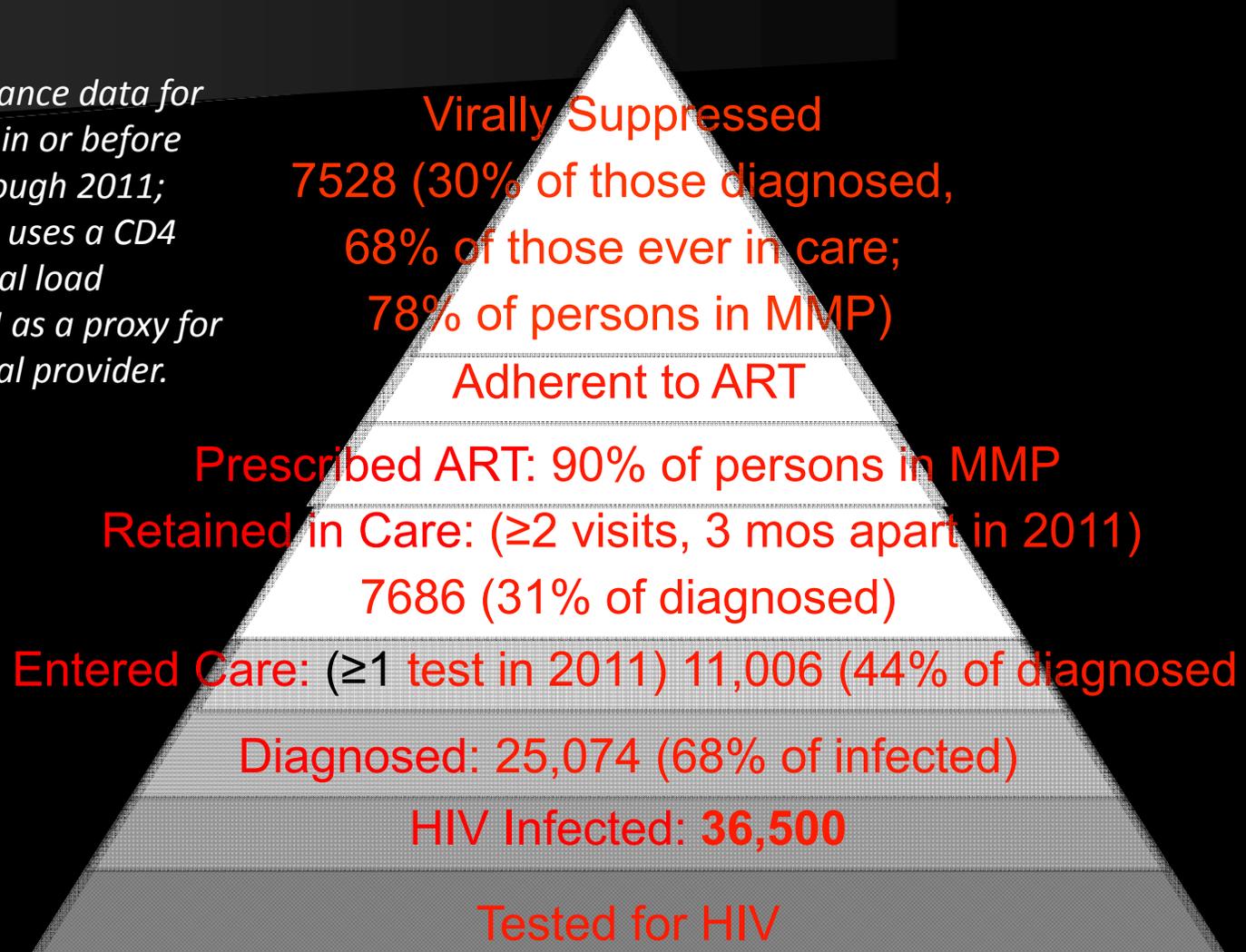
$C$  = the average number of sexual partnerships formed per unit of time

# The HIV Cascade

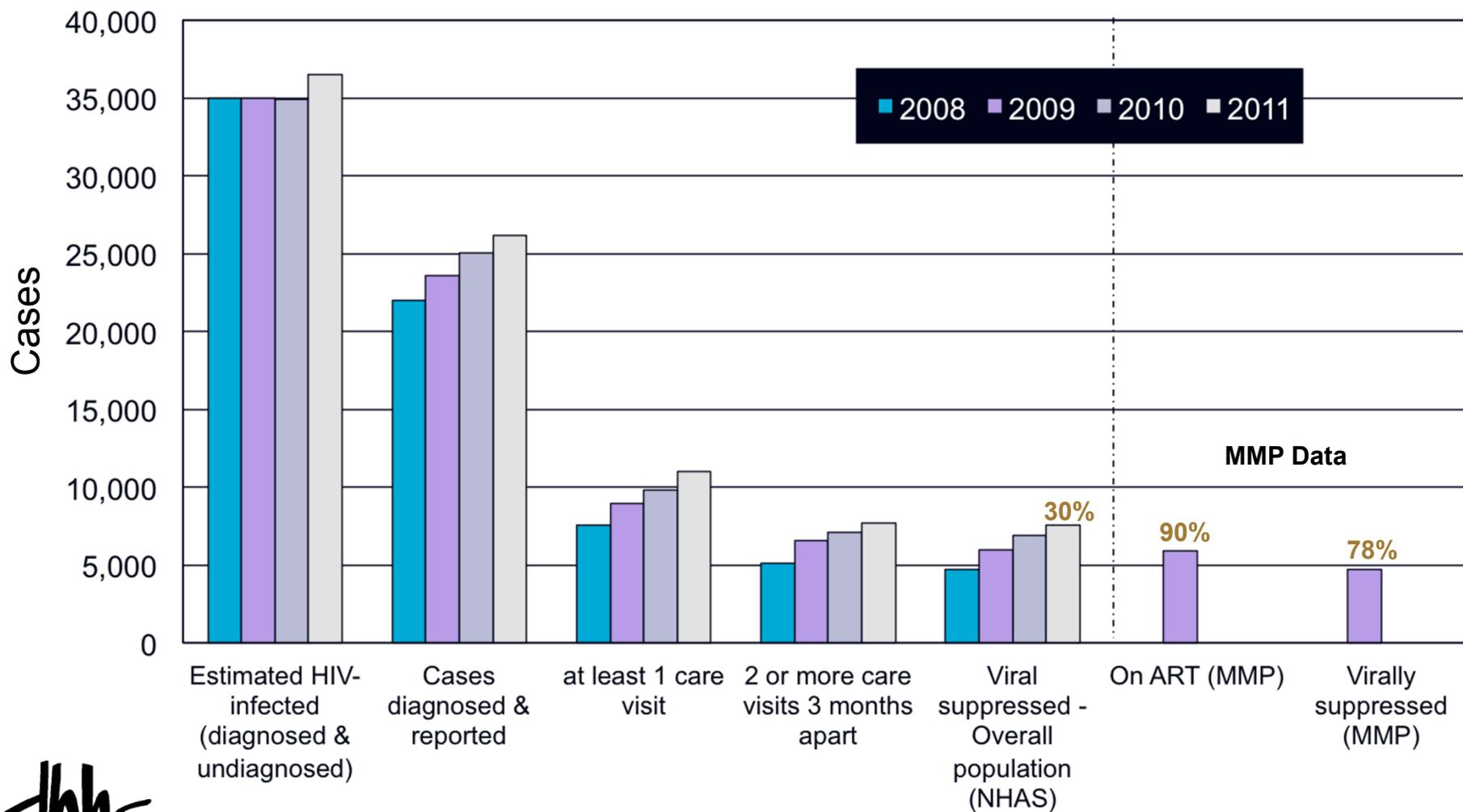


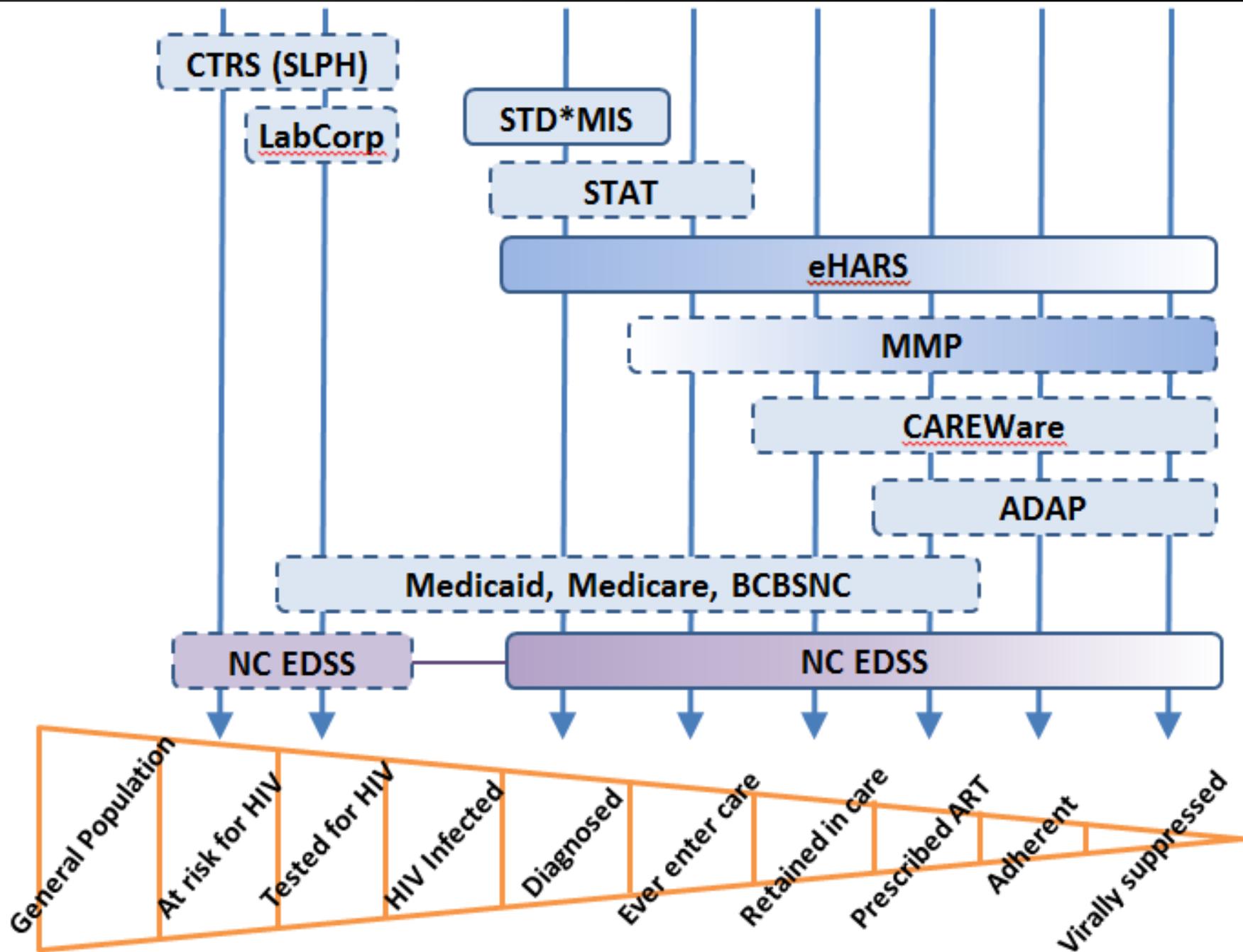
# HIV Cascade – NC Standard Estimates

*\*\*Based on surveillance data for patients diagnosed in or before 2010 and living through 2011;  
\*\*surveillance data uses a CD4 cell count or HIV viral load reported to NC DPH as a proxy for a visit with a medical provider.*



# NC HIV Cascade, overall population Diagnosed 2007-2010 and living through 2008-2011





# HIV testing & diagnosis

## The challenge:

- ❑ How many tests are being performed in NC?
- ❑ Who is being tested?
- ❑ Are we reaching who we want to reach?
- ❑ No single source of comprehensive testing data

# HIV Testing & Diagnosis in NC

508/1487 (34%) of persons newly diagnosed with HIV in 2010 were tested by the NC SLPH

- Positivity rate <0.5%

What about the other 66%?

- Partnerships with LabCorp, BCBSNC, Medicaid, Medicare being pursued to obtain aggregate & stratified HIV testing numbers
- Need to answer where best to expand testing to identify those either undiagnosed and/or not in care

# Implementation of Test and Treat

- Right Test to Right Population
- Address Contextual Factors
- Networks and core transmitters
- Link to Care
- Treat All at All CD4 and Treat Now!
- Retain in Care
- Screen for STIs

# Where Do We Go From Here?

## The Axiom

ART improves health, blocks transmission

*BUT the “AIDS Free Generation” is only an aspiration*

## The Challenge

- Humility as we go forward, *but with confidence*
  - remember, HIV is the most studied pathogen in history!
- Redouble research and implementation efforts NOW
- Identify and focus on the most critical questions
- Identify and interrupt transmission forces
- Prepare for a “long march”: tenacity, tenacity, tenacity
- Failure is NOT an option

# NC Cascade Collaborators

## NC DPH

- Jacquelyn Clymore
- Evelyn Foust
- Del Williams

## ■UNC

- Myron Cohen
- Bill Miller
- Katie Lesko (Epid)
- Pam Klein (Epid)
- Anna Barry Cope (Epid)
- Kim Powers
- Ann Dennis

## ■UNC & DPH

- Peter Leone
- Lynne Sampson
- Heidi Swygard

## Outside Organizations

- LabCorp
- Centers for Medicaid and Medicare
- Blue Cross Blue Shield of North Carolina (BCBSNC)
- Integrated Cancer Information and Surveillance System (ICISS)