Reducing Community Viral Load to Achieve HIV Prevention

Moupali Das, MD, MPH

Director of Implementation Science and Evaluation Research

San Francisco Dept. of Public Health

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
HIV PREVENTION SECTION
SFHIV
SFHIV.ORG

University of California San Francisco
UCSF
AIDS Research Institute

Outline

- Viral Load and Transmission
- A Pivotal Time
- San Francisco Comprehensive Public Health Approach
  - San Francisco Baseline Results
  - IOM Recommendations for Evaluation
- The Way Forward: Transforming our Narrative
- Revolutionizing the Research Agenda: Asking the Right Questions at this Pivotal Time

VIRAL LOAD AND PREVENTION OF TRANSMISSION

Viral Load Directly Predicts HIV Transmission

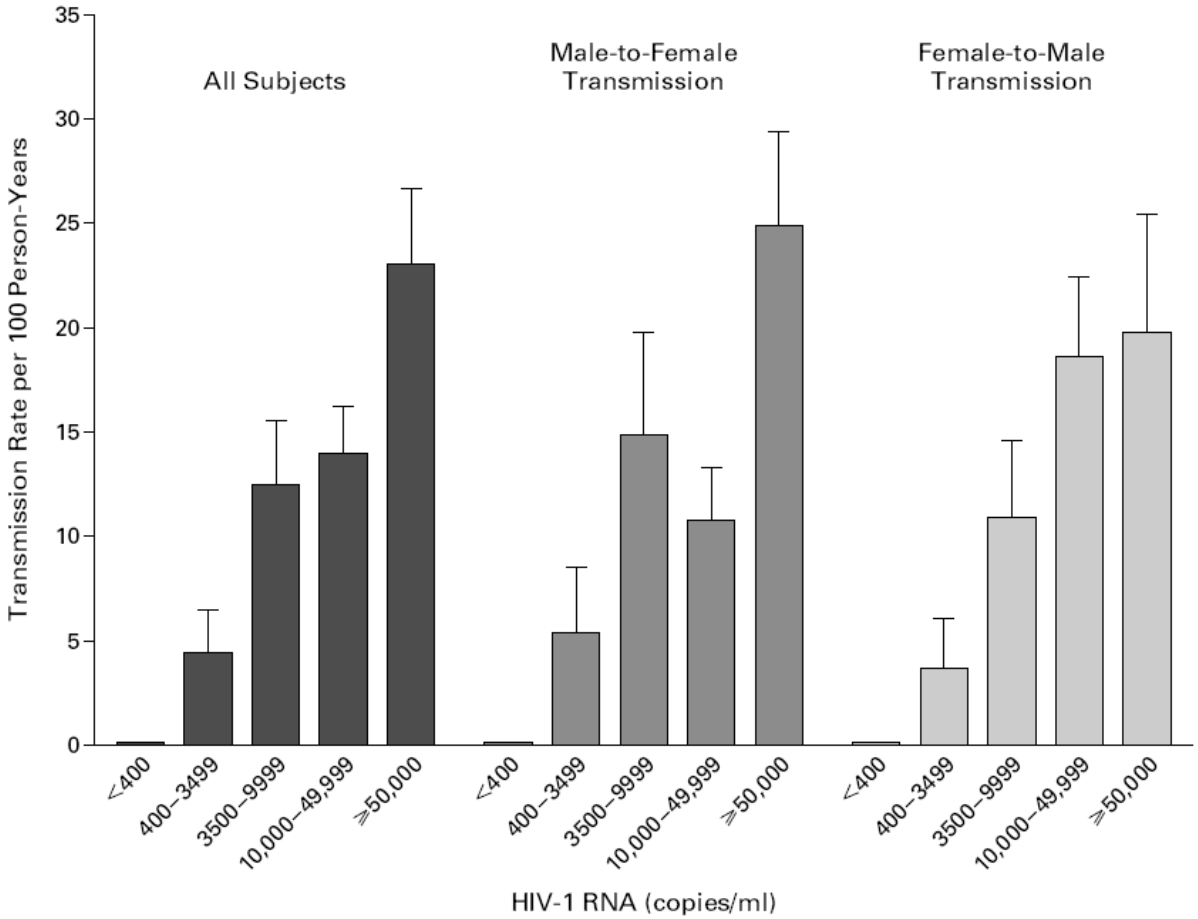


Figure 1. Mean (+SE) Rate of Heterosexual Transmission of HIV-1 among 415 Couples, According to the Sex and the Serum HIV-1 RNA Level of the HIV-1–Positive Partner.

At base line, among the 415 couples, 228 male partners and 187 female partners were HIV-1–positive. The limit of detection of the assay was 400 HIV-1 RNA copies per milliliter. For partners with fewer than 400 HIV-1 RNA copies per milliliter, there were zero transmissions.

Quinn et al NEJM 2000

Universal Testing and ART-Mediated Virologic Suppression Near Eliminates Perinatal Tx

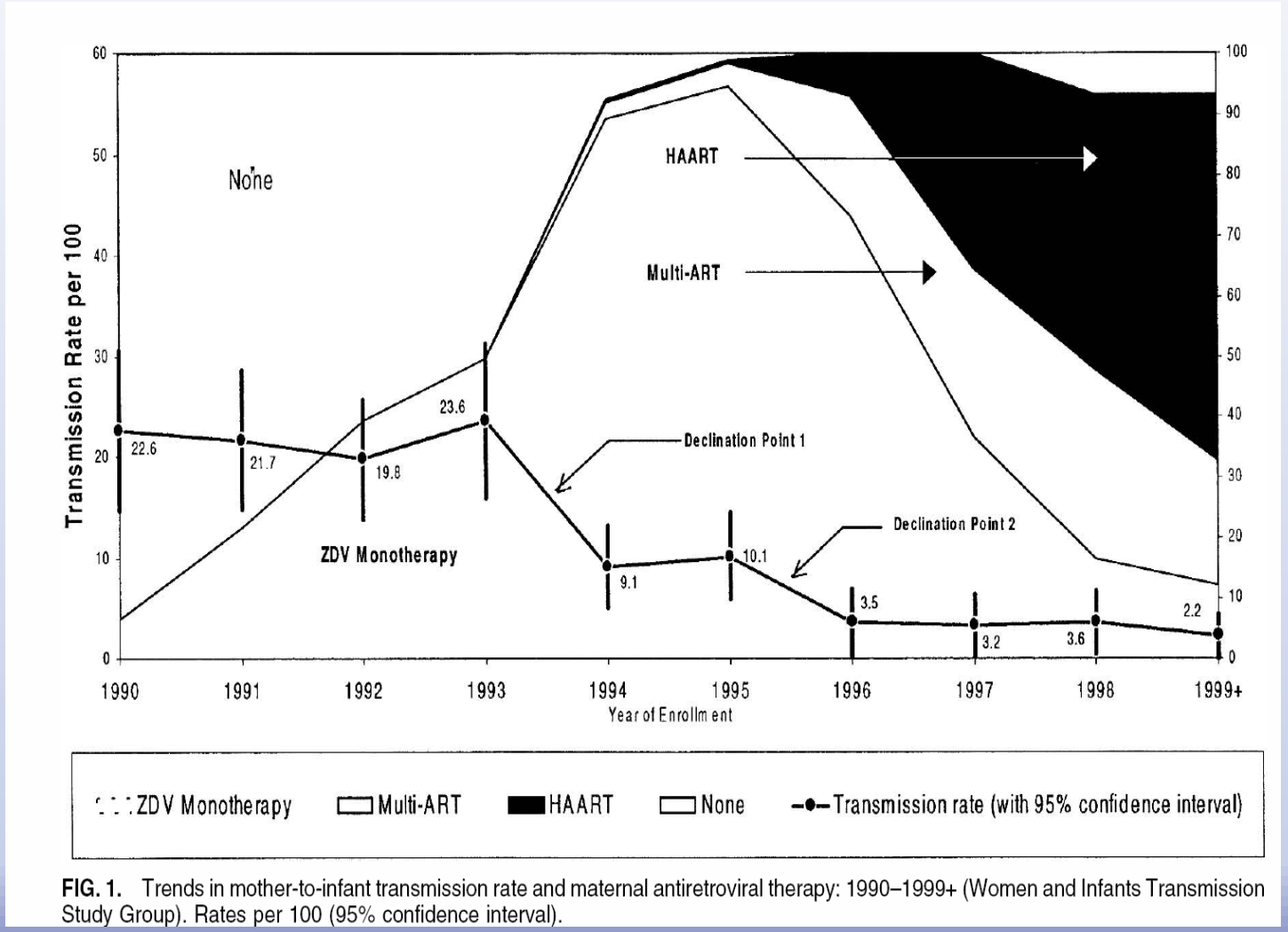


FIG. 1. Trends in mother-to-infant transmission rate and maternal antiretroviral therapy: 1990–1999+ (Women and Infants Transmission Study Group). Rates per 100 (95% confidence interval).

Cooper JAIDS 2002

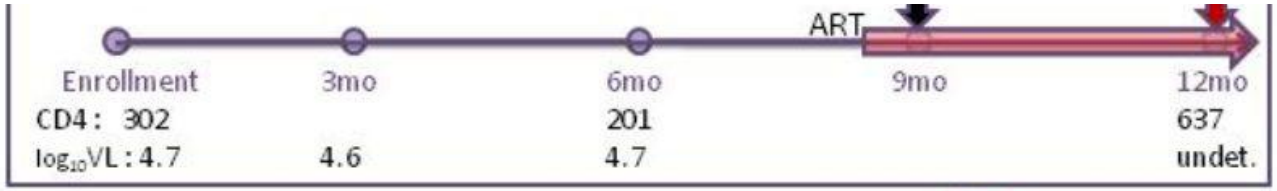
ART-mediated Virologic Suppression Near Eliminates Sexual Tx

ART and HIV-1 transmission

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 11, 2011 VOL. 365 NO. 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy



UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER
PARTNERS IN PREVENTION

Donnell D, et al. CROI 2010. Abstract 136.

It is a truth universally acknowledged that a medical intervention justified by observational data must be in want of verification through a randomized controlled trial.

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

What is already known about this topic

Parachutes are widely used to prevent death and major injury after gravitational challenge

Parachute use is associated with adverse effects due to failure of the intervention and iatrogenic injury

Studies of free fall do not show 100% mortality

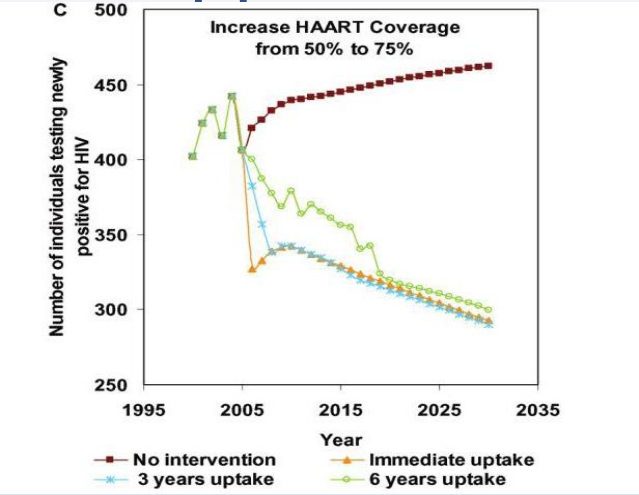
What this study adds

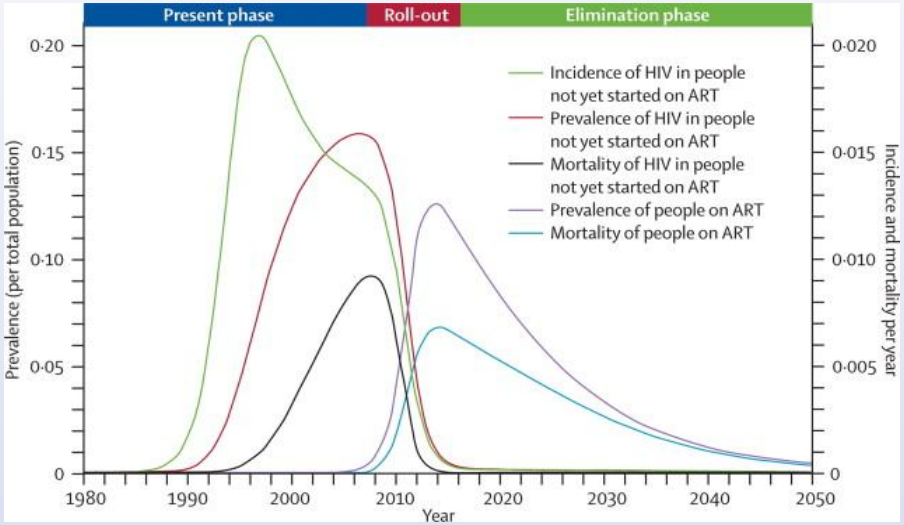
No randomised controlled trials of parachute use have been undertaken

The basis for parachute use is purely observational, and its apparent efficacy could potentially be explained by a "healthy cohort" effect

Individuals who insist that all interventions need to be validated by a randomised controlled trial need to come down to earth with a bump

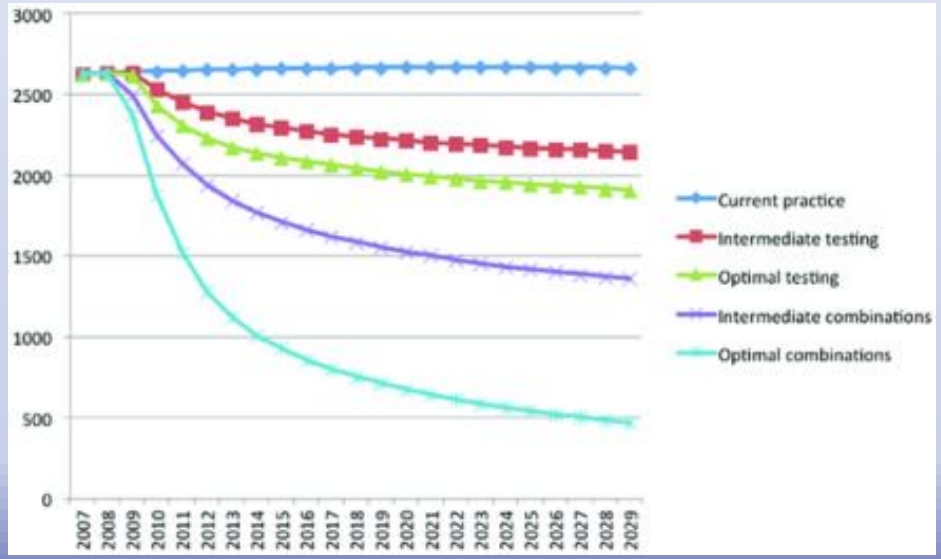
Modeling Suggests ART-mediated Virologic Suppression Reduces HIV Transmission





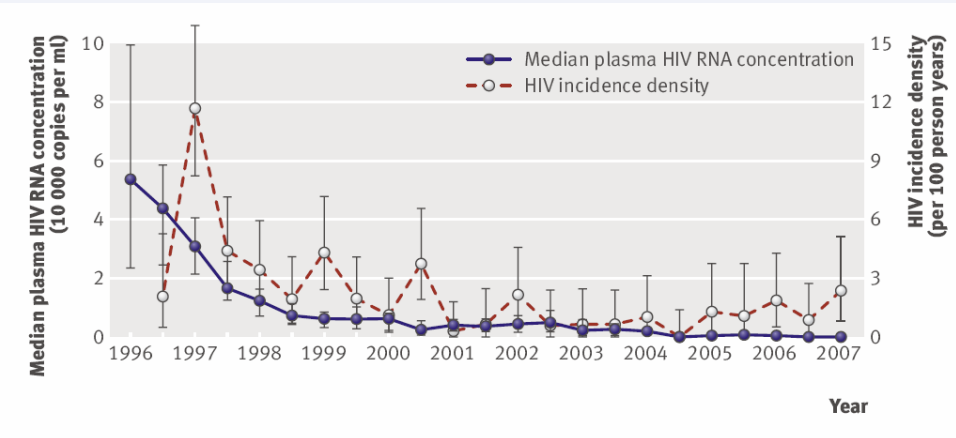
Infections Averted	Tx<500	Tx All	Test & Tx All
2014	1,554	2,169	2,810
2019	3,102	4,550	6,040
2029	4,940	8,221	12,189

Percent Reduction in New Infections	Tx<500	Tx All	Test & Tx All
2014	42%	59%	76%
2019	42%	61%	81%
2029	33%	55%	81%

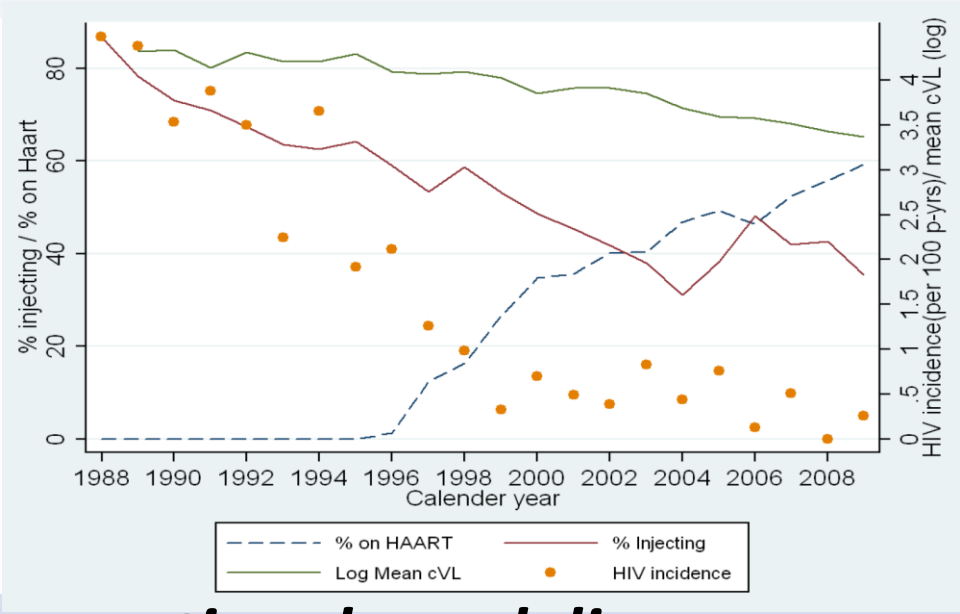


Lima JID 2008 Charlebois CID 2011 Granich Lancet 2008 Sorensen, PLoSOne, 201

Two Cohort Studies Demonstrate Reduced Cohort VL predicts decreased HIV Incidence



Estimated community plasma HIV-1 RNA concentrations and HIV incidence density, with 95% confidence intervals, among two parallel cohorts of injecting drug users. HIV incidence first estimated in second half of 1996 as enrolment started in May 1996 and repeat HIV tests to assess incidence were available only after six months of follow-up

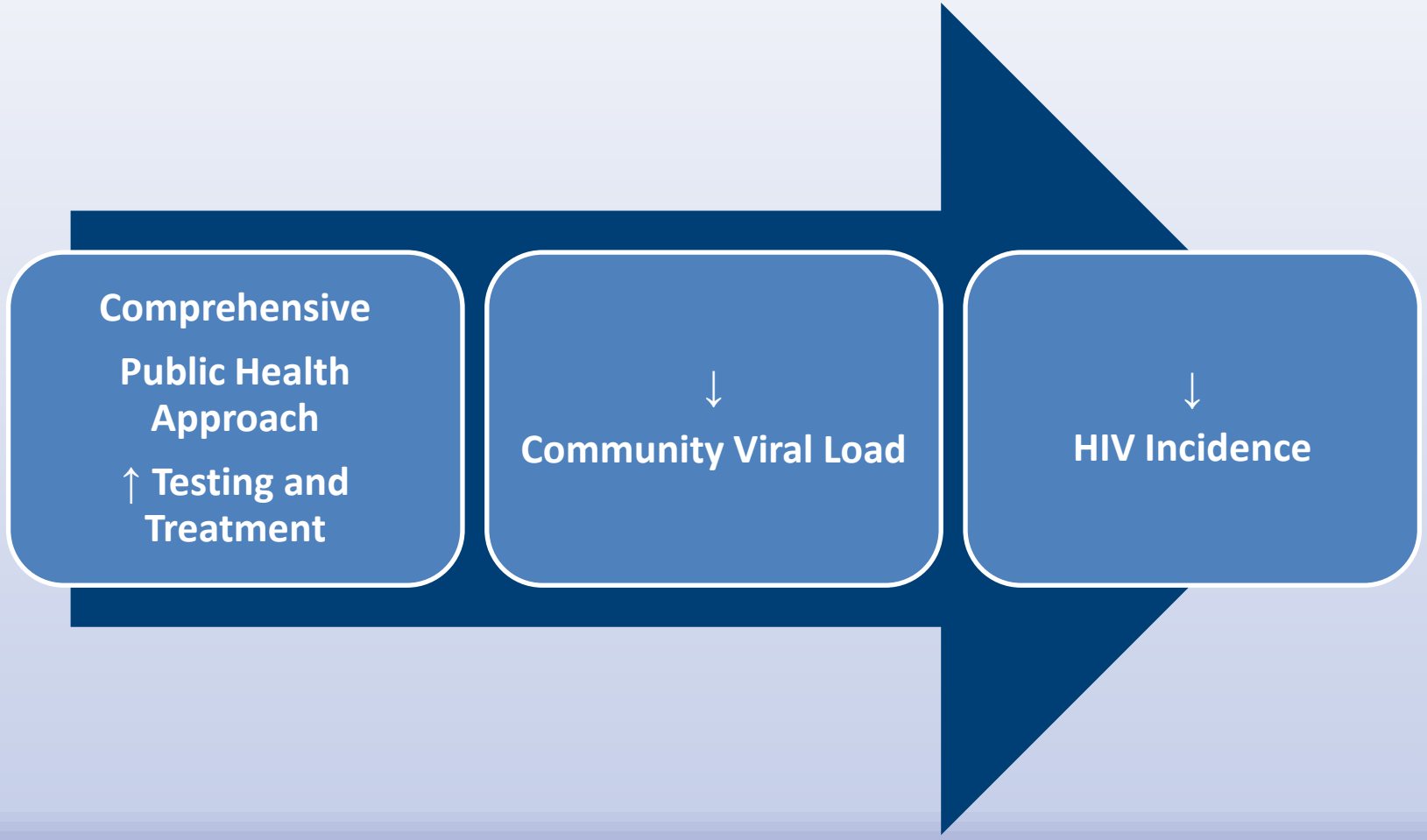


Taken together, current observational, modeling, and randomized control data demonstrates that ART-mediated virologic suppression reduces transmission at an individual level and strongly suggests community or population level effect.

Wood E et al. BMJ. 2009 Apr 30;338:b1649

Kirk, G; CROI 2011

The Hypothesis



A PIVOTAL TIME: ADVANCES IN HIV PREVENTION, TESTING & TREATMENT

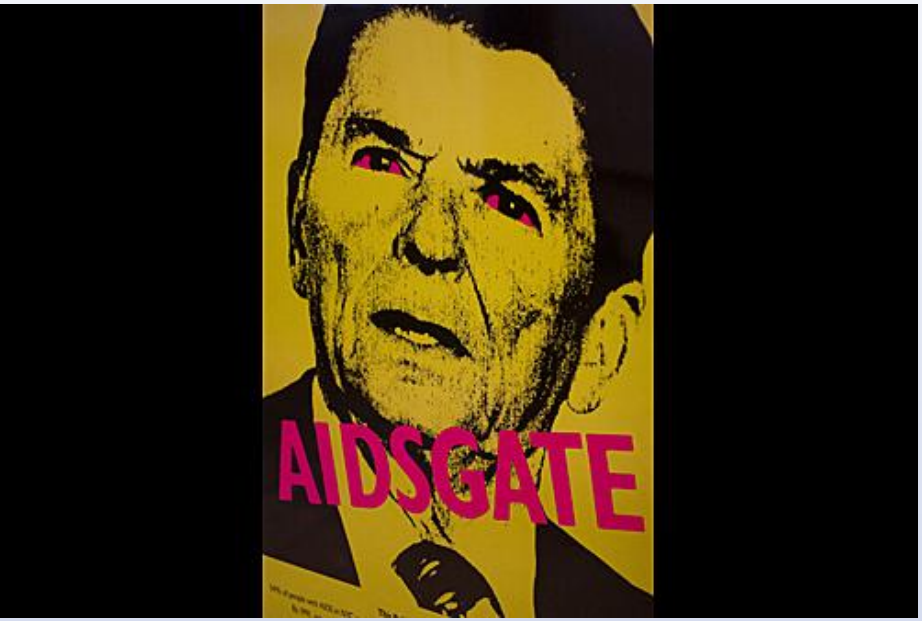
HIV in 1980s

Fear
Discrimination
Stigma
Prevention Controversial
No Testing
No Treatment

Case Finding
Surveillance
Interruption of Transmission
Systematic Treatment &
Case Management
Population Based Monitoring

Traditional Public Health Approach

President Reagan to President Obama



Testing technologies: Rapid Test, 4th gen HIV Ag/Ab, Viral load for Acute, Home testing

Prevention: US Success at near eliminating perinatal and blood-borne HIV

Wider availability of condoms, syringes

Treatment: Tremendous progress in 1st, 2nd, 3rd generation of ART

Exciting Advances in HIV Prevention

Science

AAAS

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim, *et al.*

Science **329**, 1168 (2010);

DOI: 10.1126/science.1193748

The NEW ENGLAND JOURNAL of MEDICINE

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Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

All Biomedical Interventions are BEHAVIORAL interventions

ART Brought People Back From the Brink

Haitian Patient, before and after Receiving Free Treatment for HIV Infection and Tuberculosis.

The photograph on the left was taken in March 2003, and that on the right in September 2003. Many impoverished patients in rural Haiti and Rwanda now receive comprehensive medical care through public–private partnerships.

Jim Kim and Paul Farmer, NEJM, 2006

Controversies

1998

JAMA®

Treat HIV-1 Infection Like Other Infections—Treat It

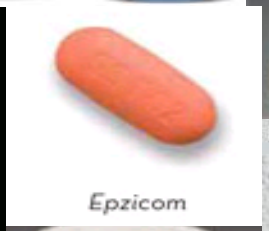
Bruce D. Walker, MD; Nesli Basgoz, MD

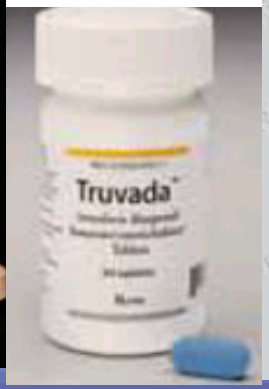
Should AIDS be renamed “Acquired Inflammatory Disease Syndrome”?

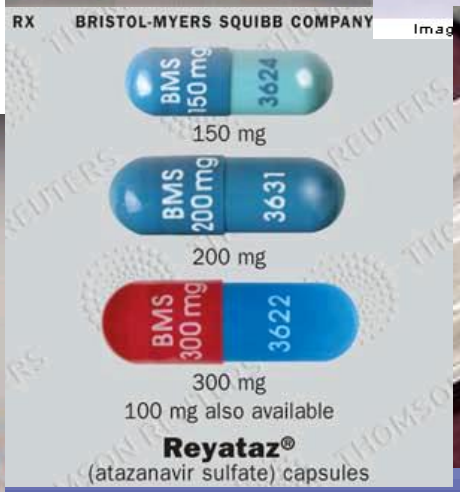
- Untreated HIV disease is associated with increased T cell activation/inflammation
- Treatment dramatically reduces inflammation
- The degree of residual inflammation during HAART is determined in part by CD4 nadir (strong effect < 200)

Slide courtesy of Steve Deeks

Expanded Treatment Options







THE VIRUS IS MORE TOXIC THAN THE MEDS

- Old paradigm: Drugs are toxic so defer therapy as long as possible
- New paradigm: Although new drugs are not completely benign, they are less “toxic” than the virus
- Rather than treating only when there was a strong reason to treat, the default is now to treat unless there is a strong reason not to treat

Slide courtesy of Steve Deeks

Universal OFFER of ART on Ward 86 and all SFDPH Community Health Clinics

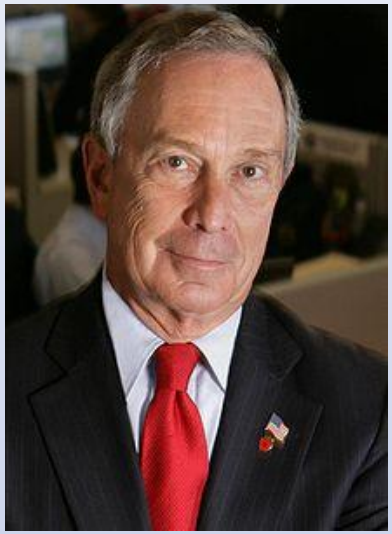
"All patients, regardless of CD4 count, will be evaluated for initiation of antiretroviral therapy (ART)"

Decision to start ART made by the individual in conjunction with the provider

Modified from slide courtesy of Brad Hare, SFGH Community Forum

NYC Recommends AIDS Drugs for any Person with HIV

NEW YORK (AP) 1 Dec 2011— Health officials in the nation's largest city are recommending that **any residents living with HIV be offered AIDS drugs as soon as the virus is diagnosed**, an aggressive move that has been shown to prolong life and stem the spread of the disease…



NYC Mayor
Michael Bloomberg

Empire State building glowing red for World AIDS Day 2011

Dr. Tom Farley
NYC Health Commissioner

Cristian Salazar, Associated Press. "NYC Recommends AIDS Drugs for Any Person with HIV." December 1, 2011. http://www.chron.com/default/article/NYC-recommends-AIDS-drugs-for-any-person-with-HIV-2337246.php.

DHHS March 2012: *ART is recommended for ALL HIV-Infected individuals*

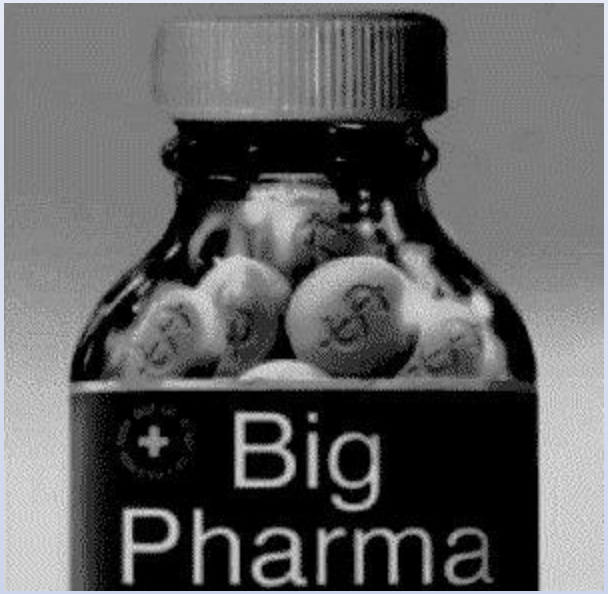
- Strength depends on CD4 strata:
  - CD4<350 AI (Strong; RCT)
  - CD4 <350- <500 AII (Strong, Obs nRT)
  - CD4>500: BIII (Moderate, Expert)
- Effective ART reduces sexual transmission
- Heterosexual AI (Strong RCT)
- All other risk groups AIII (Strong, Expert)

“Test & Treat,” or “High-Impact Combination Prevention,” or the “Medical Model”….

POZ

“Medical Ethics and the Rights of with HIV Under Assault”

by Sean Strub



“Going too far to battle AIDS? Drug experiment on blacks looms in Washington, D.C.” by Terry Michael *Washington Post* March 17 2010

Simply Testing and Treating will not eliminate the epidemic...

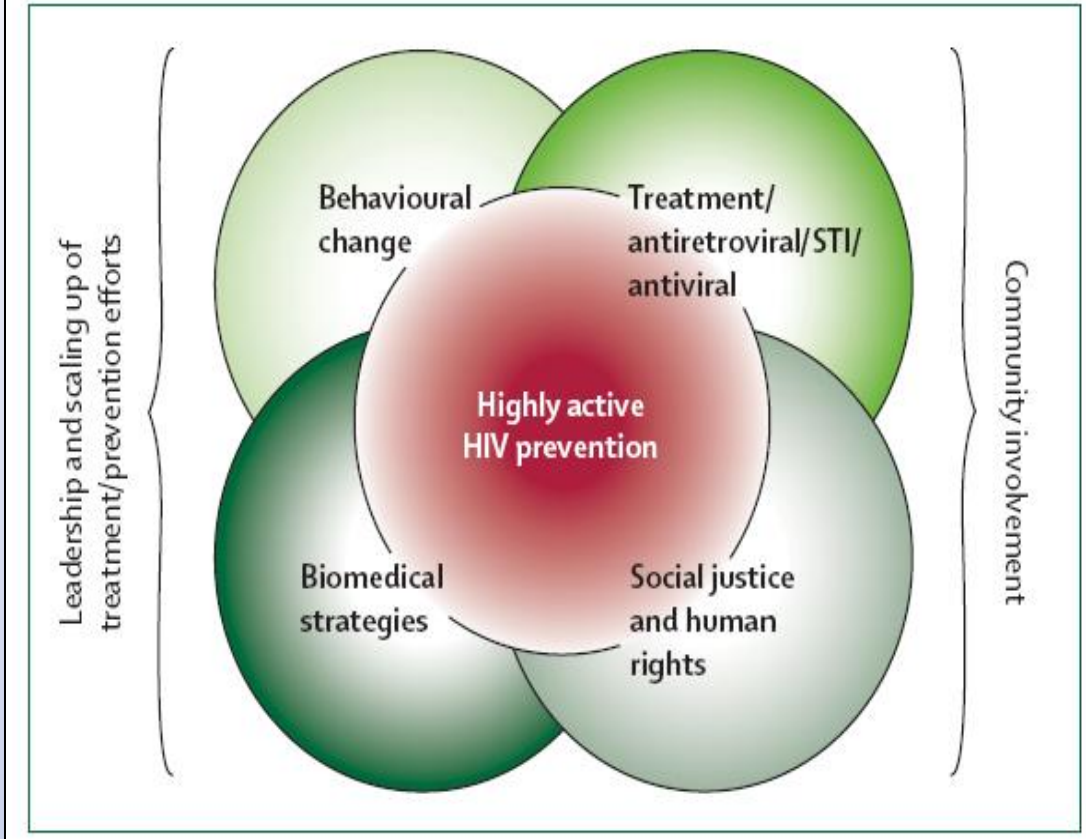


Figure 1: **Highly active HIV prevention**
This term was coined by Prof K Holmes, University of Washington School of Medicine, Seattle, WA, USA.[5] STI=sexually transmitted infections.

Coates. *Lancet*, 2008.

“Si-w bay medikaman san manje, se lave men, siye até”

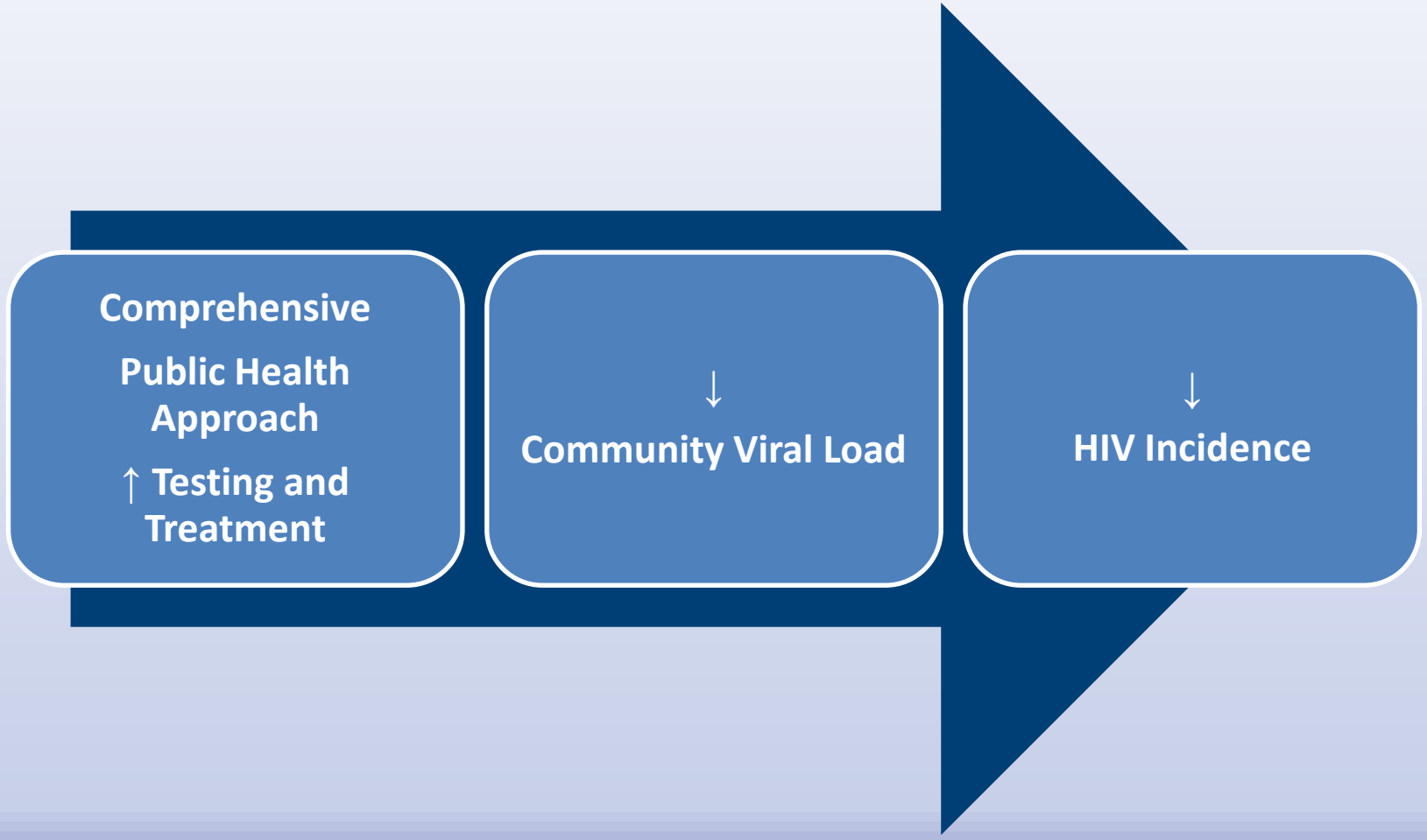
"Giving drugs without food is like washing your hands and drying them in the dirt."

Patient Care is more than ART provision

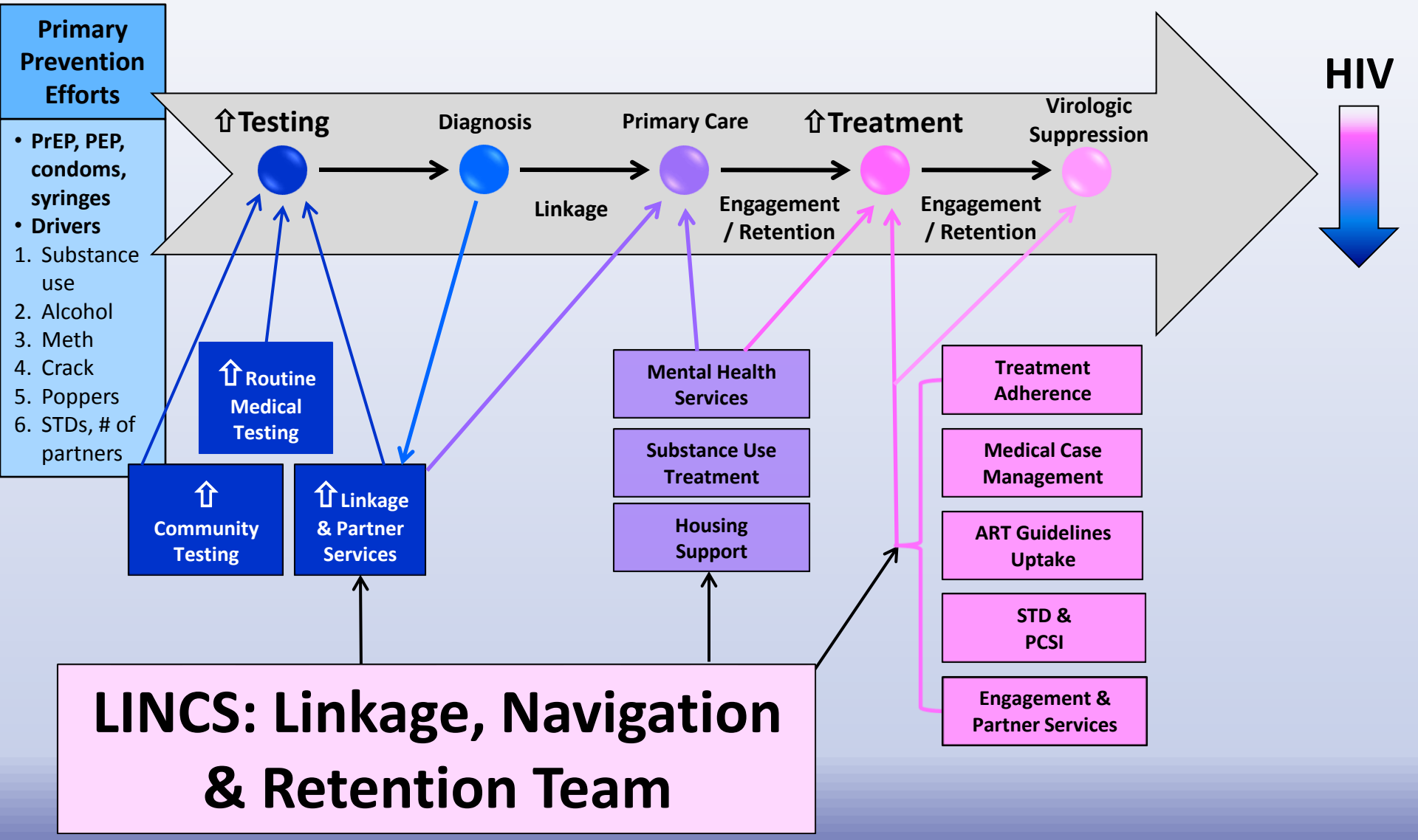
- Primary care provider (NP, Int Med, FP, ID/HIV)
- Social workers
  - Screening and referral for substance use or mental health concerns (HIV Specialty Psychiatry/Psychology)
  - Housing, disability, benefits (including ADAP enrollment)
- **Pharmacist lead ART adherence program**
  - 1:1 Assessments of barriers, education, medicine reviews, ongoing monitoring
- Patient education program and support groups
- **Linkage to care/retention support team (PHAST)**
- *Could not be done without political will →Healthy SF covers undocumented; System of Prevention*

SAN FRANCISCO'S COMPREHENSIVE STRATEGY TO MAXIMIZE CASCADE OUTCOMES

The Hypothesis



San Francisco's Approach to Maximizing the Continuum of Prevention, Care and Treatment



NATIONAL HIV/AIDS STRATEGY FOR THE UNITED STATES

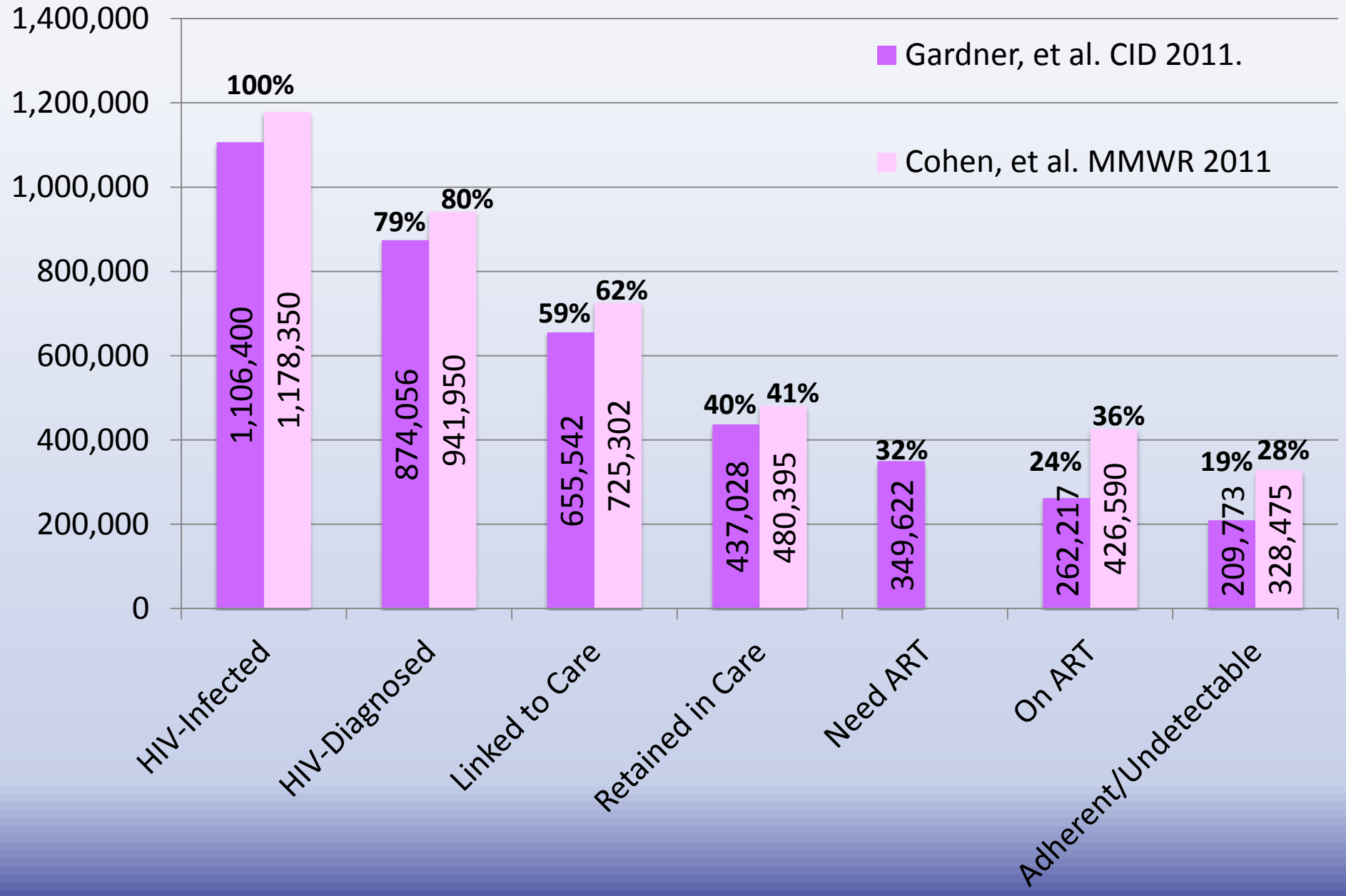
There are three primary goals for the NHAS:

- Reducing HIV incidence
- Increasing access to care and optimizing health outcomes
- Reducing HIV-related health disparities

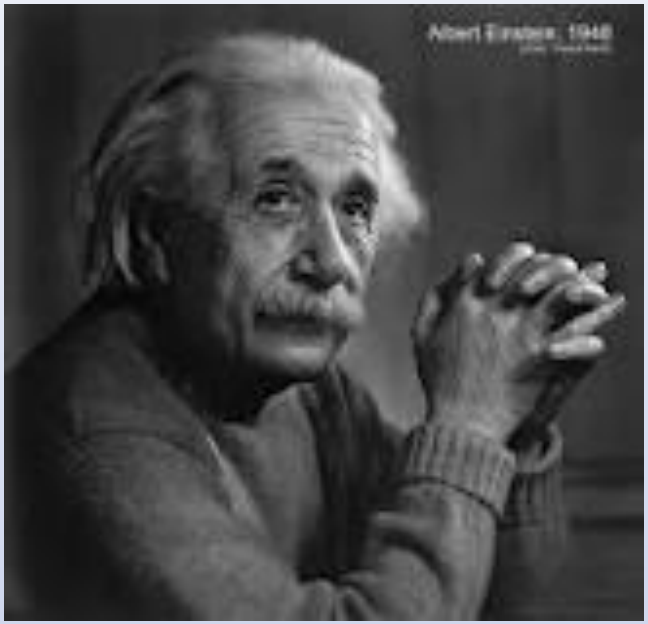
12 Cities Project and ECHPP:

Enhanced Comprehensive HIV Prevention Planning and Implementation for Metropolitan Statistical Areas Most Affected by HIV/AIDS

Major Challenges in U.S. Implementation Cascade



Be Not Discouraged



- **“Not everything that counts can be counted, and not everything that can be counted counts."**

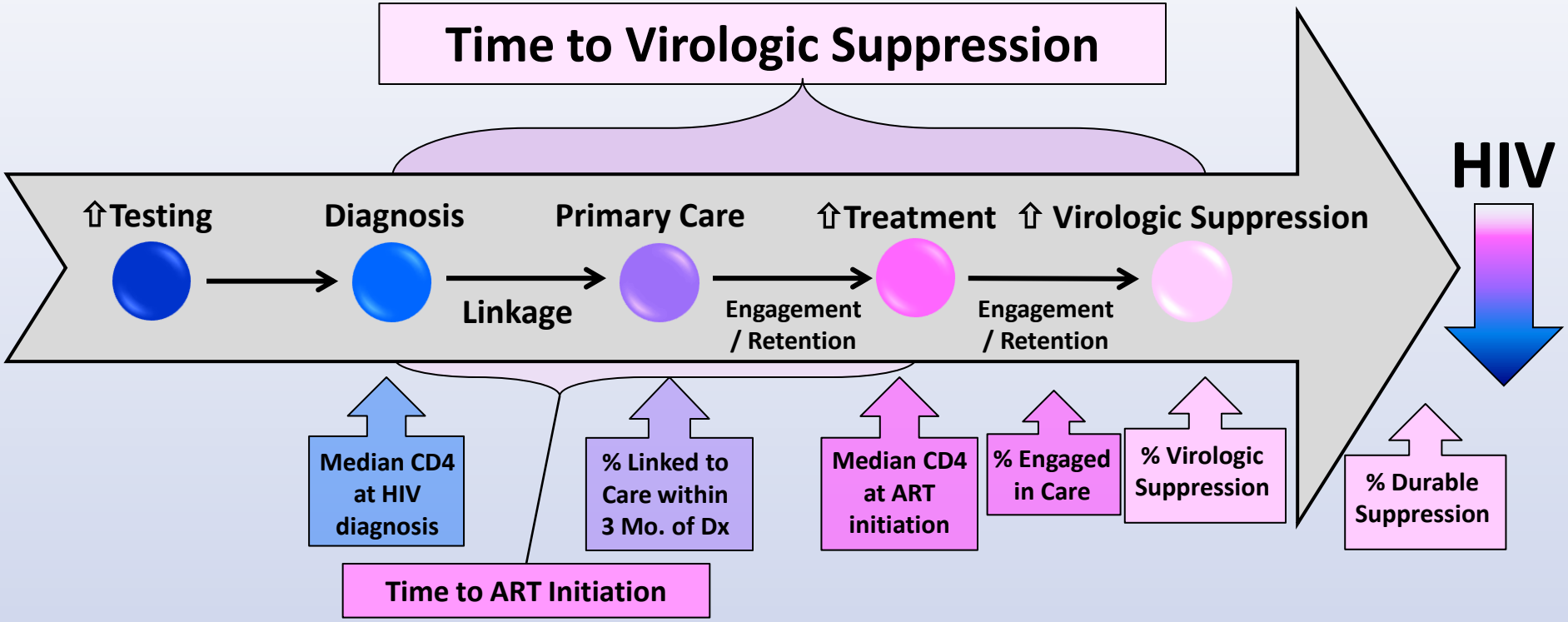
  ---Albert Einstein

When the data are in hand, we should use it!

"But once the data are in hand, it is the failure to use those data for public health purposes that must be justified." (Fairchild, 2007)

- Surveillance data and other data could not only be used to monitor and evaluate, but for real-time quality improvement: ***Maximize Cascade***
  - Prior Diagnosis
  - Current and Past Location of care: Medical records
  - Treatment history, co-infections, resistance
  - For Linkage, Engagement, Retention & Re-Engagement

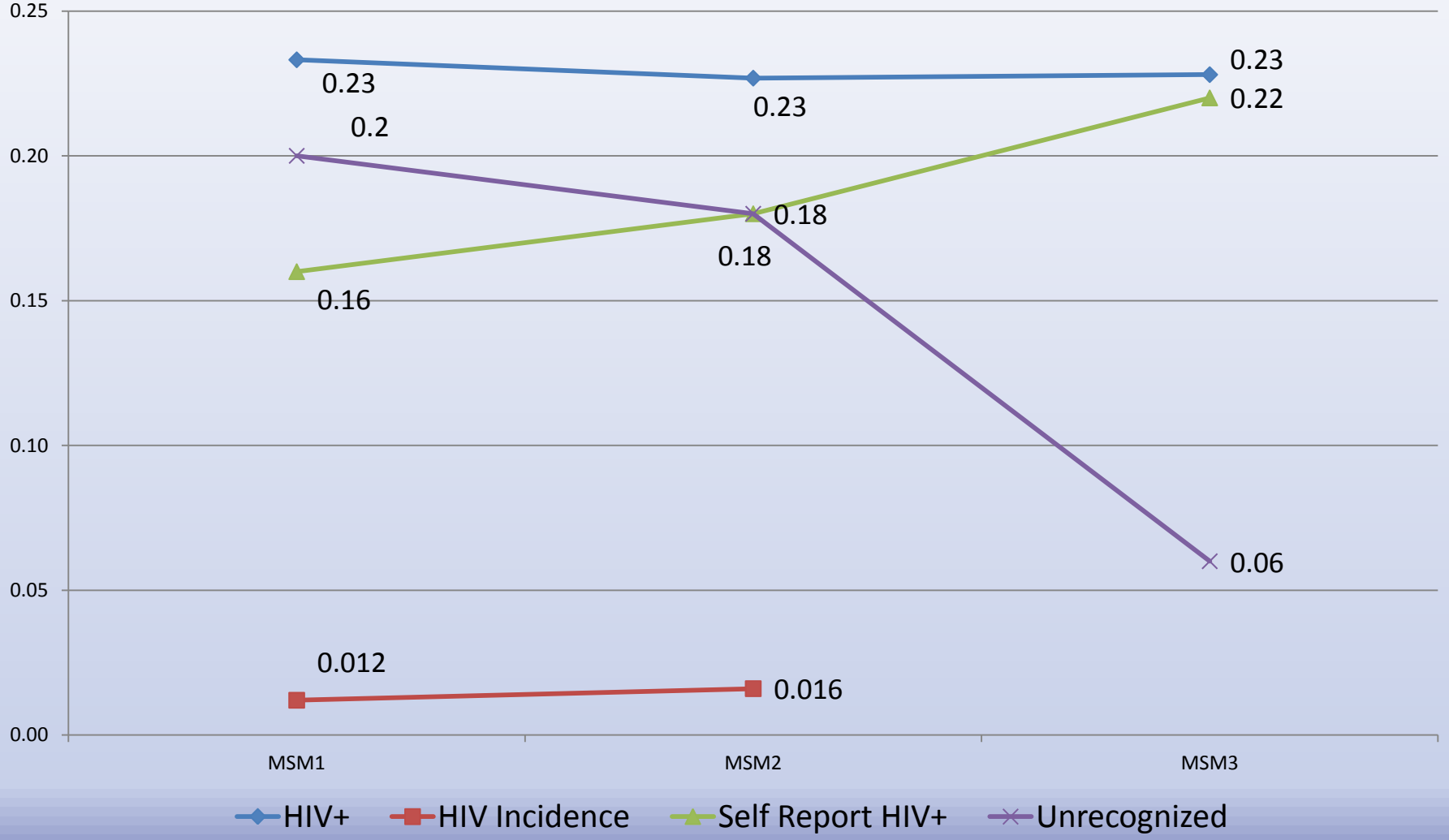
Using San Francisco's Surveillance Data to Evaluate Our Continuum of Prevention, Care and Treatment



Community Viral Load: Unified Marker of Prevention and Treatment

Das, et al. *CROI*, 2012.

HIV prevalence, incidence, self-report and unrecognized infections: 2004-2011



* MSM3 Incidence not complete

Testing (Now)

Populations by Race/Ethnicity	United States	San Francisco
Total	182	388
White	239	426
Other/Unknown	180	464
African American	175	351
Hispanic/Latino	160	328
Asian/Pacific Islander	225	319

Below 350

Below 500

~350 or below

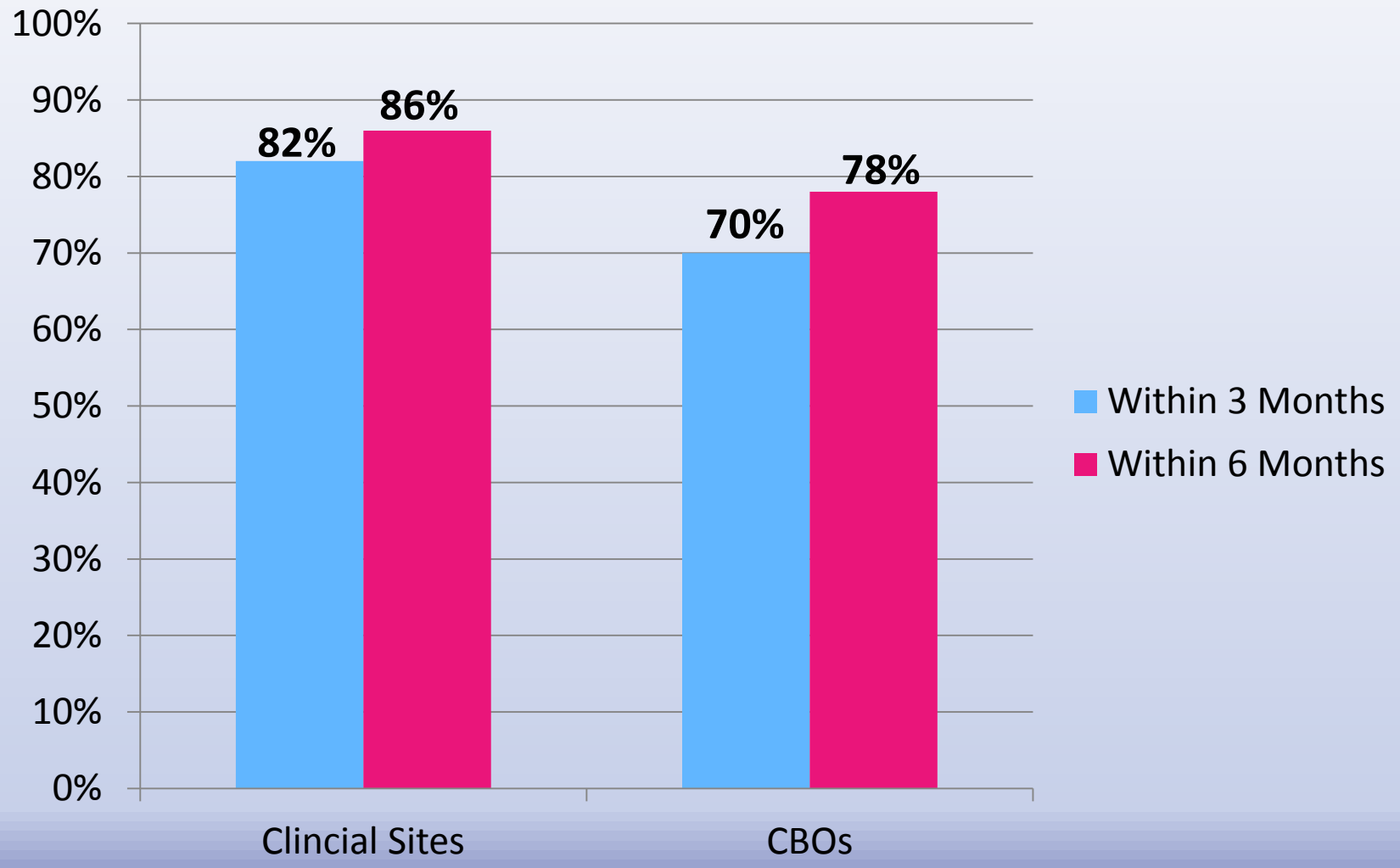
CDC HIV Surveillance Supplemental Report, Volume 16, Number 1

SFDPH HIV Epidemiology 2010 Annual Report

Linkage (Now)

- **% of PLWHA linked to medical care within 3 months after diagnosis**
  - Surveillance: CD4, VL

Linkage at SFDPH Sites



Testing and Linkage (Future)

Testing

- # of Tests (Insurance/claims)
- Testing Frequency (Need to know negatives)
- Percent Unaware of serostatus (NHBS)
- Percent Positivity (Need to know negatives)

Linkage (instead of using CD4/VL from surv)

- Self-report CTL programs
- Clinic visit schedules/EMR
- Reimbursement/Insurance

Engagement in Care (Future)

Engagement in Care

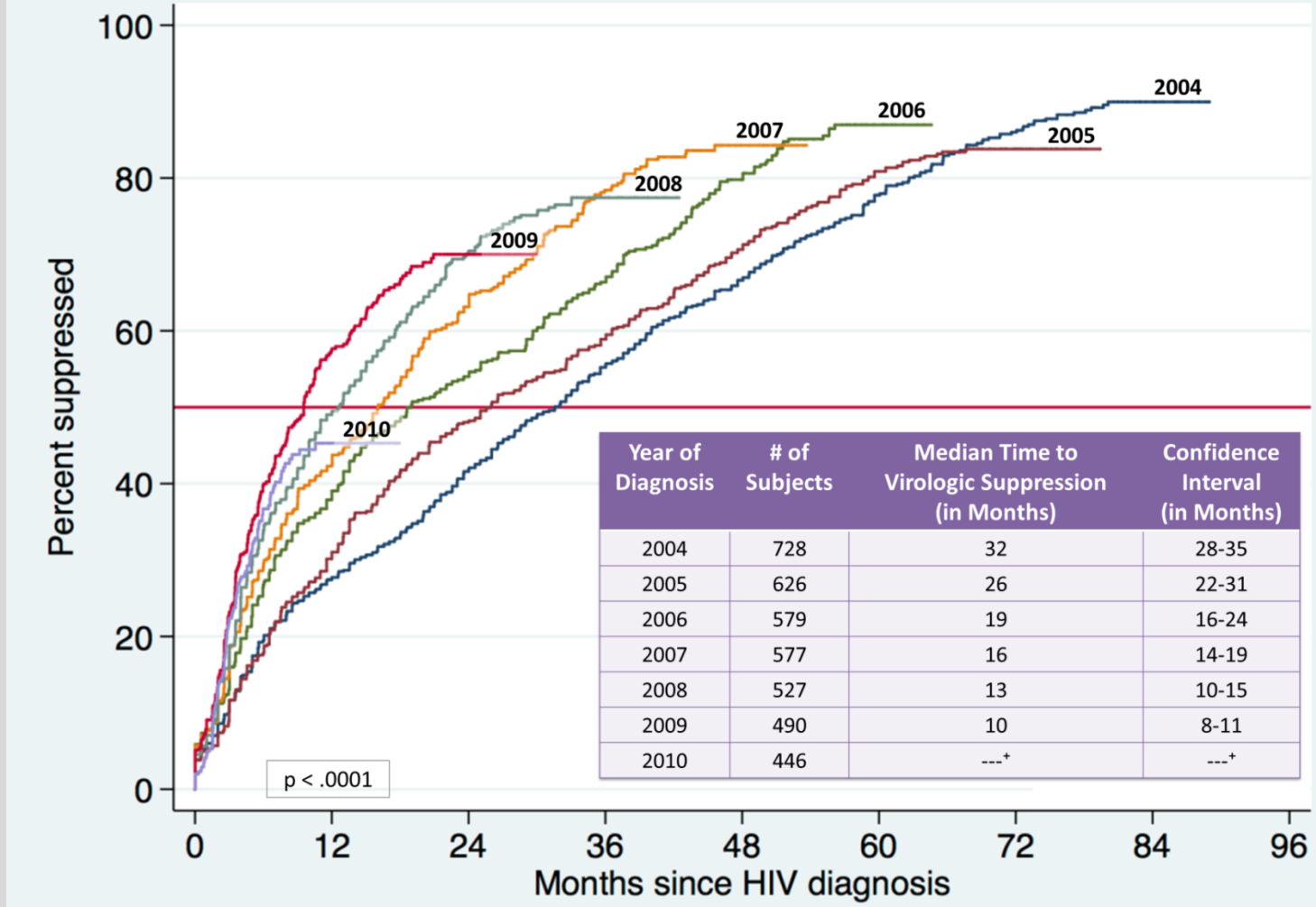
- Primary Care Visit Frequency in time period (Clinic EMR)
- Missed visits
- ER visits or hospitalizations

Treatment Indicators (Future)

- Median CD4 at treatment initiation
- Time from Diagnosis to ART initiation
- Percent in Continuous Care w/CD4>350
- Percent w/CD4<500 on ART (active surveillance or linkage with insurance, pharmacy/EMR, claims)
- Percent undetectable who've been on ART 12 months (EMR, ART data)
- Mortality

Treatment (Now)

FIGURE 1: MEDIAN TIME IN MONTHS FROM HIV DIAGNOSIS TO VIROLOGIC SUPPRESSION AMONG PERSONS DIAGNOSED WITH HIV, 2004-2010, SAN FRANCISCO



Year of Diagnosis	# of Subjects	Median Time to Virologic Suppression (in Months)	Confidence Interval (in Months)
2004	728	32	28-35
2005	626	26	22-31
2006	579	19	16-24
2007	577	16	14-19
2008	527	13	10-15
2009	490	10	8-11
2010	446	---⁺	---⁺

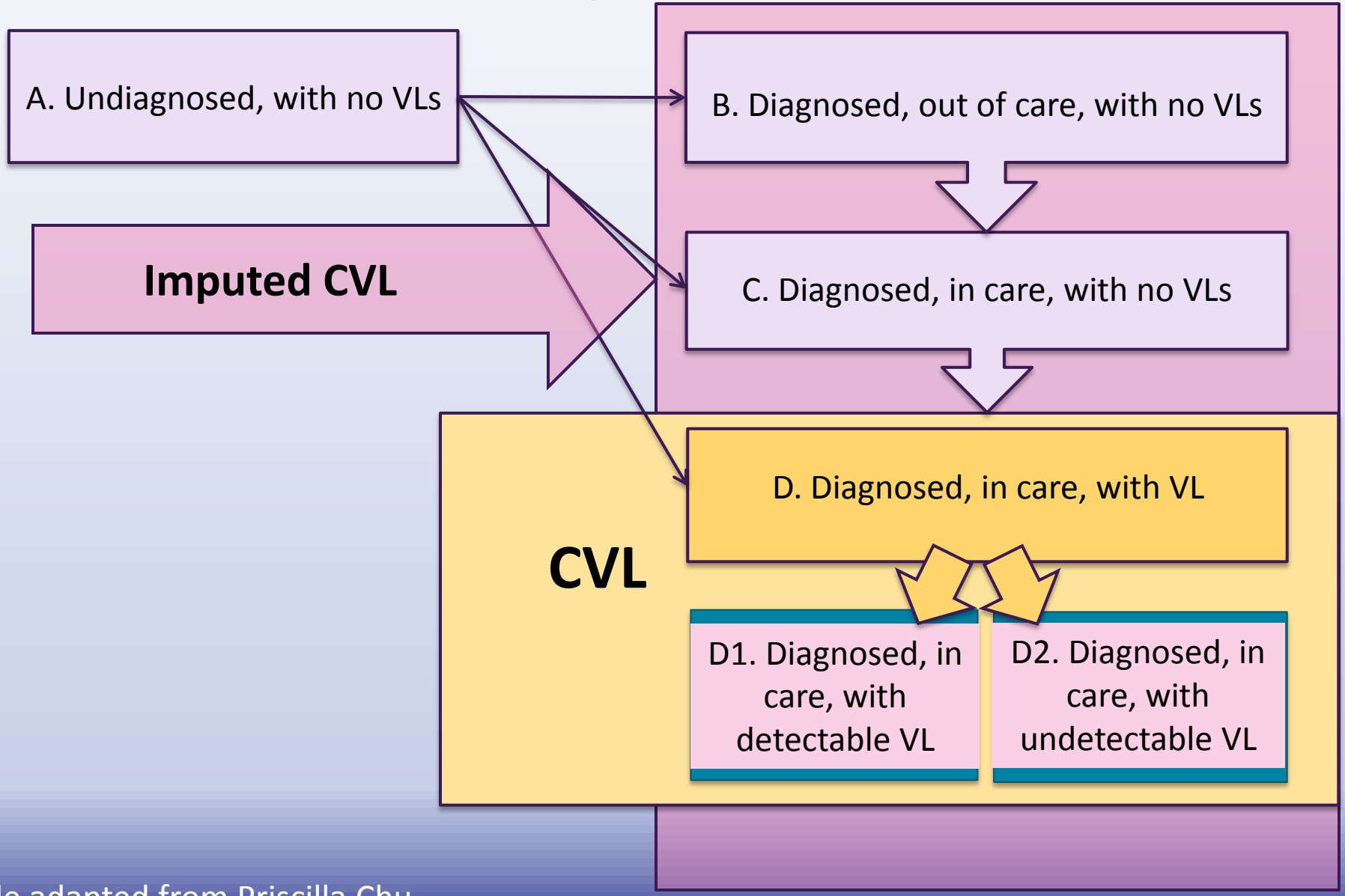
⁺Median time to suppression was undefined for 2010 (the K-M curve does not cross 50%)

Das, et al. *CROI,* 2012.

Engagement in care

- **Surveillance of CD4/VL monitoring frequency**
  - Proportion in continuous care (2 or more visits in preceding 12 months at least 3 months apart)

Conceptual Framework for Community Viral Load Measures among HIV-infected Persons



Slide adapted from Priscilla Chu

Calculation of CVL

- Used San Francisco's comprehensive HIV/AIDS surveillance system
- Calculated two measures of CVL:
  - Total: $$tCVL = \left(\sum_{i=1}^{n} mostrecentVL \right)$$
  - Mean: $$CVL = \left(\frac{\sum_{i=1}^{N} (VL)}{N} \right)$$

Applications of the Measures

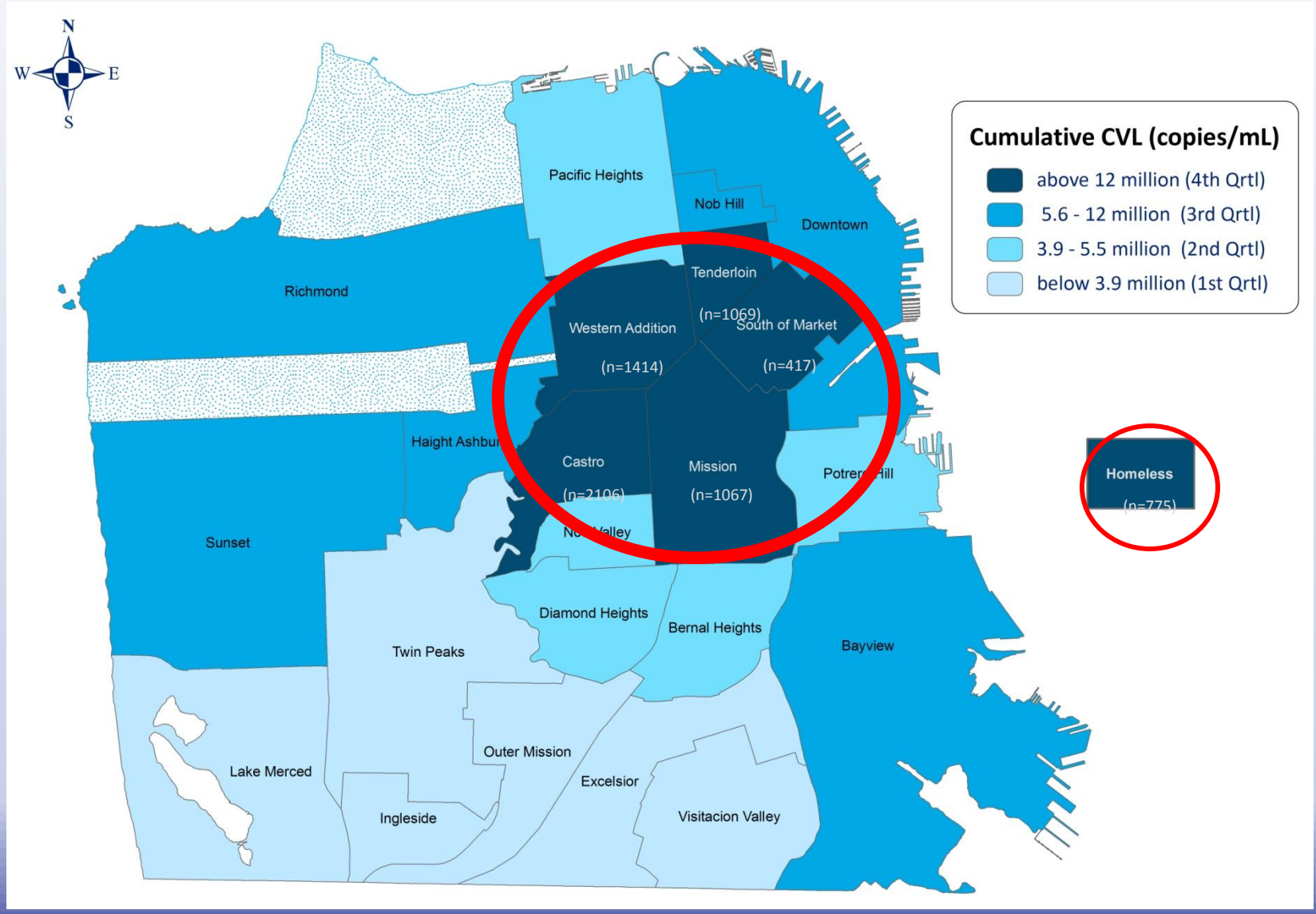
- Calculate cross-sectional CVL and examine geographic distribution and other disparities
  - San Francisco *(Das CROI 2009, CROI 2010, PLOS 2010)*
  - Washington DC *(Castells, CROI 2011)*
  - New York *(Laraque, CROI 2011)*
- Calculate annual measures of CVL and relate to new HIV Infections (Program and Research)
  - Ecologic
  - Cohort Study

CVL Disparities, SF 2004-2008

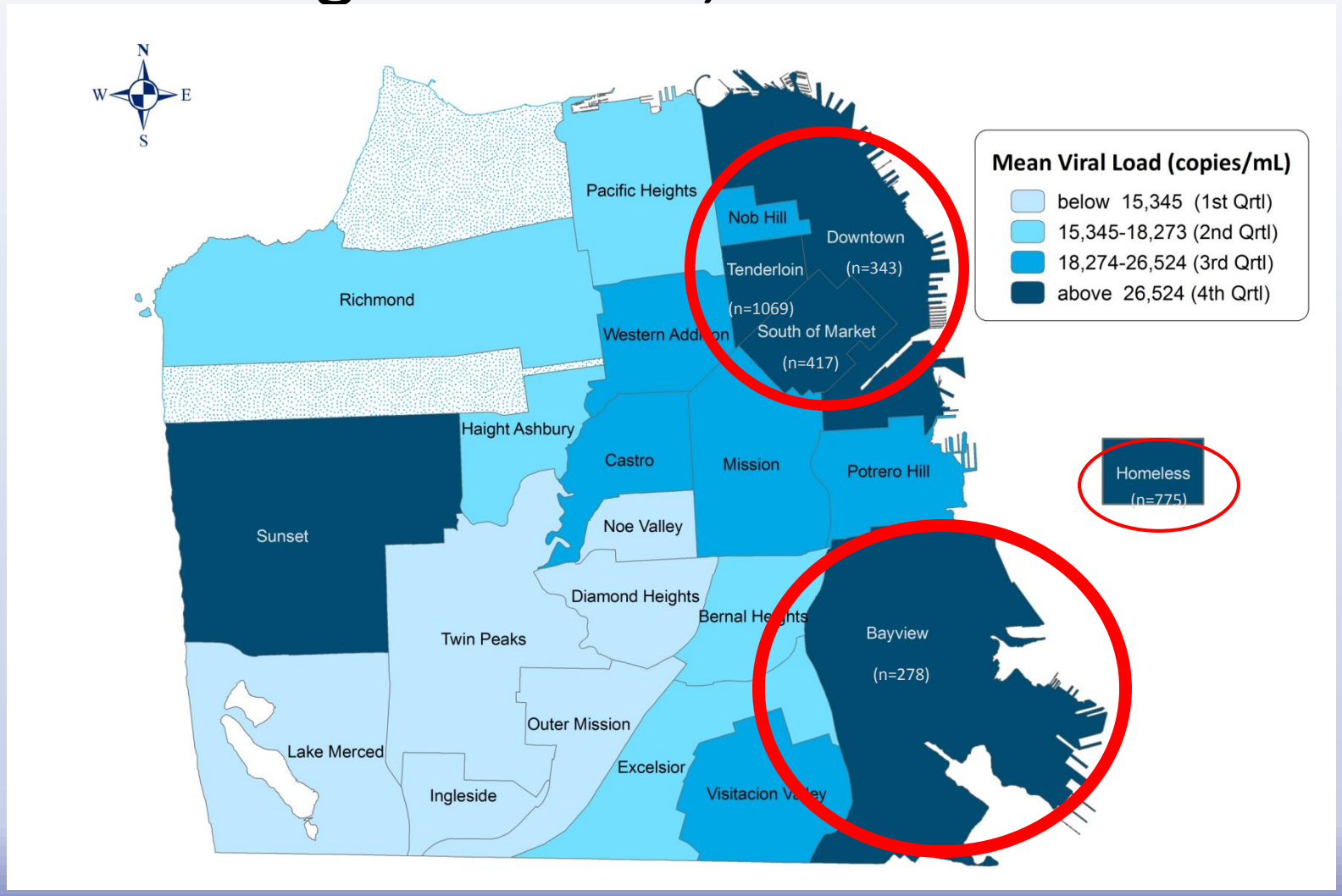
Overall	N	(%)	Mean CVL*
San Francisco	12,512	(100)	23,348
Sub-groups	**N**	**(%)**	**Mean CVL***
Latino	1822	(15)	26,744
African-American	1825	(15)	26,404
Women	786	(6)	27,614
Transgender	291	(2)	64,160
IDU	1011	(8)	33,245
MSM-IDU	1791	(14)	36,261
Not on treatment	2924	(23)	40,056
Not engaged in care	4637	(37)	36,992

*($p<0.001$ by Kruskal-Wallis test) in mean CVL by treatment history, race/ethnicity, age, gender, HIV transmission risk category, insurance status, and clinical status.

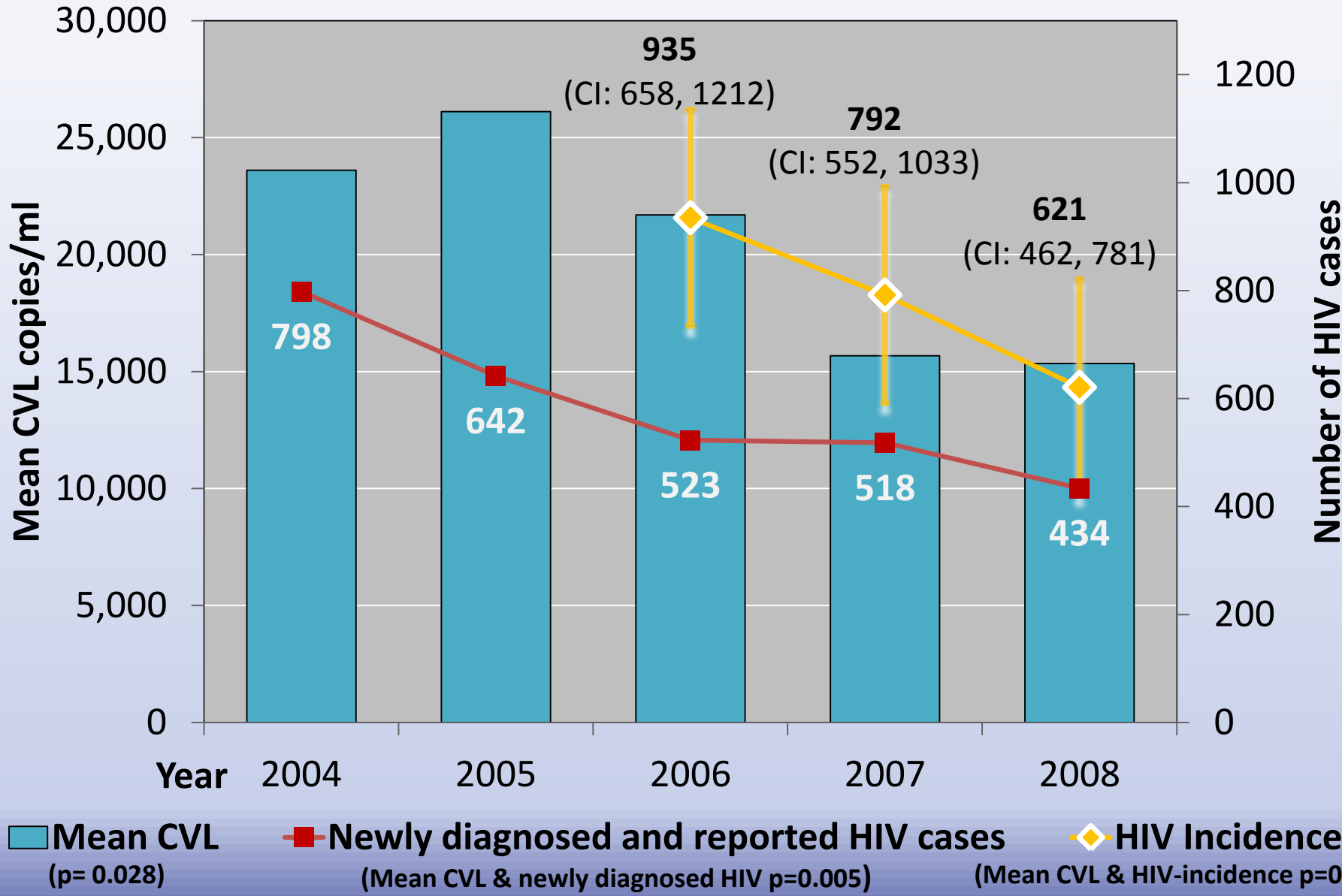
Spatial Distribution of Total CVL by Neighborhood, 2005-2008



Spatial Distribution of Mean CVL by Neighborhood, 2005-2008

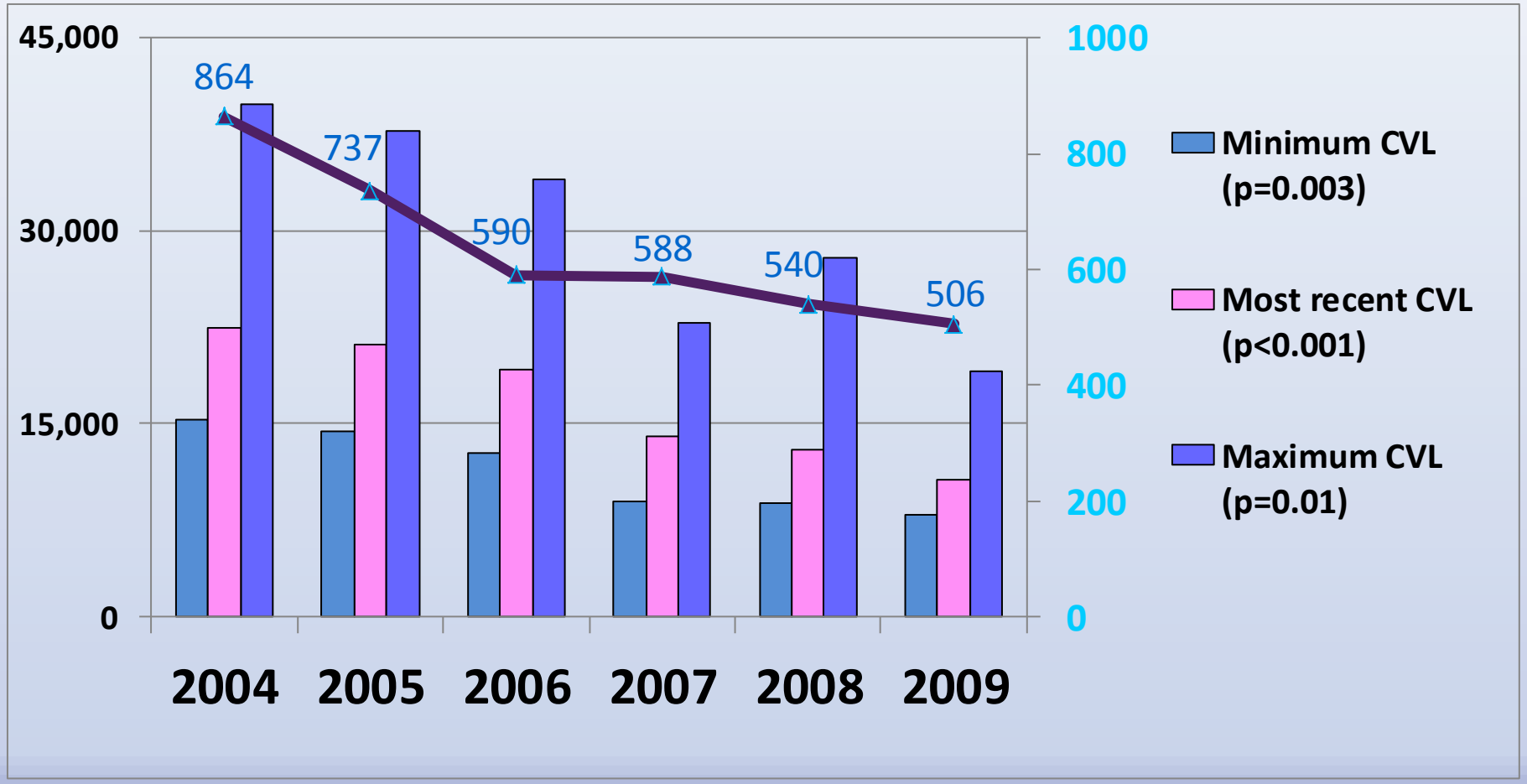


Mean CVL and New HIV Infections, 2004-2008



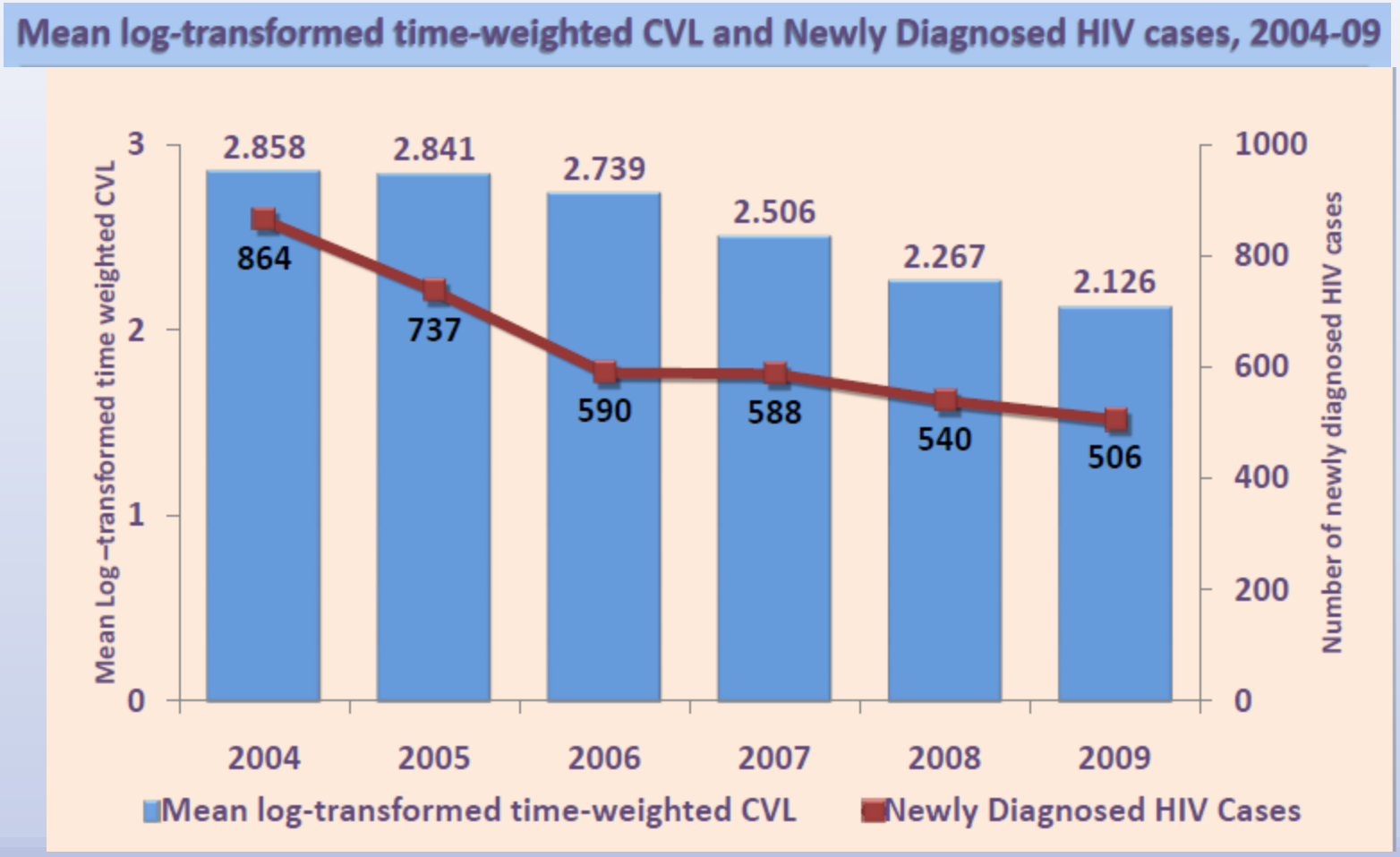
Das, et al. 2010.

Minimum, Most Recent, Maximum CVL and Newly Diagnosed and Reported HIV cases

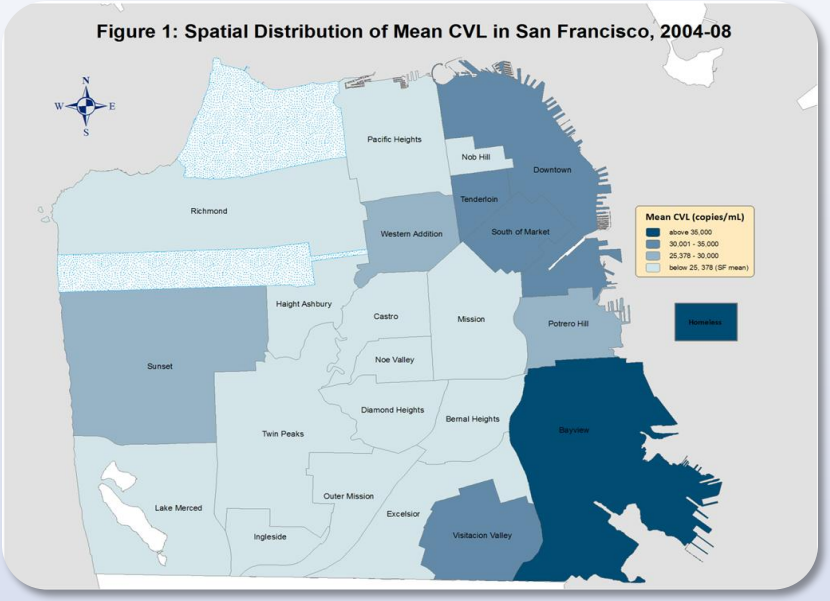


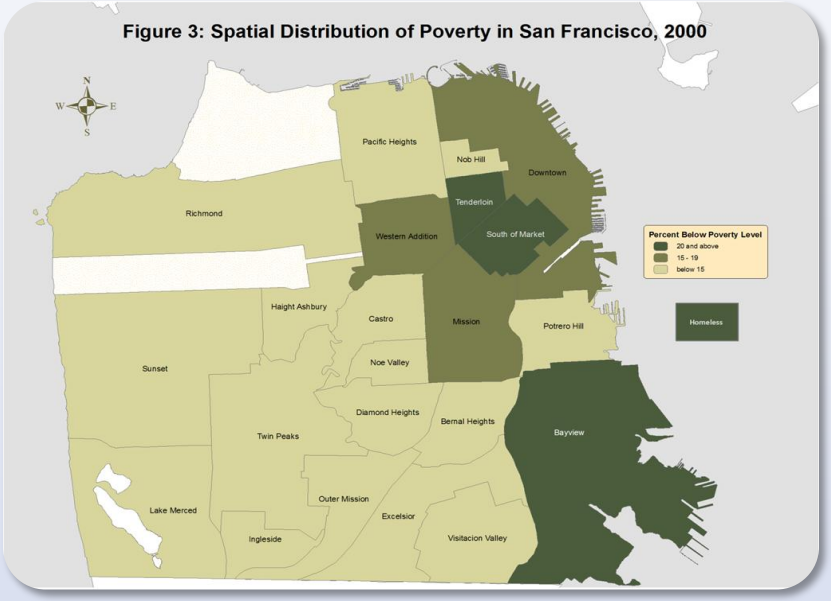
Das, et al. *CROI,* 2011.

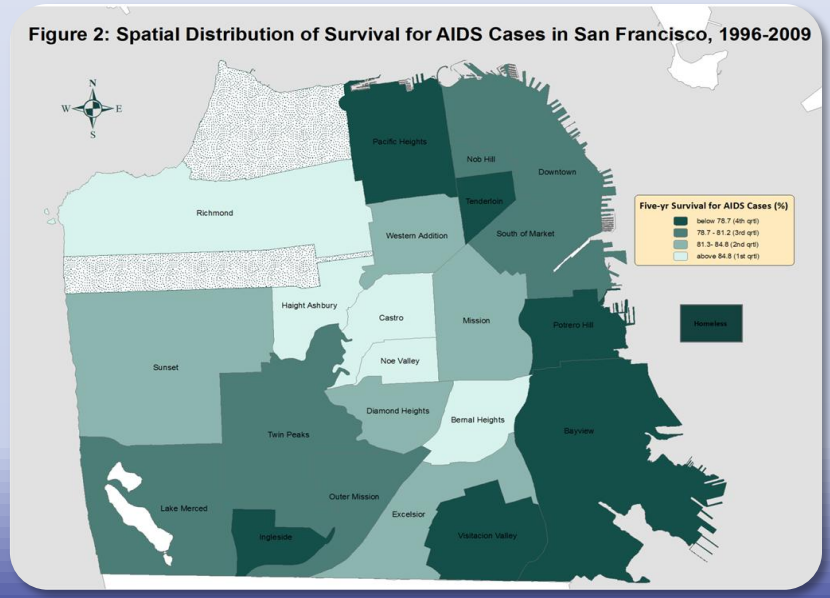
Refining CVL Calculation with Time-Weighted Averaging (AUC)



Community Viral Load Disparities

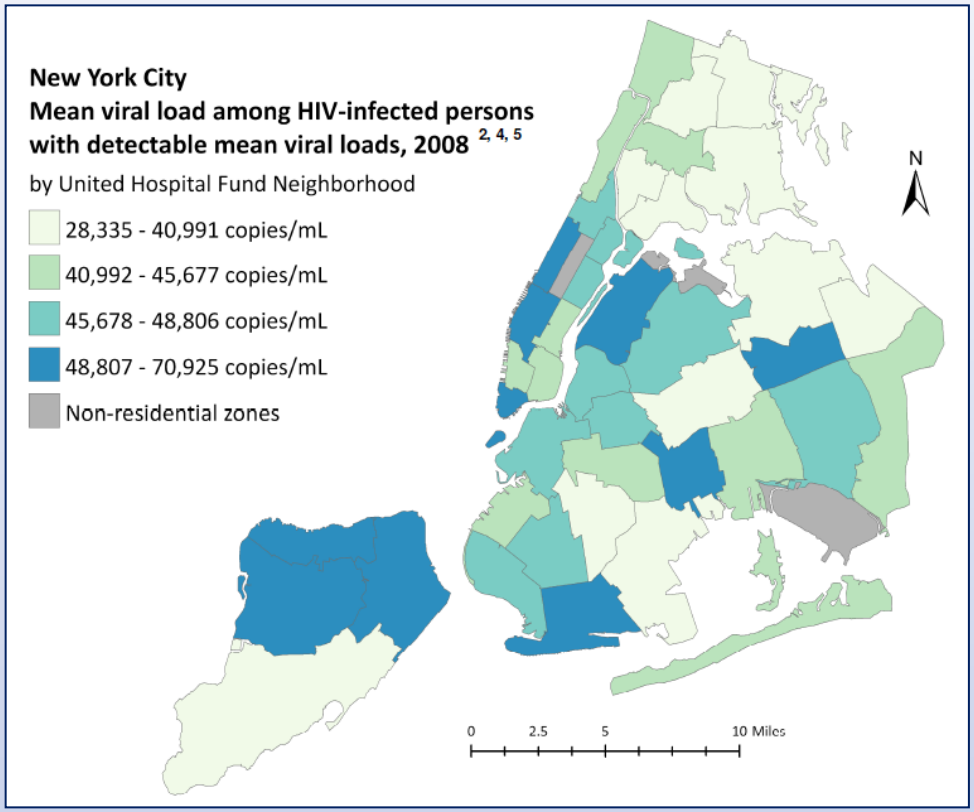




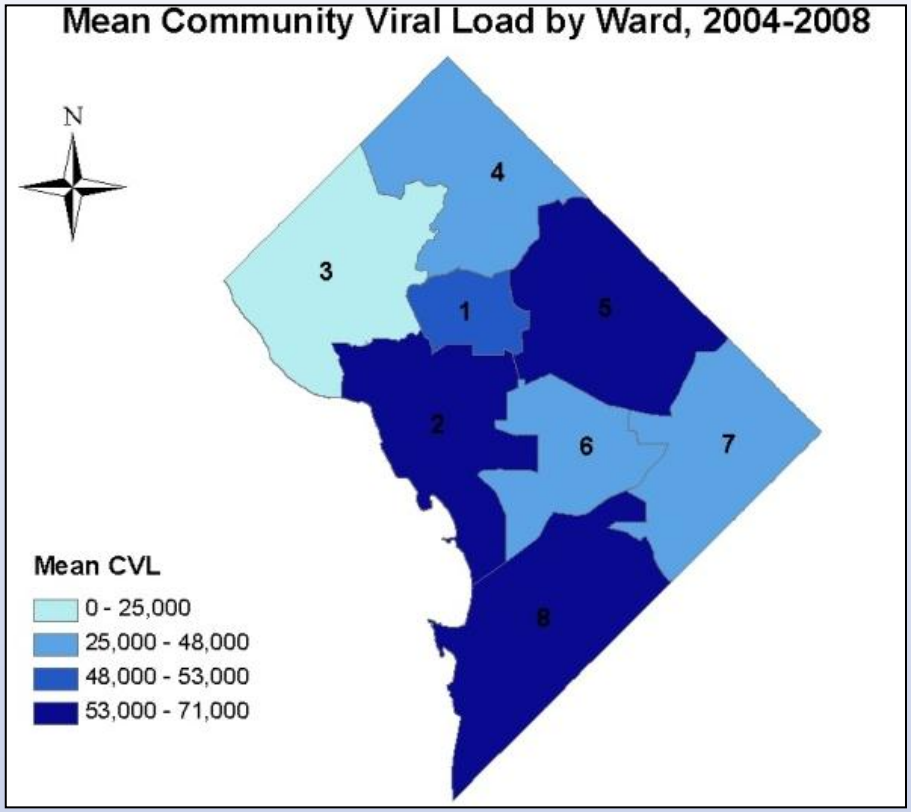


- **Even in relatively richly-resourced San Francisco, disparities in CVL track with poor 5-year survival and neighborhood concentration of poverty**
- **CVL may be a useful marker for public health departments to target resources and address geographic disparities in HIV transmission and survival**

CVL: New York & Washington D.C.



Laraque, et al. *CROI*, 2011. Abstract #1024.



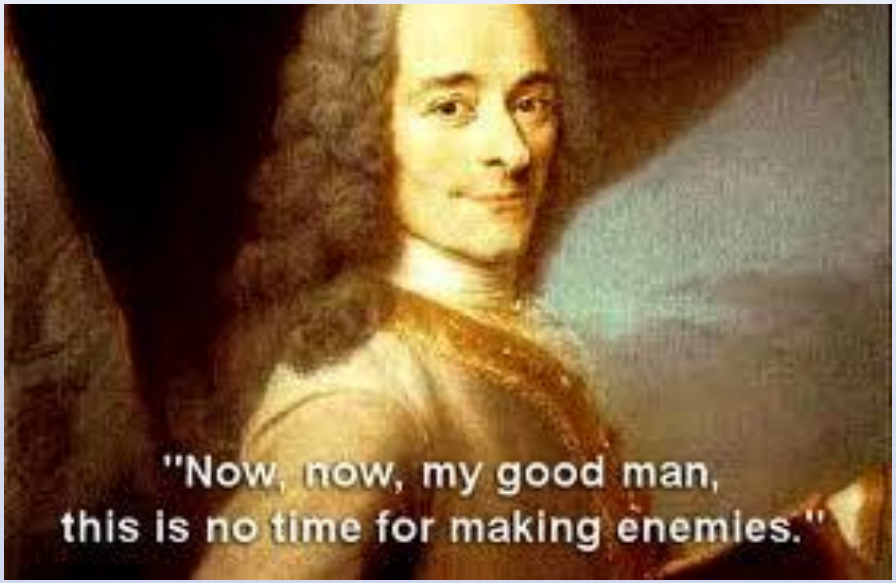
Castel, et al. *CROI*, 2011. Abstract #1023.

Caveats, Concerns, Limitations, Critiques

- Surveillance Limitations (denominator issues)
  - Sample “undiagnosed” with NHBS
  - Cohort Data Evidence; Cluster RCT evidence
- Different VL assays
- Acute Infection (Stop Study Ag/Ab vs. RNA)
- Multiple Imputation: Does MAR assumption hold?
- Ecologic Fallacy (Alternative secular trends→STI, syphillis, gonorrhea, risk behaviors, serosorting)

Let Not the Perfect Be the Enemy of the Good!

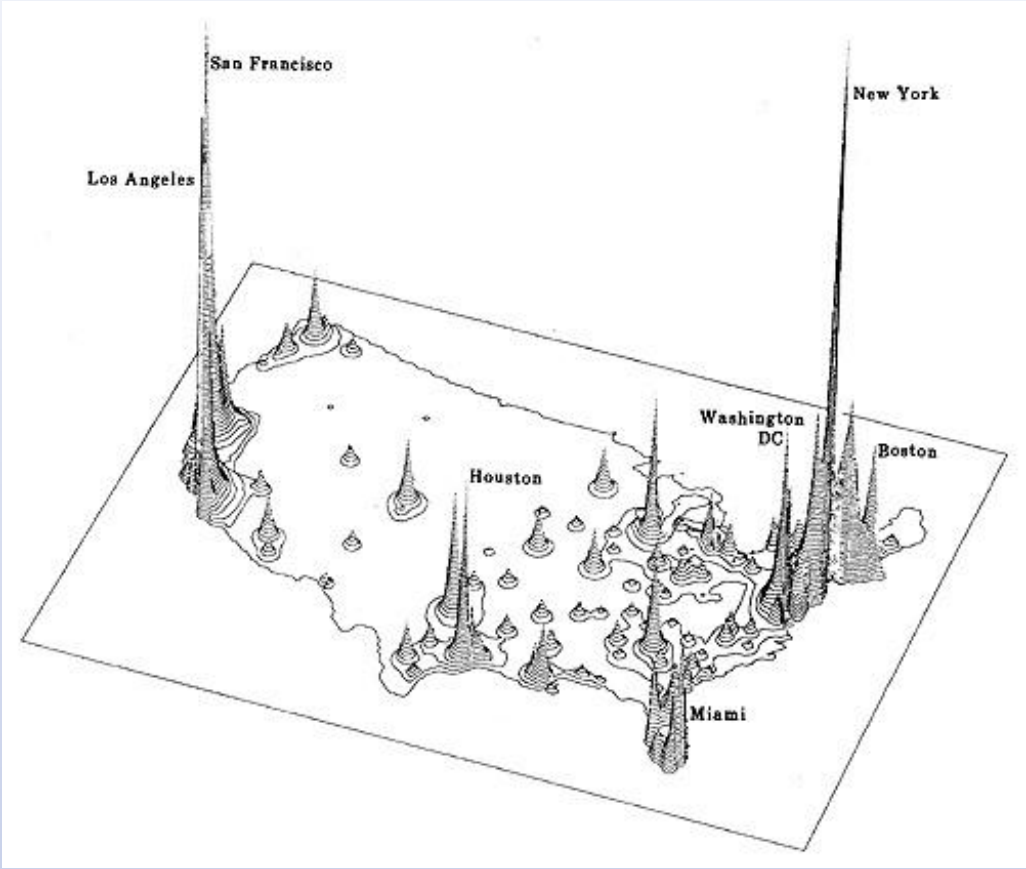
- “The perfect is the enemy of the good.”



Voltaire 1772

Can we get to a National or Global CVL Estimate?

- Yes, we can!
- Establish the baseline
- **Must modernize surveillance in the United States**
- We should pursue the exercise to delineate missing data, gaps in resources, technology, or other issues
- What will the added value be?
  - ***Follow trends in CVL → HIV Incidence***
  - ***Single Indicator of Prevention and Care Success***

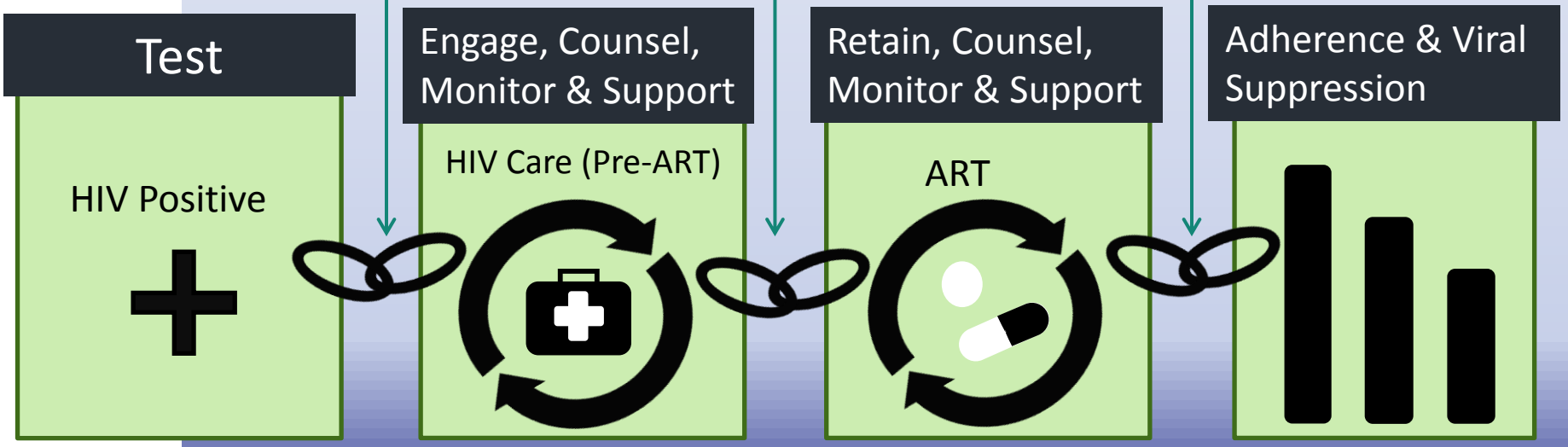


THE WAY FORWARD: TRANSFORMING OUR NARRATIVE

MAXIMIZING USE OF DATA, MAXIMIZING SERVICES

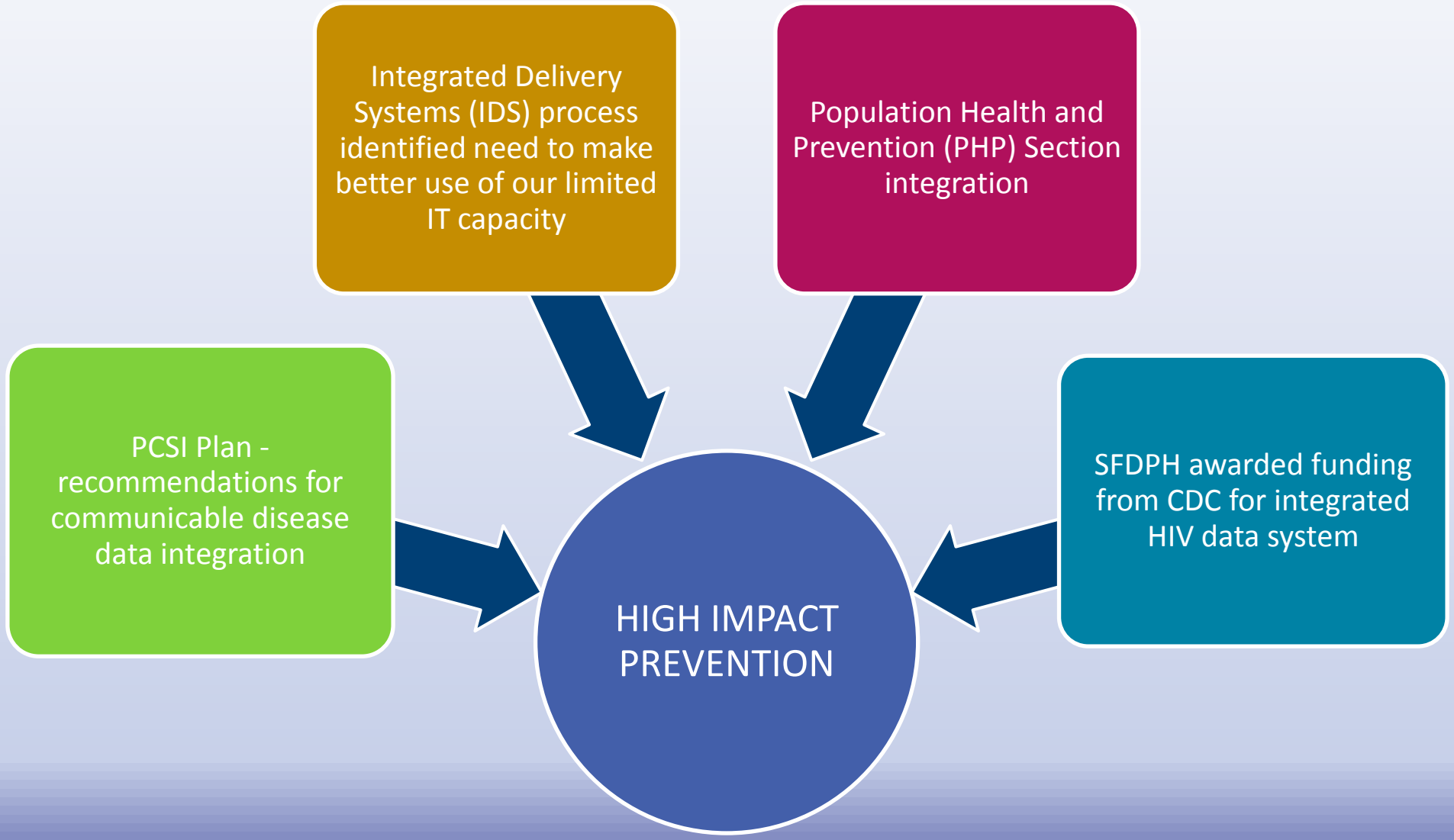
Data linkages are broken given our siloed databases and policies that make sharing information difficult

We must update our polices to improve the sharing of data along continuum



Components of slide adapted from el Sadr, CROI 2012

Measuring High-Impact Prevention



Institute of Medicine Report

Monitoring HIV Care in the United States

Indicators and Data Systems

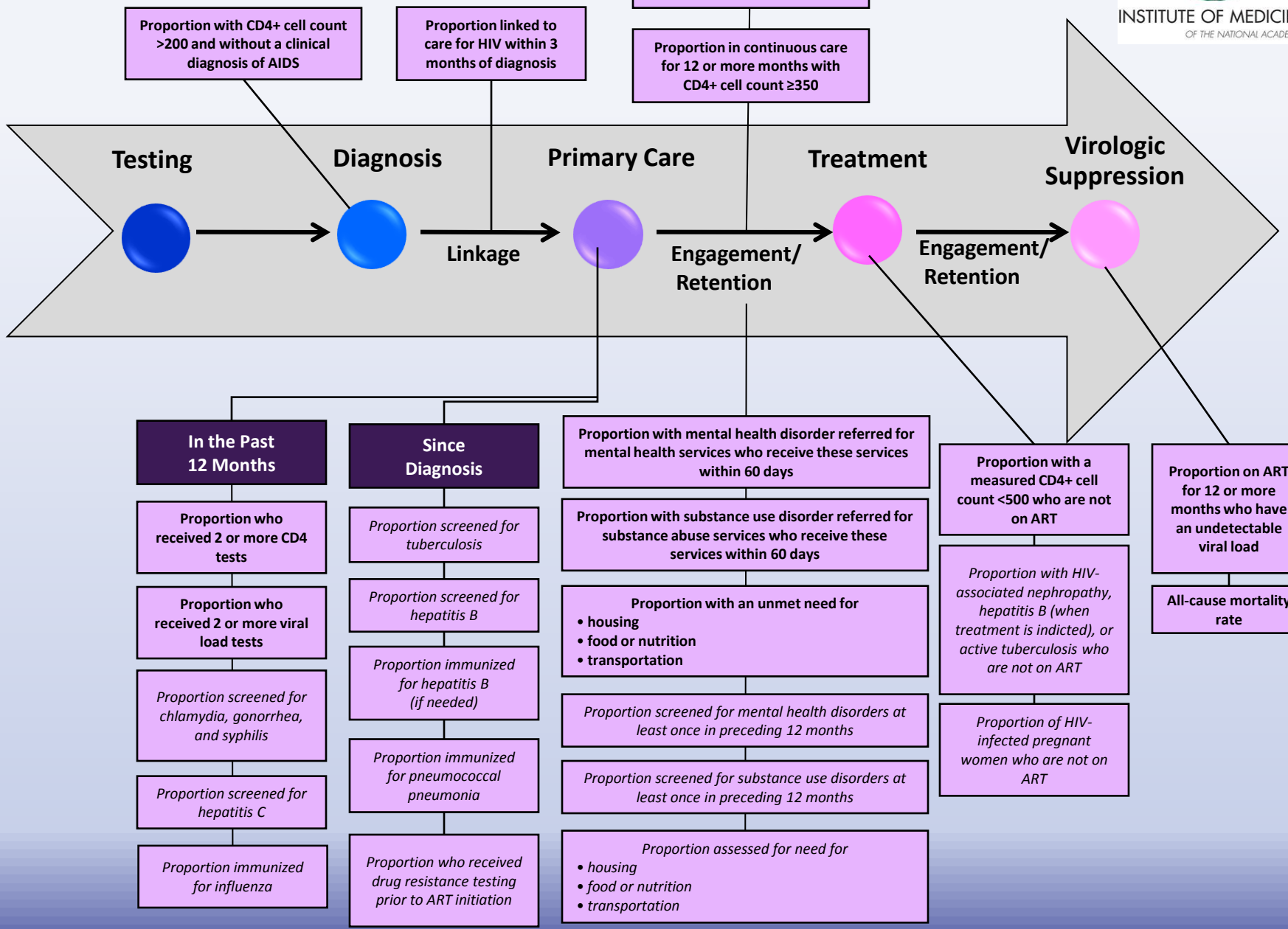
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the nation • Improving health

Committee's approach to its charge

- Use NHAS targets and existing indicators (PEPFAR, HP 2020), quality measures (NQF), and treatment standards (HHS Guidelines) as a basis for the recommended indicators
- Review public and private data systems pertinent to HIV care
- Identify critical points along care continuum
- Review the literature, expert presentations
- Were mindful of need to minimize reporting burden and cost
- Limited scope to adults diagnosed with HIV

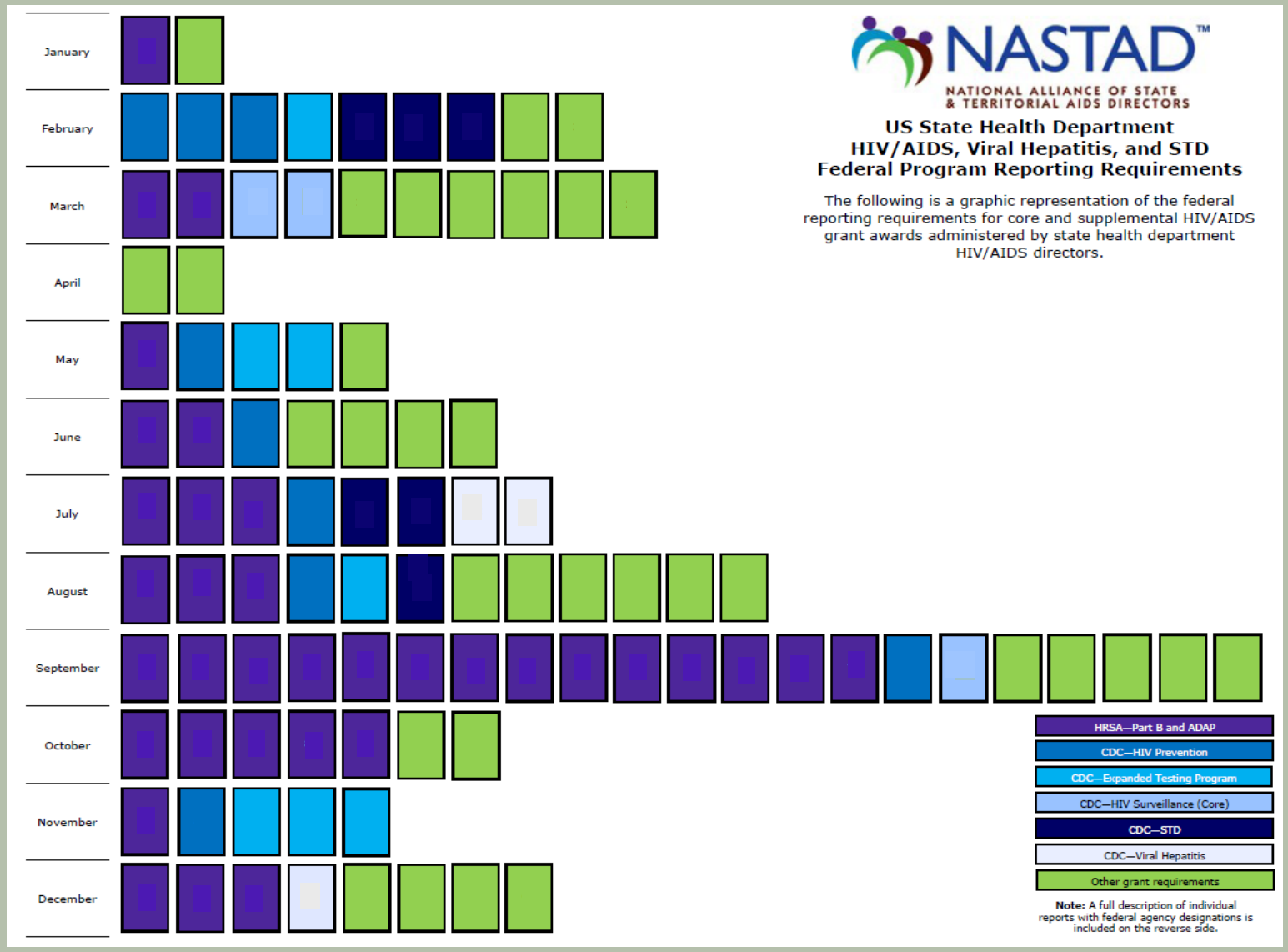
Continuum of HIV care mapped to indicators of HIV care and supportive services



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

IOM Report: Monitoring HIV Care in the United States: Indicators and Data Systems 2012

BARRIERS TO DATA COLLECTION


January
February
March
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September
October
November
December
NASTAD™
NATIONAL ALLIANCE OF STATE & TERRITORIAL AIDS DIRECTORS
US State Health Department
HIV/AIDS, Viral Hepatitis, and STD
Federal Program Reporting Requirements
The following is a graphic representation of the federal reporting requirements for core and supplemental HIV/AIDS grant awards administered by state health department HIV/AIDS directors.
HRSA—Part B and ADAP
CDC—HIV Prevention
CDC—Expanded Testing Program
CDC—HIV Surveillance (Core)
CDC—STD
CDC—Viral Hepatitis
Other grant requirements
Note: A full description of individual reports with federal agency designations is included on the reverse side.

Other barriers to data collection:

- Reimbursement policies and practices
- Variation in reporting requirements across states
- Incomplete reporting by providers
- Lack of mechanisms for health departments to share data across jurisdictions
- Staffing, administrative, and budgetary constraints
- Shifts in care coverage and across health care providers
- State variations in implementation of ACA
- Anonymous HIV testing

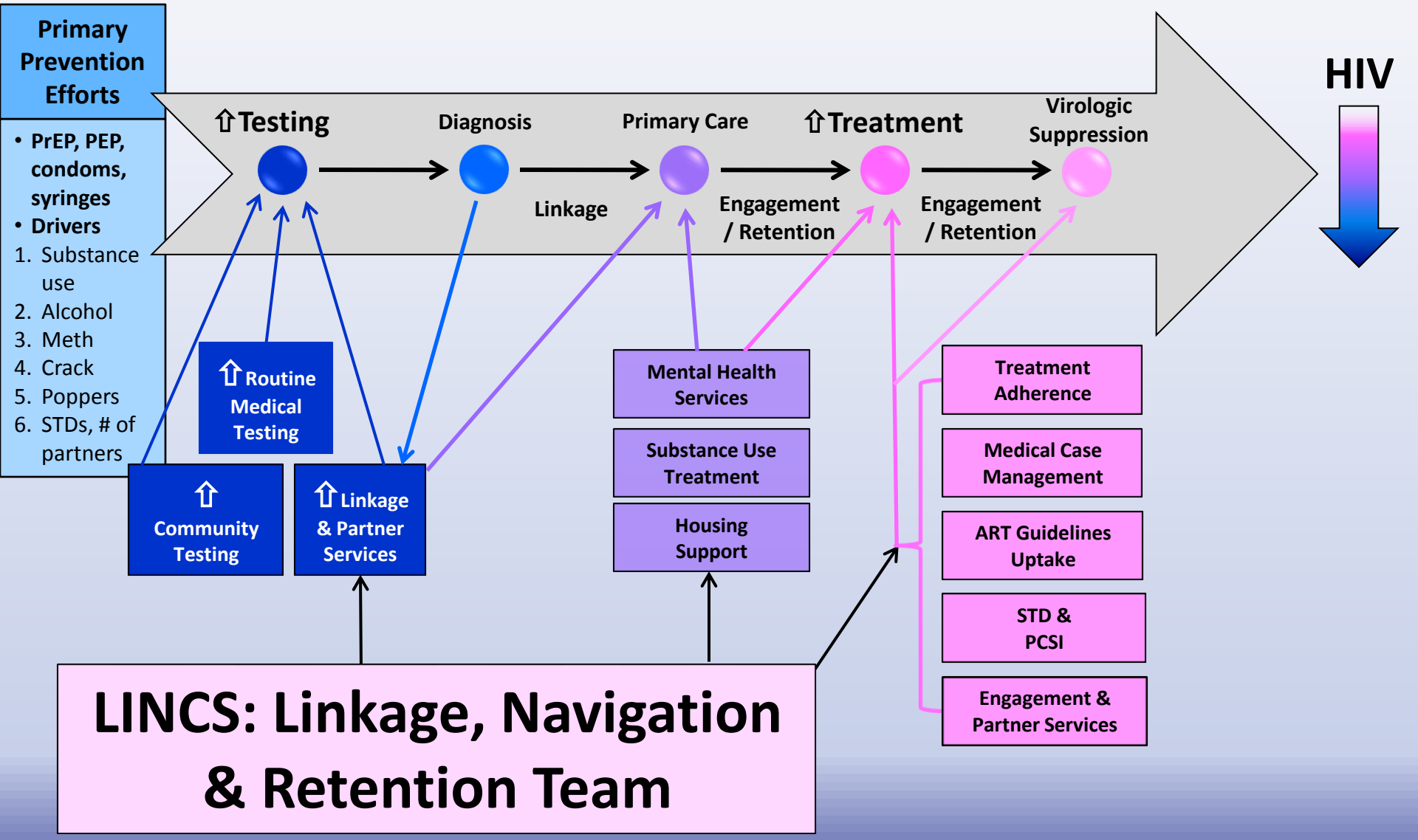
Recommendations

- **HHS should maintain and institutionalize the existing effort to streamline data collection and reduce reporting requirements for grantees of federally funded HIV/AIDS programs.**

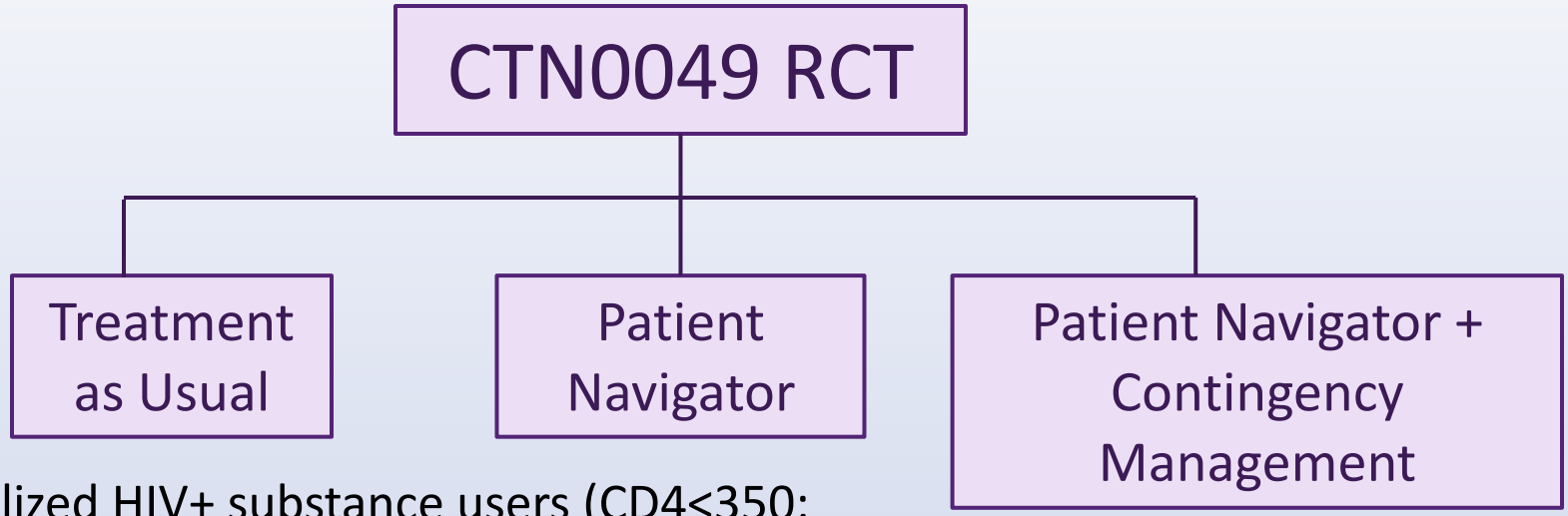
- **HHS should issue guidance to the HIV care community to clarify what patient information is permissible to share given federal and state privacy laws.**

REVOLUTIONIZING THE RESEARCH AGENDA

San Francisco's Approach to Maximizing the Continuum of Prevention, Care and Treatment

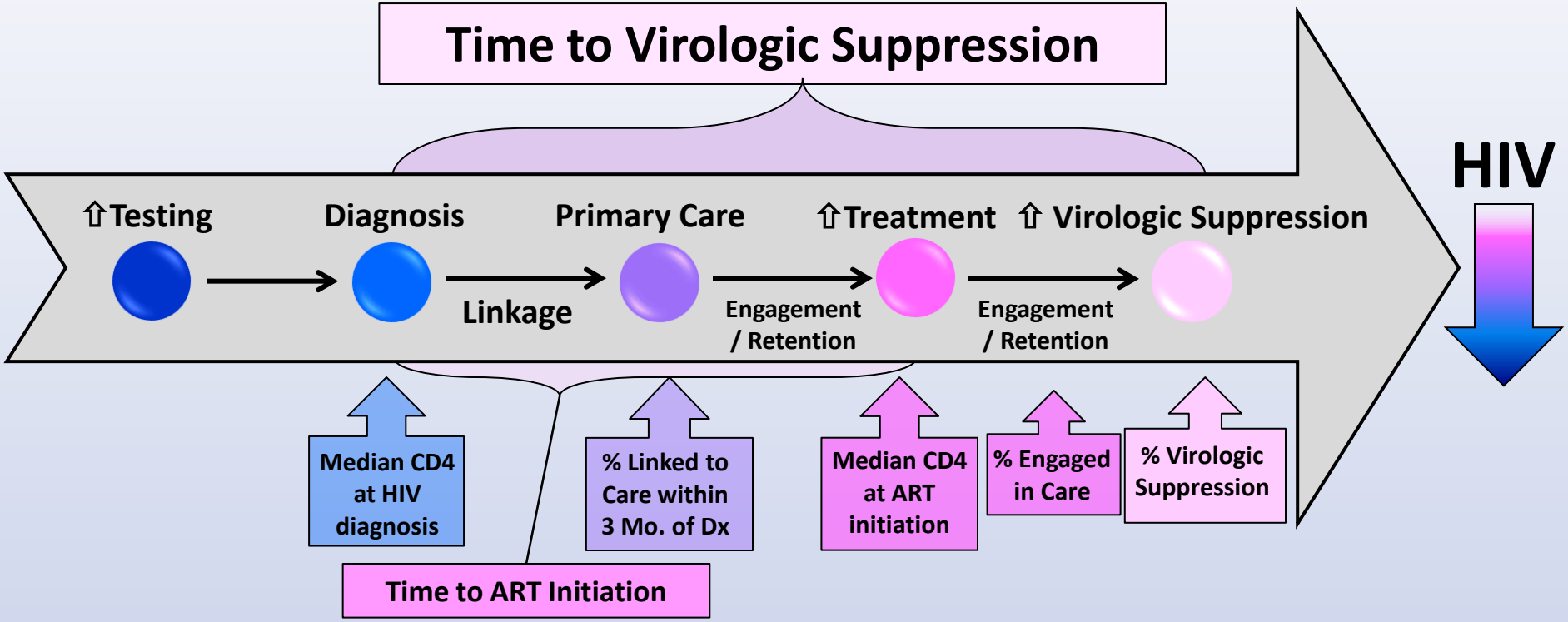


Hospital Visit as Opportunity for Prevention & Engagement for HIV+ Drug Users



- Hospitalized HIV+ substance users (CD4<350; detectable VL)
  - 800 participants
  - 10 sites
    - Miami
    - Atlanta
    - Baltimore
    - Boston
    - Philadelphia
    - Chicago
    - Dallas
    - Pittsburgh
    - Los Angeles
    - Birmingham

Modeling to Augment Evaluation: CVL in each compartment including those who fall off continuum



What CVL or % Supp→ R<1?

Das, et al. *CROI*, 2012.

Acknowledgments

People living with HIV/AIDS in San Francisco

SFDPH

Priscilla Chu, Glenn-Milo Santos, Susan Scheer, Willi McFarland, Taylor Maturo, H. Fisher Raymond, Israel Nieves-Rivera, Isela Gonzalez, Tracey Packer, Dara Geckeler, Bill Blum, Susan Philip, Stephanie Cohen, Nicholas Moss, Noah Carraher, Erin Antunez, Tomas Aragon, Barbara Garcia

UCSF

Diane Havlir, Elvin Geng, Edwin Charlebois, Steve Morin, Eric Vittinghoff, Steve Deeks, Brad Hare

CDC

Candice Kwan, Thomas Frieden, Kate Buchacz

Univ of Miami

Lisa Metsch, Dan Feaster, Lauren Gooden

White House Office of National AIDS Policy

Greg Millet, Jeff Crowley, and Grant Colfax

Municipalities Learning from Each Other: Strategic Implementation of Universal Antiretroviral Treatment to Maximize Reductions in HIV Incidence

SAVE THE DATE!

Friday, July 20, 2012

Renaissance Ballroom, 830-5pm

ABA Community Partner: Urban Coalition for HIV/AIDS Prevention Services (UCHAPS)

Chairs: Moupali Das, Peter McLloyd, and Blayne Cutler

UCSF University of California San Francisco

UCHAPS Urban Coalition for HIV/AIDS Prevention Services

Academic, government and community public health leaders will strategize regarding best practices in scaling up ART for both individual and public health benefit within their home communities.

-- Overview of Jurisdictions offering Universal Treatment

--Moving from the Emergency to Sustainable Response

--Finding New Partners and Forging New Relationships with the old to Finance Universal Treatment

--Harmonization of Data Systems and Innovative Uses of Technology to Improve Treatment Outcomes

--Politics, Policies, Protocols, and Philosophies