Untangling the racial disparities in HIV infection among men who have sex with men

Eli Rosenberg, PhD
Assistant Professor
Department of Epidemiology
Emory University RSPH

UCLA Seminar
March 4, 2016

Outline for today

1. Epidemiology of HIV infection among MSM in the US

2. Evaluating a causal framework for HIV racial disparities
   1. The “partner pool”: How HIV prevalence and care contribute to incidence disparities
   2. Individual-level risk behaviors revisited
   3. Biological co-factors

3. A model to put it all together

4. How do we fix this?

PRISM Health, Dept. of Epidemiology

Patrick Sullivan
Professor

Travis Sanchez
Associate Professor

Colleen Kelley
Assistant Professor

Eli Rosenberg
Assistant Professor

RESEARCH PROGRAMS INNOVATION
PRISM
IN SEXUAL MINORITY HEALTH

Amazing team

- 25 staff
- 7 PhD students
- 3 postdoctoral fellows
- Many MPH students

Jodie Guest
Professor

Aaron Siegler
Assistant Professor

Samuel Jenness
Assistant Professor

Kristin Wall
Assistant Professor

Epidemiology of HIV infection among MSM in the United States

HIV infection in the United States

- 1.2 million people in living with HIV infection in 2012
- 40,000 – 50,000 new infections per year
- Characterized by
  - Risk group
    - Men who have sex with men
    - Injection drugs users (IDU / PWID)
    - Heterosexual males/females
  - Sex
  - Age
  - Race
  - Region

New infections disproportionately among MSM, Black MSM

Figure 2: Estimated New HIV Infections, 2009, by Transmission Category

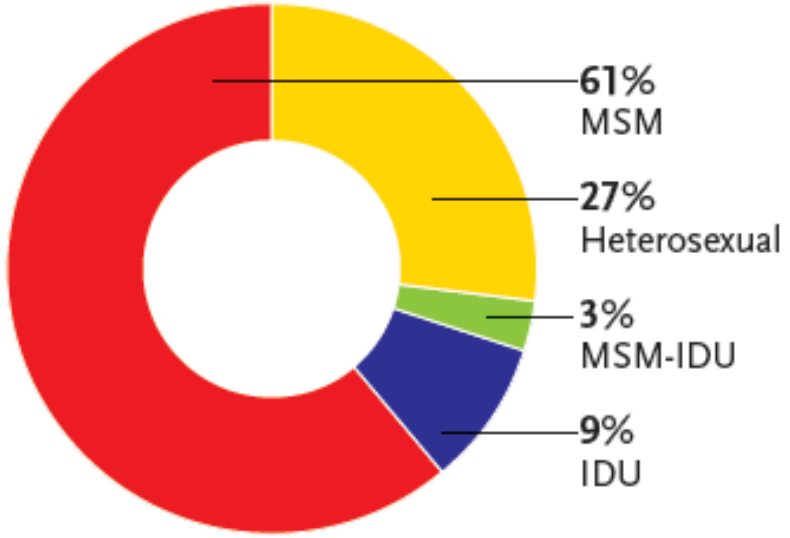
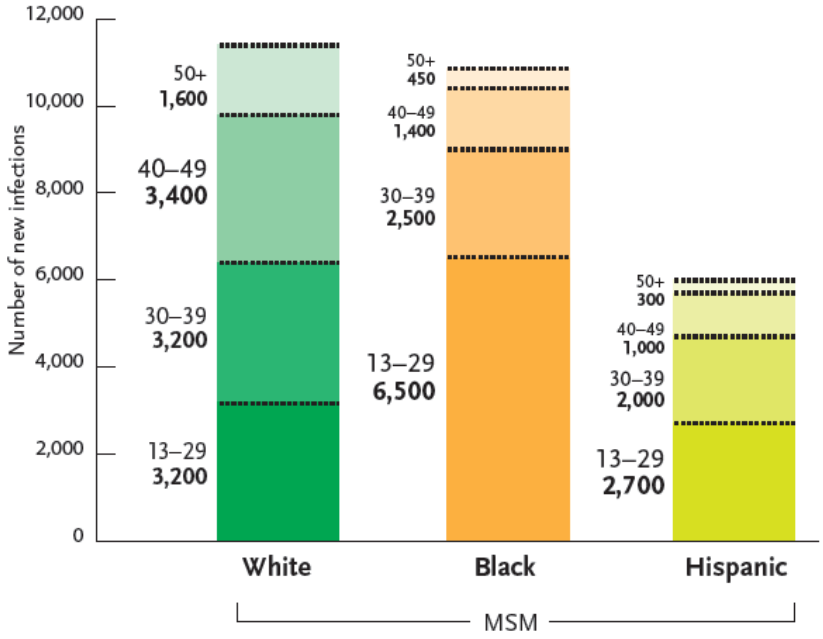


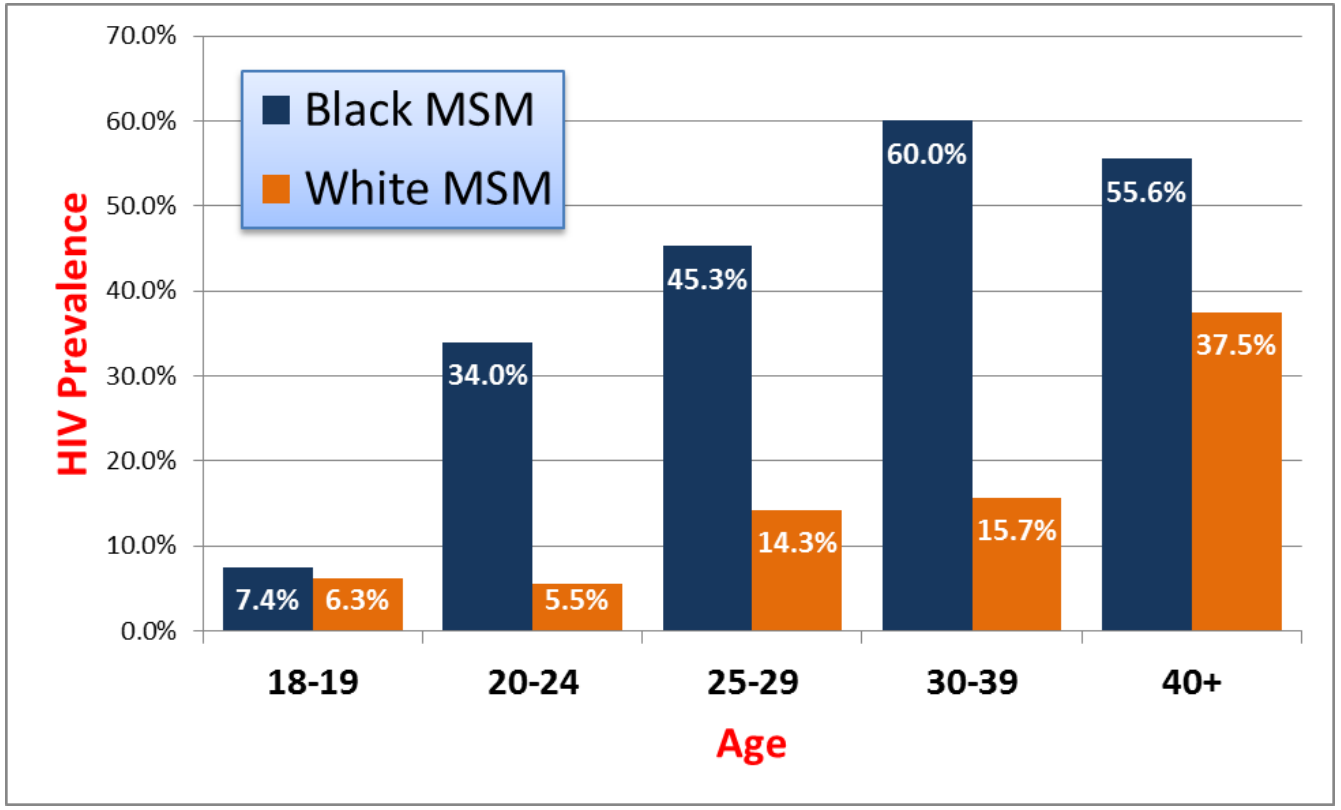
Figure 3: Estimated Number of New HIV Infections among Men Who Have Sex with Men (MSM), 2009, by Race/Ethnicity and Age†



CDC Fact Sheet 2011

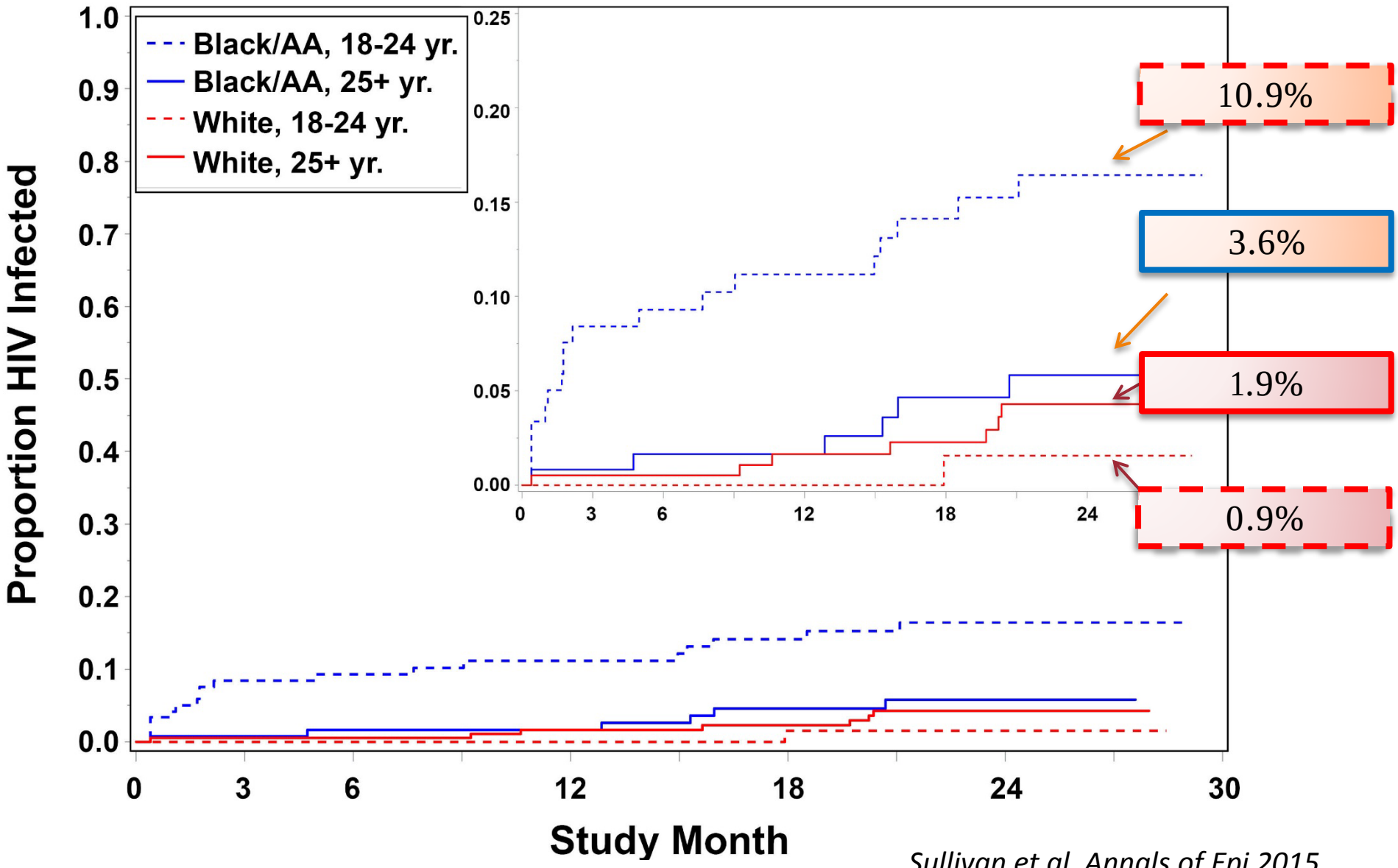
Involve[men]t Study

- Atlanta: 2010 - 2014
  - 803 MSM enrolled
  - 30% HIV-positive (BMSM: 44%, WMSM: 13%)



Sullivan et al, PLOS One 2014

MSM HIV incidence by race, age



Sullivan et al, Annals of Epi 2015

An unproductive view of the epidemiology

THURSDAY, FEB. 25, 2016 myAJC | AJC.com $2

The Atlanta Journal-Constitution
Credible. Compelling. Complete.

Partly cloudy
High: 51, Low: 37
0% chance of rain
Friday: Sunny, 52/32
Saturday: Sunny, 56/36
Sunday: Sunny, 64/39
Details on the back of Metro

Nevada win puts Trump on path to GOP nomination
Donald Trump's dominating victory in the Nevada caucuses pushes him further ahead of his nearest competitors, giving his candidacy a major boost heading into Super Tuesday contests next week, A4

NATION & WORLD
Ryan: GOP has votes to stop Gitmo plan
The House speaker said Republicans are taking legal steps to stop the closing of the U.S. prison, A2

» Health care: A report finds fault with the efforts to combat fraud involving the president's health care law, A3

BUSINESS
Airport, TSA to discuss long lines
Hartsfield-Jackson's threat to privatize security screenings has prompted talks with the agency, A9

» Jobs: Job growth in Georgia will slow to about 76,000 new positions in 2016, A9

METRO
House considering fireworks sale bill
The sale of fireworks would be used to help fund trauma care in Georgia, B1

» DeKalb: Raises may be on the way for police officers and firefighters, B1

SPORTS
Familiar face back for spring training
Jeff Francoeur reported for his second stint with the Braves, this time without a guaranteed job, C1

Dear Abby D3 | Peach Buzz D2
Classifieds D6 | Puzzles D3
Comics D8 | Scoreboard C5
Obituaries B6 | Television D2

©2016 AJC. VOL. 68, NO. 56
PRINTED WITH SOY INK ON RECYCLED PAPER

CDC REPORT ON HIV

1 in 2: Number of gay black men who will be diagnosed with HIV if the current rate continues.

1 in 4: HIV Rate for gay Latino men.

1 in 6: Overall average HIV rate for all gay and bisexual men who will be affected by the HIV epidemic in the U.S.

1 in 11: HIV Rate for white gay men.

LaMar Yarborough greets a friend at the 25th Annual AIDS Walk Atlanta & 5K Run in Piedmont Park last October. In 2013, black Georgians accounted for 66 percent of people living with HIV in the state, says the CDC. CONTRIBUTED BY STEVE SCHAEFER

HIV risk soars for black men

CDC: About half of all gay and bisexual black men in the U.S. will be diagnosed with AIDS.

By Jeremy Redmon
jredmon@ajc.com
and Ernie Suggs
esuggs@ajc.com

The CDC announced a stunning statistic this week: About half of all gay and bisexual black men in the U.S. will be diagnosed with the AIDS virus during their lifetime. But LaMar Yarborough wasn't surprised by the news.

Yarborough, 23, who is black and has AIDS, lives in Georgia, where HIV – the virus that causes his illness – is still raging. Abstinence-only sex education and poverty are contributing to its spread, said Yarborough, an HIV-prevention activist.

"We kind of saw this coming," said Yarborough, who was diagnosed with AIDS about five years ago after having unprotected sex with men and women. "It is not shocking."

Presented this week at a conference in Boston, the study by the U.S. Centers for Disease Control and Prevention found that one in six gay and bisexual men will be diagnosed with HIV: 1 in 2 blacks;

HIV continued on A7

"When people come in for an HIV screening, there is always something that leads up to it."
— DeWayne Ford, associate director of education and prevention services for AID Atlanta.

FULTON COUNTY
School chief finalist bows out

Criticism follows handling of charge that 3 raped Clarke student.

By Rose French
rose.french@ajc.com

The educator Fulton County chose to be its next school superintendent has withdrawn as a candidate amid criticism over how his administration handled the alleged rape of a Clarke County high school student.

Philip Lanoue, who has been school superintendent in Athens since 2009, is no longer in the running to lead Fulton, Georgia's fourth-largest school system with close to 95,000 students.

When reached by phone by The Atlanta Journal-Constitution on Wednesday, Lanoue declined to comment or say if he was withdrawing because of the fallout from the reported rape at a high school.

Fulton continued on A5

The administration of Phil Lanoue, Clarke County schools chief, has been criticized.

CAMPUS SUSPENSION
Sanctions lifted on Tech fraternity

Members had been accused of yelling racial slurs at student.

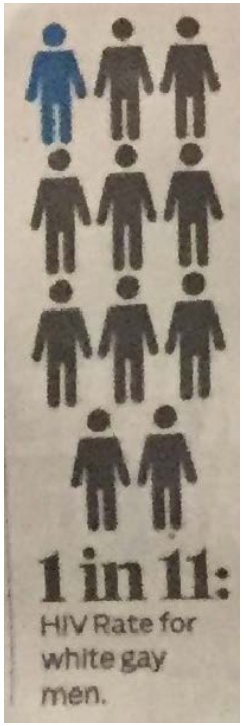
CDC "lifetime risk of HIV diagnosis" extrapolation model - CROI 2016

HIV risk soars for black men

CDC: About half of all gay and bisexual black men in the U.S. will be diagnosed with AIDS.

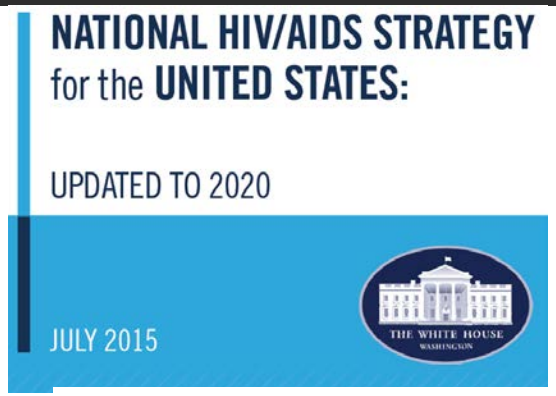
1 in 2: Number of gay black men who will be diagnosed with HIV if the current rate continues.

1 in 4: HIV Rate for gay Latino men.



1 in 11: HIV Rate for white gay men.

HIV infection in MSM, BMSM, South: National priority



GOAL 1: REDUCING NEW HIV INFECTIONS

HIV does not impact all Americans equally. While anyone can become infected, the HIV epidemic is concentrated in key populations and geographic areas. In 2010, the Strategy called for a path that followed epidemiological data. This Update continues along that path by calling for Federal agencies to ensure that funding is allocated according to the current epidemiological profile of each jurisdiction, and that cost-effective, scalable interventions are prioritized in the communities where HIV is most concentrated for the following groups:

- **Gay, bisexual, and other men who have sex with men of *all races and ethnicities***
  (noting the particularly high burden of HIV among Black gay and bisexual men)
- **Black women and men**
- **Latino men and women**
- **People who inject drugs**
- **Youth aged 13 to 24 years**
  (noting the particularly high burden of HIV among young Black gay and bisexual men)
- **People in the Southern United States**
- **Transgender women**
  (noting the particularly high burden of HIV among Black transgender women)

Evaluating a causal model for the MSM HIV racial disparity in Atlanta

Meta-analysis: differences between B and W MSM

Individual

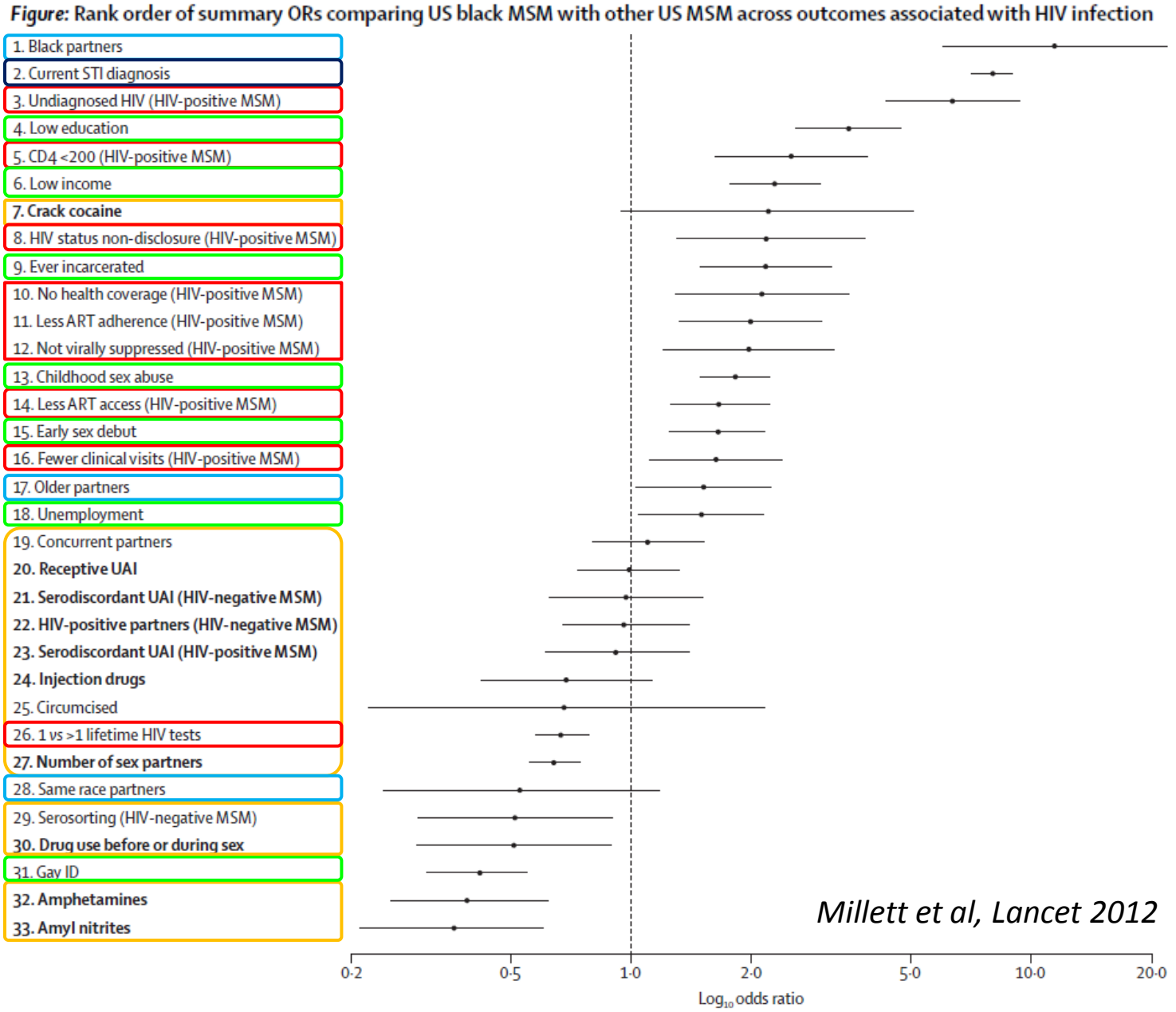
Partner demo.

Inadequate suppression of HIV+

Partner pool/network

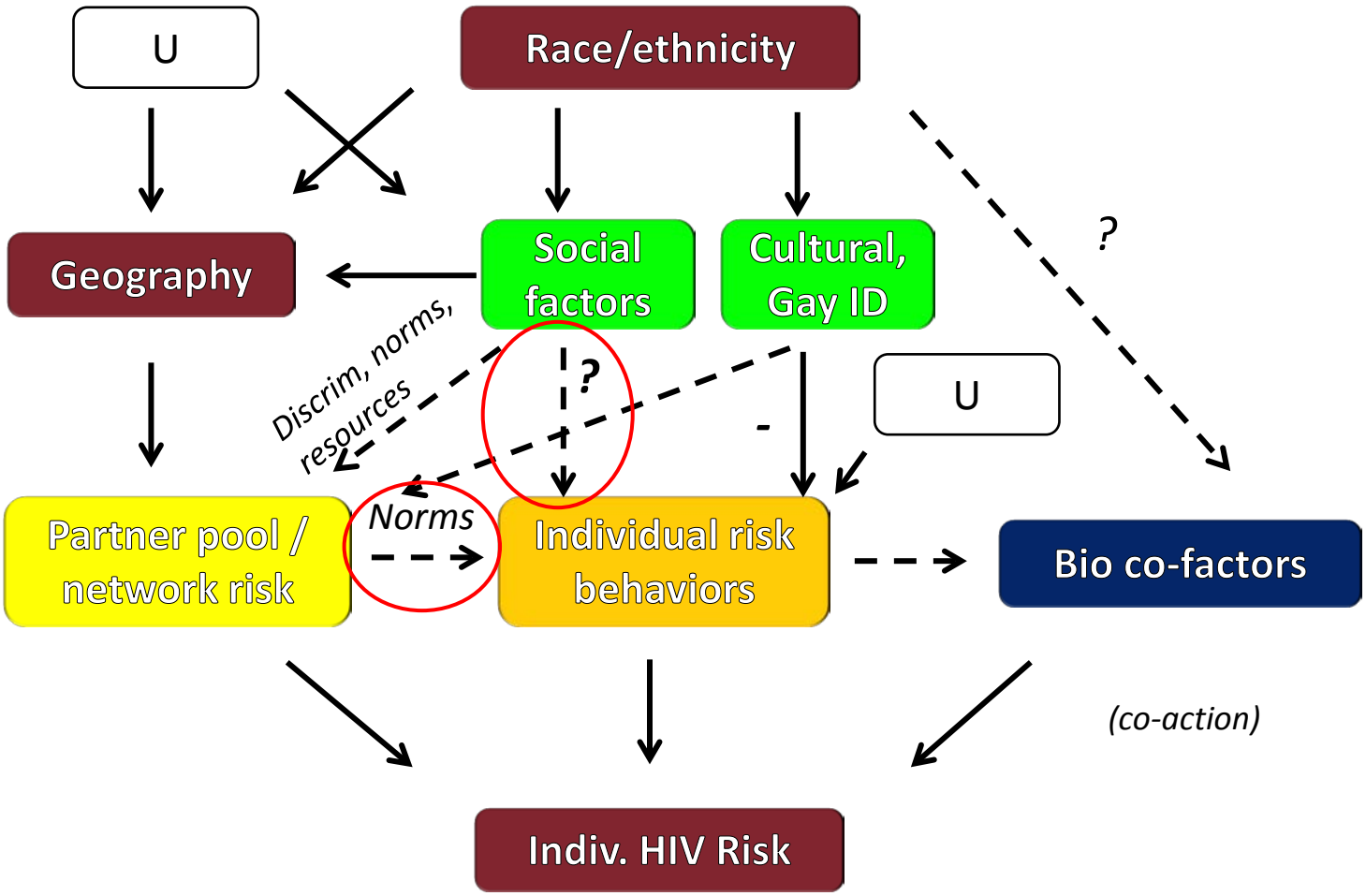
Social / cultural

Bio co-factors

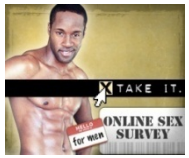


Millett et al, Lancet 2012

Empirical findings suggest causal diagram for MSM racial HIV disparities

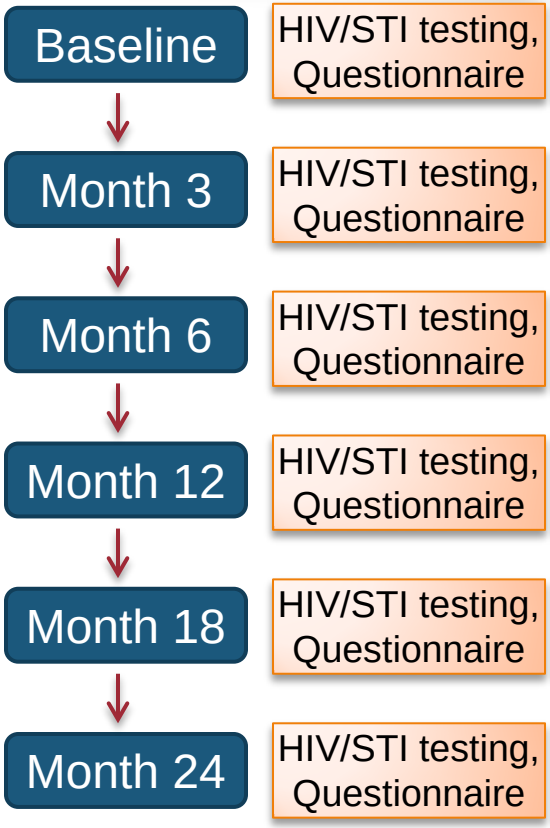


Research program on MSM HIV disparities

	Fund period	Mech.	Design
 **BOPR:** Barriers to Online Prevention Research	2009	CFAR micro	Online cross-sectional: recruitment and retention methods feasibility
CHECKING IN. THE SEX STUDY FOR MEN	2009 – 2012	RC1 NIMHD	Online cohort: retention methods and at-home HIV incidence; *sex-behaviors*
involve[men]t	2009 – 2014	R01 NIMH	HIV/STI incidence cohort (Atlanta)
The MAN Project The Men's Atlanta Networks Project	2010 – 2013	R01 NICHD	HIV/STI, cross-sectional networks design (Atlanta)
SIBANYE HEALTH PROJECT	2011 – 2015	R01 NIAID	Combination prevention package pilot trial (South Africa)
MARDHAM: Modeling Analyses for Racial Disparities in HIV in American MSM	2013 – 2015	R21 NICHD	Agent-based network modeling (Atlanta)
ele[men]t	2014 – 2019	R01 NIDA	HIV/STI incidence cohort (Atlanta)
EMORY CAMP	2014 – 2019	CDC CoAG	Numerous modeling studies to address HIV/STI transmission & prevention
engage[men]t	2015 – 2019	R01 NIAID	HIV care engagement cohort (Atlanta)

Study Design

- Prospective HIV/STI incidence cohort study: 2010-2014
  - Sexually active black and white MSM in Atlanta
  - Ages 18 - 39
- Recruitment
  - MSM community venues, Facebook
- Procedures
  - Testing: HIV, Chlamydia, Gonorrhea, Syphilis
  - Behavioral questionnaire
- Enrollment
  - 803 men enrolled
  - 30% HIV-positive (BMSM: 44%, WMSM: 13%)
  - 562 HIV-negative MSM observed for 24 months
  - 79% retained in study at 24-months



A unique study for Atlanta and US

- The only study of its kind
  - Two-group comparison of black and white MSM to understand disparities
  - Sharp geographic focus and large enrollment
  - Detailed data on multiple levels:
    - Individual features and behaviors
    - Sexual partnerships
    - Neighborhoods

- Complements but distinct from recently completed HPTN-061 (BROTHERS Study)
  - Also documented high HIV incidence among BMSM
  - Involve[men]t enrolled WMSM as well, and larger Atlanta sample

Meta-analysis: differences between B and W MSM

Individual

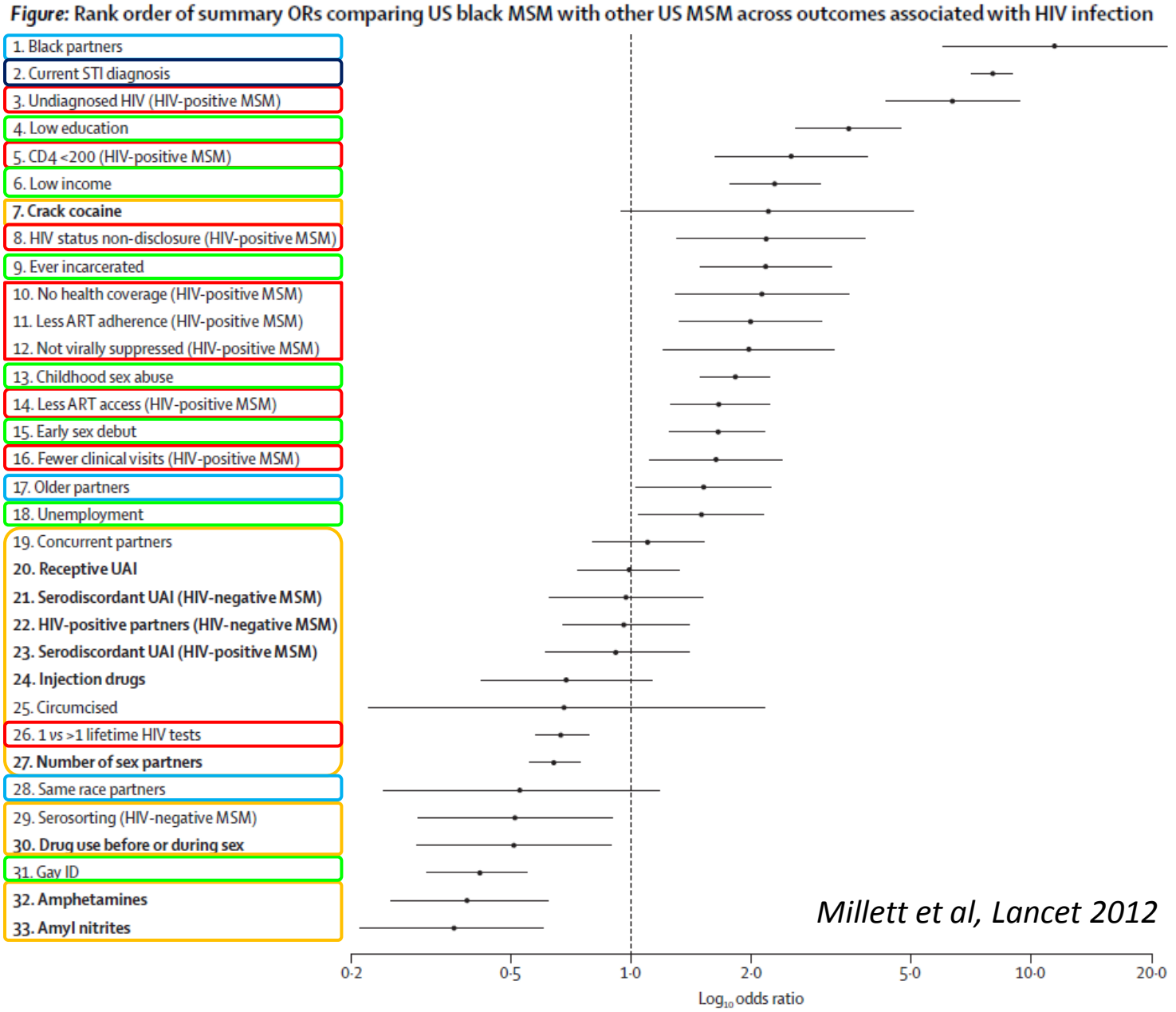
Partner demo.

Inadequate suppression of HIV+

Partner pool/network

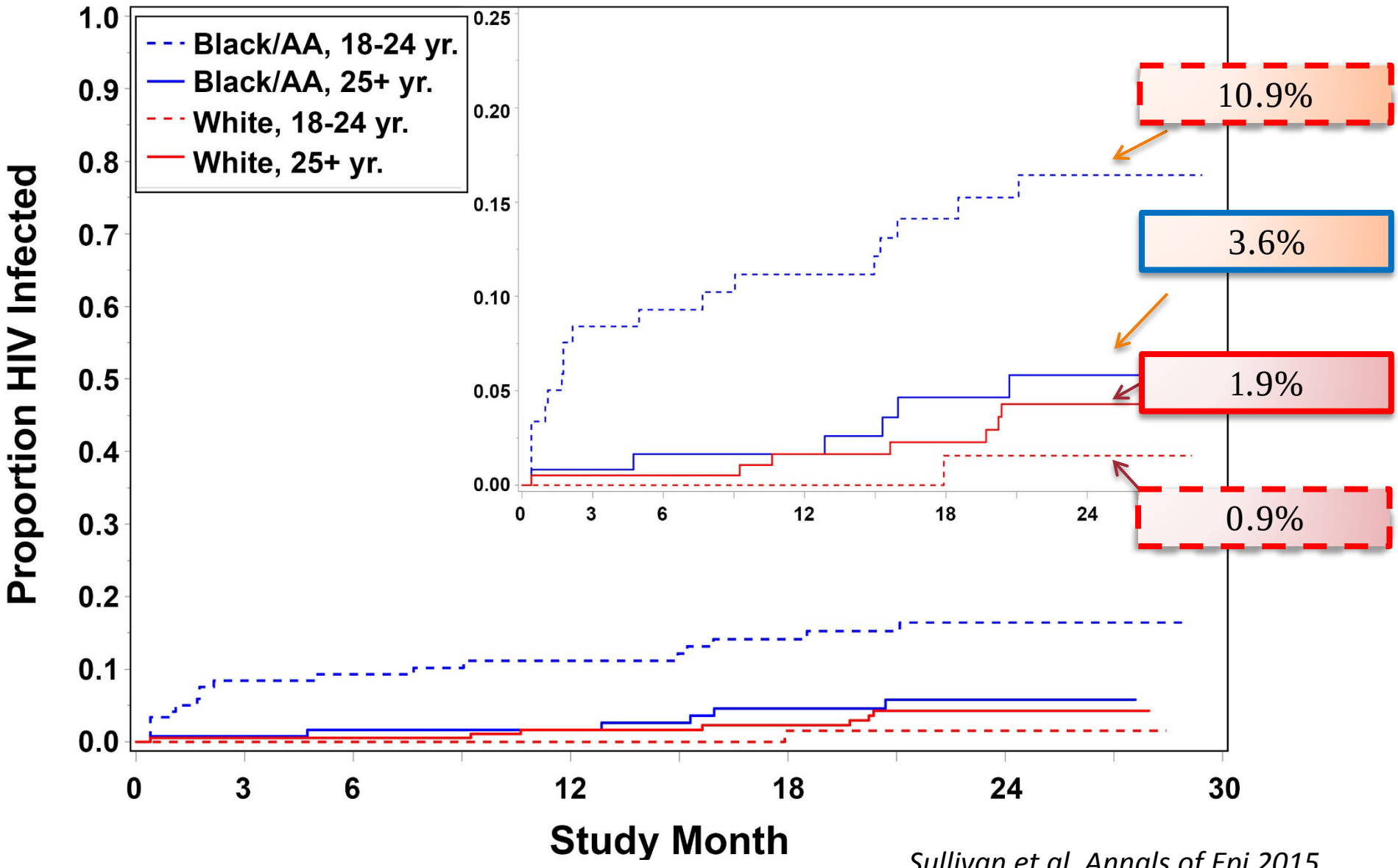
Social / cultural

Bio co-factors



Millett et al, Lancet 2012

MSM HIV incidence by race, age



Sullivan et al, Annals of Epi 2015

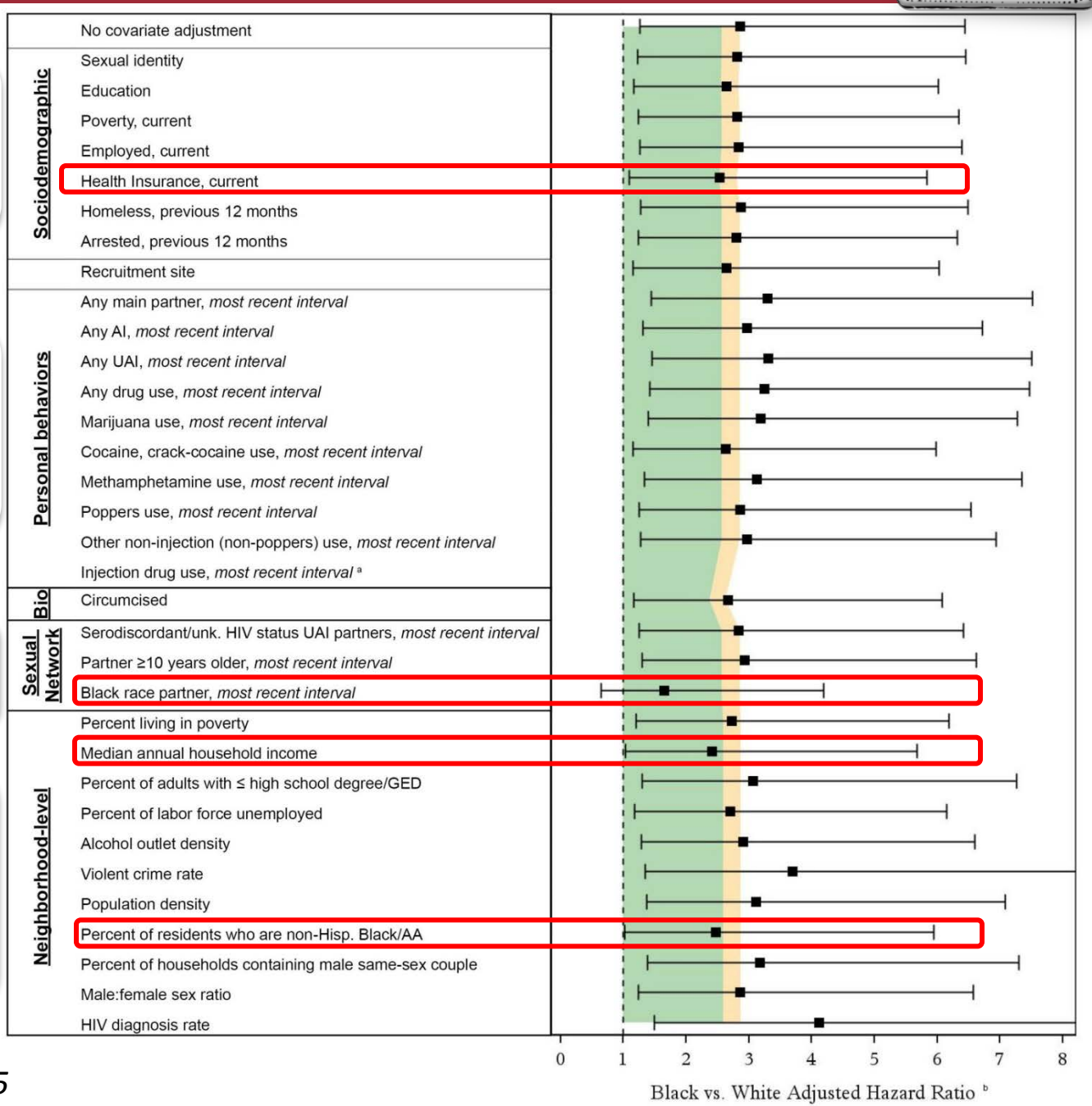
Mediation analysis to explain HIV incidence disparity

Social determinants

Individual behaviors

Partner pool / network

Neighborhood



Sullivan et al, Annals of Epi 2015

Incidence conclusions

- In Atlanta, MSM and BMSM face high-incidence epidemics of HIV
  - >1 in 10 for young, black MSM per year
- Individual behavioral risk factors associated with HIV incidence, but do not account for race disparity
- Sexual network factors and social determinants may supersede individual characteristics and behaviors as drivers of HIV disparities.
- Important to recognize the limitations – both socially and epidemiologically – of ascribing risk to network by race

Now what? Big, related questions to address

- What are the mechanisms by which partner pools confer risk?
- How do social forces shape partner pool risk?
- How do we best intervene to reduce disparities?
- (What gave rise to prevalence disparities?)

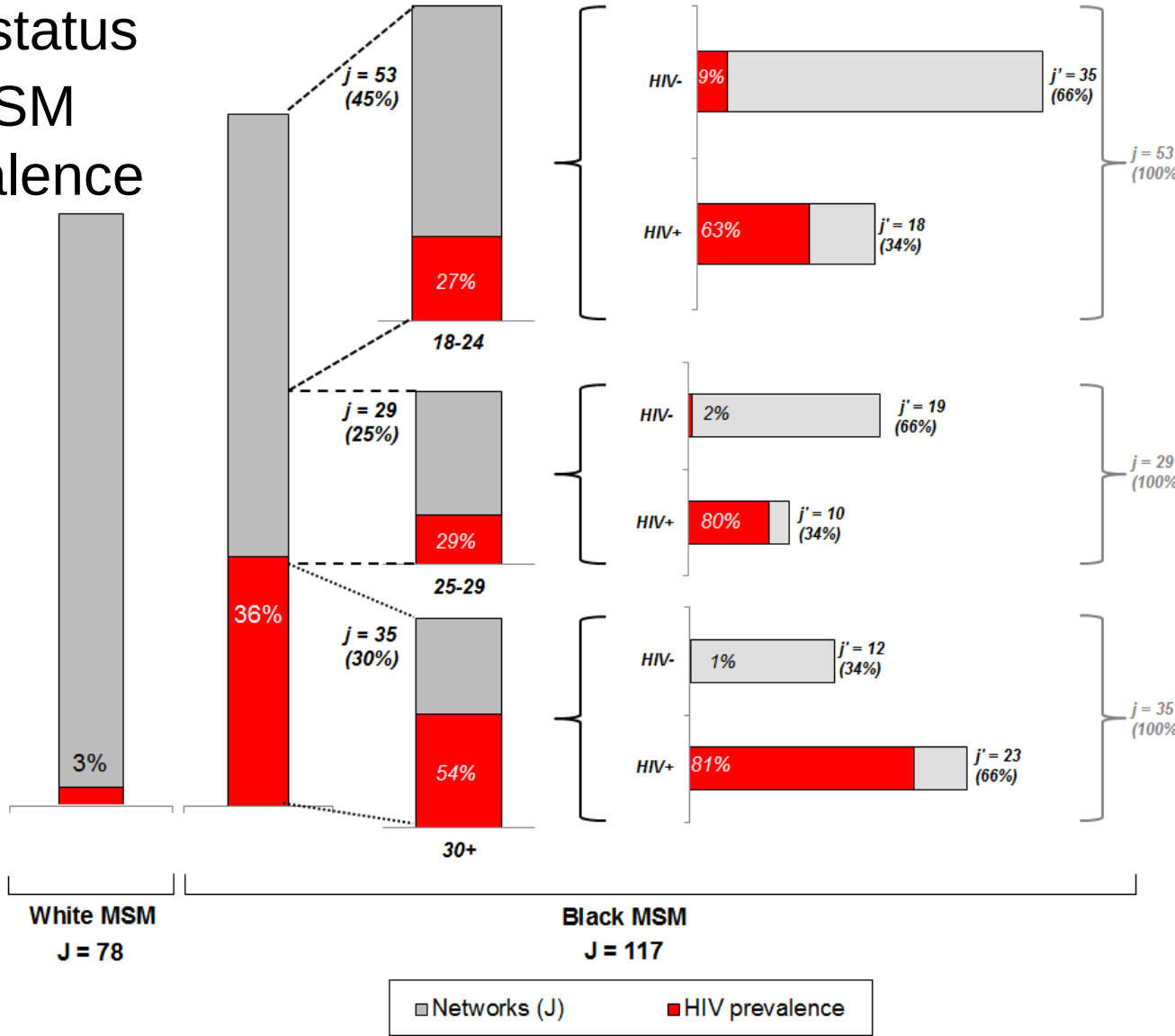
The “partner pool”: How HIV prevalence and care contribute to incidence disparities

Heterogeneity of HIV prevalence in BMSM networks

The MAN Project
The Men's Atlanta Networks Project

- Prevalence is not uniform
- Clustering by HIV status
- HIV-negative YBMSM have highest prevalence among partners

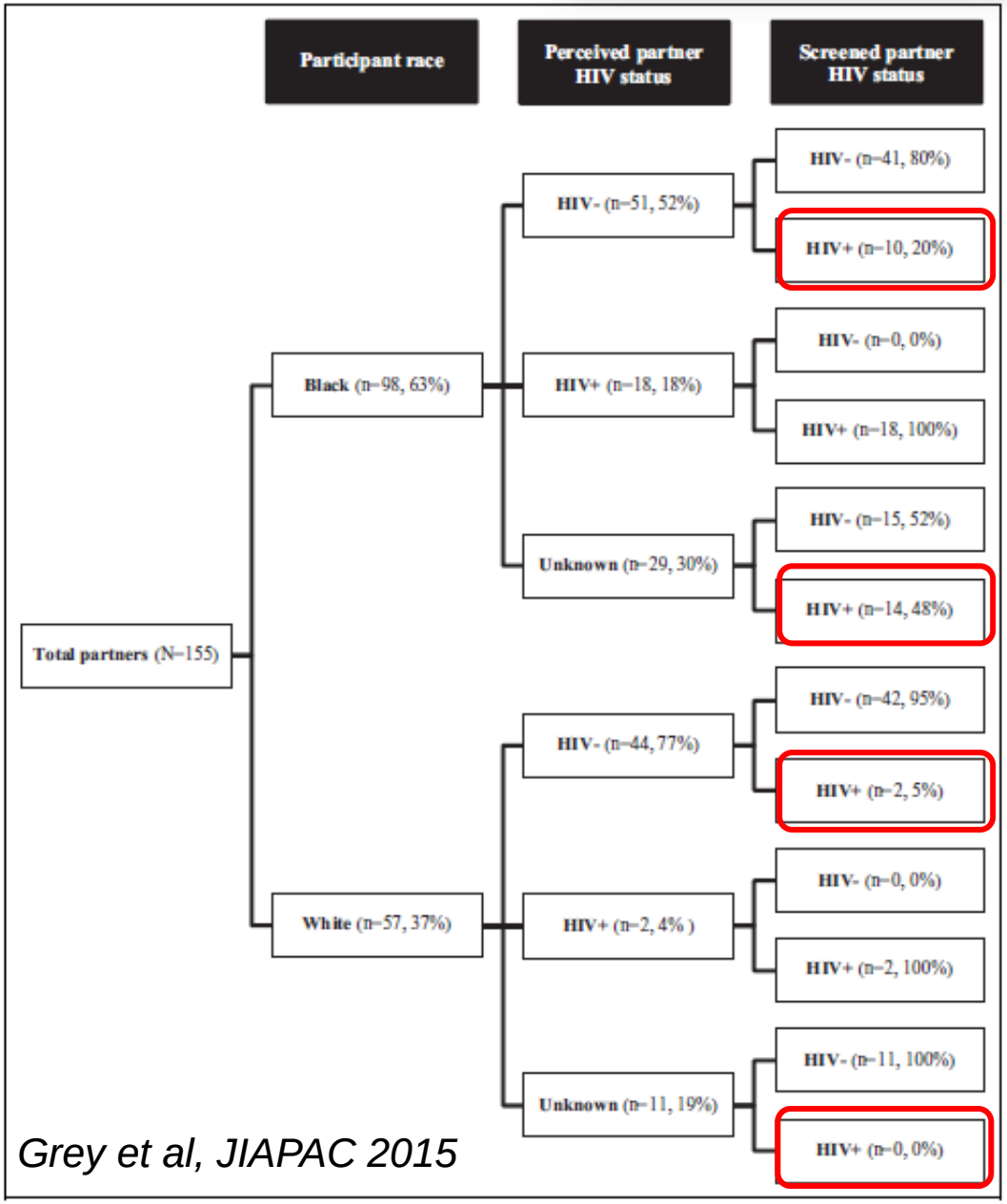
Hernandez-Romieu et al., STD 2015



Higher chance of HIV serosorting failure among BMSM

The MAN Project
The Men's Atlanta Networks Project

- HIV serosorting
  - Deviation from random HIV status mixing
    - HIV+ with HIV+
    - HIV- with HIV-
  - In theory a conscious selection process
  - Protective?
- BMSM more likely to inadvertently have HIV-positive partners
  - ↑ prevalence
  - ↓ infection awareness
  - ↓ pre-sexual discussion of HIV status



Grey et al, JIAPAC 2015

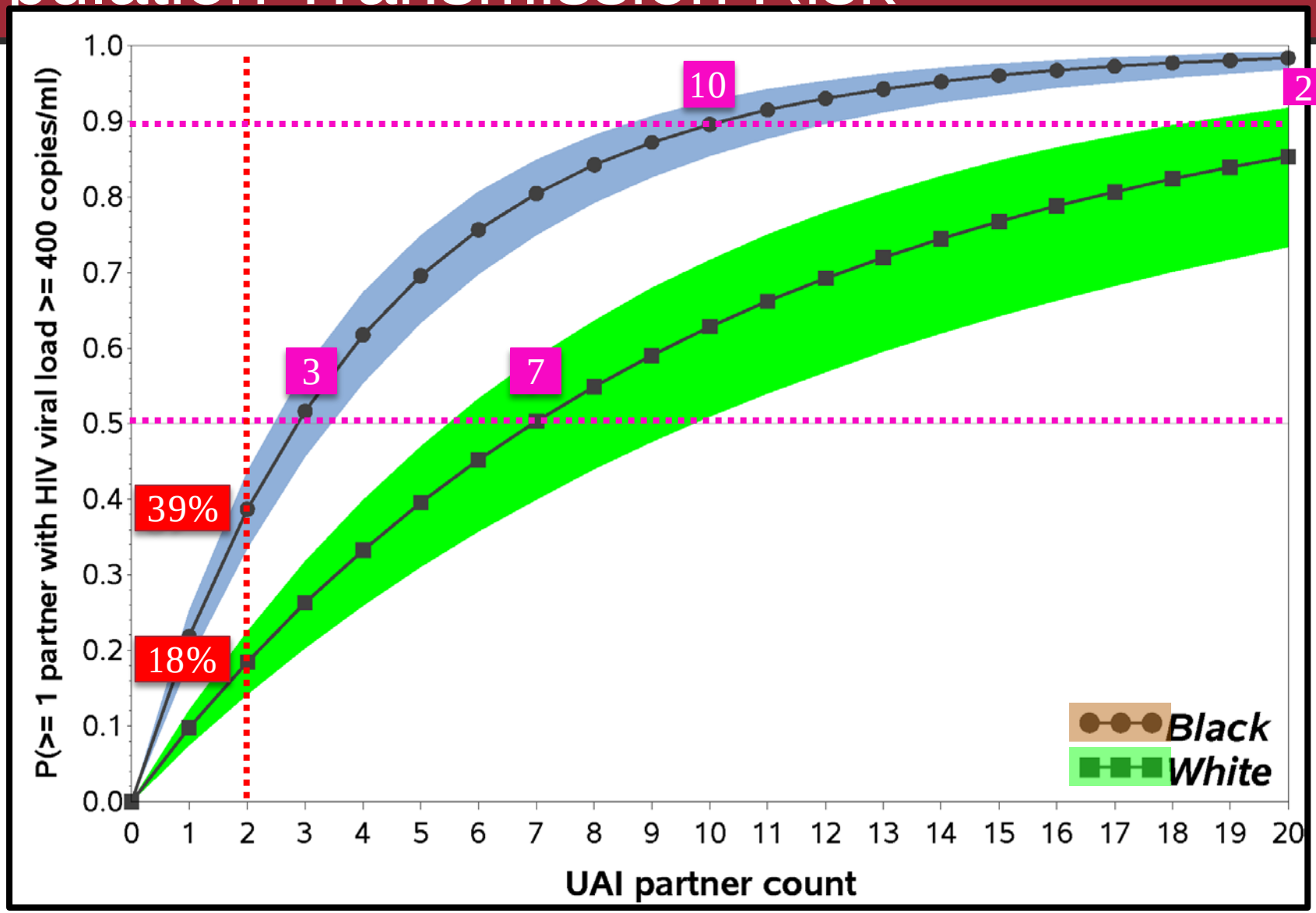
Population Transmission Risk

- HIV prevalence is insufficient *Kelley et al, Plos One 2012*
  - Differences in proportion of partners with unsuppressed virus are what matter for disparate HIV risk

- 'Community viral load' does not capture disparities in HIV exposure between groups because does not incorporate HIV prevalence.
  - No difference in CVL or PVL between black and white MSM

- Synthesized data on disparities in HIV prevalence, viral load with racial-patterns in sexual partnering
  - Calculated prevalence of HIV viremia: 25% of BMSM vs. 8% of WMSM had HIV VL>400 copies/ml
  - Racially concordant partnerships: BMSM 71%; WMSM 70%

Population Transmission Risk



- At similar levels of sexual risk behavior, BMSM have higher chance of encountering an HIV-infected and unsuppressed partner
- Driven largely by differences in HIV prevalence.

Taking the role of HIV care further

- Can we apply the population transmission risk view more broadly to understand racial incidence disparities?

- HIV care continuum important framework for understanding care
  - Can view all new HIV transmissions from perspective of those living with HIV using continuum
  - Synthesized CDC surveillance reports to create care continuum for US black and white MSM
  - Static model to translate prevalent continuum → transmissions → incidence

Taking the role of HIV care further

Rosenberg et al, Lancet HIV 2014

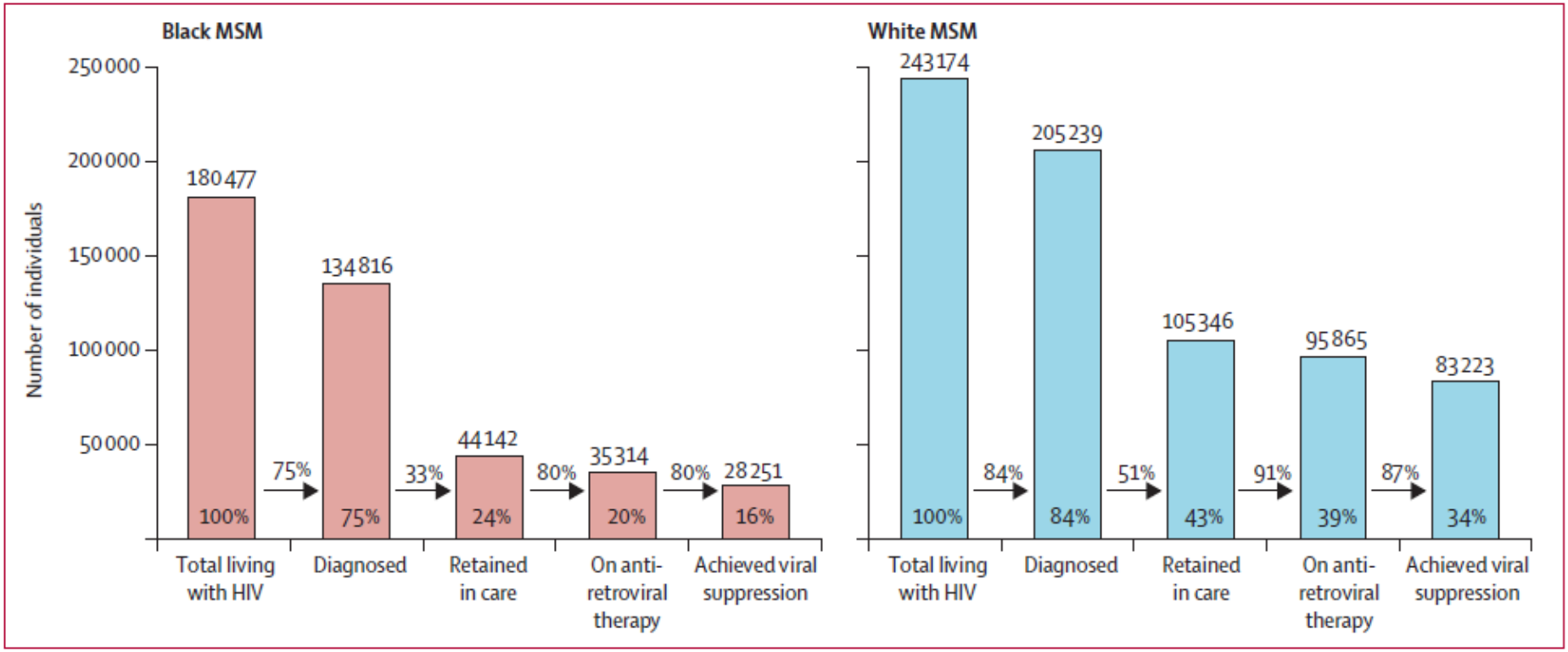
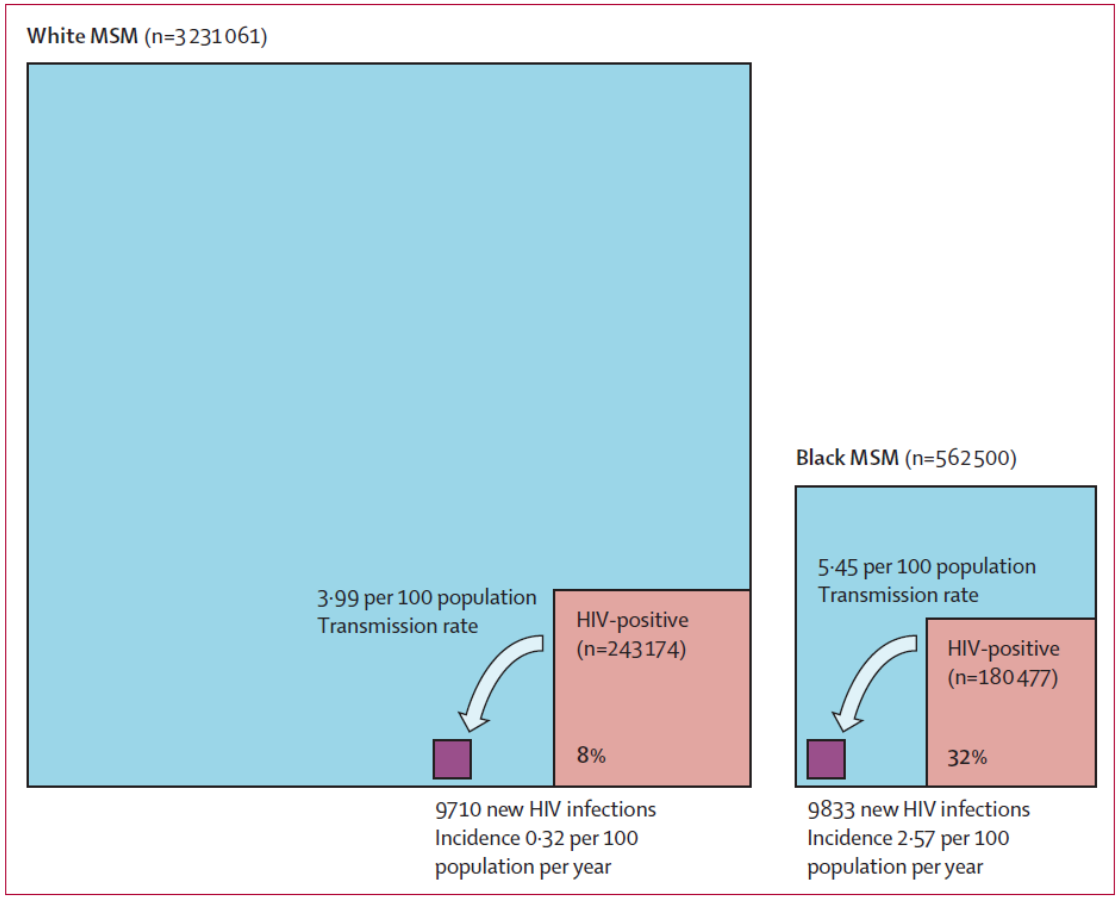


Figure 2: Estimated HIV care continuum for black and white MSM in the USA during 2009–10

9833 transmissions

9710 transmissions

Care gaps become gaps in new infections



- Imbalances in prevalence and care yield similar numbers of B & W transmissions
  - But entering communities of different sizes
  - Yields disparate rates of new infections

Care gaps become gaps in new infections

- Marked improvements in care only decrease incidence gaps by 27% in the short term
  - Equalizing BMSM and WMSM care
  - 95% diagnosis or 95% retention
- The rest is current prevalence of HIV driving tomorrow's new infections
  - Disparity will likely persist for some time, without drastic changes
- Modeling approach is intentionally simplistic… more complex results coming

Individual risk-behaviors revisited: Differential measurement of key HIV variables by race

Challenging the narrative…

- BMSM report lower or equivalent levels of risk behaviors, compared to WMSM
- In parallel, clear evidence of stigma and historical biases impacting BMSM…
- Yet misclassification often ruled out
- Studies of Involvement and MAN Project data showed racially differential validity of self-reported:
  1. Drug use
  2. Risk behaviors
  3. Awareness of HIV infection
  4. Main/casual partner typology

- Need more validity studies and understanding of the 'why'

Biological cofactors

STI and HIV Incidence

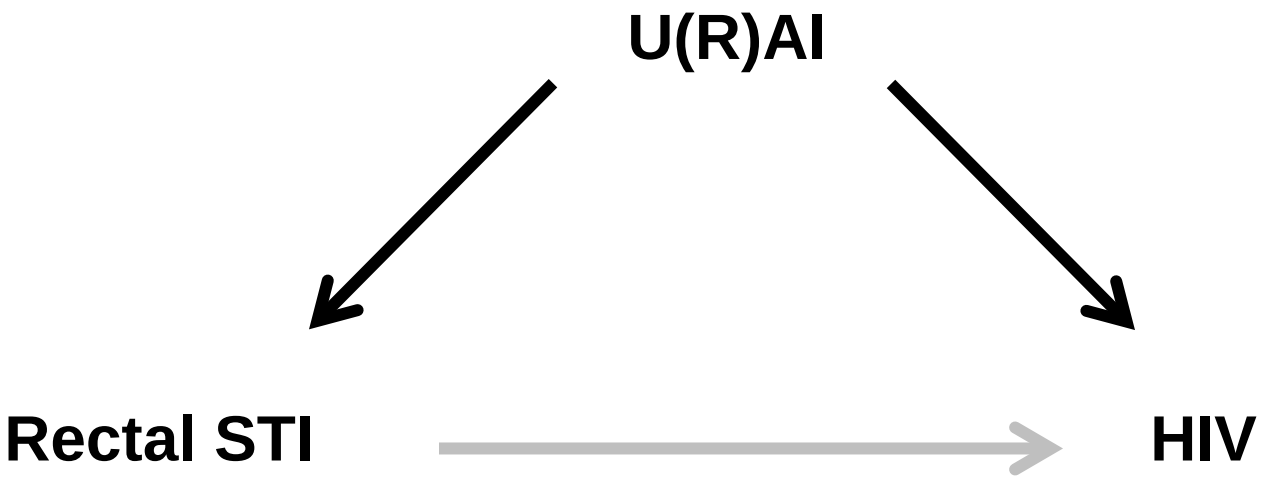
Kelley et al ARHR 2015, Vaughan et al BMC Res Meth. 2015

	BMSM		WMSM		B v. W Rate Ratio
	Infections	Rate (% / year)	Infections	Rate (% / year)	
Urethral Chlamydia	17	4.7	14	3.0	1.6
Urethral Gonorrhea	8	2.2	1	0.2	10.3
Rectal Chlamydia	34	10.8	22	5.5	2.0
Rectal Gonorrhea	30	9.4	15	3.7	2.6
Syphilis	22	6.1	0	0.0	$+\infty$
HIV	24	6.5	8	1.7	3.8

What explains parallel disparities?

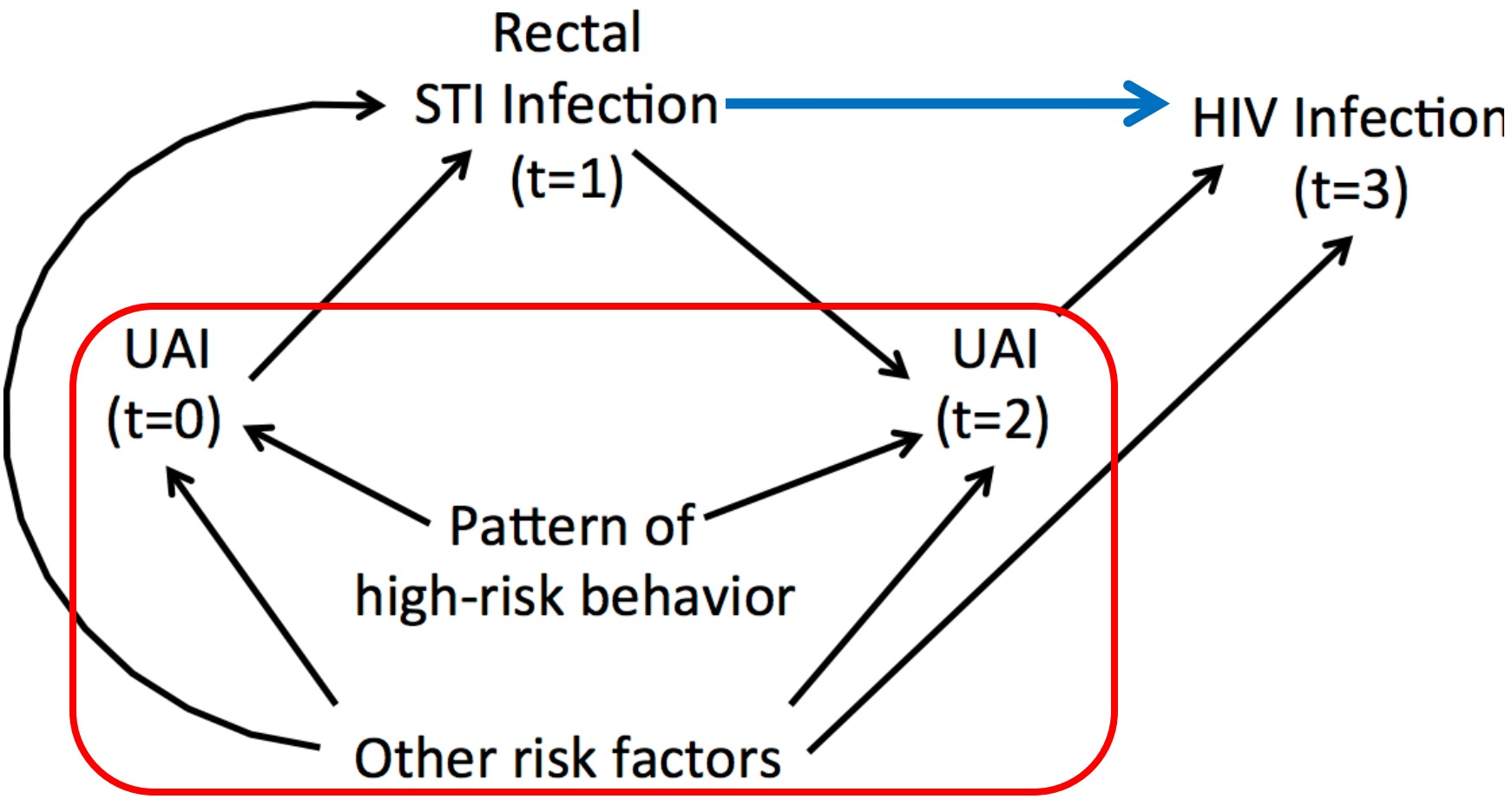
- Association?
  - Common social disparities
  - Common network features
- Causal?
  - STI -> HIV
  - HIV -> STI
- Combination of the above?

Behavioral confounding of the STI->HIV relationship



- Unprotected, receptive AI is a common cause to STI and HIV, indicating confounding
- Want to determine if causal pathway exists

More realistic DAG for STI->HIV



To isolate the causal effect of STI on HIV, need to 'control' for these pathways where people with risk behaviors are predisposed to both

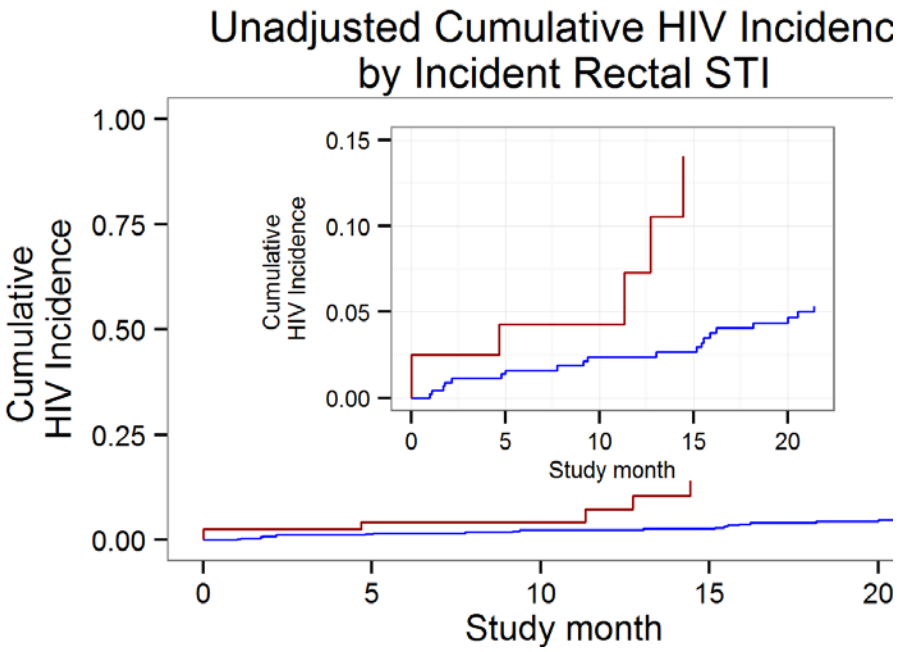
Undoing the confounding is tricky

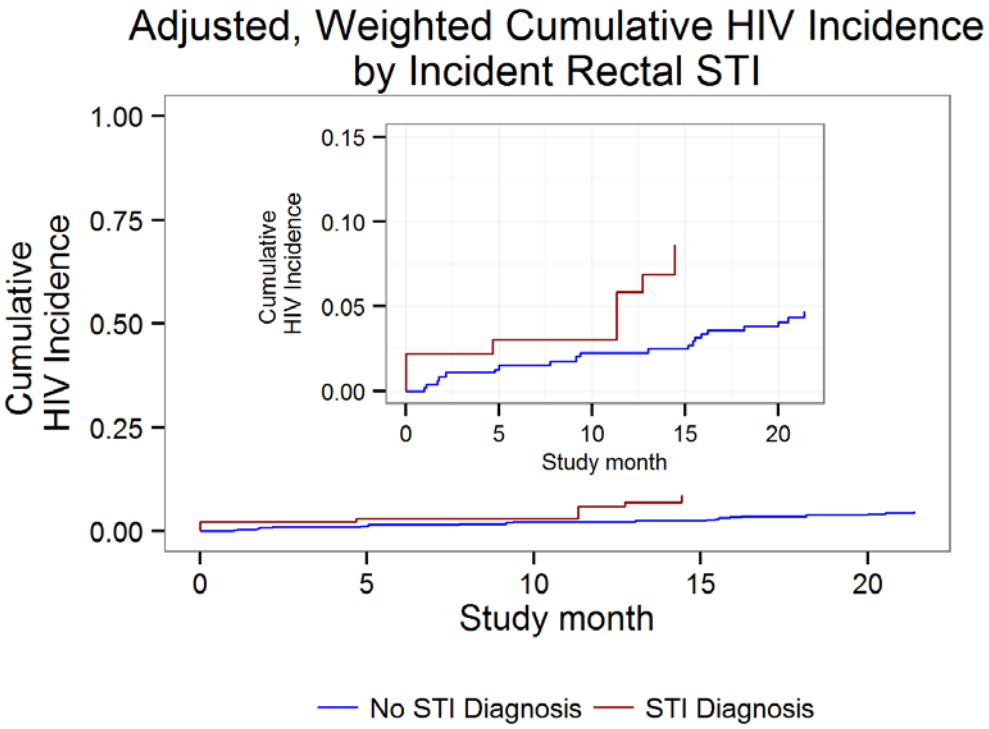
- Ideal is RCT. Not happening for MSM.

- Challenges to typical regression approaches
  - HIV outcome is rare
  - STI exposure is uncommon, but more than HIV
  - Confounding often time-varying

- Propensity-score weighted regression (*MSM for MSM*)
  - Adjust for multiple confounders, even though few outcomes
  - Adjust for time-varying confounders
  - Correctly specified, it approximates an RCT with observational data by balancing measured covariates across the exposure groups

STI -> HIV analysis results





Unadjusted HR: 3.7 (1.4, 9.4)

Adjusted, weighted HR: 2.8 (1.2, 6.4)

- Estimates 'causal' effect of rectal STI on HIV incidence
- Thus, adjustment for behavioral confounders attenuates the association by 24%

Rectal STI -> HIV conclusion

- Population attributable fraction: 14.6% (6.8, 31.4)
  - Despite significant ‘causal’ HR, rectal STI modestly contributes to HIV incidence in the population.
  - PAF driven by both HR and STI incidence

- Limitations
  - Can only adjust for known confounders
  - No STI data of HIV-positive partners (ie: transmissibility issues…)
  - No network dynamics
  - Lack of power to detect associations between specific STIs, multiple infections with a single STI, or multiple infections with multiple STIs

Genetic susceptibility?

- CCR5Δ32 homozygote confers 100% non-susceptibility
  - Almost exclusively white, non-Hispanic genotype
- Hardly discussed: what about CCR5Δ32 heterozygote?
  - HPTN VPS (Marmor et al, JAIDS 2001):

TABLE 1. *CCR5 genotypes by race among participants in the HIV Network for Prevention Trials Vaccine Preparedness Study*

	CCR5-Δ32/32		CCR5-+/Δ32		CCR5-+/+		
Race	*n*	(%)	*n*	(%)	*n*	(%)	Total
White, not Hispanic	39	(2.1)	335	(17.6)	1527	(80.3)	1901
Black, not Hispanic	0	(0.0)	21	(3.4)	601	(96.6)	622
Hispanic	1	(0.3)	18	(5.0)	342	(94.7)	361
Other	0	(0.0)	12	(10.8)	99	(89.2)	111
Total	40	(1.3)	386	(12.9)	2569	(85.7)	2995[a]

  - HIV adj. HR for heterozygote vs. WT = 0.30!
- Population-level effects of 20% WMSM vs. 3% of BMSM with >= partial immunity?

A model to put it all together

MARDHAM Project (PI: Goodreau, UW)

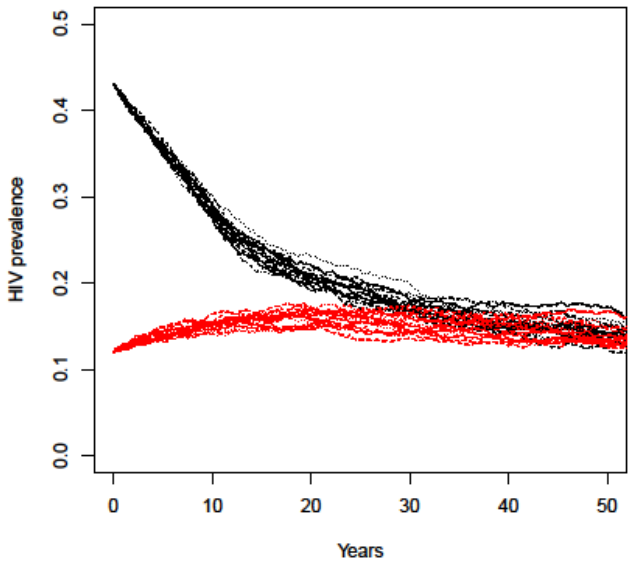
- Modeling Approaches to Racial Disparities in HIV among Atlanta MSM
- Agent-based model of MSM in Atlanta
- Comprehensive examination of possible sources of disparity:
  - Network structure
  - Behaviors within relationships
  - HIV care continuum
  - CCR5d32

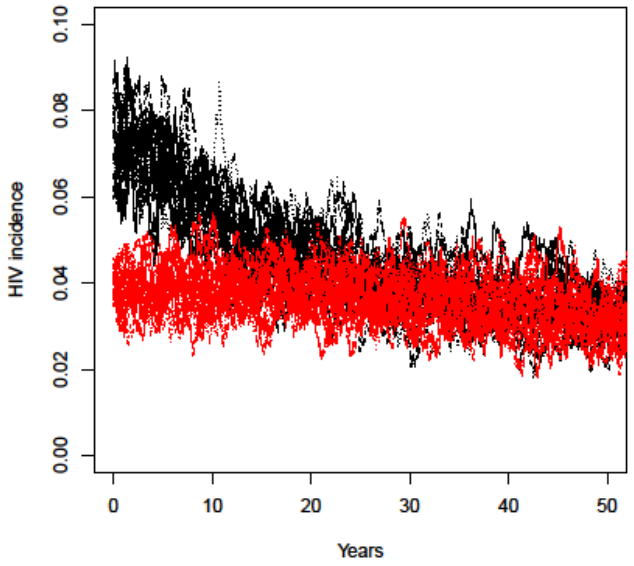
- Platform for >5 large downstream studies

MARDHAM Results (Part 0)

- How long can a pre-existing disparity persist given two groups that are now the same in all ways but have strong assortative mixing?
  - What does “partner prevalence” explain in and of itself?
  - (playing forward earlier model results)

- Disparity begins to narrow immediately. Converges within 20 years



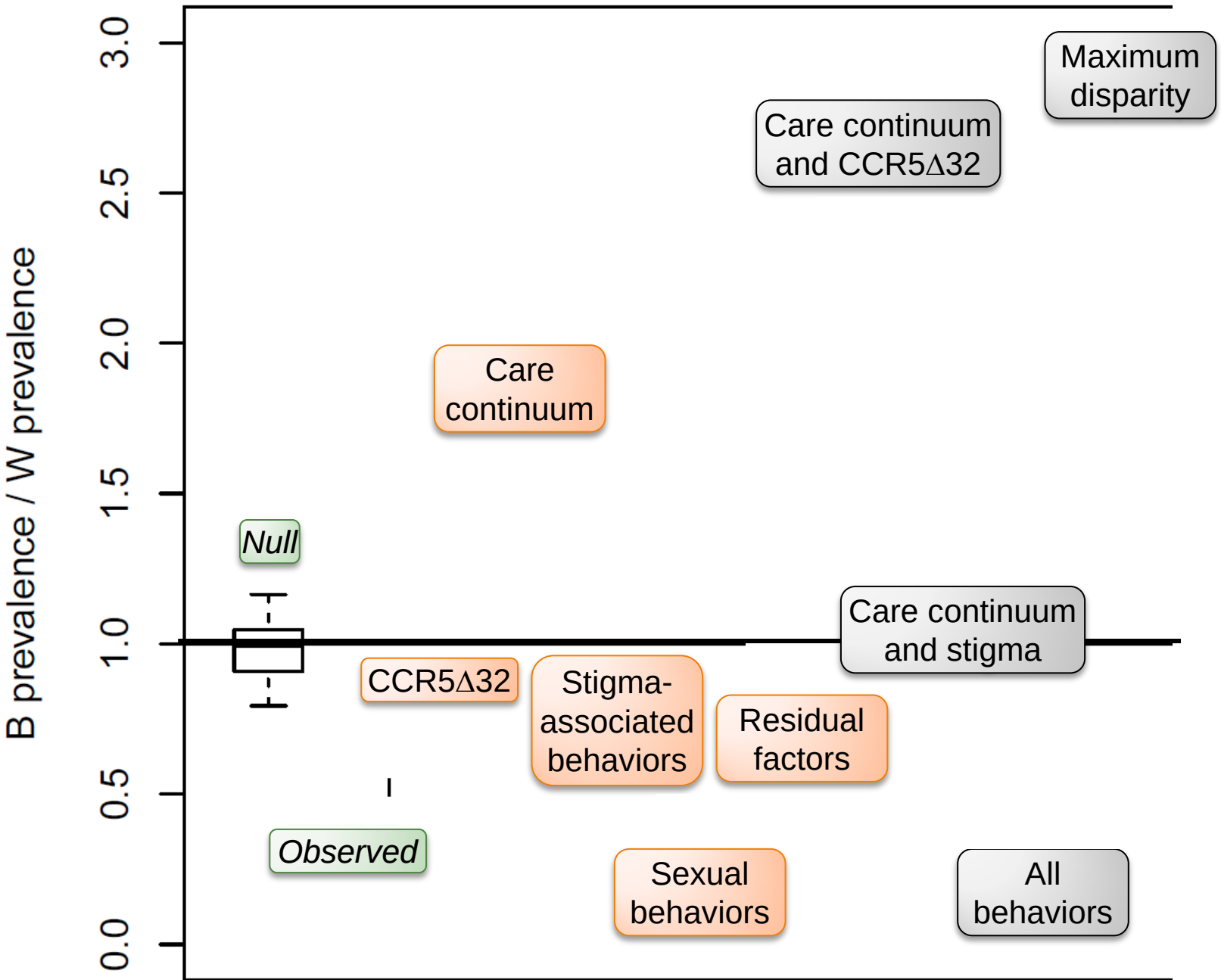


MARDHAM: Model scenarios

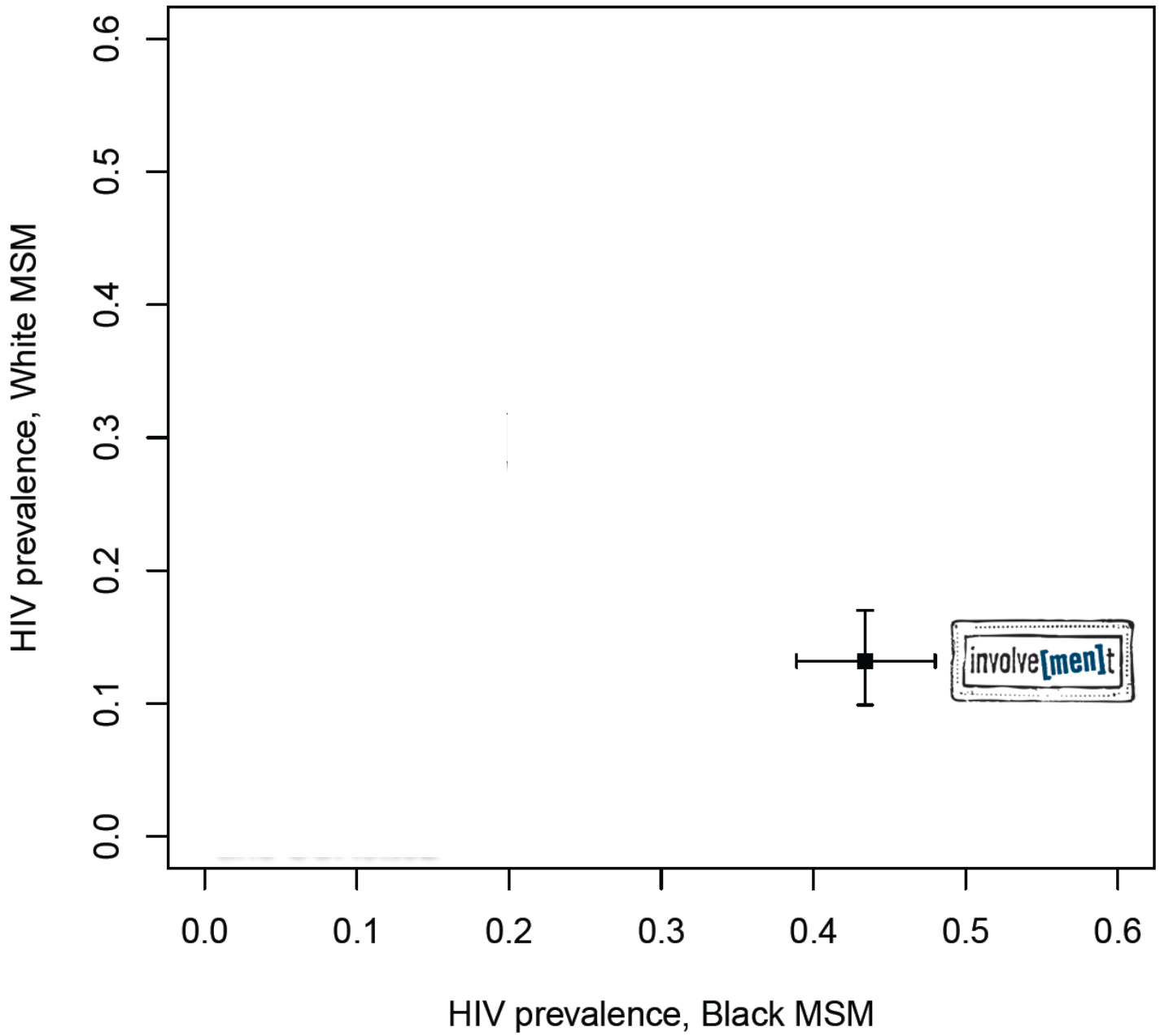
- All factors parameterized as race-specific
- Five mutually-exclusive factors groups
- Scenarios from factor groups to isolate sources of disparity

		Factor group				
	Description	**HIV care continuum**	**CCR5Δ32**	**Sexual behaviors**	**Stigma-assoc. behaviors**	**Residual determinants**
	Null *(all factors set to mean)*	-	-	-	-	-
	As-observed *(all factors race-specific)*	✓	✓	✓	✓	✓
Factor groups in isolation	Care continuum	✓	-	-	-	-
	CCR5Δ32	-	✓	-	-	-
	Sexual behaviors	-	-	✓	-	-
	Stigma-associated behaviors *(relationship duration, HIV serodiscussion)*	-	-	-	✓	-
	Residual background factors *(mortality, circ. rates)*	-	-	-	-	✓
Combined factor groups	Care continuum and CCR5Δ32	✓	✓	-	-	-
	Care continuum and stigma	✓	-	-	✓	-
	All behaviors	-	-	✓	✓	-
	Maximum disparity	✓	✓	-	✓	✓
	Misclassification of risk behaviors	✓	✓	BMSM assigned WMSM values	✓	✓

MARDHAM Results: HIV Prevalence Disparity



MARDHAM Results: HIV Prevalence Estimates



How can we fix this?

How can we fix this?

1. Large improvements to HIV care needed
   - Investments and interventions for testing, treatment
   - Greater understanding, addressing of social determinants
   - Accurate measurement of US care continuum needed

2. Need to fundamentally change the equation
   - Lower prevalence: Cure
   - Lower susceptibility: PrEP, microbicides, vaccine

3. Further modeling to understanding determinants and prioritize solutions

Research program on MSM HIV disparities – *next wave*

How can we fix this?

1. Large improvements to HIV care needed
   - Investments and interventions for testing, treatment
   - Greater understanding, addressing of social determinants
   - Accurate measurement of US care continuum needed

2. Need to fundamentally change the equation
   - Lower prevalence: Cure
   - Lower susceptibility: PrEP, microbicides, vaccine

3. Further modeling to understanding determinants and prioritize solutions

	Fund period	Mech.	Design
ele[men]t	2014 – 2019	R01 NIDA	HIV/STI incidence cohort (Atlanta)
EMORY CAMP	2014 – 2019	CDC CoAG	Numerous modeling studies to address HIV/STI transmission & prevention
engage[men]t	2015 – 2019	R01 NIAID	HIV care engagement cohort (Atlanta)

1. Engage[men]t study

- Causes of differential care achievement not comprehensively understood
  - SES – poverty, insurance, housing, …
  - Location of providers and ease of transportation Healthcare perceptions
  - Health literacy
  - Colocation of services

- Mixed-methods cohort study of black and white MSM living with HIV to understand mechanisms underlying HIV care disparities

THANK YOU!

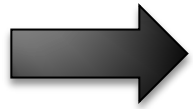
Work supported by:

- NIMH R01MH085600
- NICHD R01HD067111
- NIMHD RC1MD004370
- NICHD R21HD075662
- CDC 5U38PS004646
- CDC 12IPA1209434
- NIH P30AI050409 – the Emory Center for AIDS Research

Eli Rosenberg esrose2@emory.edu

Propensity score weighting concept

Confounder (UAI)	Exposure (STI): Yes	Exposure (STI): No
Yes	X 8	X 3
No	X 2	X 7



Confounder (UAI)	Exposure: Yes	Exposure: No
Yes	X 11	X 11
No	X 9	X 9

Weights:

Confounder (UAI)	Exposure: Yes	Exposure: No
Yes	11/8	11/3
No	9/2	9/7

Weights are the inverse probability of having the observed exposure level within strata of the confounder.