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

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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?
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Assistant Professor

Jodie Guest
Professor

Aaron Siegler
Assistant Professor

Samuel Jenness
Assistant Professor

Kristin Wall
Assistant Professor

Amazing team
• 25 staff
• 7 PhD students
• 3 postdoctoral fellows
• Many MPH students
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

- 61% MSM
- 27% Heterosexual
- 3% MSM-IDU
- 9% IDU

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

- White
  - 50+ 1,600
  - 40–49 3,400
  - 30–39 3,200
  - 13–29 6,500

- Black
  - 50+ 450
  - 40–49 1,400
  - 30–39 2,500
  - 13–29 1,000

- Hispanic
  - 50+ 300
  - 40–49 1,000
  - 30–39 2,000
  - 13–29 2,700

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

An unproductive view of the epidemiology

CDC “lifetime risk of HIV diagnosis” extrapolation model - CROI 2016

The Atlanta Journal-Constitution

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.

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

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

SPORTS
Familiar face back for spring training
Jeff Francoeur reported for his second stint with the team, this time as a non-roster player.

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.

CAMPUS SUSPENSION
Sanctions lifted on Tech fraternity
Members had been accused of yelling racial slurs at student.

1 in 4: HIV Rate for gay Latino men.

1 in 11: HIV Rate for white gay men.
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

Rank order of summary ORs comparing US black MSM with other US MSM across outcomes associated with HIV infection

1. Black partners
2. Current STI diagnosis
3. Undiagnosed HIV (HIV-positive MSM)
4. Low education
5. CD4 <200 (HIV-positive MSM)
6. Low income
7. Crack cocaine
8. HIV status non-disclosure (HIV-positive MSM)
9. Ever incarcerated
10. No health coverage (HIV-positive MSM)
11. Less ART adherence (HIV-positive MSM)
12. Not virally suppressed (HIV-positive MSM)
13. Childhood sex abuse
14. Less ART access (HIV-positive MSM)
15. Early sex debut
16. Fewer clinical visits (HIV-positive MSM)
17. Older partners
18. Unemployment
19. Concurrent partners
20. Receptive UAI
21. Serodiscordant UAI (HIV-negative MSM)
22. HIV-positive partners (HIV-negative MSM)
23. Serodiscordant UAI (HIV-positive MSM)
24. Injection drugs
25. Circumcised
26. 1 vs >1 lifetime HIV tests
27. Number of sex partners
28. Same race partners
29. Serosorting (HIV-negative MSM)
30. Drug use before or during sex
31. Gay ID
32. Amphetamines
33. Amyl nitrites

Millett et al, Lancet 2012
Empirical findings suggest causal diagram for MSM racial HIV disparities

U

Race/ethnicity

Geography

Social factors

Cultural, Gay ID

Partner pool / network risk

Norms

Individual risk behaviors

Bio co-factors

Indiv. HIV Risk

(co-action)

Discrim, norms, resources

?
<table>
<thead>
<tr>
<th>Program</th>
<th>Fund period</th>
<th>Mechanism</th>
<th>Design</th>
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<tr>
<td><strong>BOPR:</strong> Barriers to Online Prevention Research</td>
<td>2009 – 2012</td>
<td>CFAR micro</td>
<td>Online cross-sectional: recruitment and retention methods feasibility</td>
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<td><strong>CHECKING IN:</strong></td>
<td>2009 – 2014</td>
<td>RC1 NIMHD</td>
<td>Online cohort: retention methods and at-home HIV incidence; <em>sex-behaviors</em></td>
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<td><strong>involve[men]t:</strong></td>
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<td>HIV/STI incidence cohort (Atlanta)</td>
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<td><strong>The MAN Project</strong></td>
<td>2010 – 2013</td>
<td>R01 NICHD</td>
<td>HIV/STI, cross-sectional networks design (Atlanta)</td>
</tr>
<tr>
<td><strong>SIBANYE</strong></td>
<td>2011 – 2015</td>
<td>R01 NIAID</td>
<td>Combination prevention package pilot trial (South Africa)</td>
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<td><strong>MARDHAM:</strong> Modeling Analyses for Racial Disparities in HIV in American MSM</td>
<td>2013 – 2015</td>
<td>R21 NICHD</td>
<td>Agent-based network modeling (Atlanta)</td>
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<td>R01 NIAID</td>
<td>HIV care engagement cohort (Atlanta)</td>
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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

**Figure:** Rank order of summary ORs comparing US black MSM with other US MSM across outcomes associated with HIV infection

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Millett et al, Lancet 2012
MSM HIV incidence by race, age

### Social Determinants

- Sexual identity
- Education
- Poverty, current
- Employed, current
- Health insurance, current
- Homeless, previous 12 months
- Arrested, previous 12 months

### Individual Behaviors

- Any main partner, most recent interval
- Any AI, most recent interval
- Any UAI, most recent interval
- Any drug use, most recent interval
- Marijuana use, most recent interval
- Cocaine, crack-cocaine use, most recent interval
- Methamphetamine use, most recent interval
- Poppers use, most recent interval
- Other non-injection (non-poppers) use, most recent interval
- Injection drug use, most recent interval

### Partner Pool / Network

- Circumcised
- Serodiscordant/unk. HIV status UAI partners, most recent interval
- Partner ≥ 10 years older, most recent interval
- Black race partner, most recent interval
- Median annual household income

### Neighborhood

- Percent living in poverty
- Percent of adults with ≤ high school degree/GED
- Percent of labor force unemployed
- Alcohol outlet density
- Violent crime rate
- Population density
- Percent of residents who are non-Hispanic, Black/AA

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*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

- Prevalence is not uniform
- Clustering by HIV status
- HIV-negative YBMSM have highest prevalence among partners
Higher chance of HIV serosorting failure among BMSM

- **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
Population Transmission Risk

• HIV prevalence is insufficient
  ▫ 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%

Kelley et al, Plos One 2012
• 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
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*

<table>
<thead>
<tr>
<th></th>
<th>BMSM Infections</th>
<th>Rate (% / year)</th>
<th>WMSM Infections</th>
<th>Rate (% / year)</th>
<th>B v. W Rate Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethral Chlamydia</td>
<td>17</td>
<td>4.7</td>
<td>14</td>
<td>3.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Urethral Gonorrhea</td>
<td>8</td>
<td>2.2</td>
<td>1</td>
<td>0.2</td>
<td>10.3</td>
</tr>
<tr>
<td>Rectal Chlamydia</td>
<td>34</td>
<td>10.8</td>
<td>22</td>
<td>5.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Rectal Gonorrhea</td>
<td>30</td>
<td>9.4</td>
<td>15</td>
<td>3.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Syphilis</td>
<td>22</td>
<td>6.1</td>
<td>0</td>
<td>0.0</td>
<td>$+\infty$</td>
</tr>
<tr>
<td>HIV</td>
<td>24</td>
<td>6.5</td>
<td>8</td>
<td>1.7</td>
<td>3.8</td>
</tr>
</tbody>
</table>
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
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
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):
    - HIV adj. HR for heterozygote vs. WT = 0.30!

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

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

- 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

<table>
<thead>
<tr>
<th>Description</th>
<th>Factor group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>HIV care continuum</td>
</tr>
<tr>
<td>Null (all factors set to mean)</td>
<td>-</td>
</tr>
<tr>
<td>As-observed (all factors race-specific)</td>
<td>✓</td>
</tr>
<tr>
<td>Care continuum</td>
<td>✓</td>
</tr>
<tr>
<td>CCR5Δ32</td>
<td>-</td>
</tr>
<tr>
<td>Sexual behaviors</td>
<td>-</td>
</tr>
<tr>
<td>Stigma-associated behaviors (relationship duration, HIV serodiscussion)</td>
<td>-</td>
</tr>
<tr>
<td>Residual background factors (mortality, circ. rates)</td>
<td>-</td>
</tr>
<tr>
<td>Care continuum and CCR5Δ32</td>
<td>✓</td>
</tr>
<tr>
<td>Care continuum and stigma</td>
<td>✓</td>
</tr>
<tr>
<td>All behaviors</td>
<td>-</td>
</tr>
<tr>
<td>Maximum disparity</td>
<td>✓</td>
</tr>
<tr>
<td>Misclassification of risk behaviors</td>
<td>✓</td>
</tr>
</tbody>
</table>
MARDHAM Results: HIV Prevalence Disparity

- Null
- Observed
- CCR5Δ32
- Care continuum
- Stigma-associated behaviors
- Residual factors
- Sexual behaviors
- All behaviors
- Maximum disparity
- Care continuum and CCR5Δ32
- Care continuum and stigma
MARDHAM Results: HIV Prevalence Estimates

BIG SHIFT!
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?**

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1. Engagement 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

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### Propensity score weighting concept

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