

Bringing models



BRIDGING ACROSS GROUPS AND STI TRANSMISSION DYNAMICS

Locally grounded network models for HIV policy planning

Martina Morris, PhD
Departments of Statistics and Sociology
University of Washington



UW Network Modeling Group

Start by acknowledging my collaborators

Modelers

- UW Network Modeling Group
Deven Hamilton
Jeanette Birnbaum

Epidemiologists

- Joint UW/PHSKC
Sarah Glick
Roxanne Kerani

Advisory Board

- PHSKC – Amy Bennett, Susan Buskin, Katelyn Gardner Toren
- WA DOH – Jason Carr, Tom Jaenicke
- UW – Matt Golden, David Katz

Funding: NIAID R21

Outline

- Project overview: Focus on HIV bridging dynamics
- Overview of model structure and data sources
 - Demography
 - Transmission system
 - Care continuum and clinical outcomes
- Epidemic simulation results
 - Preliminary – first set of calibrated runs
- Implications for STI prevention

Project goals

- Build locally grounded projection model to support HIV policy

Models have traditionally been built at the country level

- But there is significant variation in HIV prevalence within countries
- And in the US, prevention happens at the State/Local level

- Start with the heterosexual epidemic in King County

Why?

- Small, but potential for eradication
- First step towards a more comprehensive model
- It's a challenge...

Why is it a challenge? (1)

DATA

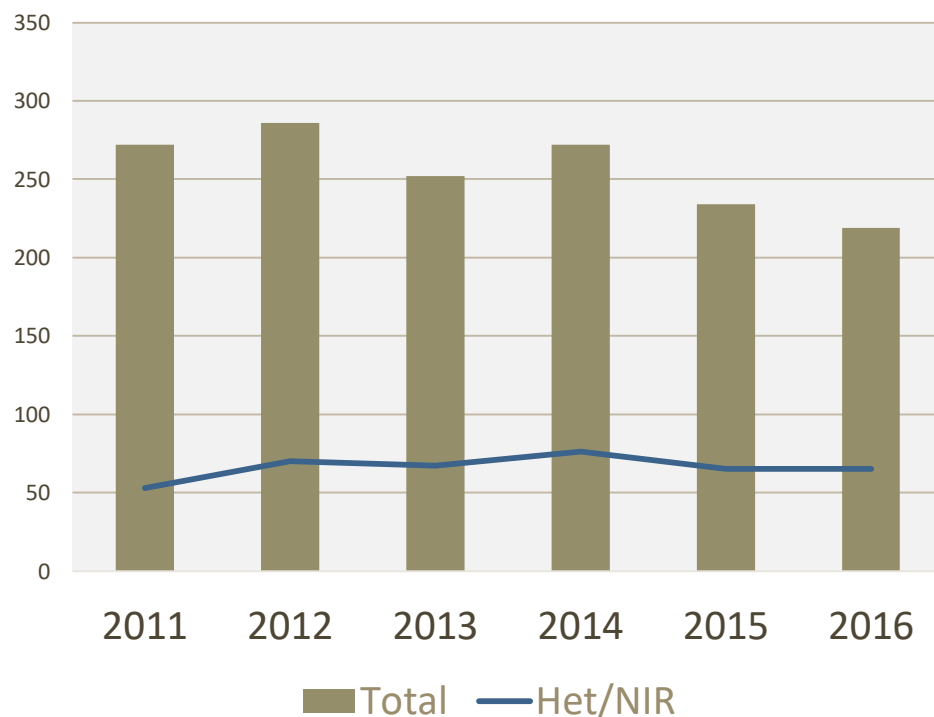
The empirical data we need are measured with significant uncertainty

- Not just the sexual behavior data
- But also the surveillance data on HIV diagnoses

Heterosexual cases of HIV

Measured with uncertainty

HIV Diagnoses in King County:
2011-2016



In King County

- **6-7%** of incidence is attributed to heterosexual contact
- Another **15-20%** is “No Identified Risk”
- Total range: **6-27%**

Why is it a challenge? (2)

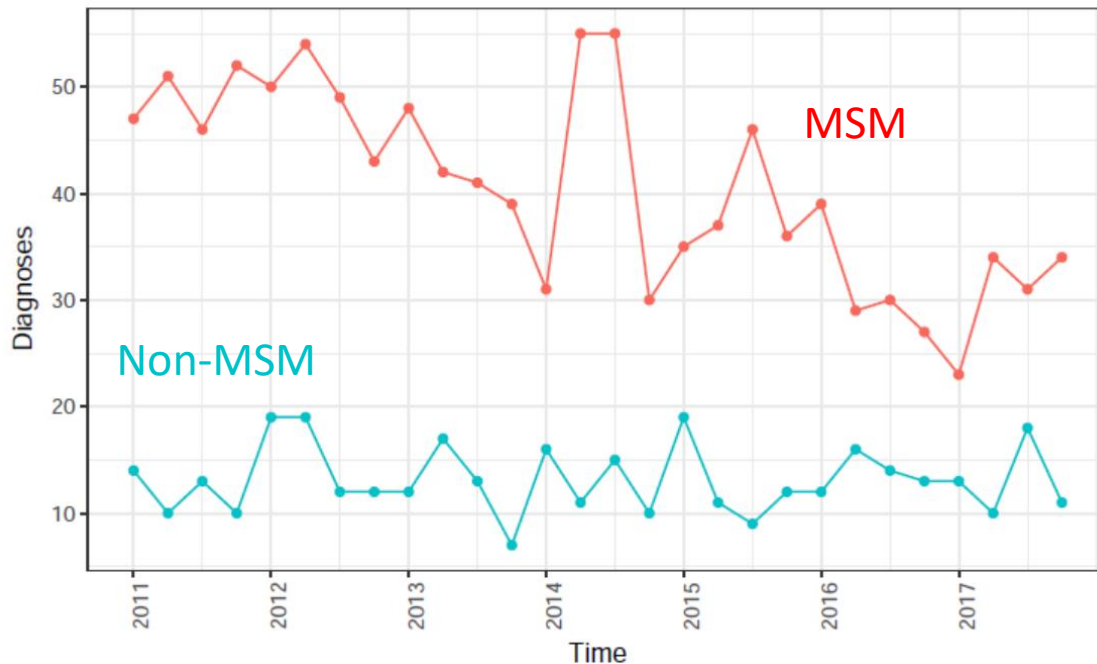
MODELS

- Modeling Het HIV in isolation
 - Do *not* generate persistent epidemics for the US
- Two primary reasons
 - Transmission within the Het population is below the epidemic threshold
 - Bridging dynamics with other risk groups must be represented

Key bridging dynamics for Seattle (1)

■ Large MSM epidemic

HIV diagnoses in King County: 2011-2017



- Majority of our epidemic is MSM
- Good progress in “bending the curve”
- But uptick in 2017 is a concern

MSM – Heterosexual bridging

- Several papers have shown evidence that there is substantial bridging across subpopulations
 - Based on phylogenetic clustering of HIV sequence data
- In the US: Oster et al. (2015)

“Of heterosexual women for whom we identified potential transmission partners,

 - 29% were linked to MSM,
 - 21% to heterosexual men
 - **a higher percentage of women in the West (52%) were linked to MSM”**

Key bridging dynamics for Seattle (2)

- Racial disparities, but with a specific local pattern

HIV Prevalence: 2016

	Estimated HIV Prevalence/100K
White	314.2
Black	1001.0
Hispanic	434.6

US Born	Foreign Born
93%	2%
56%	41%
42%	52%

We see large racial disparities

With profound differences in country of origin by race

What this suggests

- Ongoing transmission in the heterosexual population
 - could be below the reproductive threshold
 - sustained by bridging cross-boundary transmissions?
- This has implications for targeting prevention policy
 - Target the boundary to have the maximum impact
- Can be explored through simulation models

The modeling framework

Dynamic network foundation

Epidemic process spreads on the network

One slide background on modeling

Three basic types of modeling frameworks

- **Deterministic compartmental models (DCMs)**
 - The traditional approach -- most heavily used until very recently
 - Limited ability to represent partnerships
- **Stochastic Individual-based *or* Agent-based models**
 - Becoming more common
 - Limited ability to represent multiple network features
- **Stochastic Network models**
 - New – firmly grounded in statistical estimation from data
 - Able to represent the “joint distribution” of multiple network features

Network modeling for epidemics

- The result of a long research program
 - Supported by 20 years of NIH funding
- Relies on statistical methods
 - For network estimation and simulation
 - Exponential family Random Graph Models (ERGMs)
- Designed to use very simple network data
 - “Egocentric” sampled network data
 - Implemented like a traditional cross sectional sample survey

Key components of our framework

- Transmission system

- Dynamic partnership network

- Multilayer: Cohab, Persistent and one-time partnerships

- Behavior within partnerships

- Transmission

- Function of viral load/stage of infection

- Care continuum

- Testing, treatment, viral suppression

- Demography

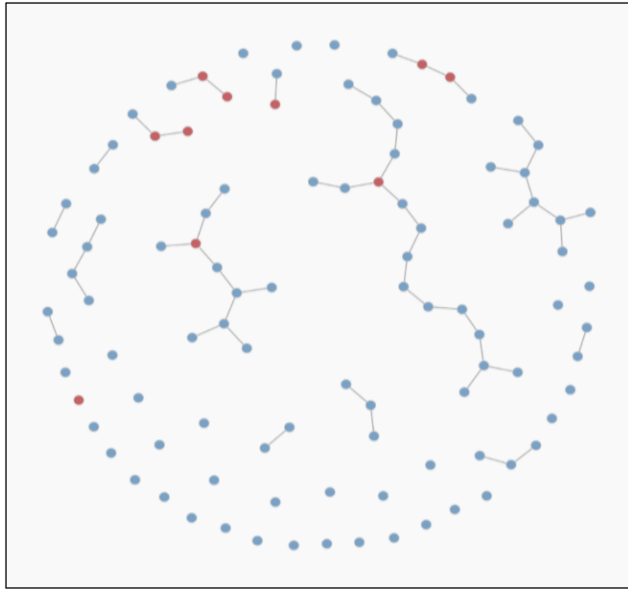
- Aging
 - Travel
 - Entry/Exit

**statnet
software**

**EpiModel
software**

All software is open
source and free

Dynamic network model(s)



Unique multi-network approach

Partnerships modeled with a separable temporal ERGM (STERGM)

- Formation model
- Dissolution model
- Estimated from egocentrically sampled data

3 different types of partnerships

- Cohabiting
- Persistent *So three different STERGMs*
- One-time

Transmission system components

Several processes are overlaid, and interact with the network

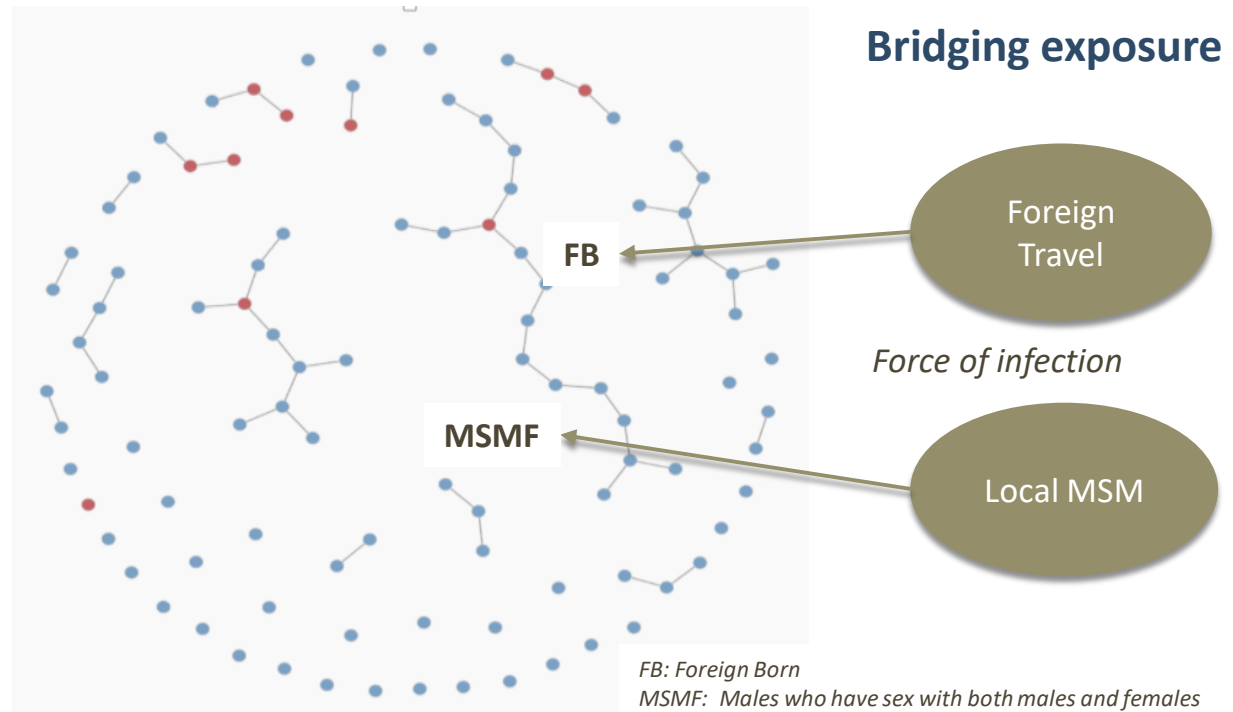
Within discordant partnerships:

Behavior

- Coital Frequency
- Condom Use

Infectivity, by

- Stage
- CC engagement
- Clinical outcome



Our population has multiple subgroups

- Race / Immigration subgroups (5)
 - US and foreign-born Black
 - US and foreign-born Hispanic
 - Other (predominantly White)
- Sex / Sexual preference subgroups (3)
 - Female (F)
 - Males who have sex with females only (MSF)
 - Males who have sex with males and females (MSMF)
- And age...

Lots of other model components

- Engagement in Care
 - HIV Testing (at sex and race-specific rates, some never test)
 - Treatment with ARVs
 - Adherence, with episodes of drop and return
 - Viral Suppression (some fraction are not full suppressors)
- Clinical progression after infection
 - 4 stages (acute rise, acute fall, chronic, AIDS)
 - Progression time: 6.4 wks, 3 wks, 10 yrs, 2 yrs
 - Stage-specific viral load (influences infectivity)
- Demography: Open population model
 - Entry at 18, exit at 45
 - Age and AIDS specific mortality rates
 - Travel for foreign born (pauses local sexual activity, activates boundary exposure)

Data sources

Locally sourced, ... when possible

Model components: **LOCAL DATA NEEDED**

Model Component	Governs:	Source
Sexual network	Partnership formation/dissolution dynamics	NSFG (18-45)
Behavior within partnerships	Coital frequency, condom use, HIV status disclosure	NSFG (18-45)
Natural history of within-host HIV infection	Viral load, CD4, symptoms and infectivity	Global Estimates
Clinical care cascade	Testing, referral, adherence, suppression	PHSKC HIV Core Surveillance
Demographics	Entries and Exits into the population (pop'n growth, mortality and in/out migration)	King County Census

National Survey of Family Growth (NSFG)

- US Data on sexual behavior & networks (2006-15)
 - Representative national sample with annual surveys
 - Age 15-45
 - Egocentric data on last 3 heterosexual partners
 - Partner attributes (age, race/immig, cohab, duration/once only, ongoing)
 - Behavior within partnerships
 - HIV testing rates

Combined sample size: ~40K

- Reweighted by age, sex, race/immigration group
 - To match King County demographics

Local data on travel back to home country: collected in public health interviews of new HIV diagnoses in KC

IMMIGRATION HX

66.

	Yes	No	Unknown	Refused	If so, where?
Were you born outside the U.S? <i>Birthplace 1</i>	<i>1</i>	<i>0</i>	<i>99</i>	<i>77</i>	<i>Birthplace - specify 1</i>

67. When did you move to the U.S?
(MM/DD/YYYY) *move us*

68. Did you ever test for HIV prior to moving to the US? *test before us*
☒ Yes. Last time: (MM/DD/YYYY) *test before us date* *0* No *99* Unknown *77* Refused

69. What was the result of that test? *test before us result*
☒ Positive *2* Negative *3* Indeterminate *99* Unknown *77* Refused

70. Have you been back to your home country/area since moving to the US?
☒ Yes *0* No *99* Unknown *77* Refused *home country return*

71. Did you have sex while back in your home area?
☒ Yes *0* No *99* Unknown *77* Refused *home country return sex*

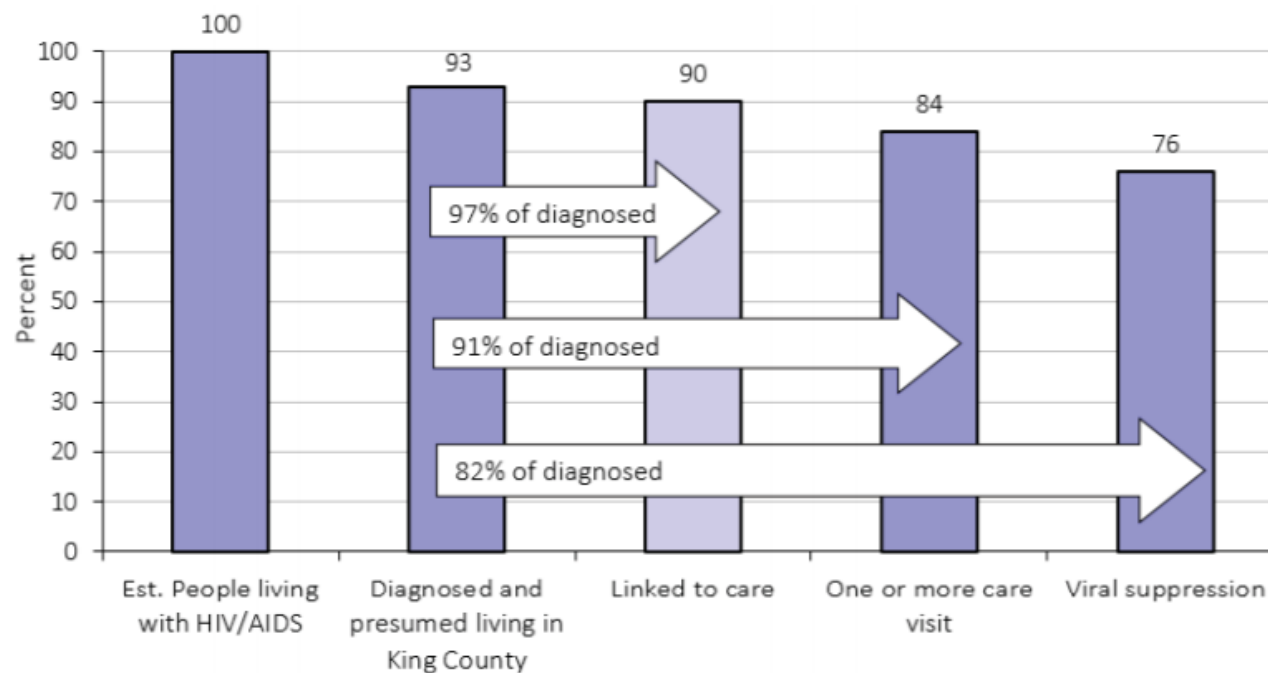
72. Have you tested HIV negative since you last had sex in your home country?
☒ Yes *0* No *99* Unknown *77* Refused *Neg Home Country sex*

73. How many people have you had sex with since moving to the US?
0 Number: *99* Unknown *77* Refused *sex partners us*
sex partners us number

Added in
2010

Local “Care Continuum” data

Figure 1: 2016 King County HIV Care Cascade (Data Reported Through June 30, 2017)



We use sex/race specific values

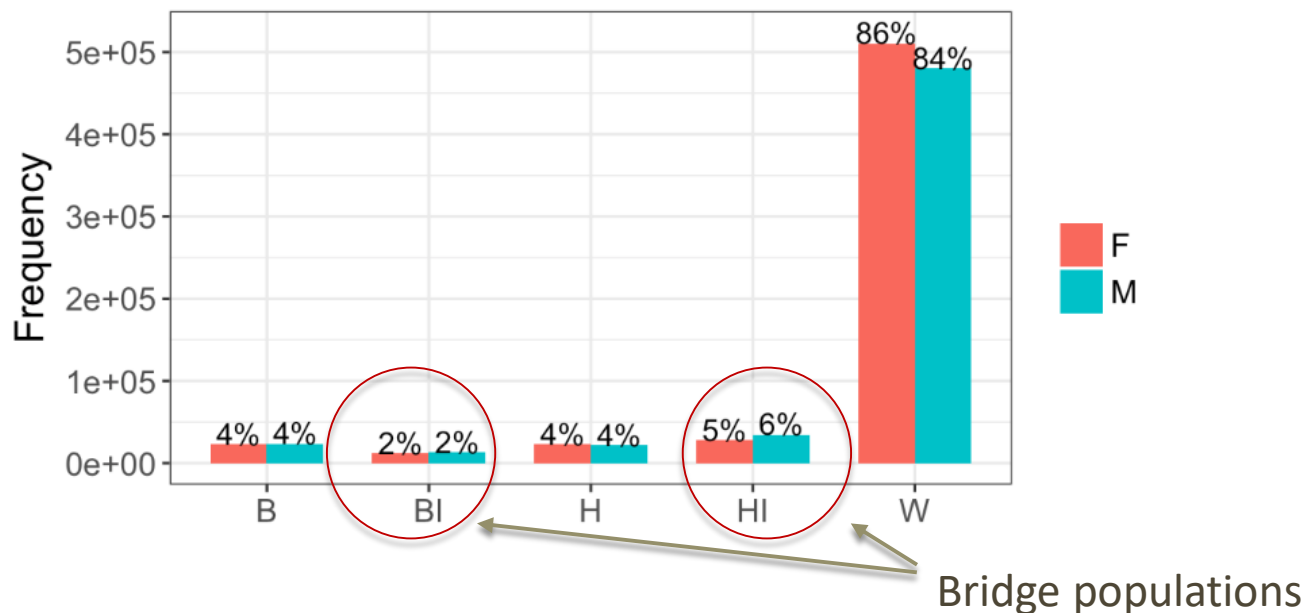
Some descriptive statistics

Population attributes

Partnerships patterns by subgroup

KC Demographics by race/imm/sex

- King County is predominantly white (68%) and Asian (18%)
- About 14% of the population is Black or Hispanic
 - About half of those are foreign born



Sexual behavior and networks

- All of these estimates are based on the NSFG survey
- Reweighted to KC demographics by
 - Age
 - Race
 - Sex

KC Sex Group estimates

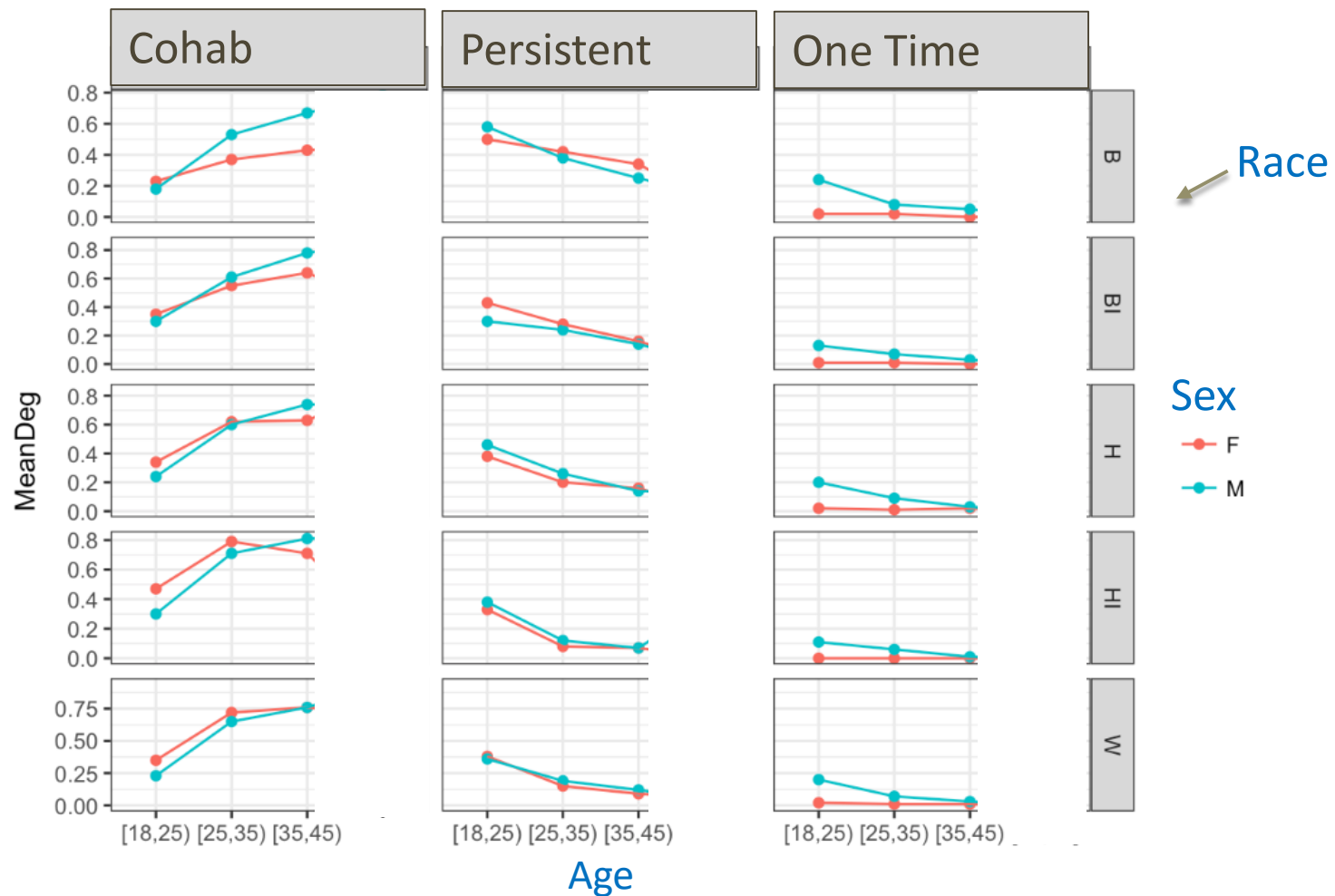
by age

About 1% of the population are MSMF



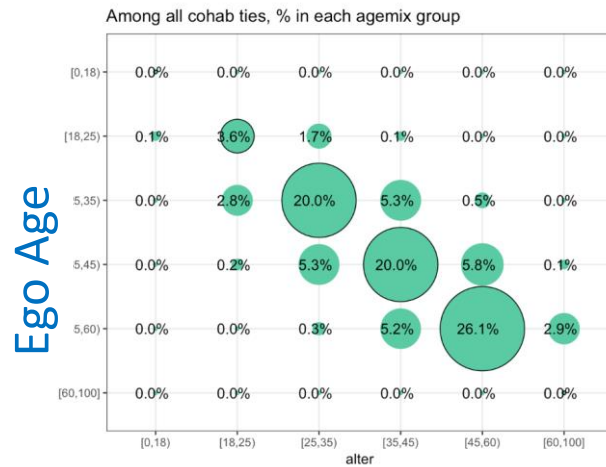
Partnership Type Prevalence

by Age, Sex, and Race

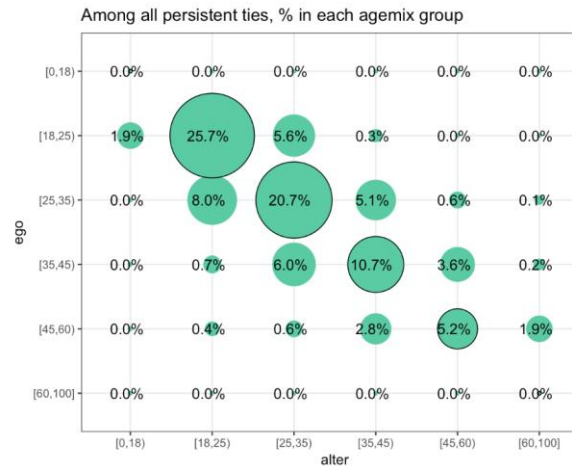


Age Mixing

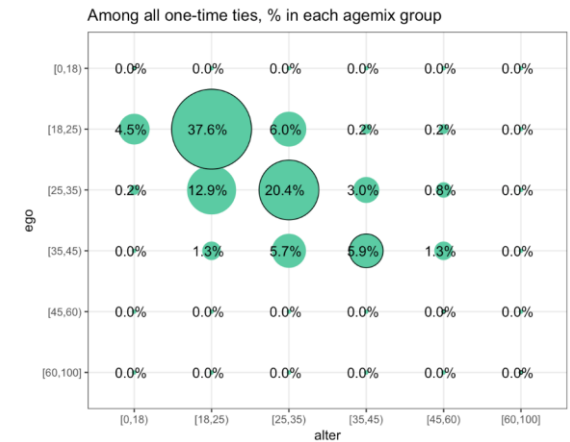
Cohabiting



Persistent



One time

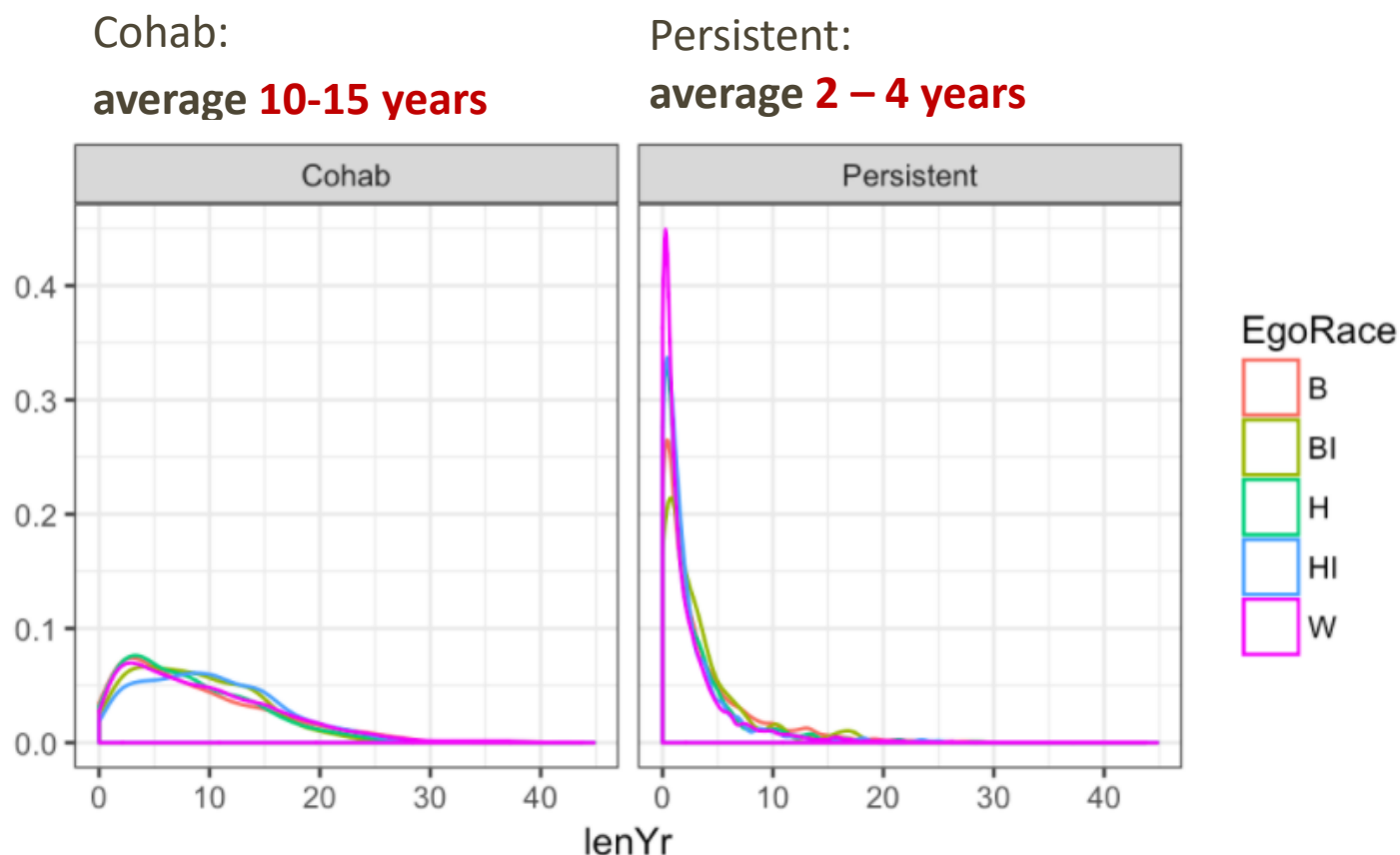


Alter Age

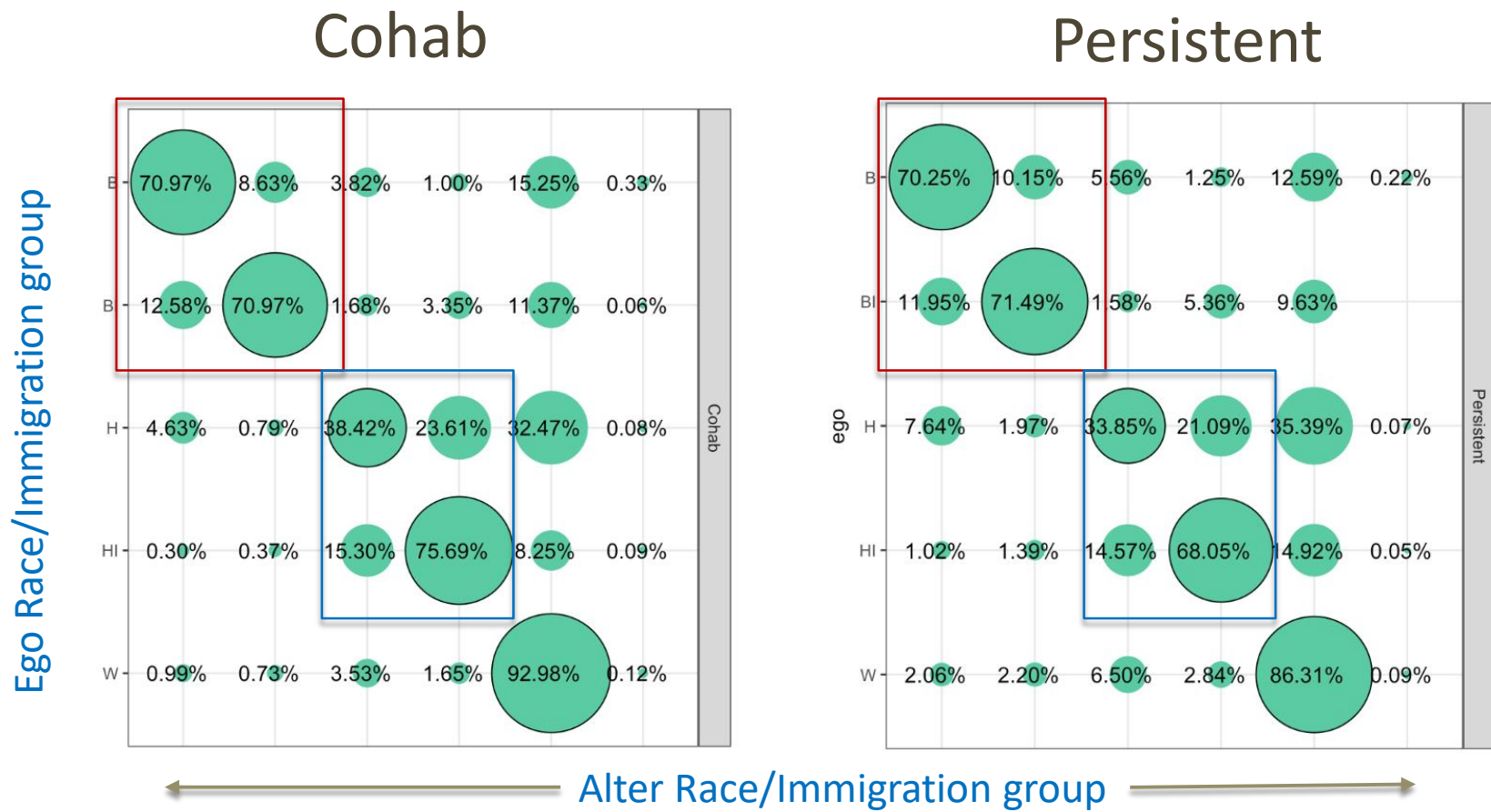
Strong age homophily for all types of partnerships

Partnership Durations: Cohab & Persistent by Race

AGE OF ACTIVE TIES



Mixing by Race/Immigration group



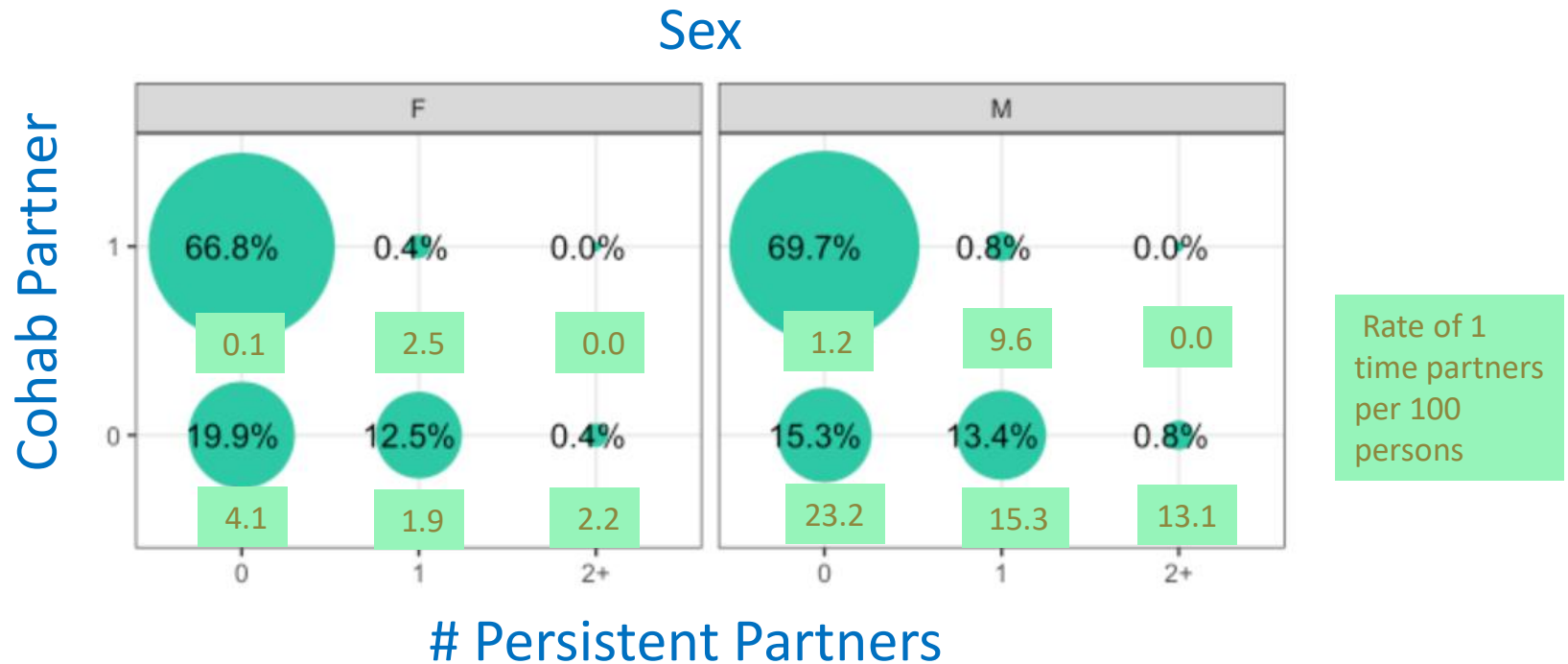
Overlapping partnerships

- Definition: When a person has more than one active sexual partnership at a time
 - Aka “concurrent partnerships”
 - Note: not the same as “multiple partners” in a specified time frame (6 mos, 12 mos, etc.)
- Has a powerful impact on network connectivity
 - Cross-sectionally: creates component sizes > 2
 - Longitudinally: increases the reachable path of infection
- And on transmission dynamics
 - Reduces the “generation interval” between transmissions
 - Supports epidemic persistence even for less active populations

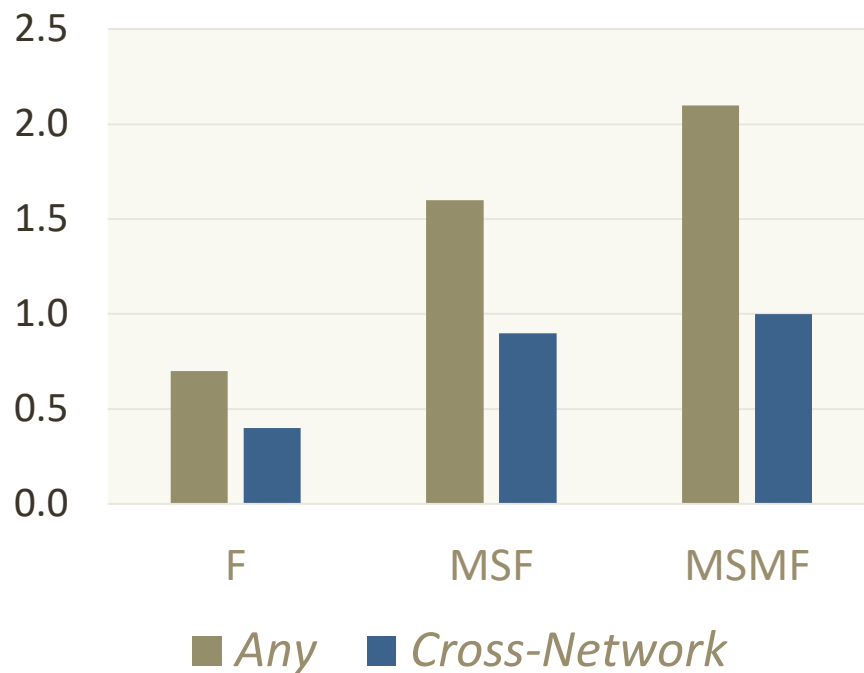
Overlapping partnership networks

On any day, a person can have none, or some of each partnership type

- About 1-2% of the population has two or more concurrent partners

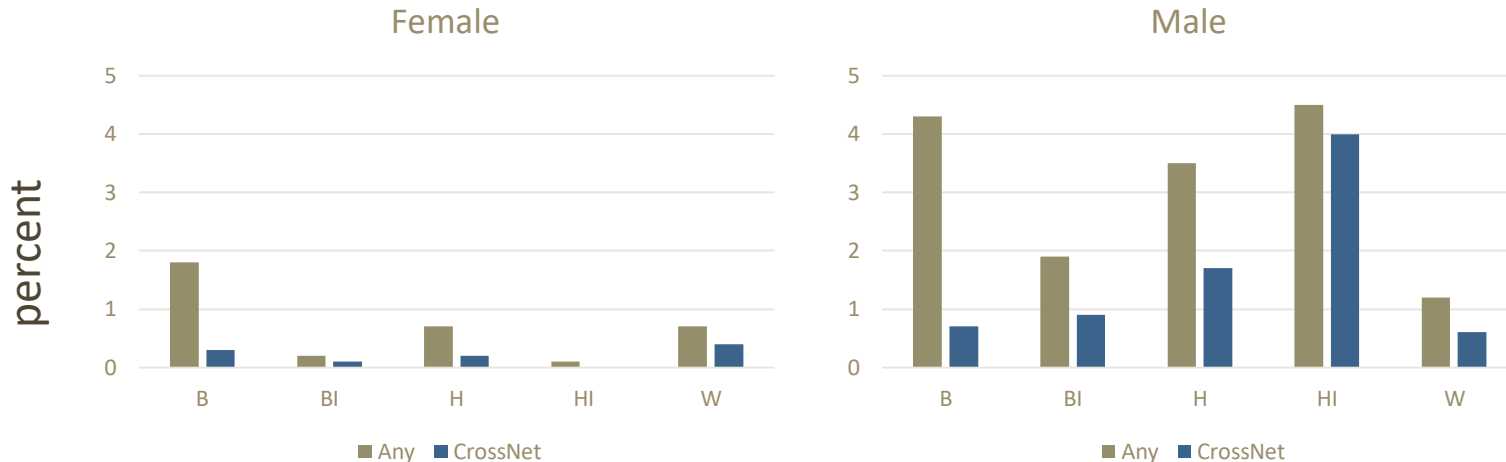


Concurrency by sex group



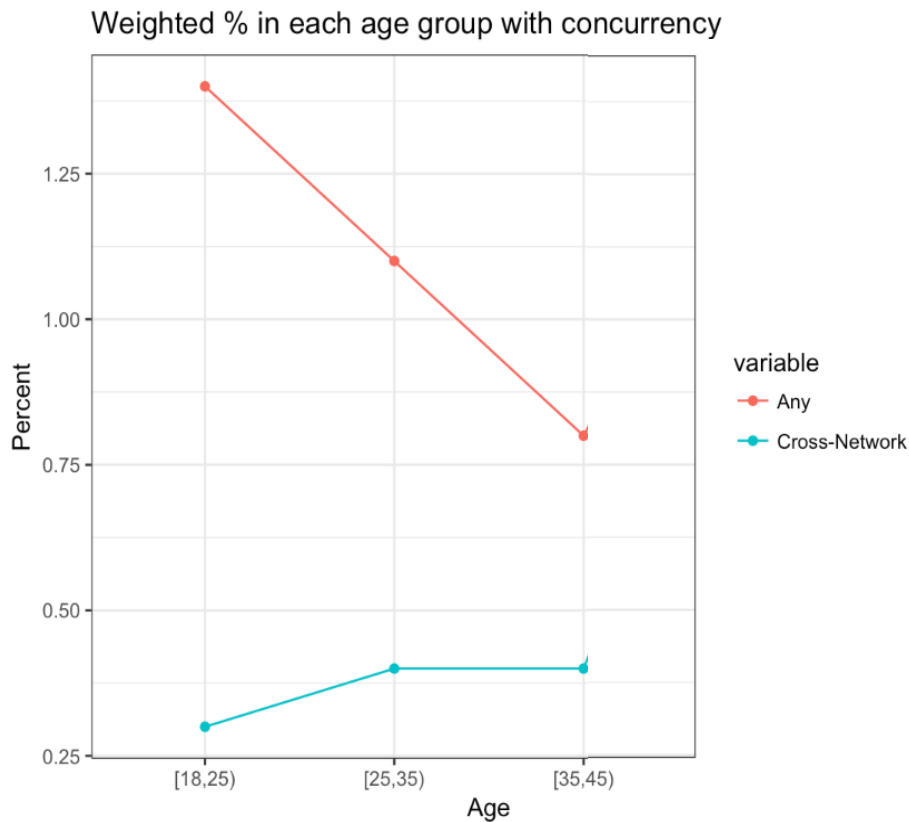
- Highest overall rates are in the bridge population: MSMF ~2%
 - About half of this is cross-network
- *This is just the concurrency with opp sex partners*
 - 65% of the MSMF also have M partners during the year
- Lowest overall rates are among women: ~0.5%

Concurrency by race/immigration group



- Highest rates are for Black, Hispanic and Hispanic immigrant men ~4%
 - Mostly multiple persistent partners for Black men
 - Mostly cross-network for Hispanic immigrants
 - Split equally for US born Hispanics
- Black women have slightly higher rates among females : ~2%

Concurrency: By age



- This is a young person's game
 - Highest rates for young men: 3-7%
- The configuration changes with age too
 - The cross-network fraction rises, as rates of cohabitation rise

Bridging force of infection

	Bridging Groups:		
	BI	HI	MSMF
Percent of population	2.3%	5.4%	1.5%
Exposure probabilities	Depart: 0.01 Return: 0.25		2.5 partners/yr
HIV acquisition probabilities *	F: 2.0e-04 M: 1.0e-04	F: 2.0e-05 M: 9.9e-06	7.2e-06

* The HIV acquisition probabilities are a function of several components, and determine the FOI at the boundary

For example for MSMF:

MSM prevalence x
condom use (.304) x efficacy (cond.rr=.4) x
P(transmission | contact)
(((.0082*1.09)+(.0031*1.09))/2) x
P(contact per week) (2.5/52)

That's a lot of numbers

Key message:

- The force of infection across these boundaries is low
 - small bridging populations
 - low sexual exposure rates
 - low probabilities of transmission
- Can such a small bridging dynamic have an impact?
 - ... we'll see

Network Model Results

Just a peek at the estimates,
and assessing the validity of the simulations

These dynamic partnership network simulations
are the foundation for the epidemic simulations

ERGM Formation model estimates

		Cohab	Pers	OT
Age		-0.87	-0.20	-0.38
Age ²		0.02	0.00	0.01
Age Diff		-3.22	-2.59	-2.40
Race (main)	Black	1.10	1.14	0.42
	Black Imm	1.14	1.61	-0.52
	Hispanic	3.17	2.00	0.52
	Hisp Imm	1.63	1.13	-0.78
Race (matching)	Black	3.35	3.21	
	Black Imm	3.85	2.86	
	Hispanic	0.01	0.27	
	Hisp Imm	2.88	2.30	
	White	3.14	2.17	
Concurrency	Cross net	-5.96	-4.36	
	Within net	NA	-2.85	

N.S.

Model assessment: Network fidelity

- The dynamic simulations should reproduce the observed network statistics (on average)

- Degree distributions (# of concurrent partners)

- Within and between networks
- By sex, age, race/imm

- Mixing patterns

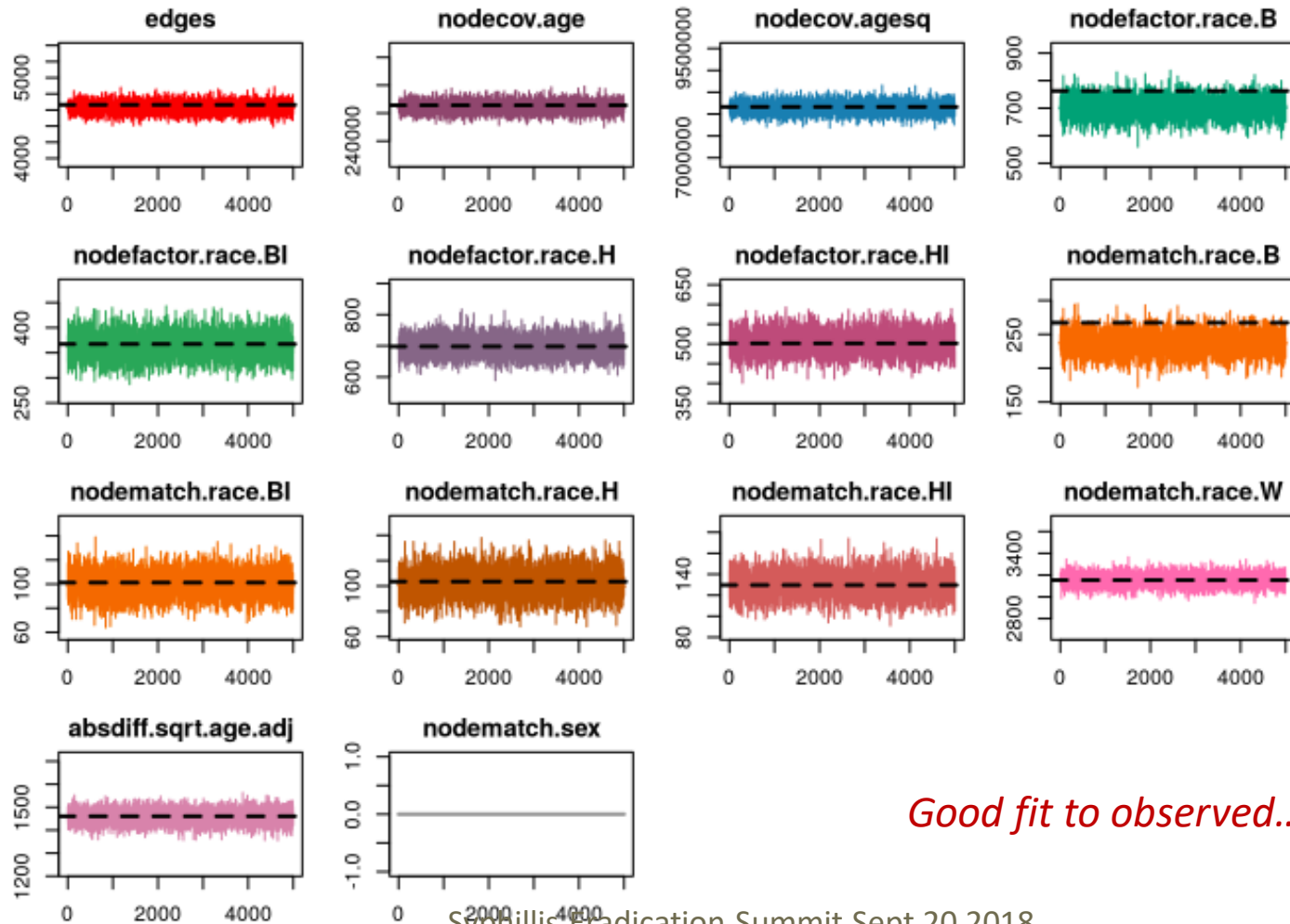
- By age, race/imm

- Partnership durations

ERGMS should be able to reproduce the joint distribution of all of the network statistics

in *each* partnership network

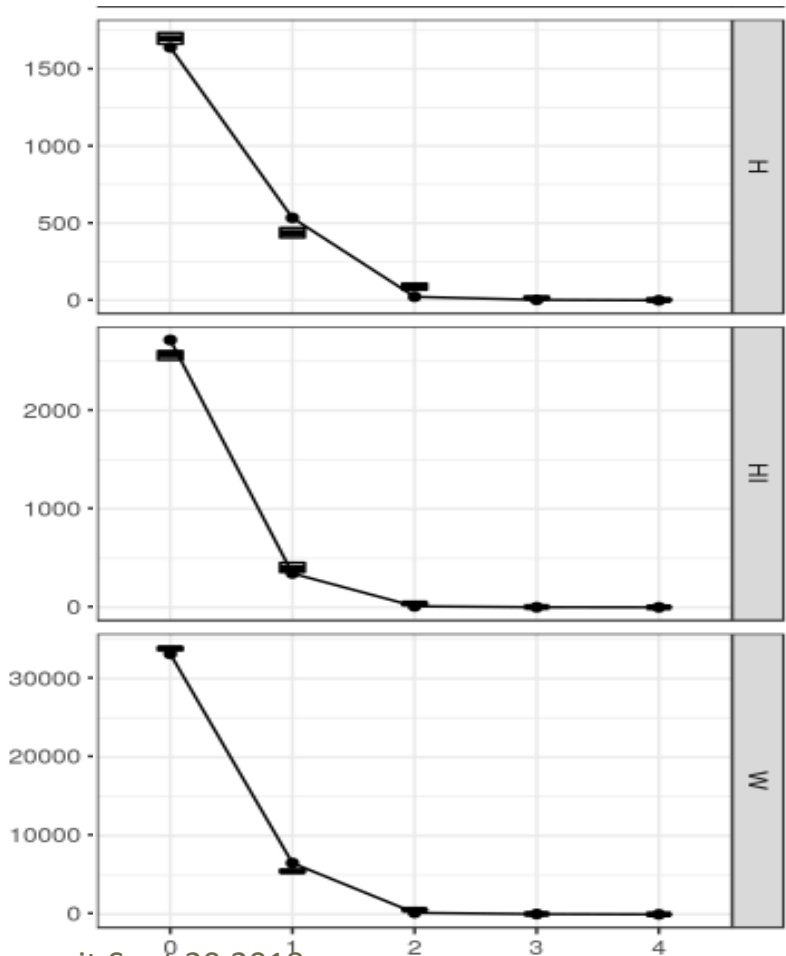
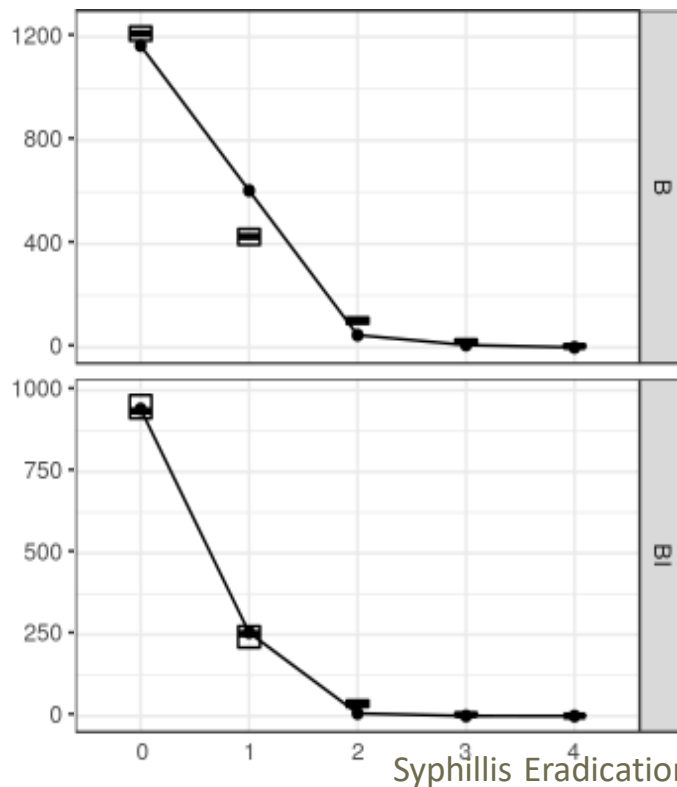
Example: Persistent network model stats



Good fit to observed...

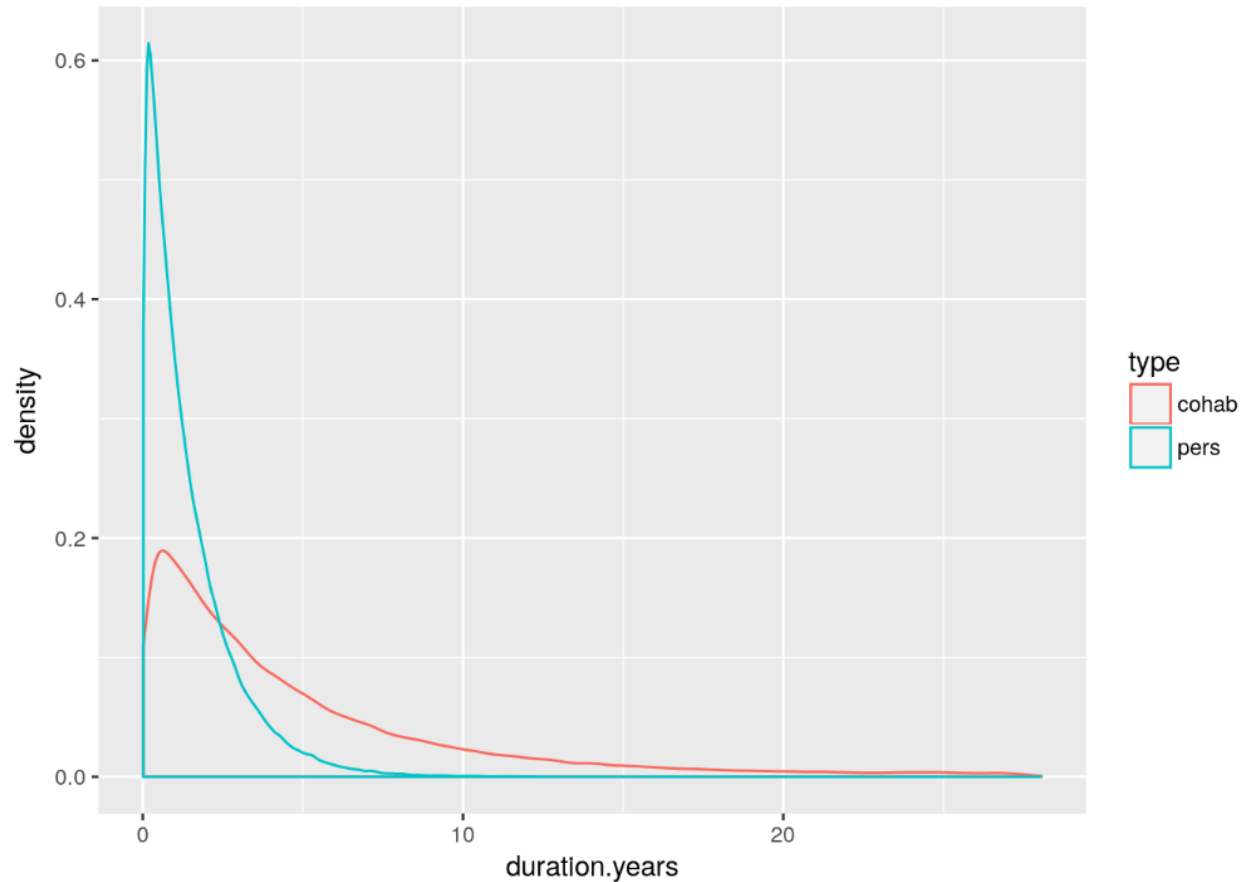
Example: Persistent degree by race

Good fit to observed, even though the degree terms are not in the model



Syphilis Eradication Summit Sept 2018

Durations by partnership type



*These also
reproduce the
observed stats*

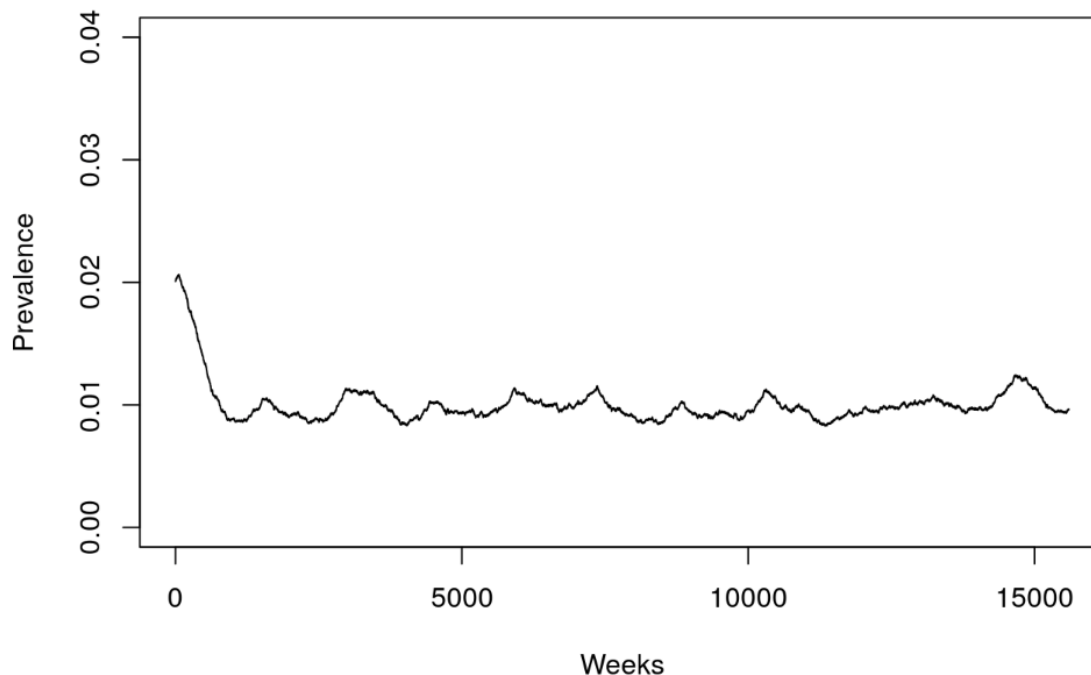
Epidemic results

Now we can simulate the epidemic,
on a network that we know closely represents the
observed data

Simulation detail

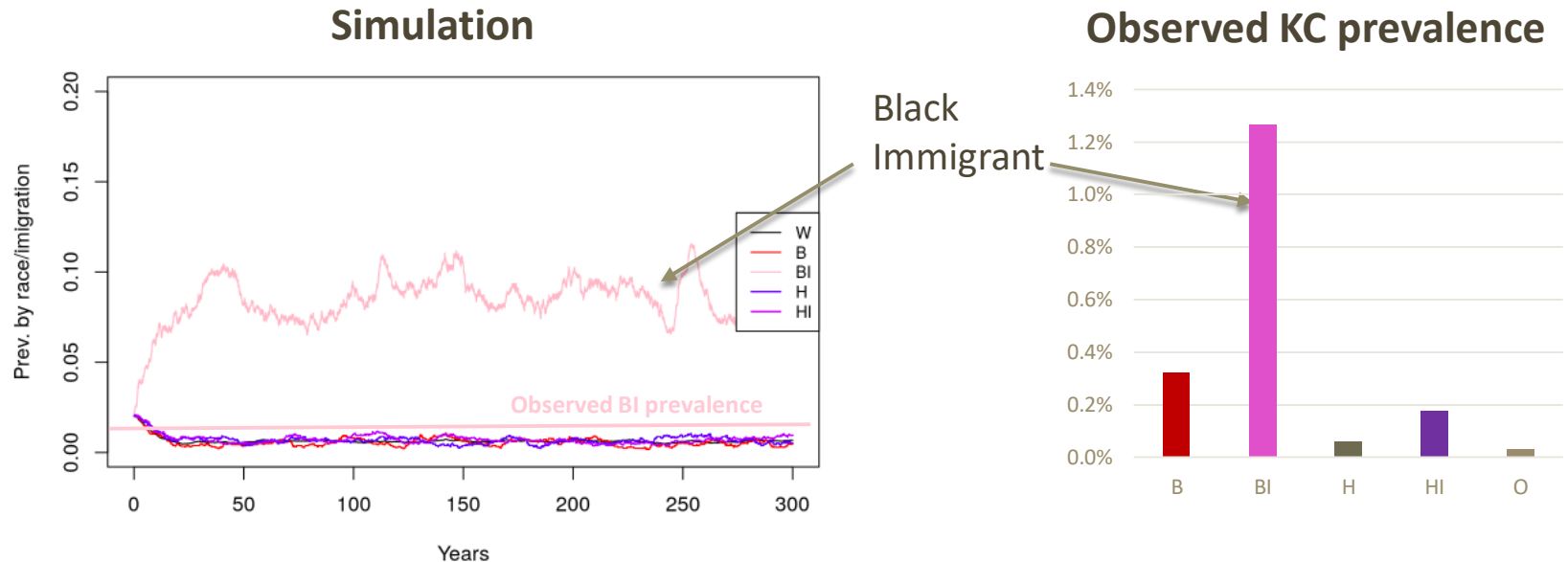
- Results here from a network size of 50,000
 - Large by most standards
 - But still not big enough
 - The prevalence of HIV in KC is low -- $\sim 0.07\%$ overall
 - So in a 50K simulation, we get very few cases: $50K * .07\% = 36$ cases
 - For this run, we bumped up the baseline transmission rate to get $\sim 1\%$ prevalence
 - We have simulations running now on networks of size 800,000
 - Should generate about 600 prevalent cases each year
- Run for ~ 300 years
 - To “equilibrium”

Persistence and equilibrium



1. We get a persistent epidemic
2. And equilibrium prevalence for Het+NIR is at our target value of 1%
 - *recall, this is about 10x higher than observed KC prevalence.*

Prevalence by race & immigration status

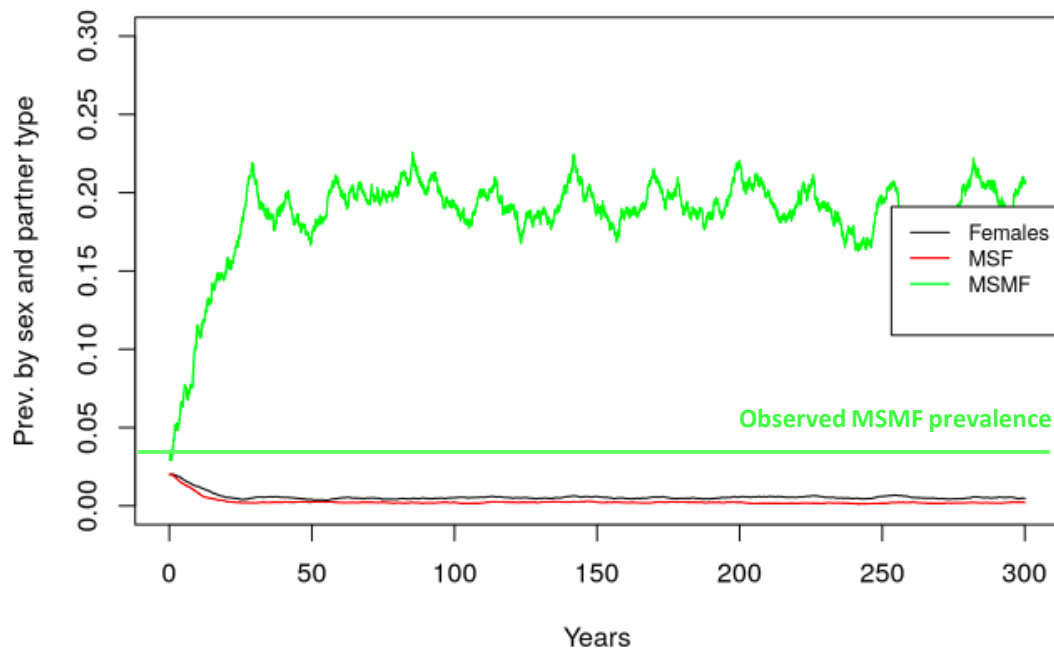


Here, the rank order is roughly correct

But the BI prevalence is too high (obs: 1.3%, sim: 7.6%)

Prevalence by sexual partner group

Simulation



Here the rank order is again correct

But estimated local prevalence for MSMF is ~4%, and our simulation is generating ~20%

So we're too high for this boundary group also (if that prevalence estimate is correct)

Our model needs to recalibrate

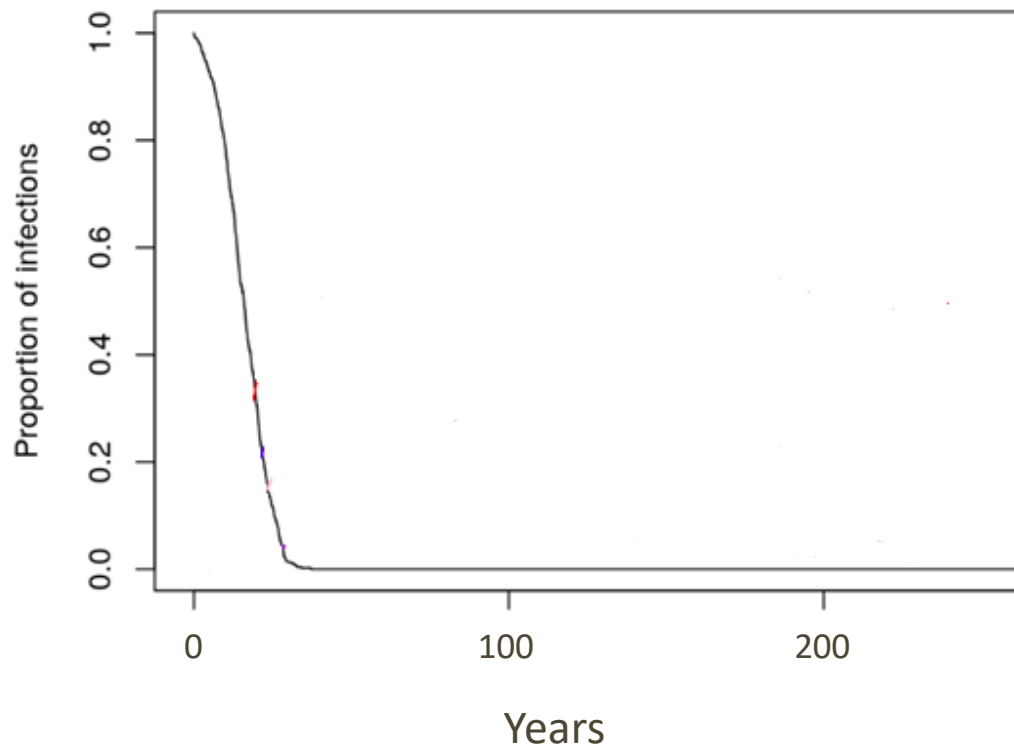
- Our boundary forces of infection need to be lowered
- There is LOTS of uncertainty in those estimates
 - Recall, they depend on national data on MSMF prevalence and behavior, as well as travel data collected only on new diagnosed HIV cases in KC
 - So we feel comfortable calibrating these as needed
- There's a much longer discussion here ...
 - But not for this presentation

Key question

What is the impact of bridging on the Heterosexual HIV epidemic?

- After the simulation run
- Break down all of the infections by source
 - Original seeds, and their downstream chain of transmissions
 - Bridge infections, and downstream chain of transmissions
 - MSMF boundary
 - Foreign boundary

Original seeds and downstream infections



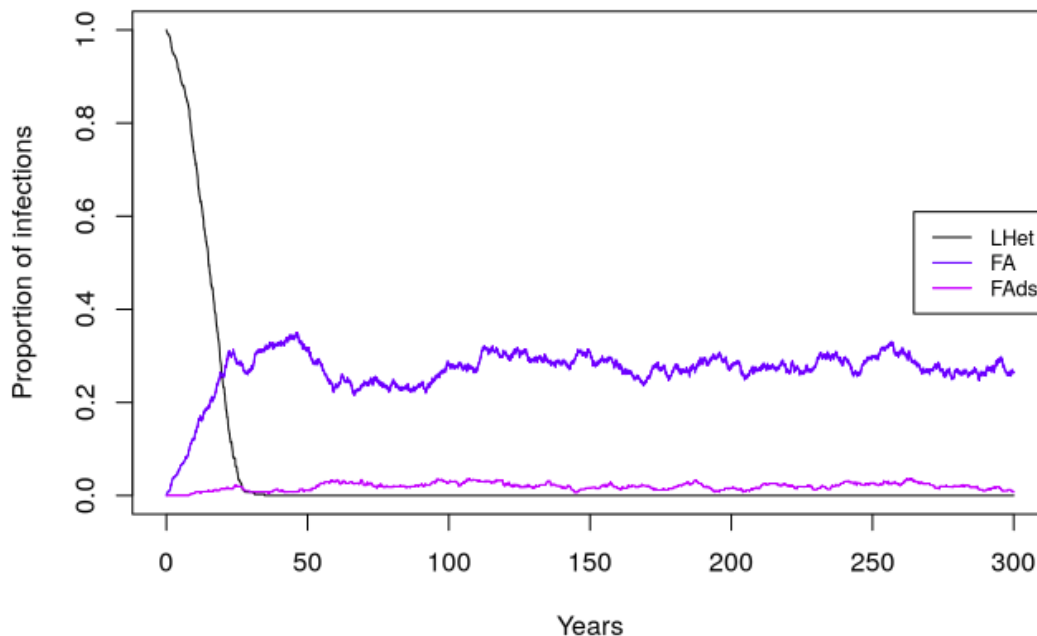
No persistence

As a fraction of all infections,

the cases in these chains decline steadily

and are extinct in about 30 years

Foreign boundary and downstream



Persistence

Bridge infections account for ~20% at equilibrium

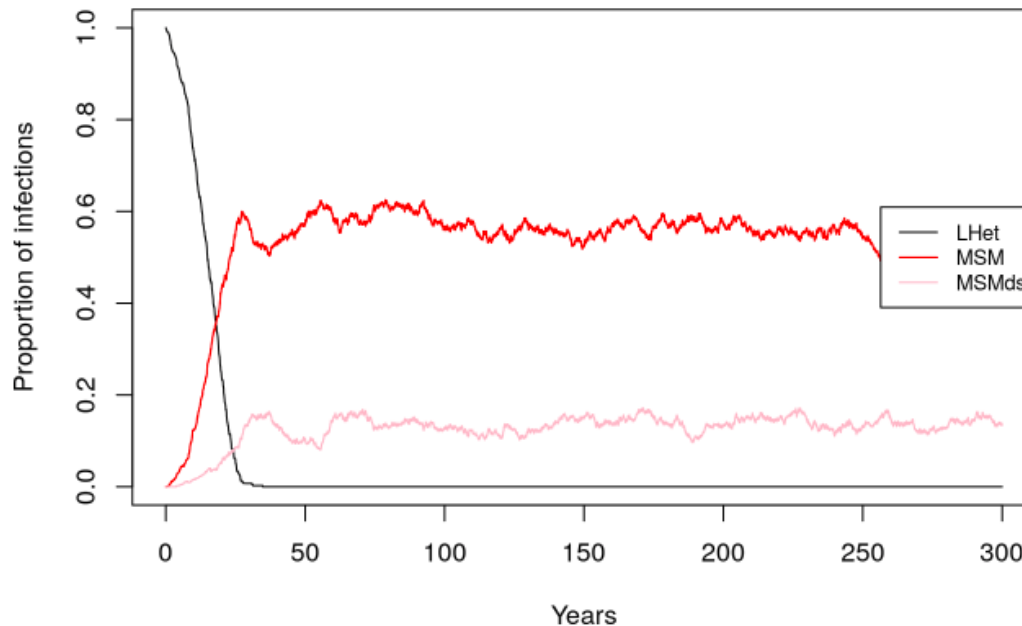
Downstream infections ~2%

So, these chains also go extinct quickly

But new ones are always being started

MSMF boundary and downstream

Persistence



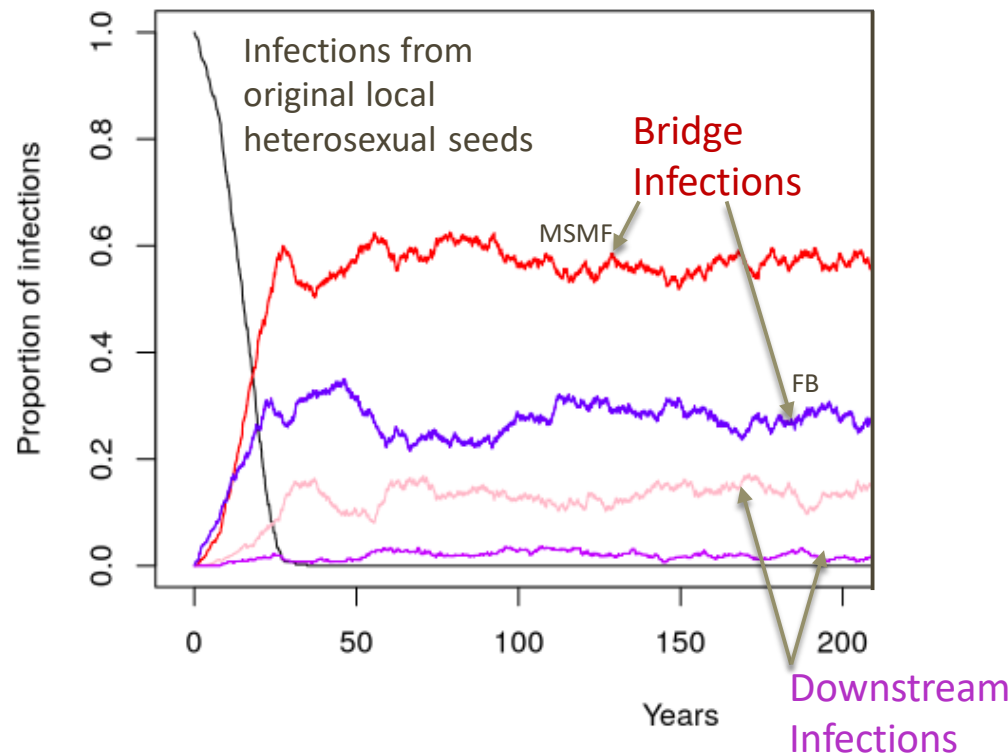
Bridge infections account for ~55% at equilibrium

Downstream infections ~23%

These chains also go extinct, but more slowly

And new ones are always being started

Summary: Infections by source



No persistence without continual infections across the bridges

The primary bridge is MSMF

No infection chains were longer than 5 generations

Implications for prevention

- HIV transmission within the heterosexual population is below the persistence threshold in Seattle/King Co.
 - *So when infections cross over a bridge to this population, the chains die out pretty quickly*
- Boundary infections are the strategic target for prevention activities
 - *These are small, identifiable bridging risk groups*
 - *Effective tailored prevention here will have a large impact*

Limitations

- These are preliminary results from a prototype model
 - We know they do not reproduce the observed epidemic yet
 - The model will need to be calibrated, using separate targets, in order to validate it
- The boundary with IDU is not represented
- The results **should not be extrapolated to other locales**
 - *This is a feature, not a bug*
 - The modeling framework is general
 - The empirical data inputs are local
 - So the model predictions are local

Take home messages

- It is now possible to model local STI epidemics with great fidelity to local empirical data
 - Transmission networks with subpopulations and bridges
 - Natural history of the specific STI pathogen
 - Care continuum
- The data can be collected at the local level
 - But are often not, esp. the network data
- The simulation results can be used to guide local policy
 - Once a model has been properly calibrated and validated

60

Thank You

Resources

Network Modeling

1. Journal of Statistical Software (v42) 2008 – Eight papers on ERGMs and statnet
2. Goodreau, S., et al. (2009). "Birds of a Feather, or Friend of a Friend? Using Statistical Network Analysis to Investigate Adolescent Social Networks." *Demography* 46(1): 103–125.
3. Krivitsky PN, Morris M. Inference for social network models from egocentrically sampled data, with application to understanding persistent racial disparities in HIV prevalence in the US. *Annals of Applied Statistics*. 2017;11(1):427-55.

EpiModel software

Jenness SM, Goodreau SM, Morris M. EpiModel: An R Package for Mathematical Modeling of Infectious Disease over Networks. *Journal of Statistical Software*. 2018;84(8). doi: 10.18637/jss.v084.i08.

We teach a weeklong intensive workshop on Network Modeling for Epidemics every summer at the University of Washington: <https://statnet.github.io/nme/>

Resources

Examples of Network Modeling for HIV/STI

1. Goodreau SM, Carnegie NB, Vittinghoff E, Lama JR, Fuchs JD, Sanchez J, Buchbinder SP. Can Male Circumcision Have an Impact on the HIV Epidemic in Men Who Have Sex with Men? Plos One. 2014;9(7). doi: 10.1371/journal.pone.0102960. PubMed PMID: WOS:000340028800021.
2. Khanna AS, Dimitrov DT, Goodreau SM. WHAT CAN MATHEMATICAL MODELS TELL US ABOUT THE RELATIONSHIP BETWEEN CIRCULAR MIGRATIONS AND HIV TRANSMISSION DYNAMICS? Mathematical Biosciences and Engineering. 2014;11(5):1065-90. doi: 10.3934/mbe.2014.11.1065. PubMed PMID: WOS:000338230600003.
3. Khanna AS, Goodreau SM, Gorbach PM, Daar E, Little SJ. Modeling the Impact of Post-Diagnosis Behavior Change on HIV Prevalence in Southern California Men Who Have Sex with Men (MSM). Aids and Behavior. 2014;18(8):1523-31. doi: 10.1007/s10461-013-0646-2. PubMed PMID: WOS:000339868100013.
4. Carnegie NB, Goodreau SM, Liu A, Vittinghoff E, Sanchez J, Lama JR, Buchbinder S. Targeting Pre- Exposure Prophylaxis Among Men Who Have Sex With Men in the United States and Peru: Partnership Types, Contact Rates, and Sexual Role. J AIDS-Journal of Acquired Immune Deficiency Syndromes. 2015;69(1):119-25. doi: 10.1097/qai.0000000000000555. PubMed PMID: WOS:000353033300023.
5. Khanna A, Goodreau SM, Wohlfeiler D, Daar E, Little S, Gorbach PM. Individualized diagnosis interventions can add significant effectiveness in reducing human immunodeficiency virus incidence among men who have sex with men: insights from Southern California. Annals of Epidemiology. 2015;25(1):1-6. doi: 10.1016/j.annepidem.2014.09.012. PubMed PMID: WOS:000346229100001.

Resources

Examples of Network Modeling for HIV / STI

7. Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, Sullivan P. Impact of the Centers for Disease Control's HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. *Journal of Infectious Diseases*. 2016;214(12):1800-7. doi: 10.1093/infdis/jiw223. PubMed PMID: WOS:000393130000005.
8. Goodreau SM, Rosenberg ES, Jenness SM, Luisi N, Stansfield SE, Millett GA, Sullivan PS. Sources of racial disparities in HIV prevalence in men who have sex with men in Atlanta, GA, USA: a modelling study. *Lancet HIV*. 2017;4(7):E311-E20. doi: 10.1016/s2352-3018(17)30067-x. PubMed PMID: WOS:000404131200011.
9. Jenness SM, Sharma A, Goodreau SM, Rosenberg ES, Weiss KM, Hoover KW, Smith DK, Sullivan P. Individual HIV Risk versus Population Impact of Risk Compensation after HIV Preexposure Prophylaxis Initiation among Men Who Have Sex with Men. *Plos One*. 2017;12(1). doi: 10.1371/journal.pone.0169484. PubMed PMID: WOS:000391641500100.
10. Jenness SM, Weiss KM, Goodreau SM, Gift T, Chesson H, Hoover KW, Smith DK, Liu AY, Sullivan PS, Rosenberg ES. Incidence of Gonorrhea and Chlamydia Following Human Immunodeficiency Virus Preexposure Prophylaxis Among Men Who Have Sex With Men: A Modeling Study. *Clin Infect Dis*. 2017;65(5):712-8. doi: 10.1093/cid/cix439. PubMed PMID: WOS:000407808400008.
11. Goodreau SM, Hamilton DT, Jenness SM, Sullivan PS, Valencia RK, Wang LY, Dunville RL, Barrios LC, Rosenberg ES. Targeting Human Immunodeficiency Virus Pre-Exposure Prophylaxis to Adolescent Sexual Minority Males in Higher Prevalence Areas of the United States: A Modeling Study. *Journal of Adolescent Health*. 2018;62(3):311-9. doi: 10.1016/j.jadohealth.2017.09.023. PubMed PMID: WOS:000425861300011.

Resources

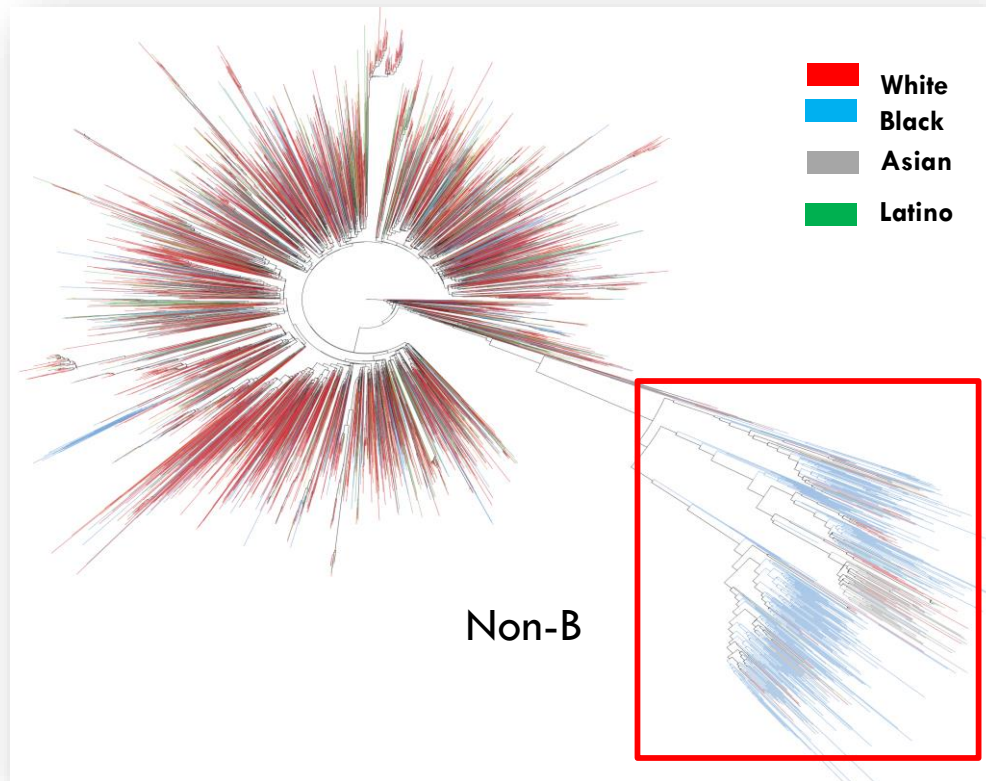
MSMW and HIV

1. Friedman MR, Stall R, Silvestre AJ, Mustanski B, Shoptaw S, Surkan PJ, Rinaldo CR, Plankey MW. STUCK IN THE MIDDLE: LONGITUDINAL HIV-RELATED HEALTH DISPARITIES AMONG MEN WHO HAVE SEX WITH MEN AND WOMEN (MSMW). *Journal of acquired immune deficiency syndromes* (1999). 2014;66(2):213-20. doi: 10.1097/QAI.000000000000143. PubMed PMID: PMC4030741.
2. Singh S, Hu X, Wheeler W, Hall HI. HIV Diagnoses Among Men Who Have Sex With Men and Women—United States and 6 Dependent Areas, 2008-2011. *American Journal of Public Health*. 2014;104(9):1700-6. doi: 10.2105/AJPH.2014.301990. PubMed PMID: PMC4151940.
3. Shadaker S, Magee M, Paz-Bailey G, Hoots BE. Characteristics and Risk Behaviors of Men Who Have Sex With Men and Women Compared With Men Who Have Sex With Men-20 US Cities, 2011 and 2014. *J Acquir Immune Defic Syndr*. 2017;75 Suppl 3:S281-s7. Epub 2017/06/13. doi: 10.1097/qai.0000000000001403. PubMed PMID: 28604429.
4. Friedman MR, Sang JM, Bukowski LA, Matthews DD, Eaton LA, Raymond HF, Stall R. HIV Care Continuum Disparities Among Black Bisexual Men and the Mediating Effect of Psychosocial Comorbidities. *J Acquir Immune Defic Syndr*. 2018;77(5):451-8. Epub 2018/01/18. doi: 10.1097/qai.0000000000001631. PubMed PMID: 29337847; PMCID: PMC5844845.

Appendix

From another project at UW

■ Phylogenetic analyses of local HIV diagnoses

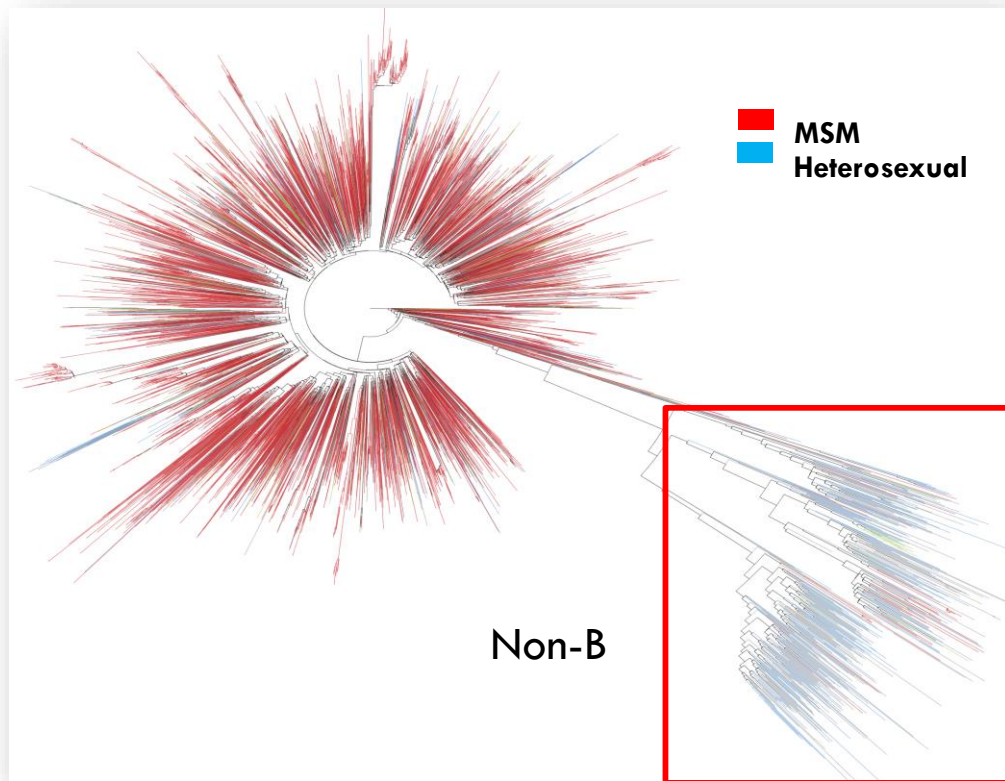


- B Clades predominate in the US
- Non-B clades predominate in Africa and Asia

They form a distinctive cluster here,
predominantly black

Herbeck & Kerani

- Phylogenetic analyses of *local* HIV diagnoses



They form a distinctive cluster here,

And predominantly heterosexual

An independent empirical calibration target

- Directly relevant for calibrating our most uncertain parameters – the FOI across the boundaries
- Separate from HIV incidence and prevalence data
 - So those can be preserved for model validation