

Introduction to EpiModelHIV

Network Models for HIV/STI Transmission Dynamics with EpiModel

June 28, 2017

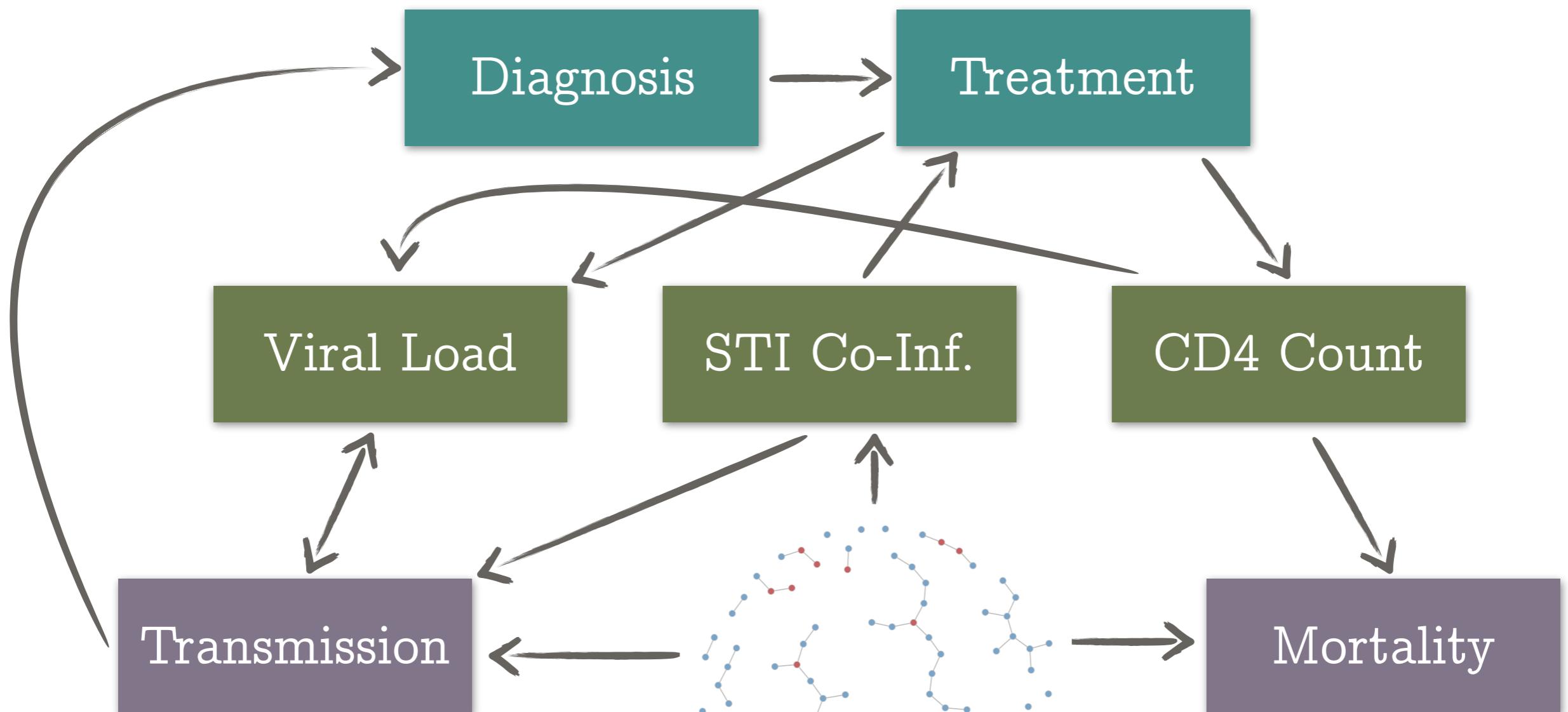
Overview

- Distinguish EpiModel from EpiModelHIV
- Demonstrate one research-level use of EpiModelHIV to address HIV prevention
- Review the different “branches” of EpiModelHIV
- Show organization and structure of current master branch

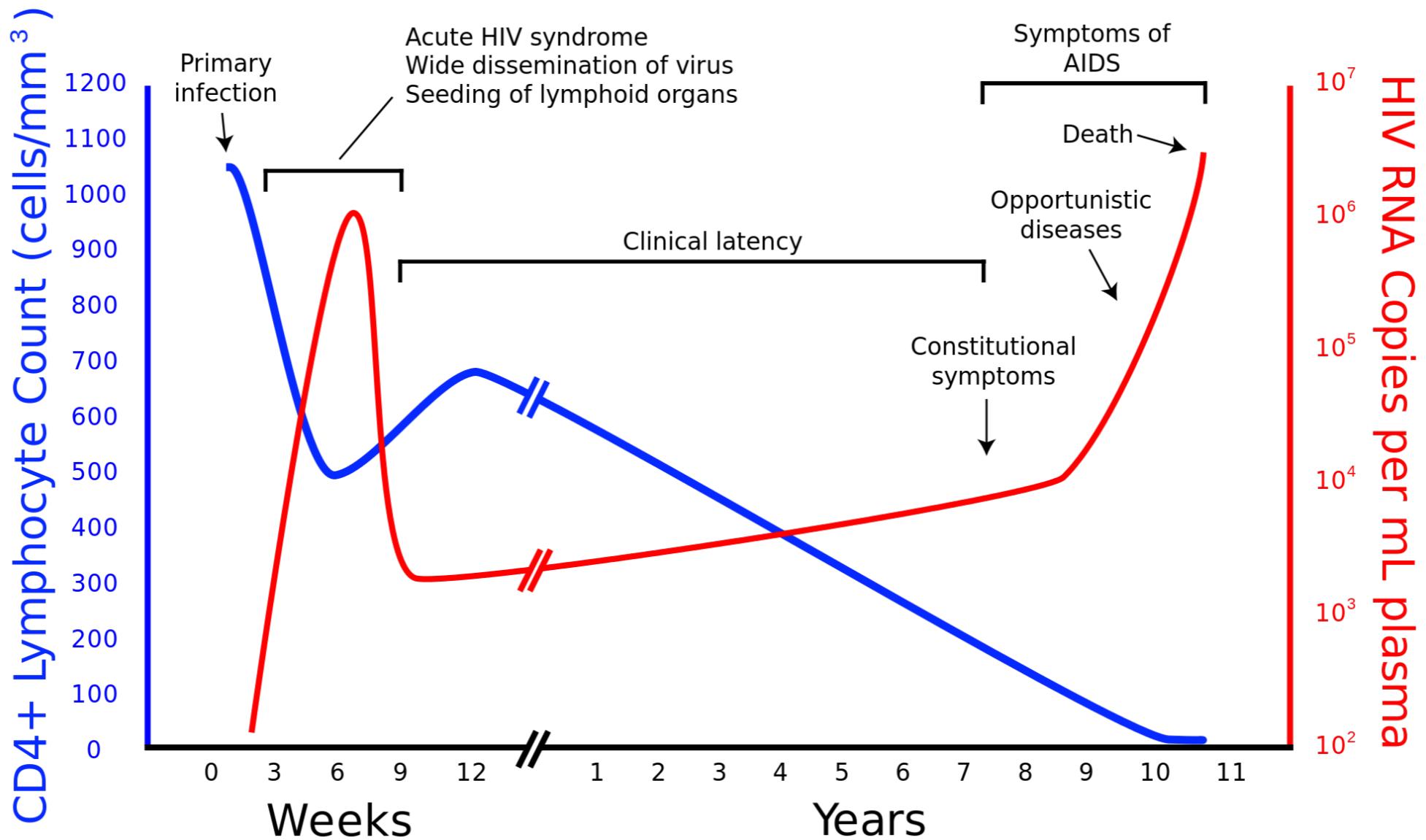
Base Modules

initialize.FUN	Module to initialize the model at time 1, with the default function of initialize.net.
deaths.FUN	Module to simulate death or exit, with the default function of deaths.net.
births.FUN	Module to simulate births or entries, with the default function of births.net.
recovery.FUN	Module to simulate disease recovery, with the default function of recovery.net.
edges_correct.FUN	Module to adjust the edges coefficient in response to changes to the population size, with the default function of edges_correct that preserves mean degree.
resim_nets.FUN	Module to resimulate the network at each time step, with the default function of resim_nets.
infection.FUN	Module to simulate disease infection, with the default function of infection.net.
get_prev.FUN	Module to calculate disease prevalence at each time step, with the default function of get_prev.net.
verbose.FUN	Module to print simulation progress to screen, with the default function of verbose.net.

Conceptual Diagram for HIV/STI Transmission Model



HIV Stages



- In absence of treatment, HIV viral load and CD4 counts are co-evolving after initial time of infection
- In individual-based models, we can model these processes continuously to handle constant progression over the long chronic period

EpiModelHIV

- EpiModelHIV contains the set of modules built on top of the EpiModel platform specifically for modeling HIV (and now STI) transmission dynamics
- Uses the core STERGM methods shown here but in a self-contained R package for ease of extensibility
- Uses the same EpiModel modular approach for adding new epi functionality, but with several helper functions to get from empirical data to simulation to analysis
- Contains code and functionality for both US MSM populations and SSA heterosexual populations

EpiModelHIV

- Major differences between EpiModel and EpiModelHIV:
 - Top-down versus bottom-up platform
 - Specific to HIV/STI and specific to at-risk populations
 - For MSM, big conceptual difference in networks
 - Optimized to run big, fast research-level models on HPCs

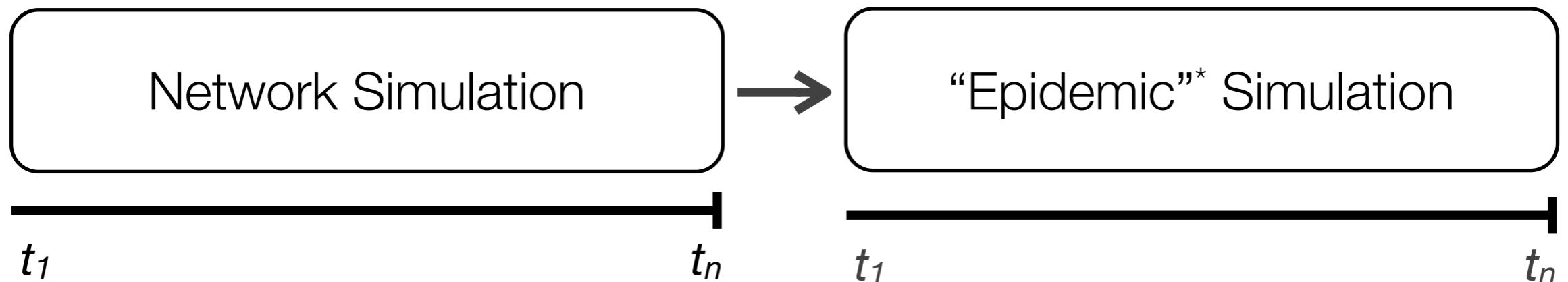
- Top-down versus bottom-up
 - Top-down (EpiModelHIV): We start with a research question and build software to answer that question
 - Bottom-up (EpiModel): We start with a method build software to help (us and others!) answer that question
 - Implications for ongoing software development and innovations that may be useful for us versus others

- Specific to HIV/STI and specific to at-risk populations
 - Given the top-down approach, we use EpiModelHIV in applied research in HIV/STI prevention science in populations for which we are interested in and have empirical data
 - For MSM code, simulations include modules specific to what drives transmission in this population, and new prevention methods
 - One major difference from tutorials so far is the “3-network” approach of main, casual, and one-off partnerships
 - Tomorrow will involve reviewing each module of the simulation and component of the software in minute detail

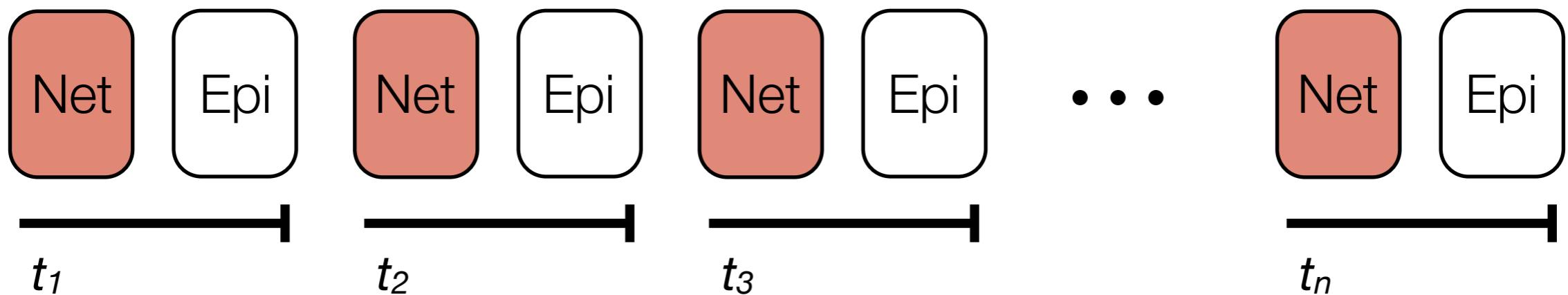
- Optimized to run big, fast research-level models on HPCs
 - Dynamic network models like any ABM will always be slower than DCMs, and increase with N
 - Network models have been slowed by the network resimulation process

Model Dependence

Independent Models



Dependent Models



"Epidemic"*= biological, behavioral, demographic, etc., changes

- Optimized to run big, fast research-level models on HPCs
 - Dynamic network models like any ABM will always be slower than DCMs, and increase with N
 - Network models have been slowed by the network resimulation process
 - Huge strides in improving this (7 days → 7 minutes);
 - tergm vs tergmLite
 - This involves a tradeoff between speed and information retention (e.g., movies)
 - Built workflows specific to our HPC systems

Model Example 1



Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, Sullivan PS. Impact of CDC's HIV Pre-Exposure Prophylaxis Guidelines among MSM in the United States. *Journal of Infectious Diseases*. 2016; 214(12): 1800–1807.

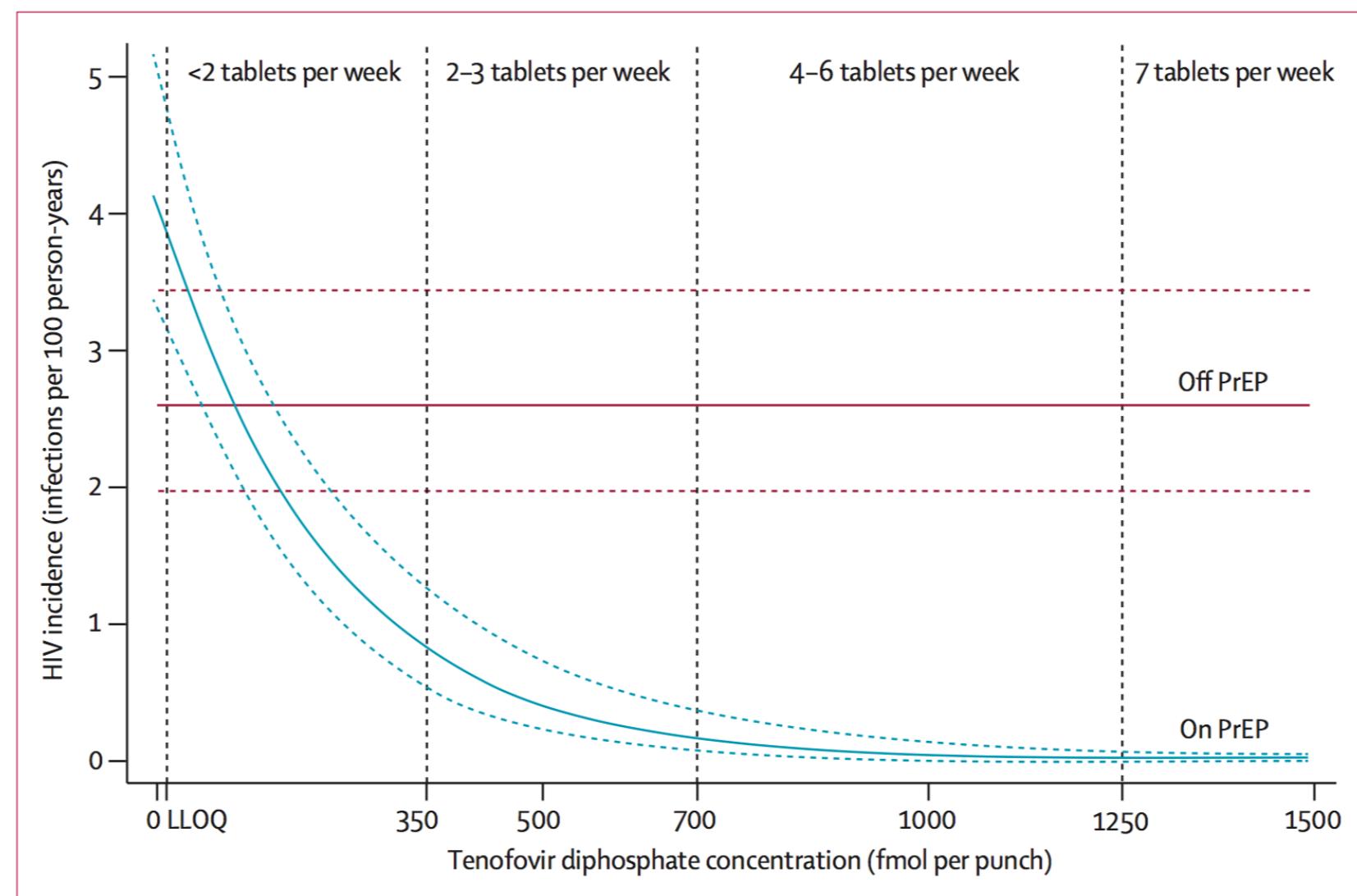
HIV Preexposure Prophylaxis

- Anti-retroviral treatment provided to HIV-uninfected persons
- Decreases biological risk of infection when HIV-infected partner has uncontrolled viral replication
- Men who have sex with men (MSM) in the US are a high-priority population for PrEP
- 5% to 10% of MSM with indications currently using it



PrEP is More Effective When Adherence is Better

- **Efficacy** of daily oral PrEP established in several RCTs
 - iPrex trial among MSM and TG women: 44% incidence reduction in intent-to-treat analyses
 - Secondary iPrEx analyses suggest non-linear dose-response effect



Grant, 2014, Lancet Infect Dis

Adherence is Better When Effectiveness is Known

Original Investigation

Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services

Albert Y. Liu, MD, MPH; Stephanie E. Cohen, MD, MPH; Eric Vittinghoff, PhD; Peter L. Anderson, PharmD; Susanne Doblecki-Lewis, MD; Oliver Bacon, MD, MPH; Wairimu Chege, MD, MPH; Brian S. Postle, BS; Tim Matheson, PhD; K. Rivet Amico, PhD; Teri Liegler, PhD; M. Keith Rawlings, MD; Nikole Trainor, MPH; Robert Wilder Blue, MSW; Yannine Estrada, PhD; Me Daniel J. Feaster, PhD; Robert Grant, MD, MPH; Susan Buchbinder, MD; Michael A. Kolber, PhD, MD

Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study

Robert M Grant, Peter L Anderson, Vanessa McMahan, Albert Liu, K Rivet Amico, Megha Mehrotra, Sybil Hosek, Carlos Mosquera, Martin Casapia, Orlando Montoya, Susan Buchbinder, Valdilea G Veloso, Kenneth Mayer, Suwat Chariyalertsak, Linda-Gail Bekker, Esper G Kallas, Mauro Schechter, and the iPrEx study team

Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial

Sheena McCormack, David T Dunn*, Monica Desai, David I Dolling, Mitzy Gafos, Richard Gilson, Ann K Sullivan, Amanda C... Gabriel Schembri, Nicola Mackie, Christine Bowman, Charles J Lacey, Vanessa Apea, Michael Brady, Julie Fox, Stephen Taylor, Saye H Khoo, James Rooney, Anthony Nardone, Martin Fisher, Alan McOwan, Andrew N Phillips, Anne M Johnson, Brian Gazzola, and the PROUD study team*

No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting

Jonathan E. Volk,¹ Julia L. Marcus,² Tony Phengrasamy,¹ Derek Blechinger,¹ Dong Phuong Nguyen,¹ Stephen Follansbee,¹ and C. Bradley Hare¹

CDC PrEP Guidelines for Clinical Practice

- **US PHS/CDC** released clinical practice guidelines indicating PrEP for those at “substantial risk” in **2014**
- For MSM, prescription **indications** were:
 - Unprotected anal intercourse (UAI) in monogamous partnership with person not recently tested for HIV
 - UAI outside of a monogamous partnership
 - AI (including with condoms) in a known serodiscordant partnership
 - Any non-HIV STI diagnosis
- Clinicians recommended to screen for conditions in past 6 months, **reevaluate** risk every 12 months

Study Aims

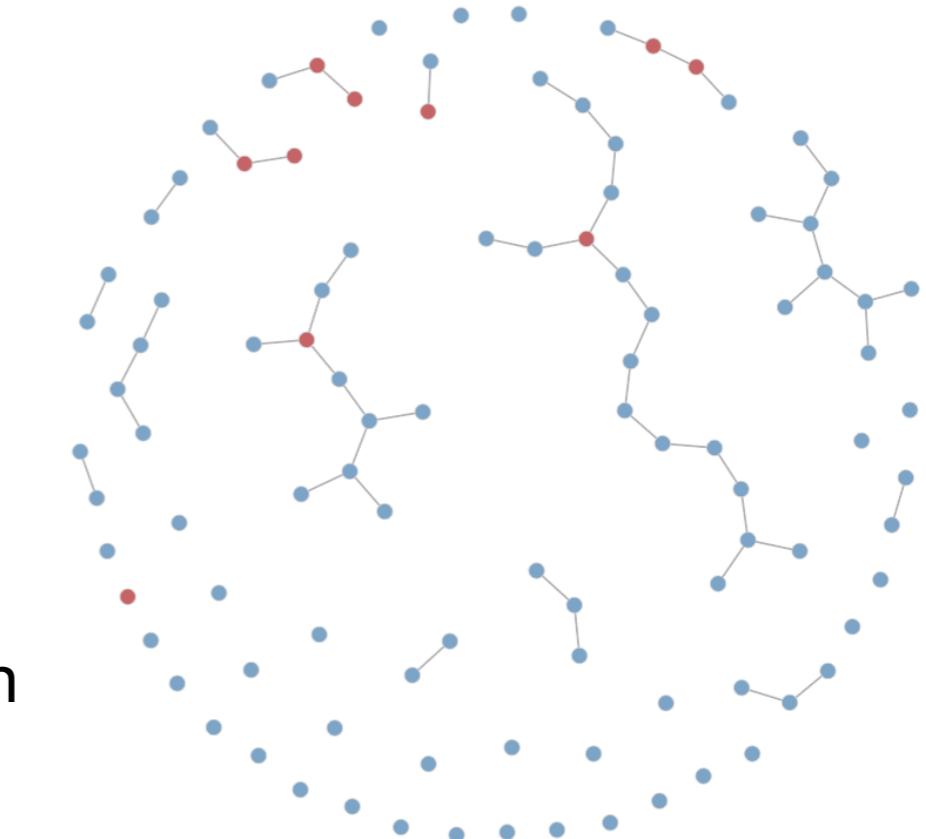
- Model HIV transmission dynamics among MSM in the US after implementation of PrEP according to CDC guidelines
 - Use a robust mathematical framework to represent complex MSM bio-behavioral population evolution
- Quantify reduction in HIV incidence associated with:
 - Individual behavioral criteria in the guidelines, separately and jointly
 - Varying levels of PrEP coverage, adherence

Methods Overview

- Stochastic network-based mathematical model
- Sexual behavior and clinical epidemiology based on two HIV incidence cohorts of MSM in Atlanta
- Epidemiological, demographic, and intervention modules designed in **EpiModel** software (www.epimodel.org)
- Simulates open population of MSM, aged 18 to 40, in the US over a 10-year time span

HIV Transmission on Dynamic Sexual Networks

- Temporal exponential random graph models (ERGMs) define partnership formation and dissolution
 - Sexual network types: main, casual, one-off
 - Men form partnerships according to model terms based on numbers of each partner type, mixing on race and age, sexual role segregation
- HIV epidemiology
 - Natural history (disease stages, continuous VL, HIV-related mortality)
 - ART initiation and adherence
 - HIV transmission dynamics within serodiscordant partnerships
- Demographic processes



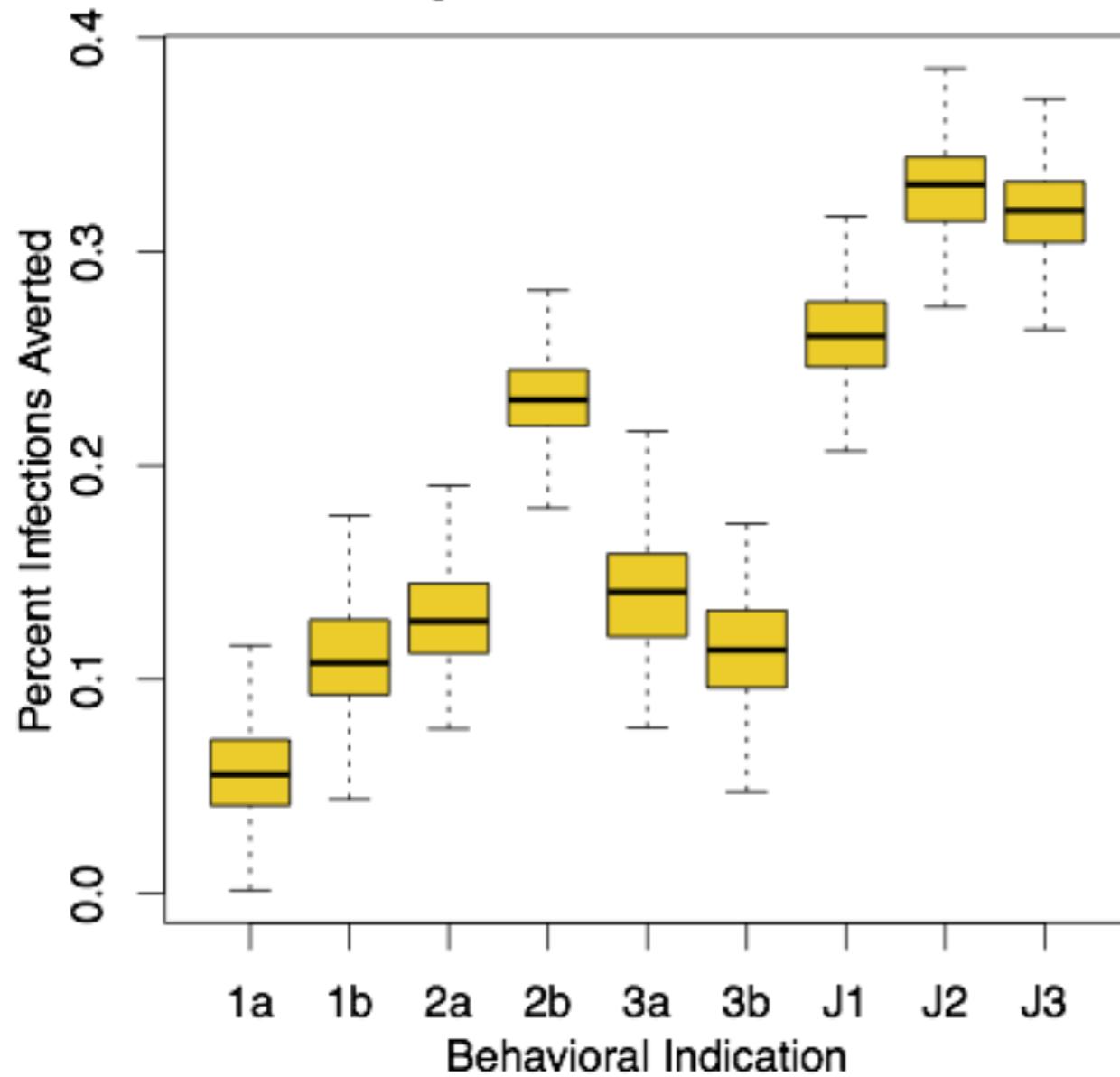
PrEP Initiation and Adherence

- Initiation
 - HIV-uninfected men encounter diagnostic HIV testing
 - Risk assessment for PrEP over past 6-month window based on CDC **behavioral** indications
 - Indicated men start PrEP if the % of already initiated men is less than a **fixed coverage threshold** (40% in base models)
- Adherence
 - Men assigned a **fixed adherence profile** following PrEP demonstration project data (62% high, 10% moderate, 7% low, and 21% null adherence)
 - Adherence translates into a 95%, 81%, 31%, and 0% reduction in transmission risk
 - Men **discontinued** from PrEP if, at yearly follow-up visit, no longer behavioral indications

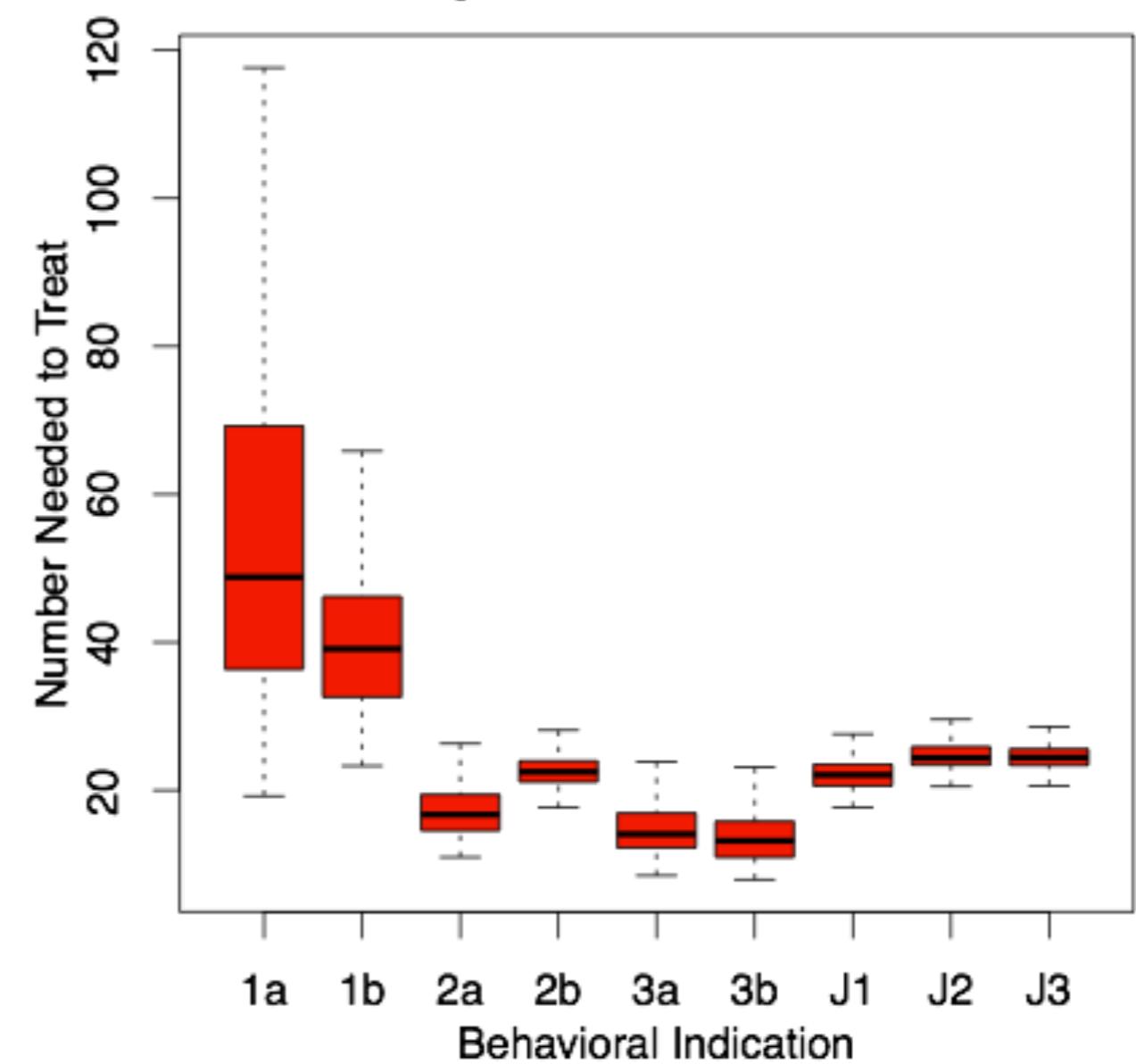
Results by CDC Guideline Indication

Effectiveness and efficacy across indications

PIA by Behavioral Indication

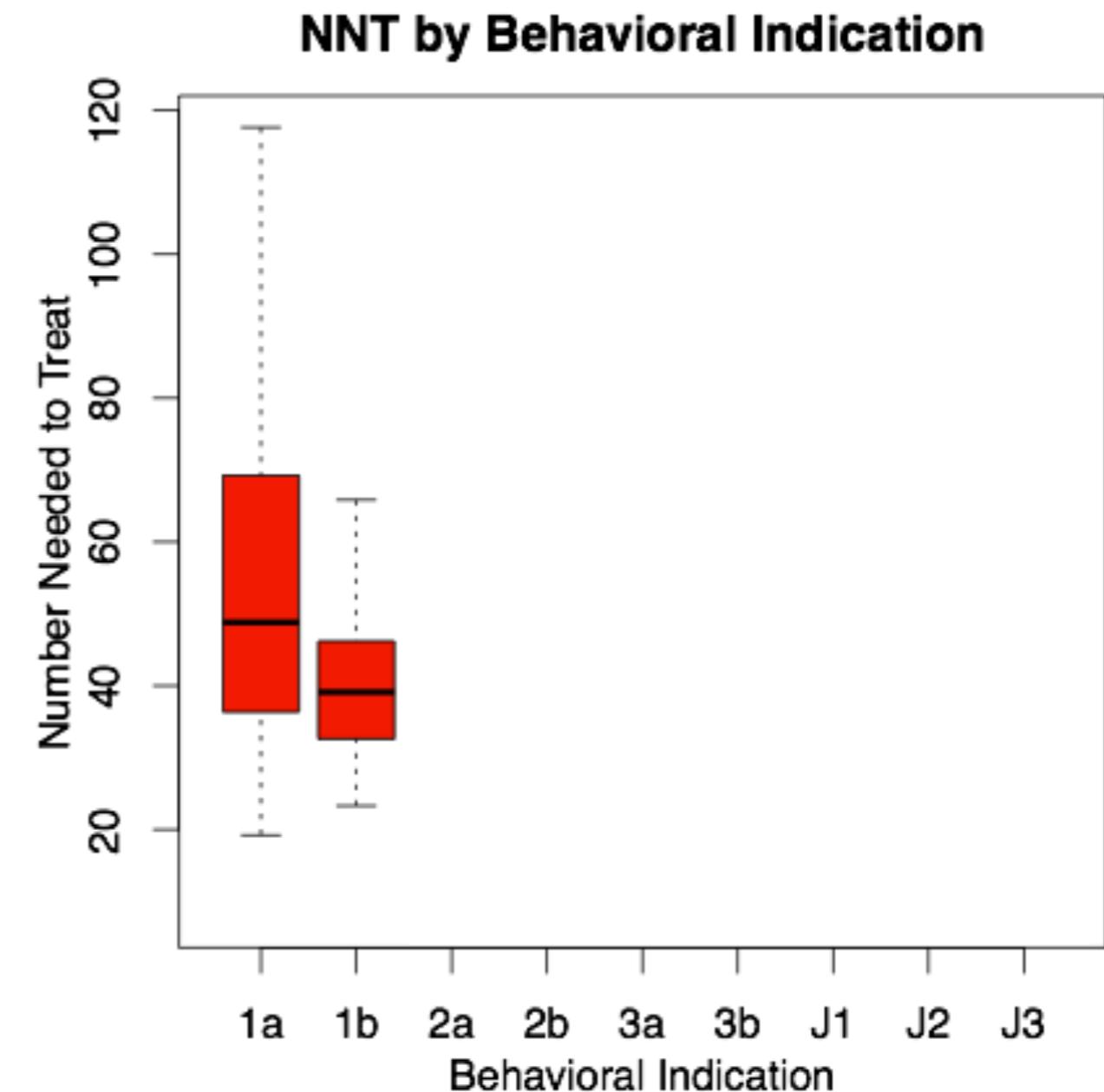
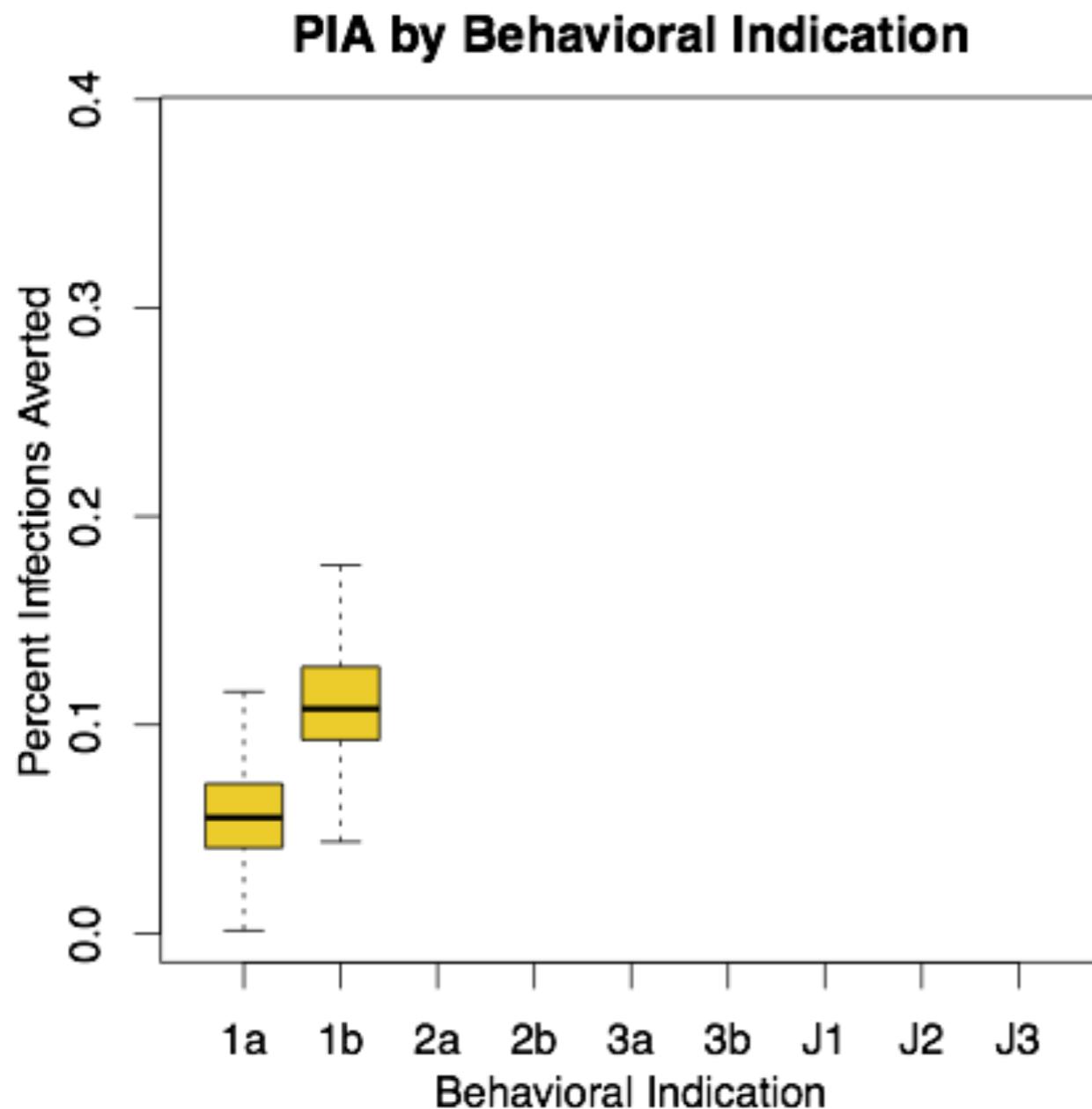


NNT by Behavioral Indication



Results by CDC Guideline Indication

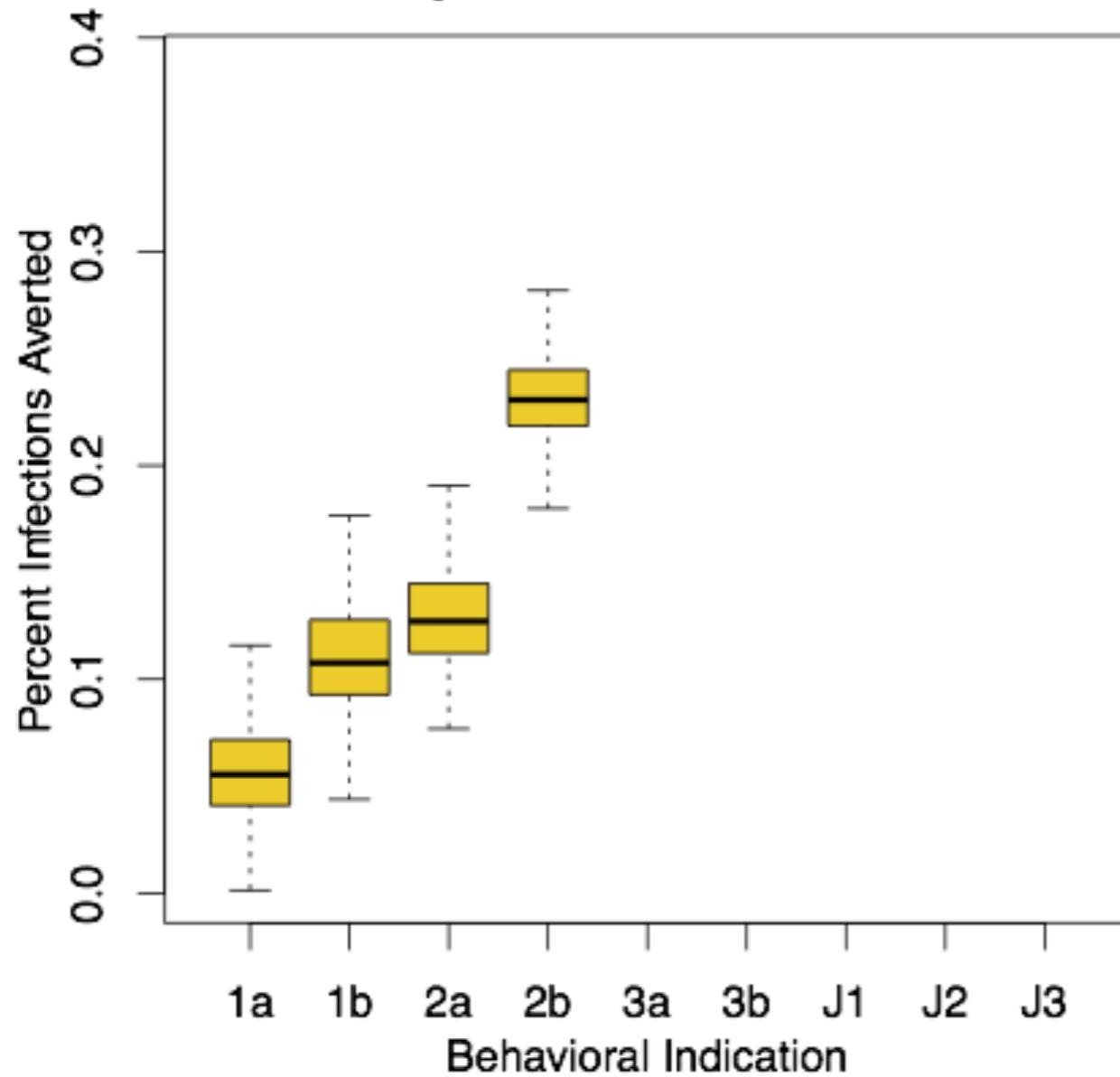
UAI with HIV status-unknown monogamous partner



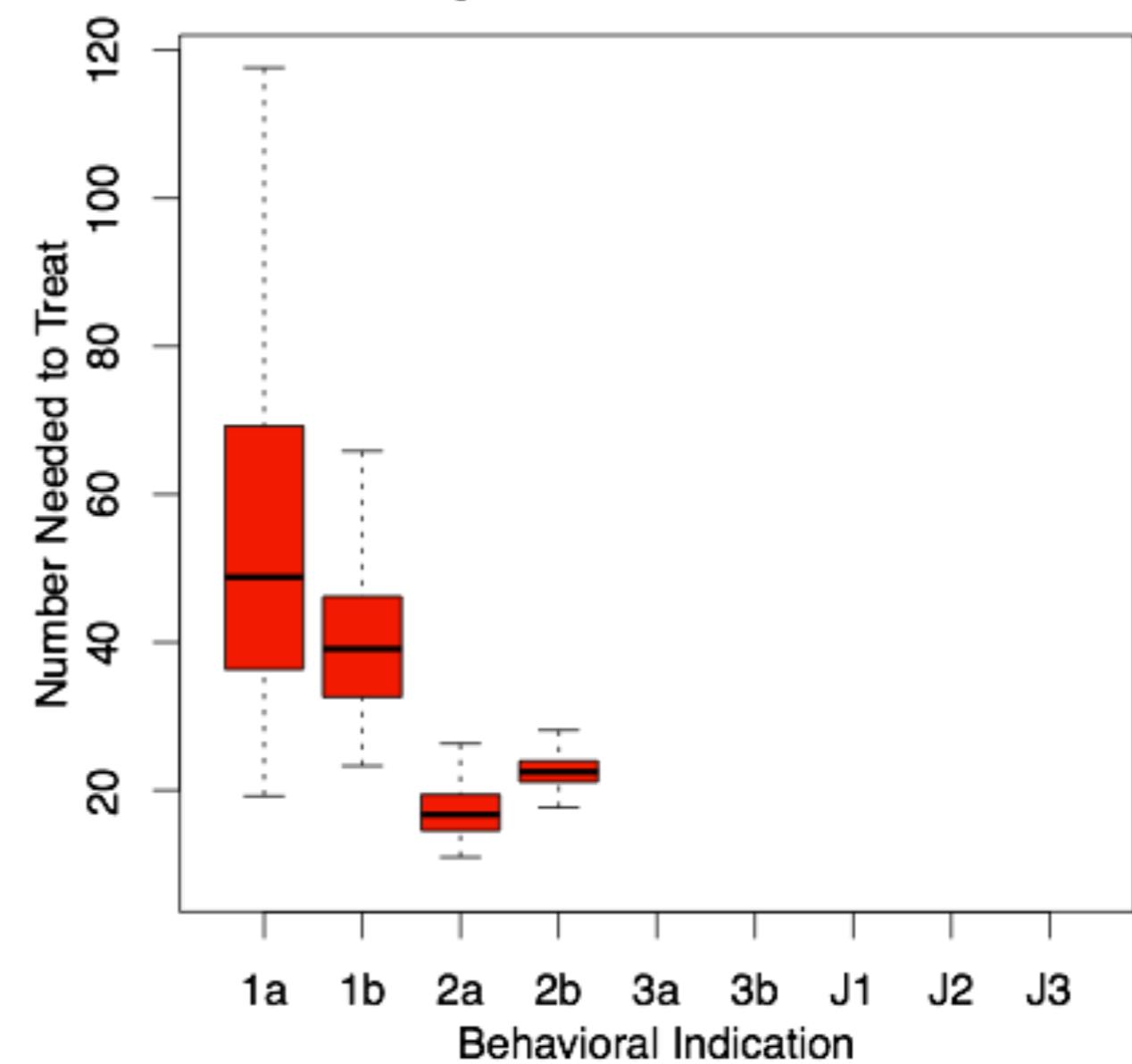
Results by CDC Guideline Indication

UAI outside of monogamous partnership

PIA by Behavioral Indication

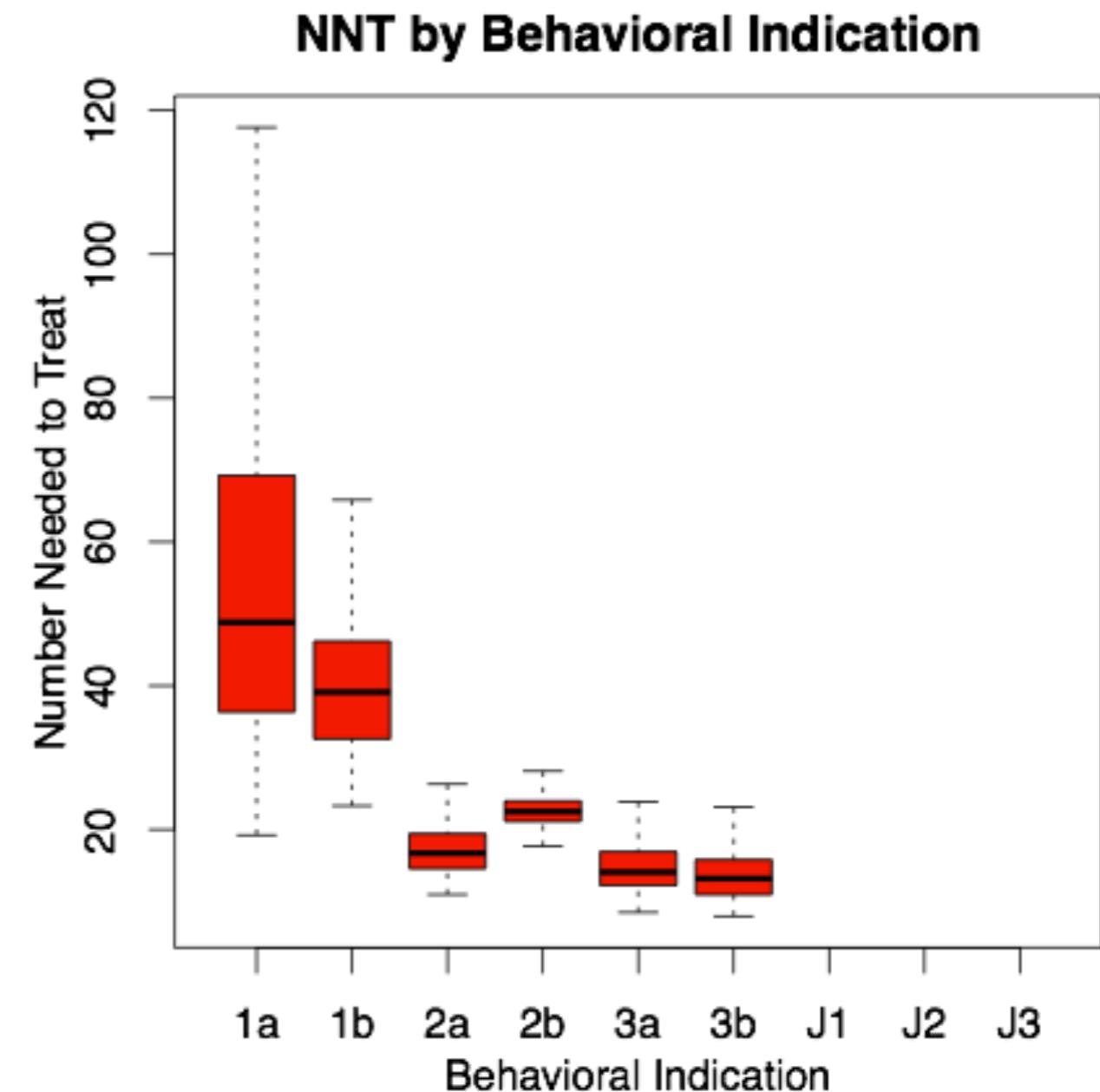
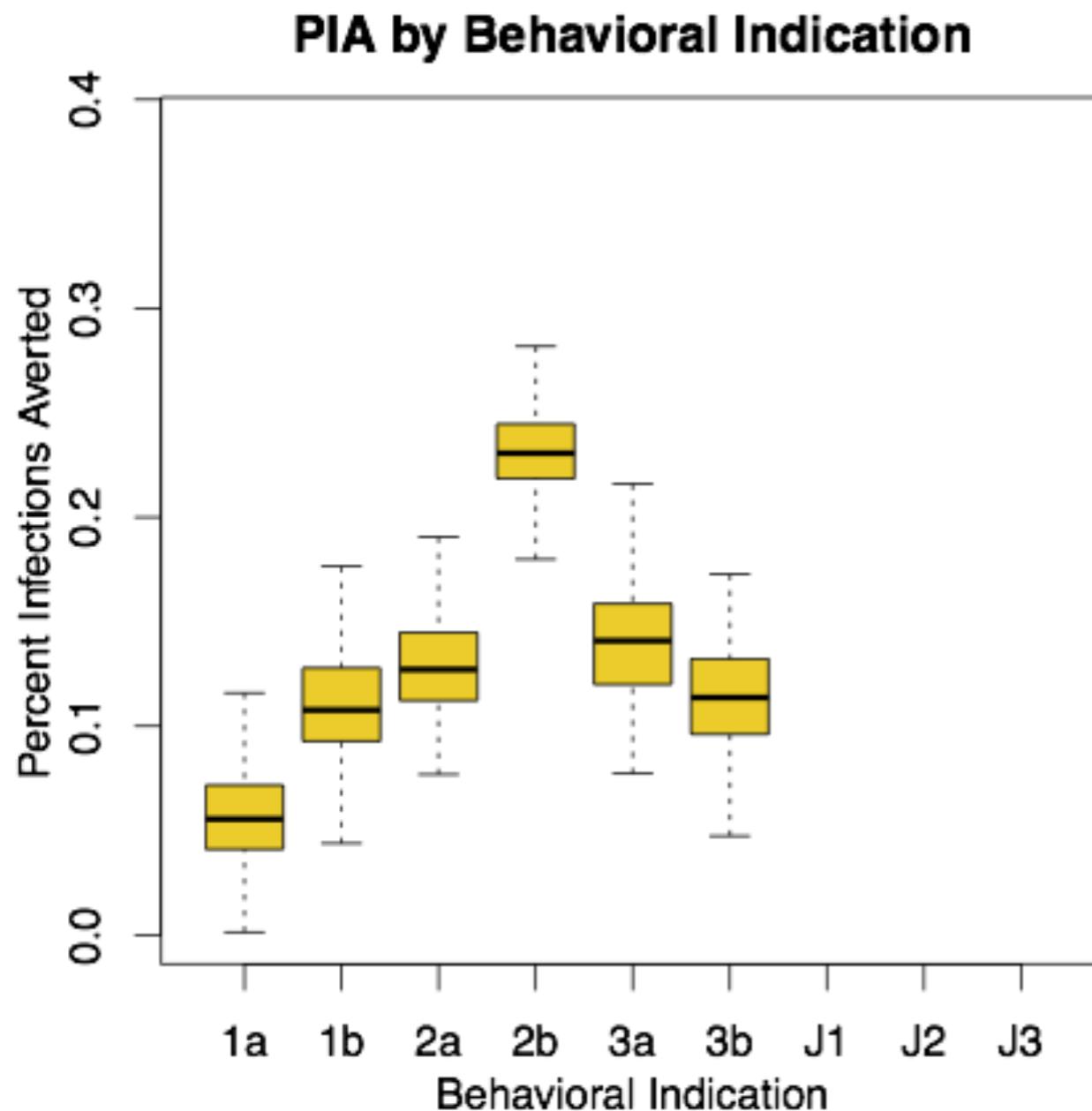


NNT by Behavioral Indication



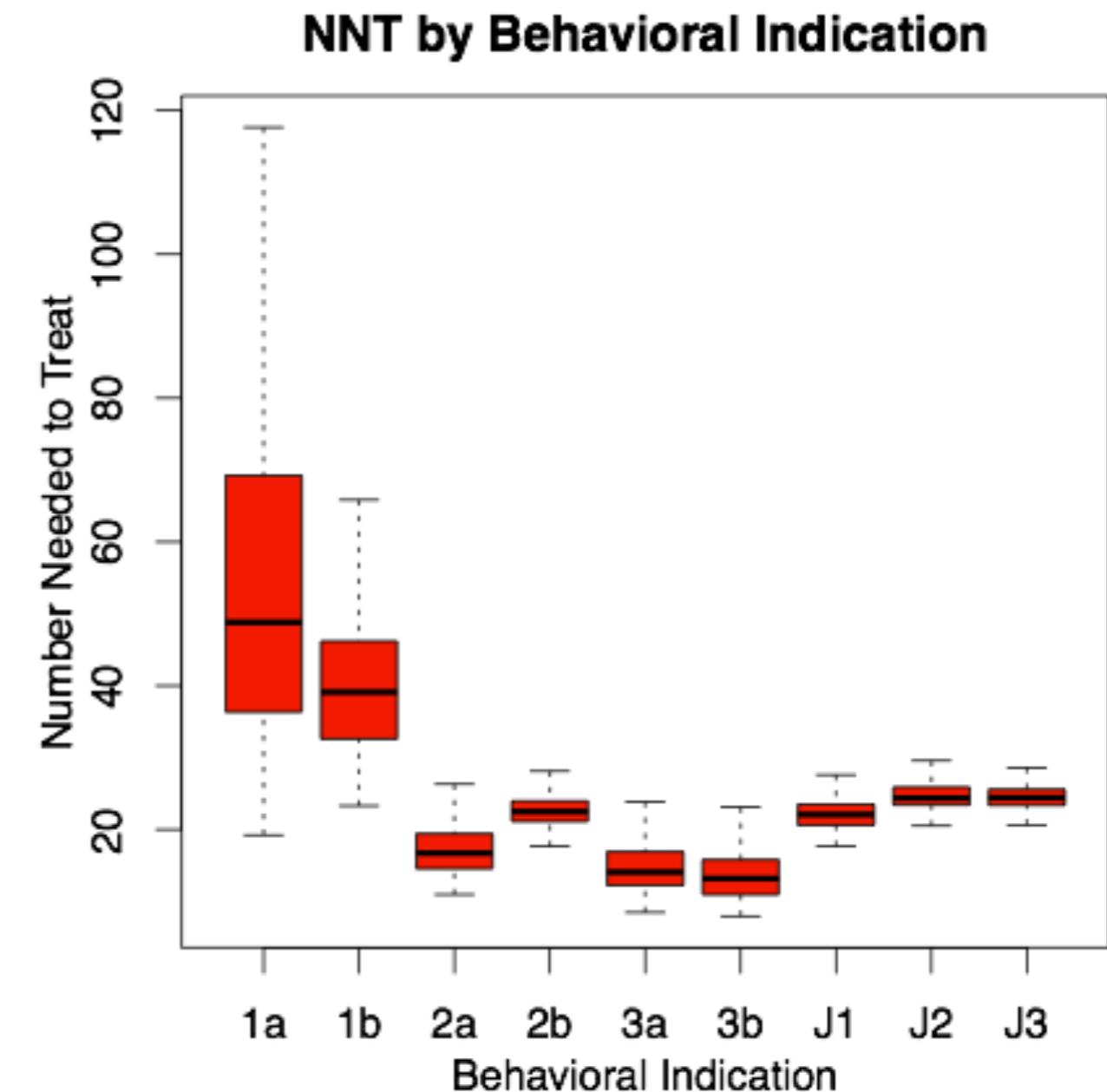
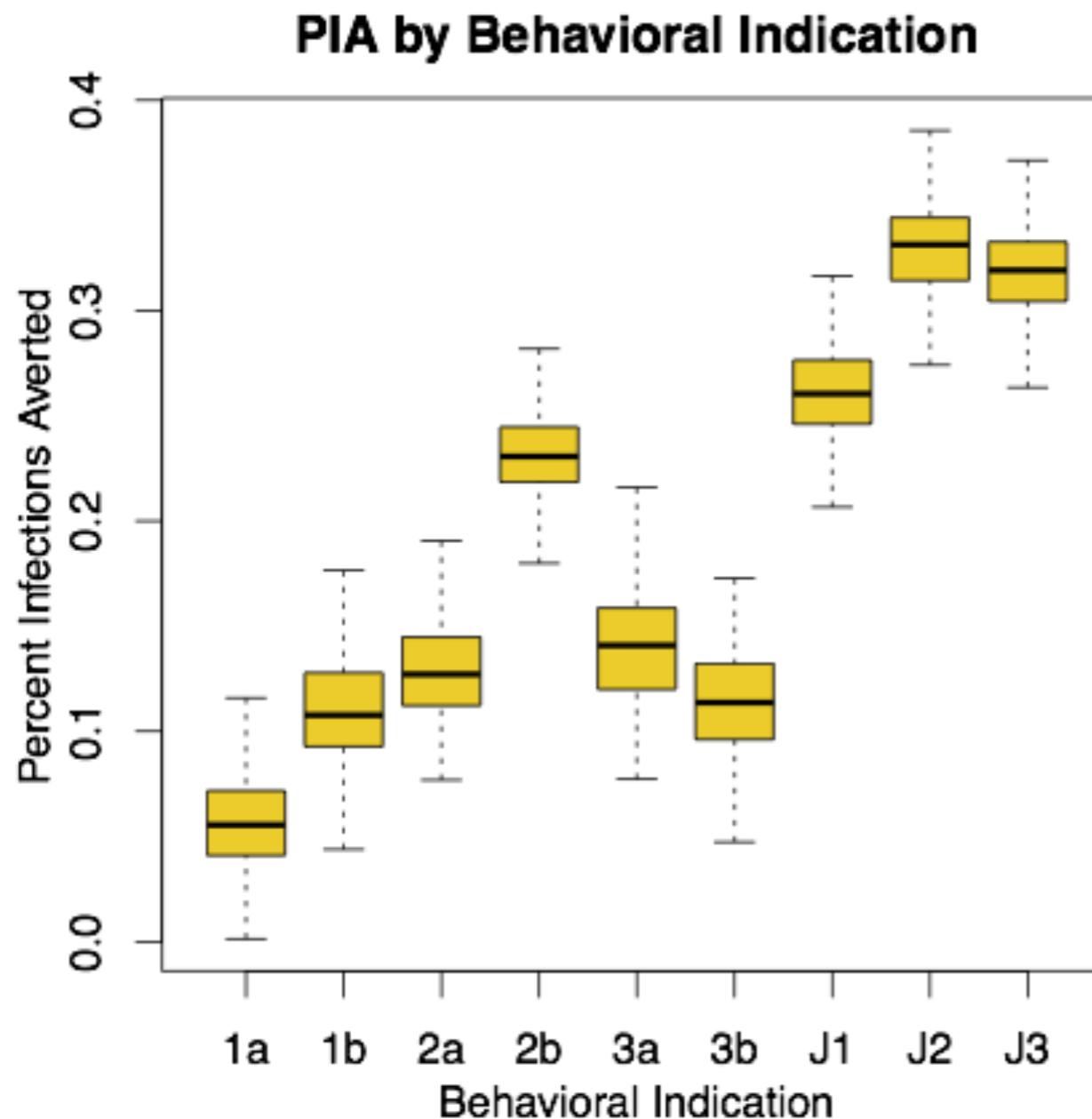
Results by CDC Guideline Indication

AI in known-serodiscordant partnership



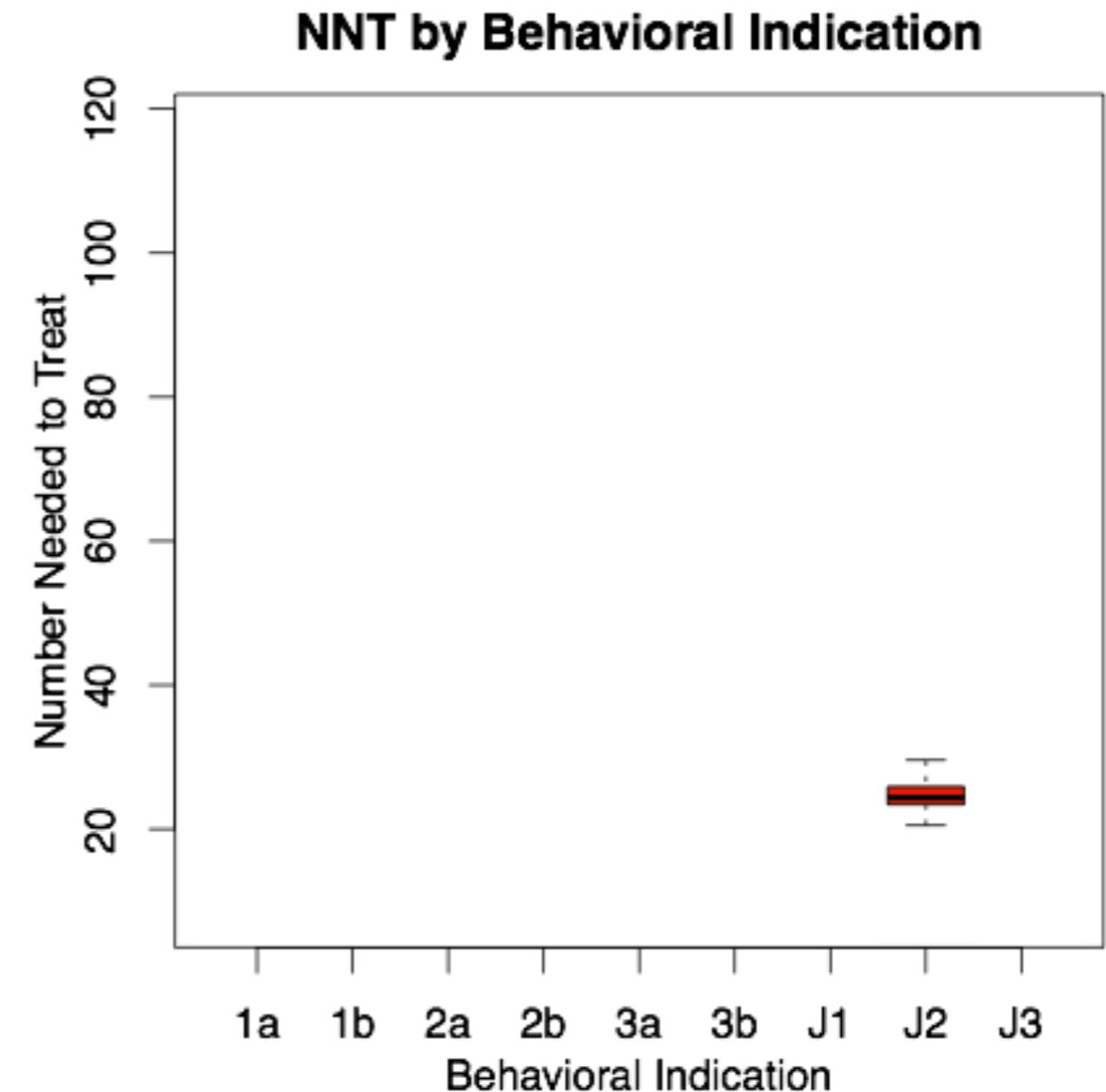
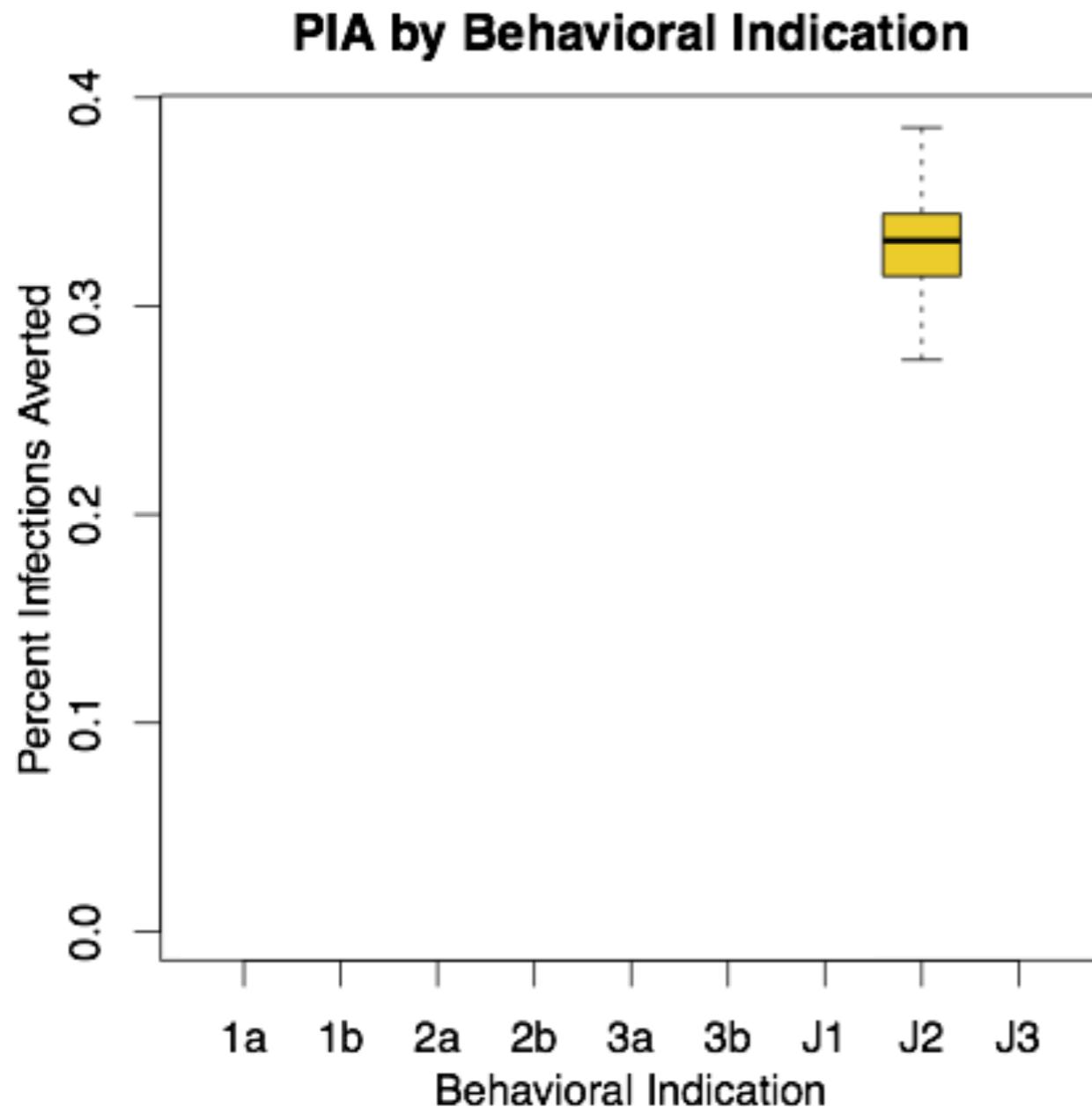
Results by CDC Guideline Indication

Joint scenarios = interpretations of CDC guidelines

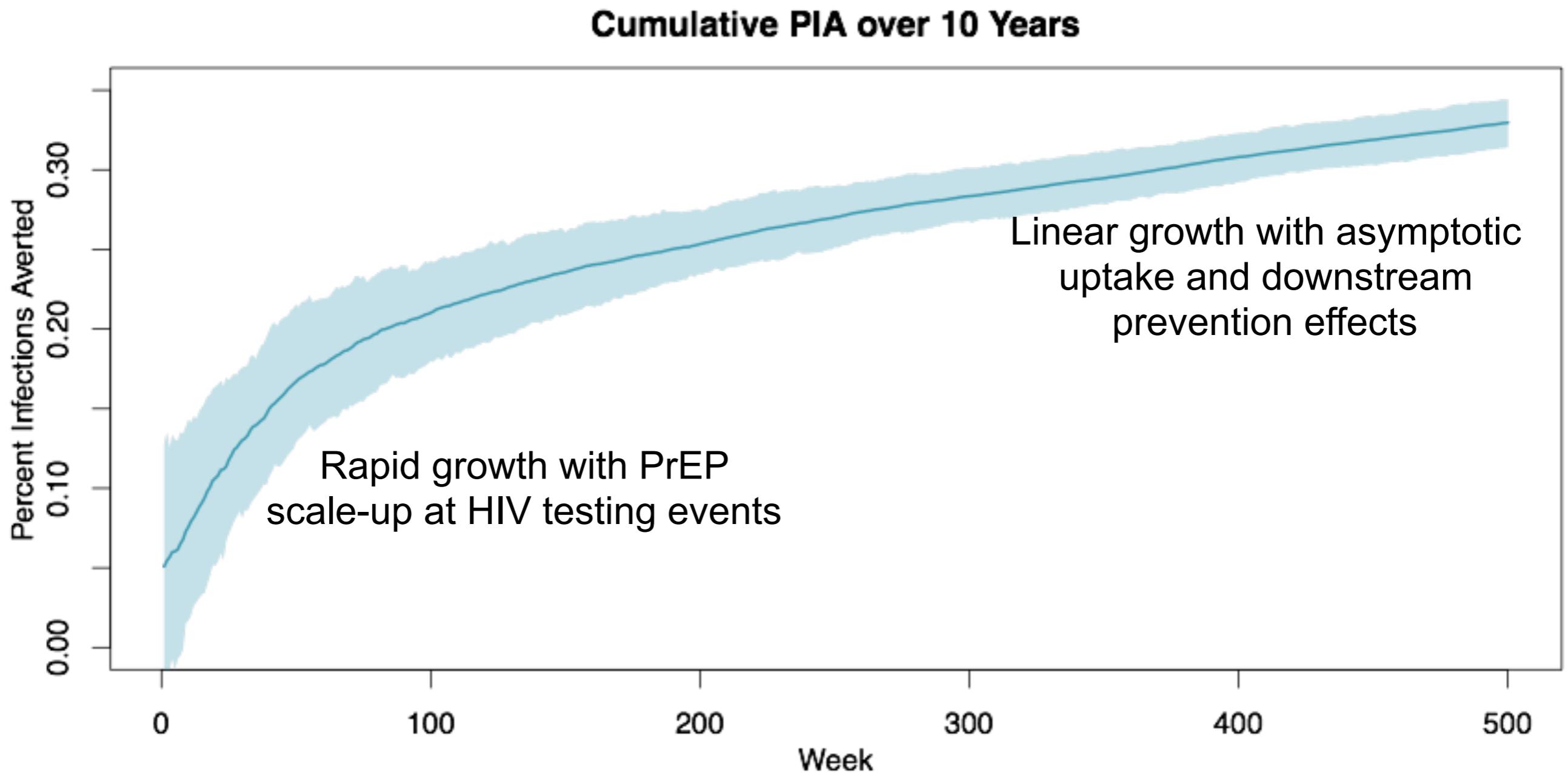


Results by CDC Guideline Indication

Joint scenarios = interpretations of CDC guidelines



Percent of Infections Averted in Joint Scenario



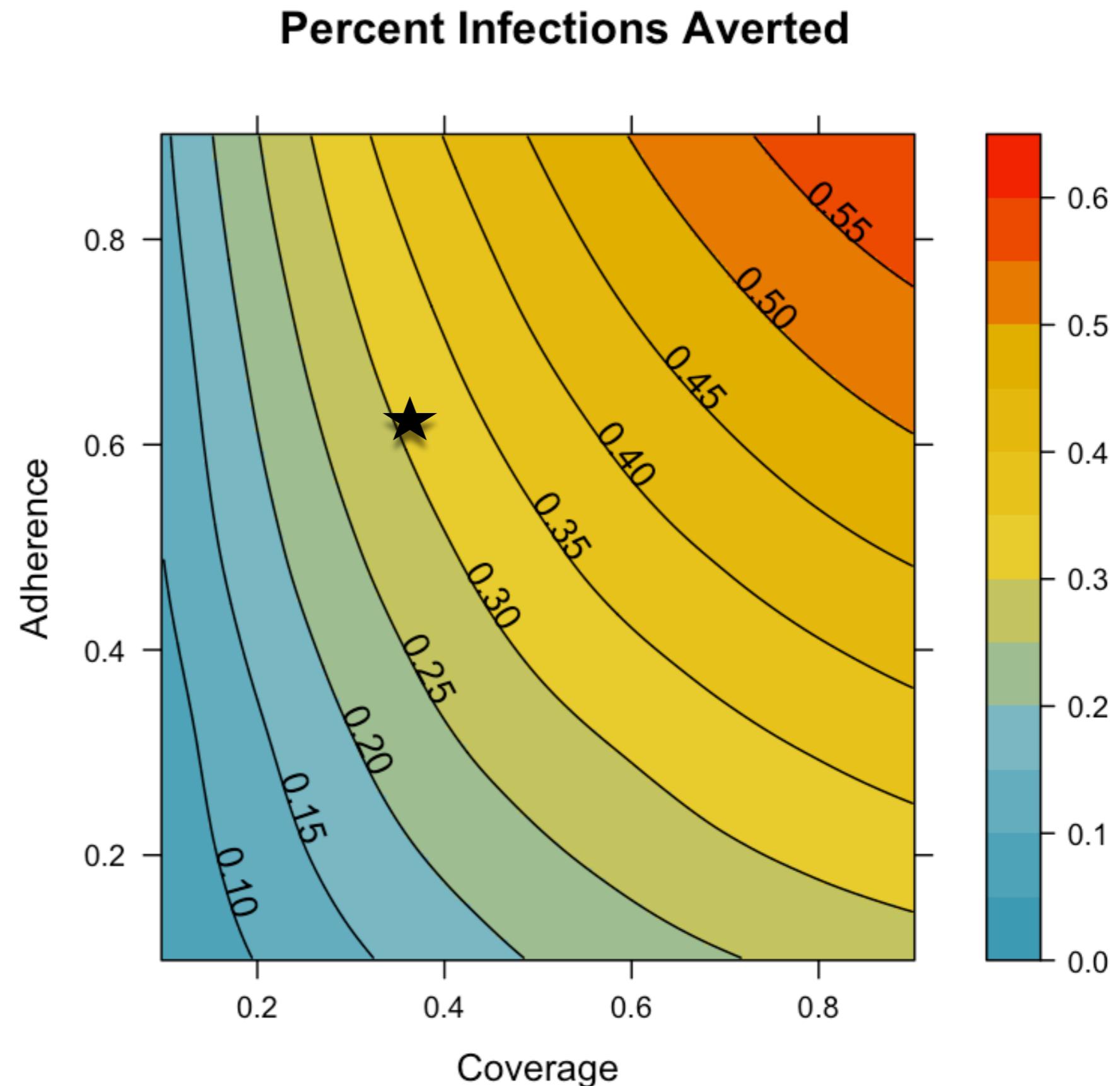
Interaction of Adherence and Coverage

Adherence

% of MSM who were highly adherent (4+ pills / week)

Coverage

% of CDC-indicated MSM who initiate PrEP



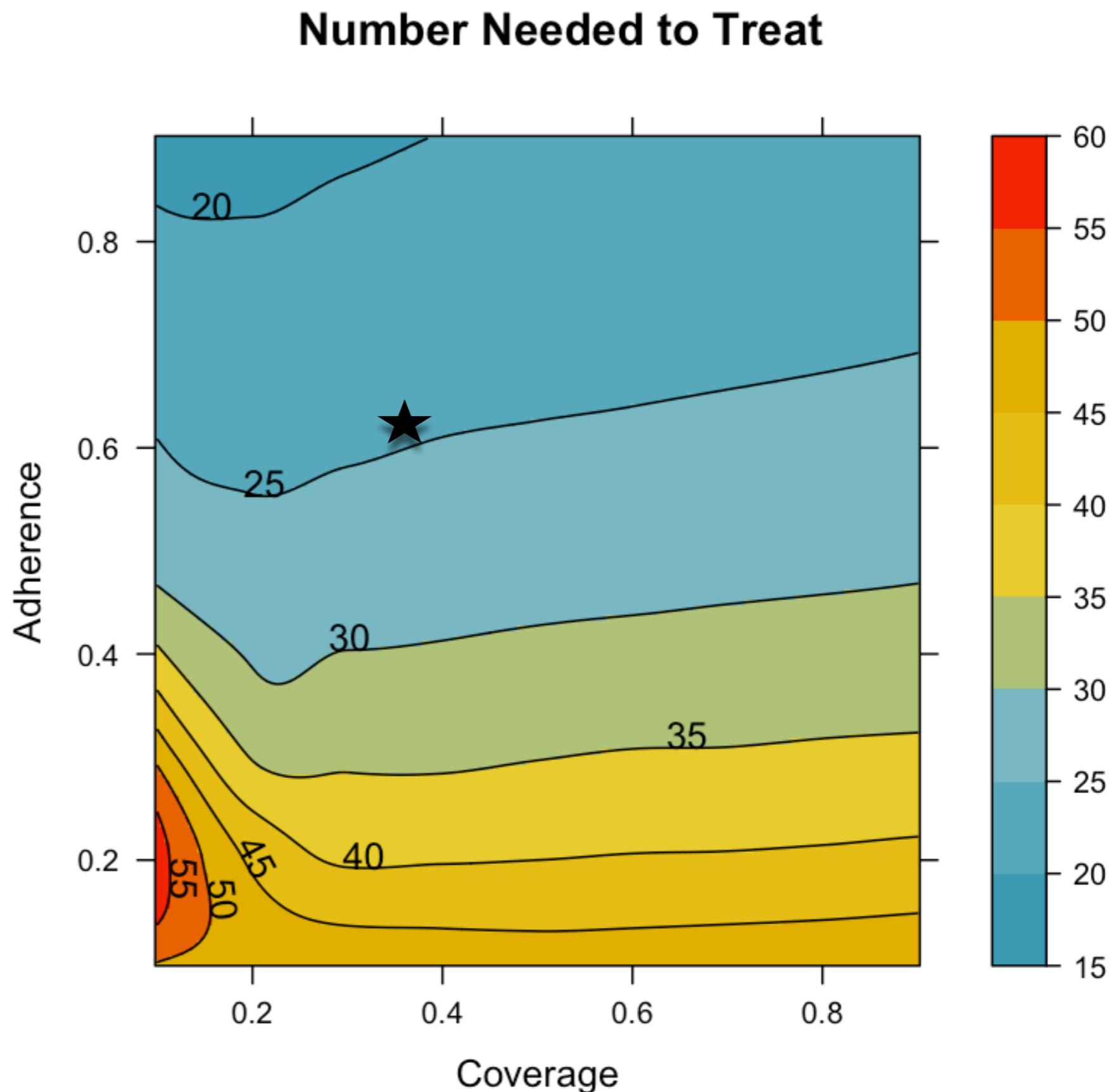
Interaction of Adherence and Coverage

Adherence

% of MSM who were highly adherent (4+ pills / week)

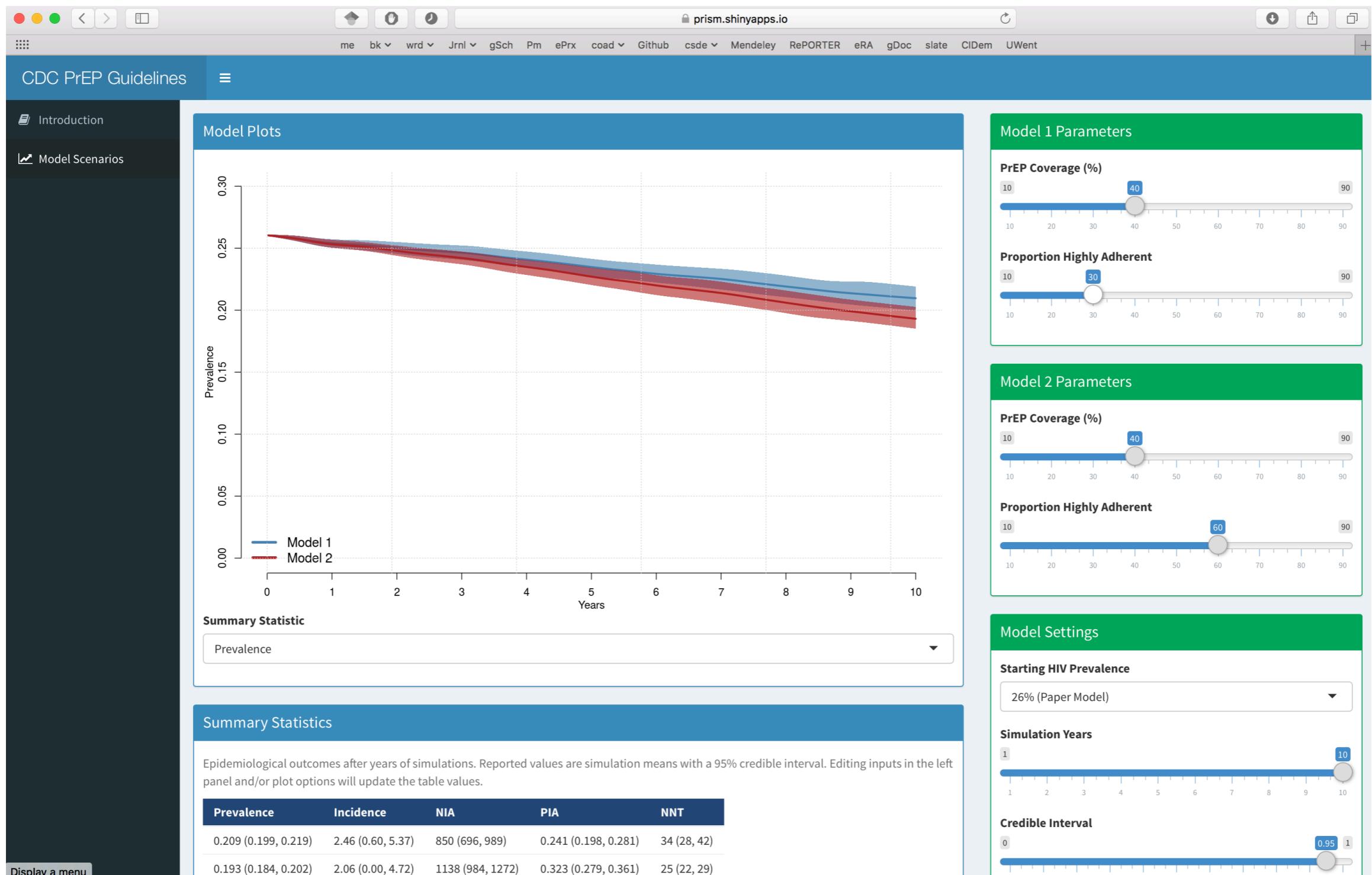
Coverage

% of CDC-indicated MSM who initiate PrEP



Web-Based Modeling Tool for Public Health Practice

<http://prism.shinyapps.io/cdc-prep-guidelines/>



Conclusions

- Implementation of CDC PrEP guidelines would avert **33% of infections** over next decade
 - Preventing one new infection would require **treating 25 MSM** for one year on PrEP
- Model-based validation of CDC guidelines for PrEP
 - Balances tradeoff of intervention effectiveness (PIA) and efficiency (NNT)
- PrEP coverage is a necessary condition, promoting adherence can only increase the PIA and reduces the NNT

Model Example 2

STI Incidence among MSM Following HIV Preexposure Prophylaxis: A Modeling Study

Samuel M. Jenness,¹ Kevin Weiss,¹ Steven M. Goodreau,² Thomas Gift,³ Harrell Chesson,³ Karen W. Hoover,³ Dawn K. Smith,³ Patrick Sullivan,¹ Eli Rosenberg¹

¹ Emory University; ² University of Washington; ³ US Centers for Disease Control and Prevention

Abstract #1034

Background

PrEP and STI Incidence among MSM

- PrEP reduces HIV risk by over 90% among MSM with high adherence.
- Public health concern about **higher incidence of bacterial STIs** among PrEP users compared to non-PrEP cohorts (Kojima, AIDS, 2016):
 - *Neisseria gonorrhoeae* (NG) rates 25 times as high (37.2 versus 4.2 per 100 PYAR).
 - *Chlamydia trachomatis* (CT) rates 11 times as high (38.0 versus 6.6 per 100 PYAR).
- Higher rates may be **causal** due to effects of PrEP or **non-causal** due to biases in comparing the two cohort groups.
- A primary **causal hypothesis is behavioral risk compensation (RC)**, where MSM may reduce condom use after starting PrEP.
- PrEP confers no biological protection against bacterial STIs.

STI Screening within PrEP Guidelines

- CDC's PrEP clinical practice guidelines recommend **biannual screening** and treatment for bacterial STIs.
- Biannual screening may **miss 40% of infections** compared to quarterly intervals (Cohen, CROI, 2016).
- **Optimizing STI screening** recommended within the guidelines may result in lower STI incidence, which would reduce HIV among non-PrEP users.

Study Aims

- To estimate how the **two potentially counteracting phenomena** surrounding PrEP use — behavioral RC and ongoing STI screening — could interact to either increase or decrease the incidence of rectal and urogenital NG and CT.

Methods

Network-Based Mathematical Model

- Extended our robust **HIV transmission model** for MSM in the United States.
- Network model for dynamics of complex predictors for main, casual, and one-off sexual partnerships using **exponential random graph models (ERGMs)**.
- Modeled **three co-circulating infections**: HIV, NG, and CT.
- **HIV model** incorporated interacting transmission and progression dynamics by HIV viral load, condom and PrEP use, sexual position, biological/genetic factors.
- **NG/CT transmission** site-specific (urethral vs rectal) with varied symptomatology.
- **NG/CT recovery** dependent on treatment status, influenced by PrEP use and symptoms.

Flowchart:

```
graph TD
    A[All MSM] --> B[Condom Use]
    A --> C[No Condom Use]
    B --> D[Asymptomatic Infection]
    B --> E[Symptomatic Infection]
    C --> F[Asymptomatic Infection]
    C --> G[Symptomatic Infection]
    D --> H[HIV Positive]
    D --> I[NG Positive]
    D --> J[CT Positive]
    E --> K[HIV Positive]
    E --> L[NG Positive]
    E --> M[CT Positive]
    F --> N[HIV Positive]
    F --> O[NG Positive]
    F --> P[CT Positive]
    G --> Q[HIV Positive]
    G --> R[NG Positive]
    G --> S[CT Positive]
    H --> T[Screening and Treatment]
    I --> T
    J --> T
    K --> T
    L --> T
    M --> T
    N --> T
    O --> T
    P --> T
    Q --> T
    R --> T
    S --> T
    T --> U[100% Not Screened and Treated]
    T --> V[75% Screened and Treated]
    T --> W[50% Screened and Treated]
    T --> X[25% Screened and Treated]
    T --> Y[10% Screened and Treated]
    T --> Z[0% Screened and Treated]
```

Results

- At 40% PrEP coverage and 40% risk compensation, 42% of GC infections and 40% of CT infections would be averted over the next 10 years.
- A **doubling of RC** would still result in **net STI prevention benefits** relative to no PrEP.

Discussion

PrEP Could Reduce STI Incidence

- Increasing uptake of PrEP along with successful completion of STI treatment after routine screening could lead to **strong and sustained declines in NG/CT incidence and prevalence among MSM**.
- PrEP-related screening would result in **early detection of many more asymptomatic rectal cases**, which often remain untreated.

No Support for the Causal Hypothesis

- Our models, calibrated to the non-PrEP cohorts, were **unable to reproduce incidence rates** close to the PrEP cohorts even under **extreme levels of RC**.
- Suggest higher incidence observed in PrEP cohorts more likely resulting from **biased comparisons between the cohorts** (e.g., selection bias) than causal from RC.

Optimizing PrEP-Related STI Screening

- **Screening interval** was strongly associated with STI incidence reductions, but even yearly screening and treatment would reduce STI incidence.
- **Clinicians have a critical role** to perform the recommended STI screening and treatment, as incidence could increase if PrEP delivered without those services.

PrEP as Combination Prevention

- MSM who are at substantial risk for HIV, and therefore indicated for PrEP, are also at risk for STIs through the same **sexual partnership networks** and behaviors.
- Our study highlights the design of PrEP not only as daily antiretroviral medication, but as a **combination HIV/STI prevention package** incorporating STI screening and treatment.

Conference on Retroviruses and Opportunistic Infections (CROI)
February 2017 // Seattle

Funding
CDC U38 PS004646
NIH R21 HD075662
NIH P30 AI050409

Contact
sjenness@emory.edu
<http://epimodel.org>
<http://samueljenness.org>

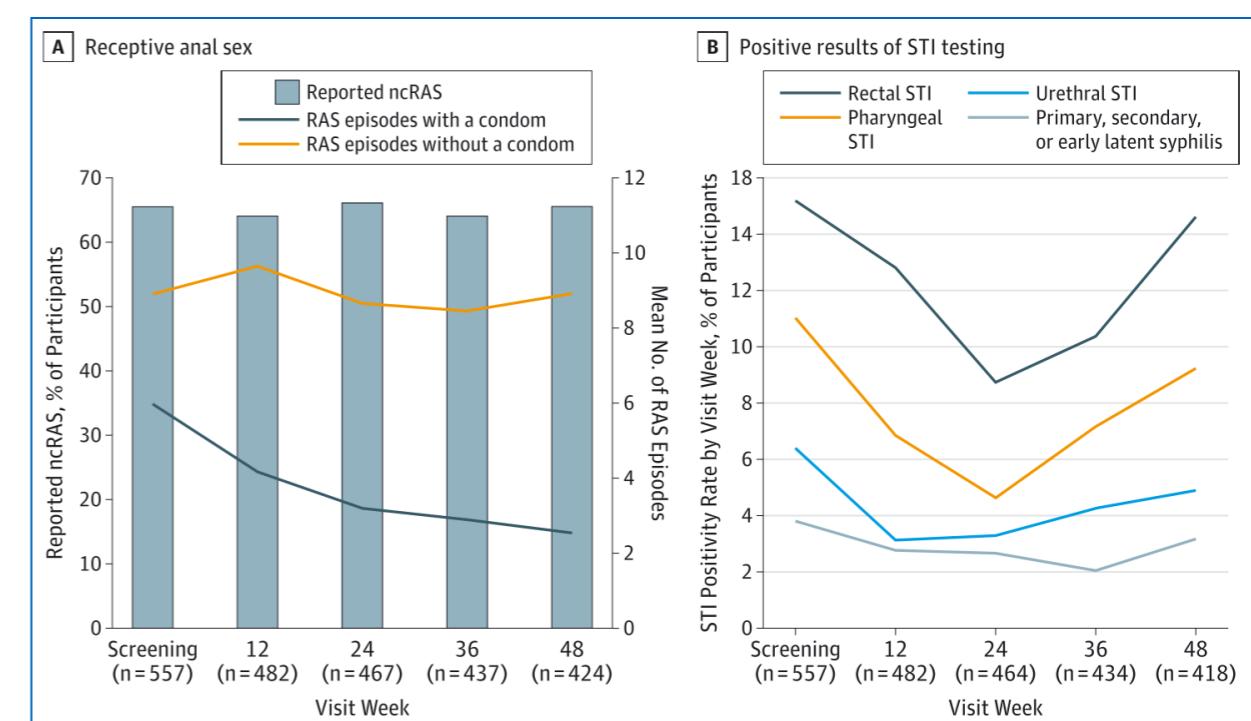
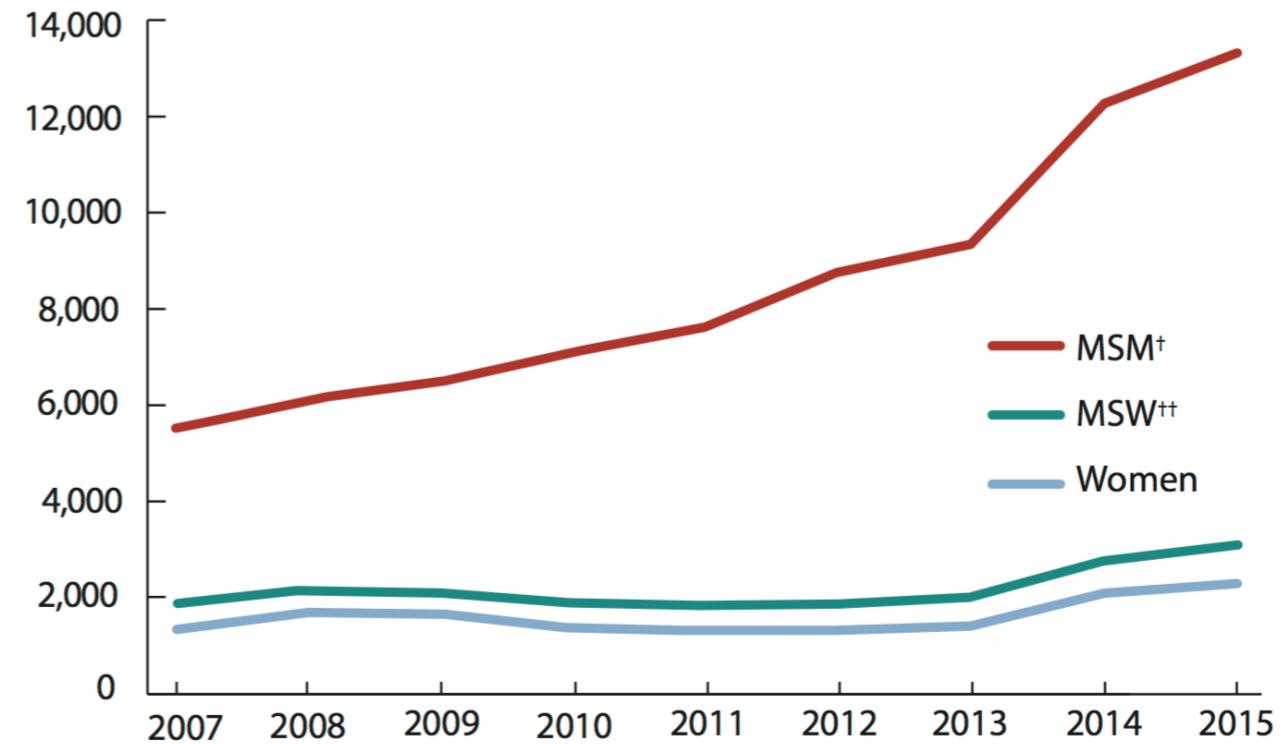
Jenness SM, Weiss KM, Goodreau SM, Rosenberg E, Gift T, Chesson H, Hoover KW, Smith DK, Liu AY, Sullivan P. Incidence of Gonorrhea and Chlamydia Following HIV Preexposure Prophylaxis among Men Who Have Sex with Men. *Clinical Infectious Diseases*. Epub ahead of print. DOI: 10.1093/cid/cix439.

33

STIs as Unintended Consequence of PrEP Uptake

- Limited but growing evidence to show that men who initiate PrEP may reduce use of condoms: risk compensation
- PrEP protects against HIV but not other STIs
- STI incidence rising before PrEP and continuing higher as PrEP use increases

Rates of Syphilis by Risk Group



The Causal Question

Table 1. Meta-analysis of studies of sexually transmitted infection incidence among men who have sex with men using pre-exposure prophylaxis for HIV versus MSM not using pre-exposure prophylaxis for HIV

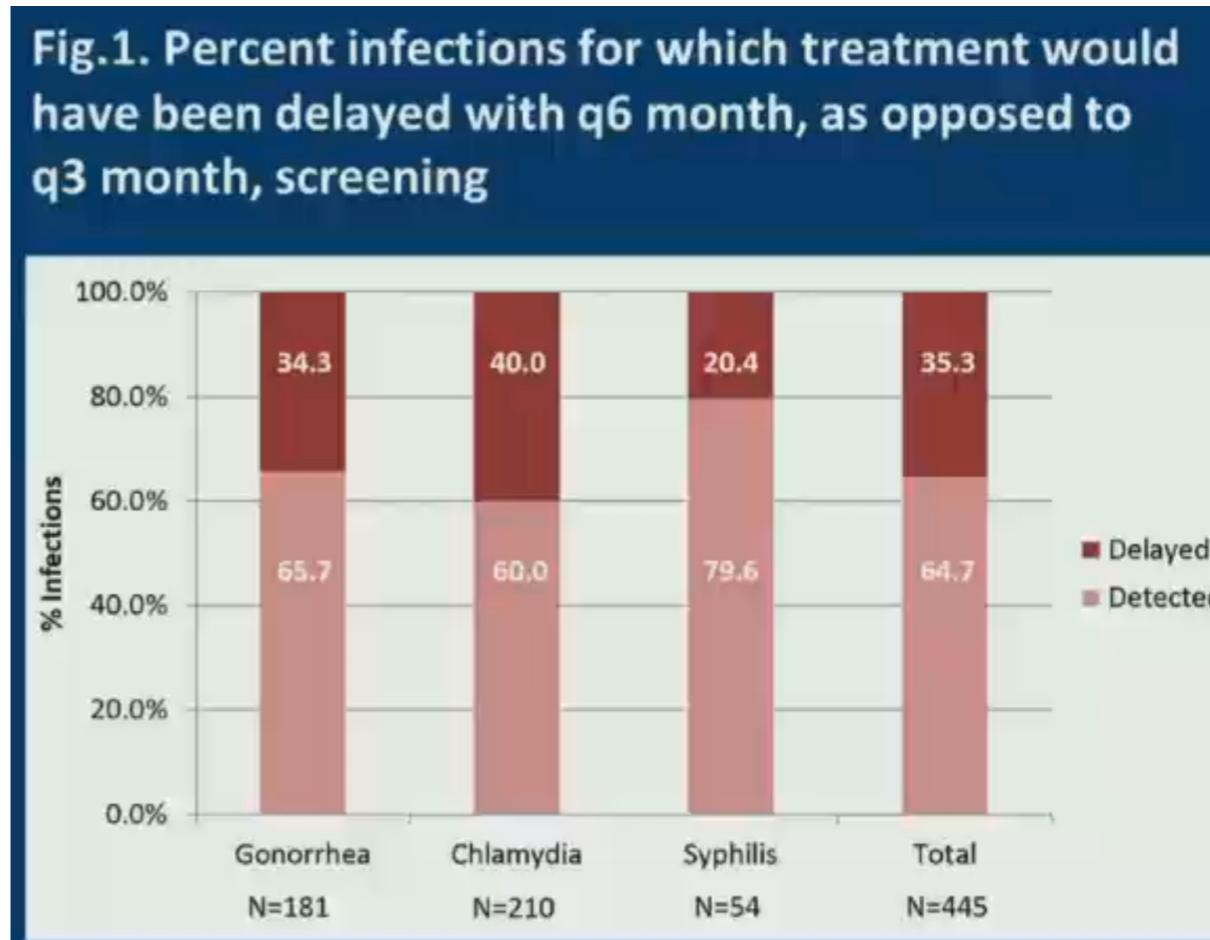
Sexually transmitted infections	MSM using PrEP			MSM not using PrEP			Incidence rate ratio, 95% CI	<i>P</i> value
	Incidence per 100 person-years, 95% CI	Number of studies	Total person-years followed	Incidence per 100 person-years, 95% CI	Number of studies	Total person-years followed		
Any <i>Neisseria gonorrhoeae</i> infection	37.5 (24.3, 50.7)	4	1561	4.2 (2.7, 5.7)	5	43 294	25.3 (22.6, 28.4)	<0.001 or <0.001
Any <i>Chlamydia trachomatis</i> infection	38.0 (20.3, 55.7)	4	1561	6.6 (3.8, 9.4)	6	54 703	11.2 (10.2, 12.3)	<0.001 or <0.001
Syphilis	14.5 (3.8, 25.2)	5	4887	0.9 (0.6, 1.3)	11	50 957	44.6 (39.1, 51.1)	<0.001 or <0.001

Shown are crude incidence per 100 person-years and crude incidence rate ratios with 95% confidence intervals and *P* values. Studies included are from 2010 to 2016 for MSM using PrEP infection and from 1998 to 2016 for studies in MSM not using PrEP infection. CI, confidence interval; PrEP, pre-exposure prophylaxis.

- STI incidence 11 to 45 times higher in “PrEP cohorts” compared to “non-PrEP cohorts”
- Several potential explanations why, but is it causal? Non-causal explanations include secular trends, diagnostic biases, selection effects

Optimizing STI Screening and Treatment

- Cohen et al. found that biannual STI screening would delay treatment of 35% of STIs in MSM using PrEP compared to quarterly screening
- Prevention issue: 3 more partners (median) exposed with less frequent testing
- Questions about how to optimize the CDC guidelines with respect to STIs



Study Aims

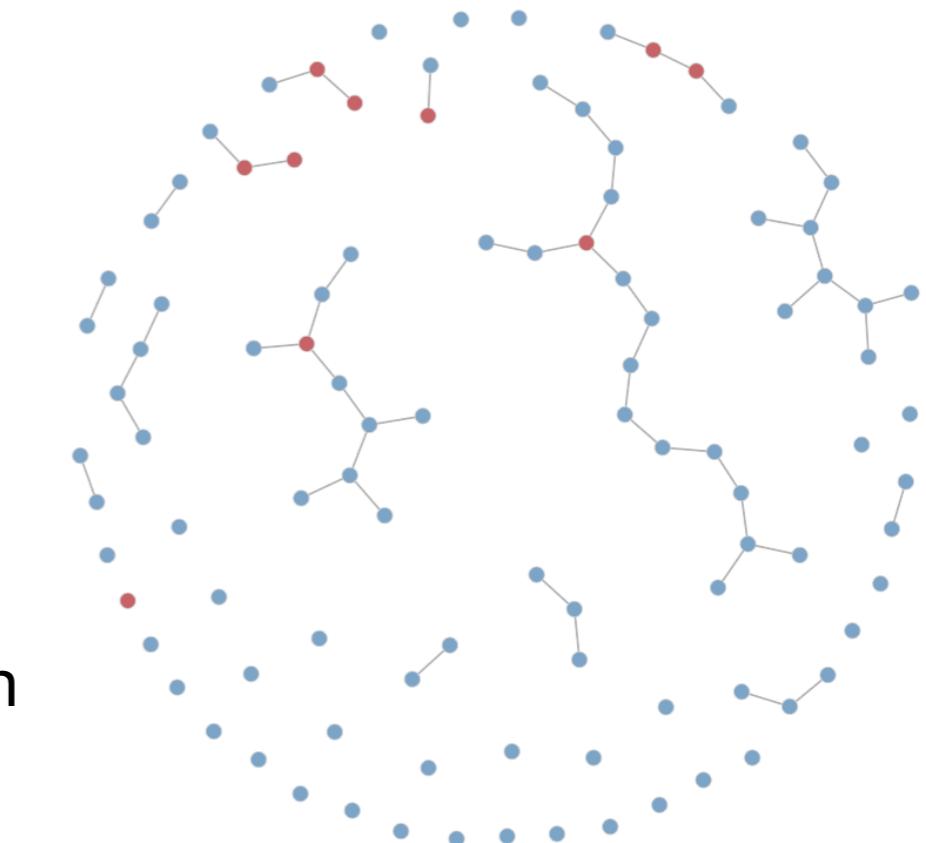
- Develop a mathematical model for transmission of urogenital and rectal GC and CT transmission dynamics among MSM in the US
- Investigate evidence for the causal versus non-causal contributions of risk compensation to higher STI incidence in PrEP users
- Estimate the impact of the CDC PrEP guidelines on STI incidence among MSM

Methods Overview

- Stochastic network-based mathematical model
- Robust sexual behavioral and clinical epidemiology based on local (Atlanta) and national parameters
- Epidemiological, demographic, and intervention modules designed in EpiModel software (www.epimodel.org)
- Simulates open population of adult MSM in the US over a 10-year time span

Disease Transmission over Dynamic Sexual Networks

- Temporal exponential random graph models (ERGMs) define partnership formation and dissolution
 - Sexual network types: main, casual, one-off
 - Men form partnerships according to model terms based on numbers of each partner type, mixing on race and age, sexual role segregation
- HIV epidemiology
 - Natural history (disease stages, continuous VL, HIV-related mortality)
 - ART initiation and adherence
 - HIV transmission dynamics within serodiscordant partnerships
- Demographic processes (births and deaths)

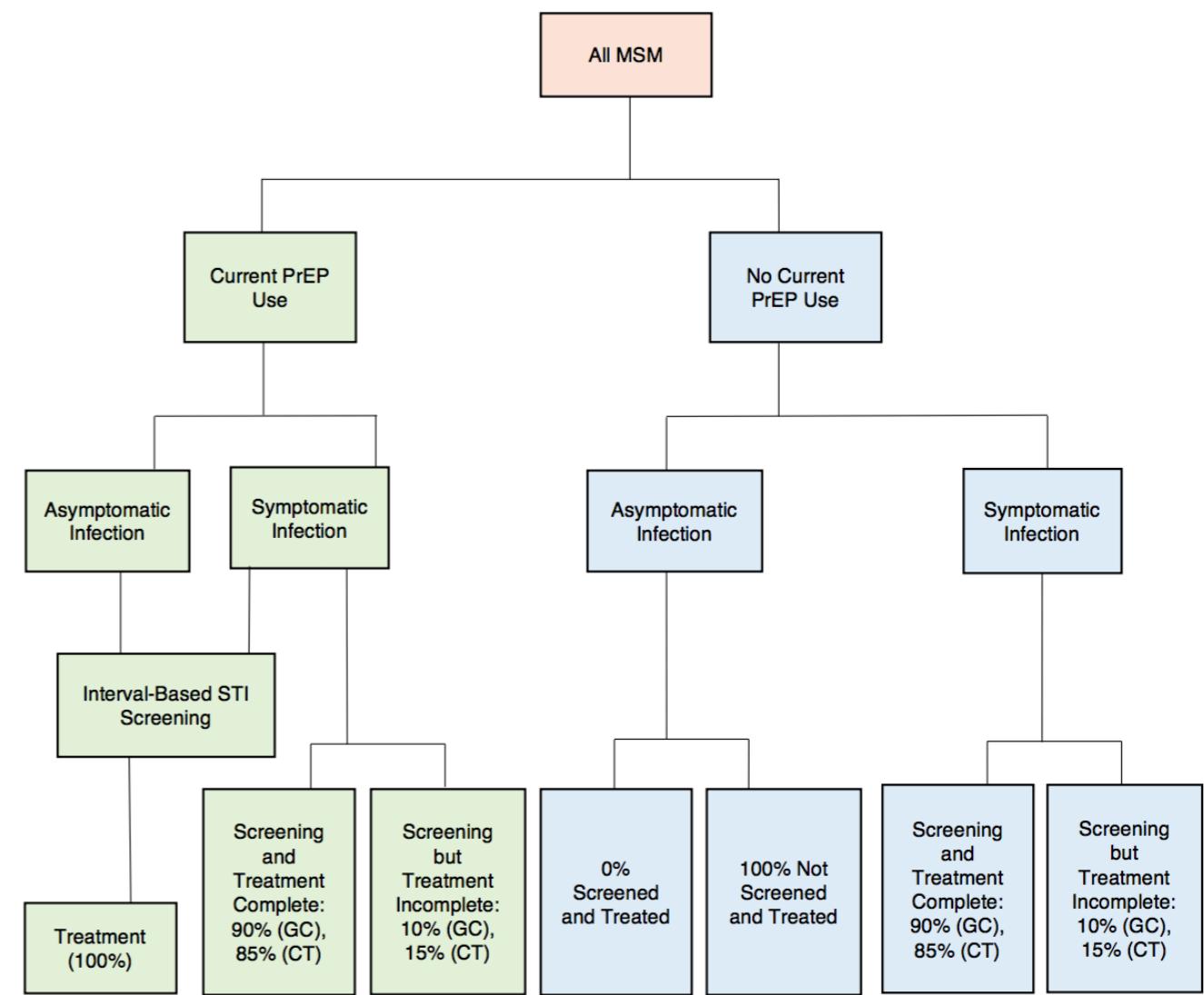


PrEP Initiation and Adherence

- Initiation
 - HIV-uninfected men encounter diagnostic HIV testing
 - Risk assessment for PrEP over past 6-month window based on CDC indications
 - Indicated men start PrEP if the % of already initiated men is less than a **fixed coverage threshold** (40% in base models)
- Adherence
 - Men assigned a **fixed adherence profile** following PrEP demonstration project data (62% high, 10% moderate, 7% low, and 21% null adherence)
 - Adherence translates into a 95%, 81%, 31%, and 0% reduction in transmission risk
 - Men **discontinued** from PrEP if, at yearly follow-up visit, no longer behavioral indications

GC/CT Transmission, Treatment, and Recovery

- Urogenital and rectal GC and CT transmission directional by receptive versus insertive sexual act
- Infection site strongly associated with probability of disease symptoms
- Disease symptoms strongly associated with treatment outside of PrEP
- PrEP added biannual interval-based screening and treatment for both symptomatic and asymptomatic infections
- MSM on PrEP could exhibit varying levels of condom-related risk compensation
- Other sensitivity analyses for PrEP coverage and STI screening interval



GC and CT Incidence by Coverage and RC

Table 1. Gonorrhea and Chlamydia Incidence Rates, Hazard Ratios, Percent of Infections Averted, and Number Needed to Treat (NNT) on PrEP, by PrEP Coverage Level and Behavioral Risk Compensation Level among Men Who Have Sex with Men in the United States

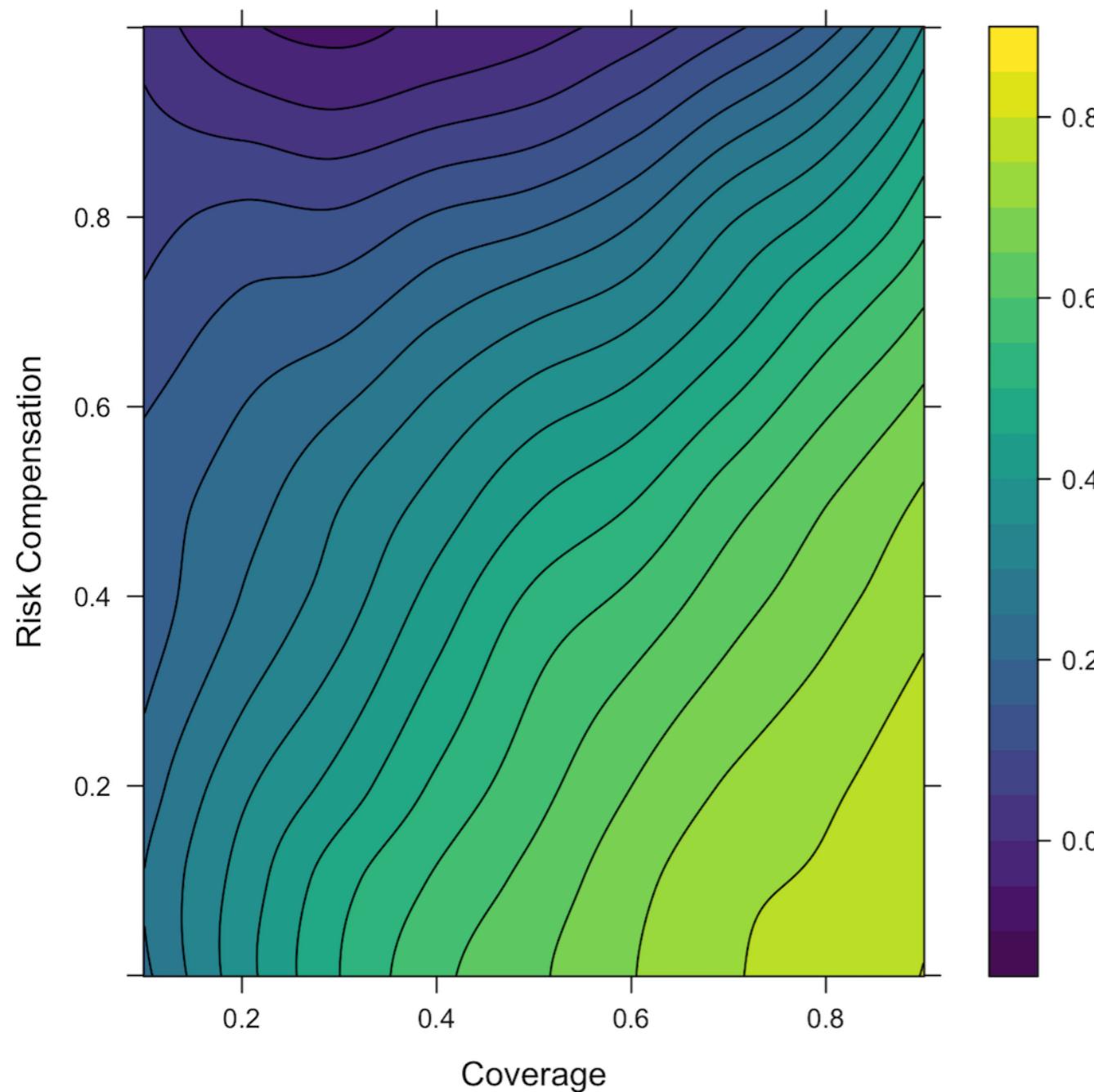
Model Scenario	Gonorrhea			Chlamydia		
	Incidence (IQR)	Hazard Ratio (IQR)	PIA (IQR)	Incidence (IQR)	Hazard Ratio (IQR)	PIA (IQR)
Base Model (No PrEP)	4.35 (2.57, 5.73)	1.00	-	6.76 (5.47, 8.03)	1.00	-
PrEP Coverage						
10%	3.36 (2.57, 4.38)	0.76 (0.53, 1.13)	15.5 (-13.0, 41.5)	5.38 (4.54, 6.57)	0.83 (0.64, 1.06)	10.5 (-9.1, 23.9)
40% (Ref)	1.38 (0.80, 2.18)	0.32 (0.19, 0.48)	41.6 (20.8, 56.7)	2.08 (1.57, 2.61)	0.30 (0.22, 0.42)	40.3 (23.5, 49.3)
90%	0.00 (0.00, 0.06)	0.00 (0.00, 0.02)	73.2 (62.2, 80.8)	0.04 (0.00, 0.17)	0.01 (0.00, 0.03)	70.5 (63.3, 74.9)
Risk Compensation						
0%	0.51 (0.19, 0.92)	0.11 (0.05, 0.24)	58.0 (39.1, 71.6)	1.13 (0.80, 1.51)	0.17 (0.11, 0.24)	51.0 (41.8, 59.4)
40% (Ref)	1.38 (0.80, 2.18)	0.32 (0.19, 0.48)	41.6 (20.8, 56.7)	2.08 (1.57, 2.61)	0.30 (0.22, 0.42)	40.3 (23.5, 49.3)
100%	5.64 (3.81, 7.08)	1.21 (0.83, 1.86)	-3.2 (-39.9, 23.9)	5.74 (4.77, 6.74)	0.84 (0.66, 1.08)	6.2 (-11.3, 21.1)

IQR = interquartile range (25% and 75% percentiles) of the simulation outcomes. Incidence expressed per 100 person-years at risk.

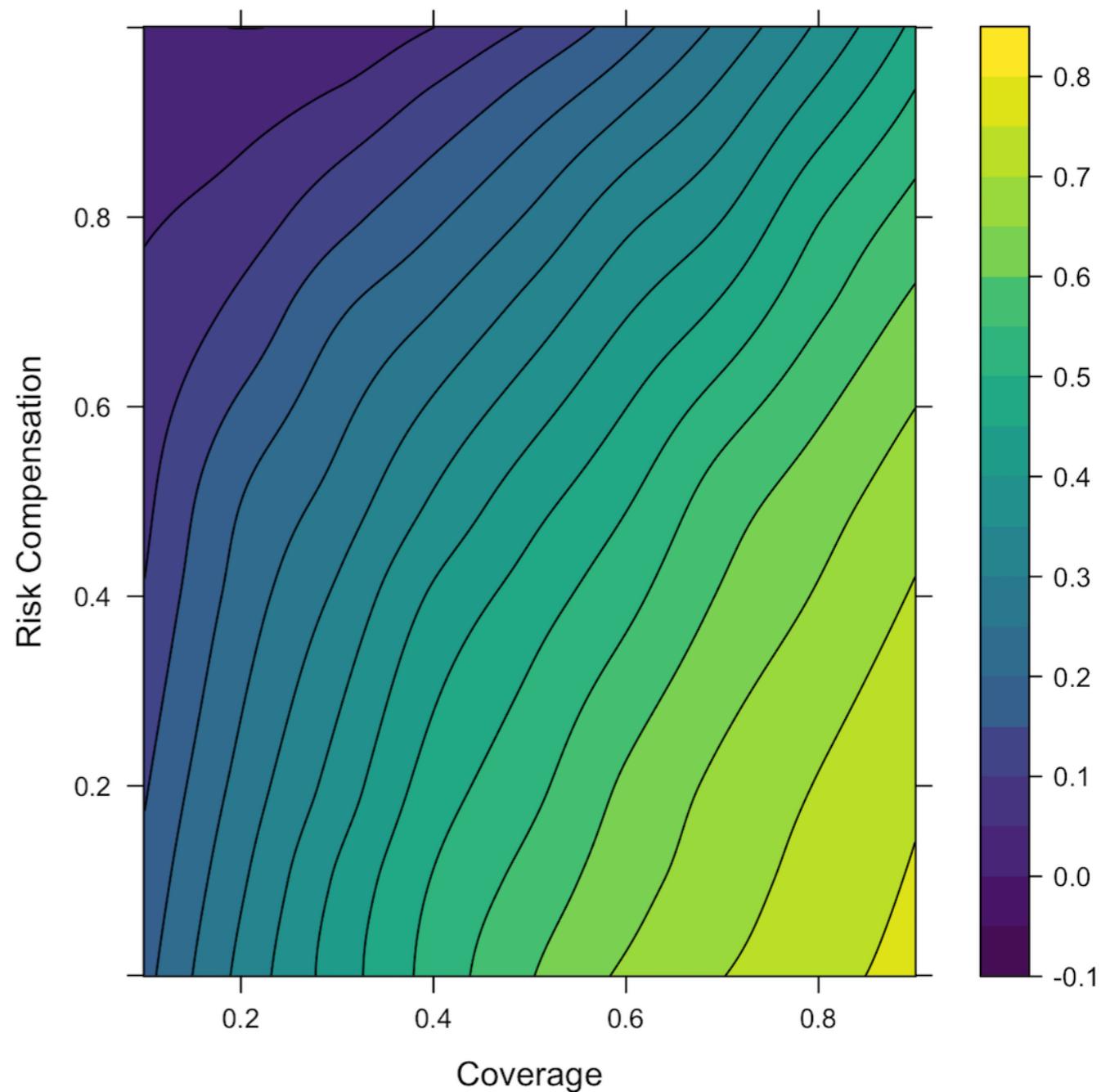
- Compared to no PrEP (base model), 40% coverage and 40% RC associated with a major reduction in both GC and CT incidence
- Measured reduction in hazard ratio at end of time series (HR) and percent of infections averted (relative to base model) cumulatively

GC and CT Infections Averted by Coverage and RC

Percent GC Infections Averted

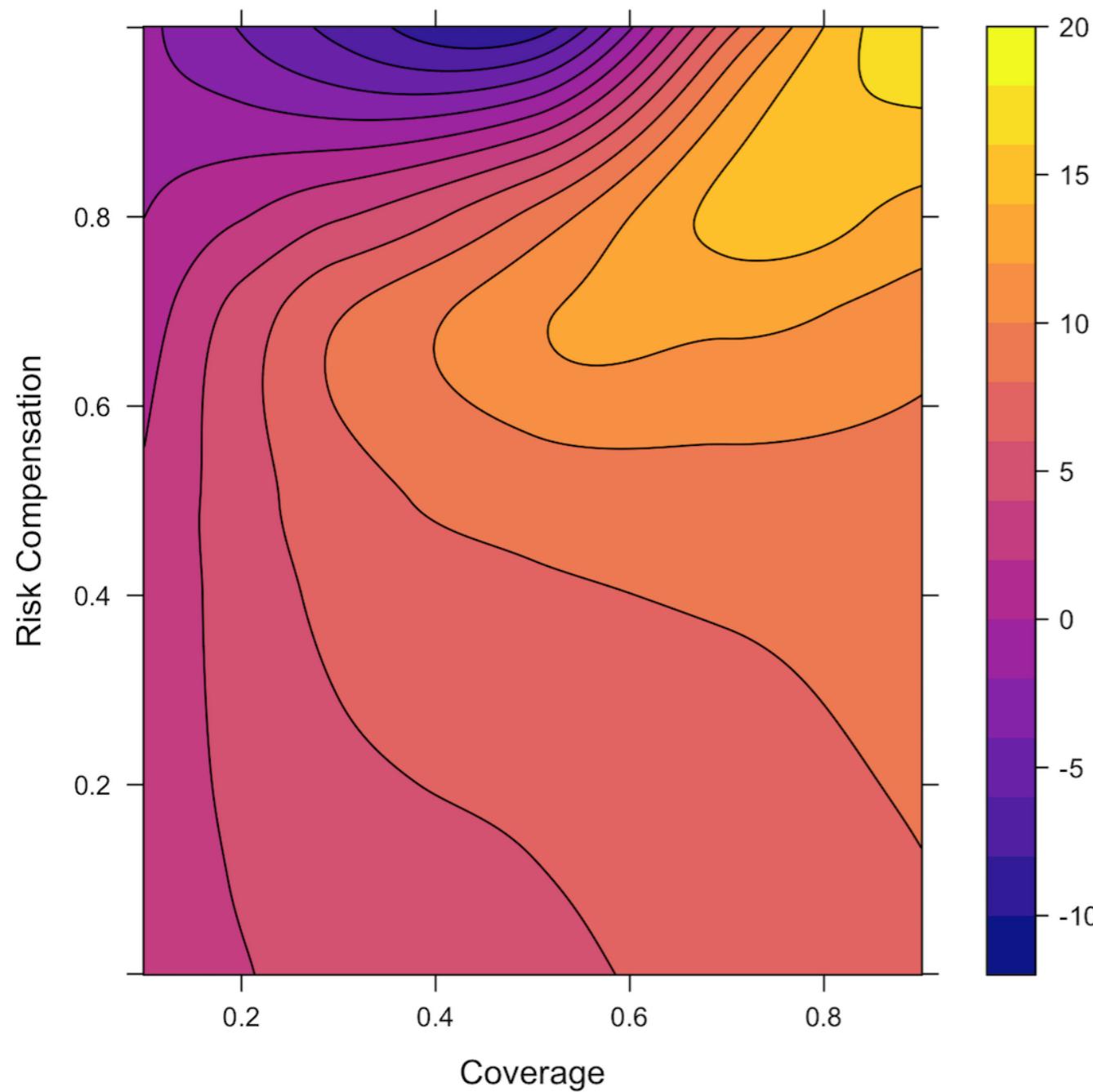


Percent CT Infections Averted

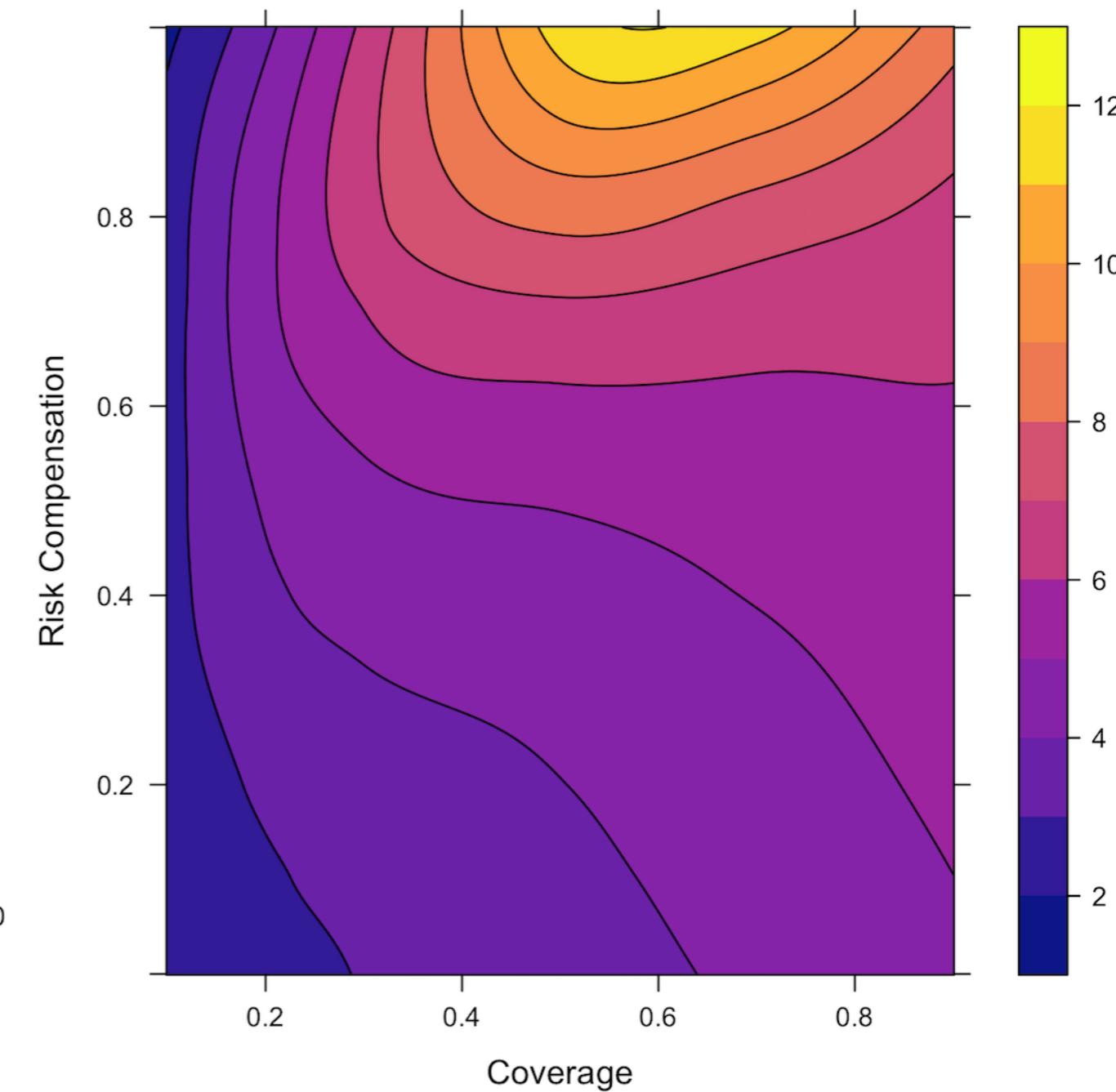


NNT on PrEP to Prevent One New GC or CT Infection

Number Needed to Treat (GC)



Number Needed to Treat (CT)



Mechanisms of PrEP-Related STI Prevention

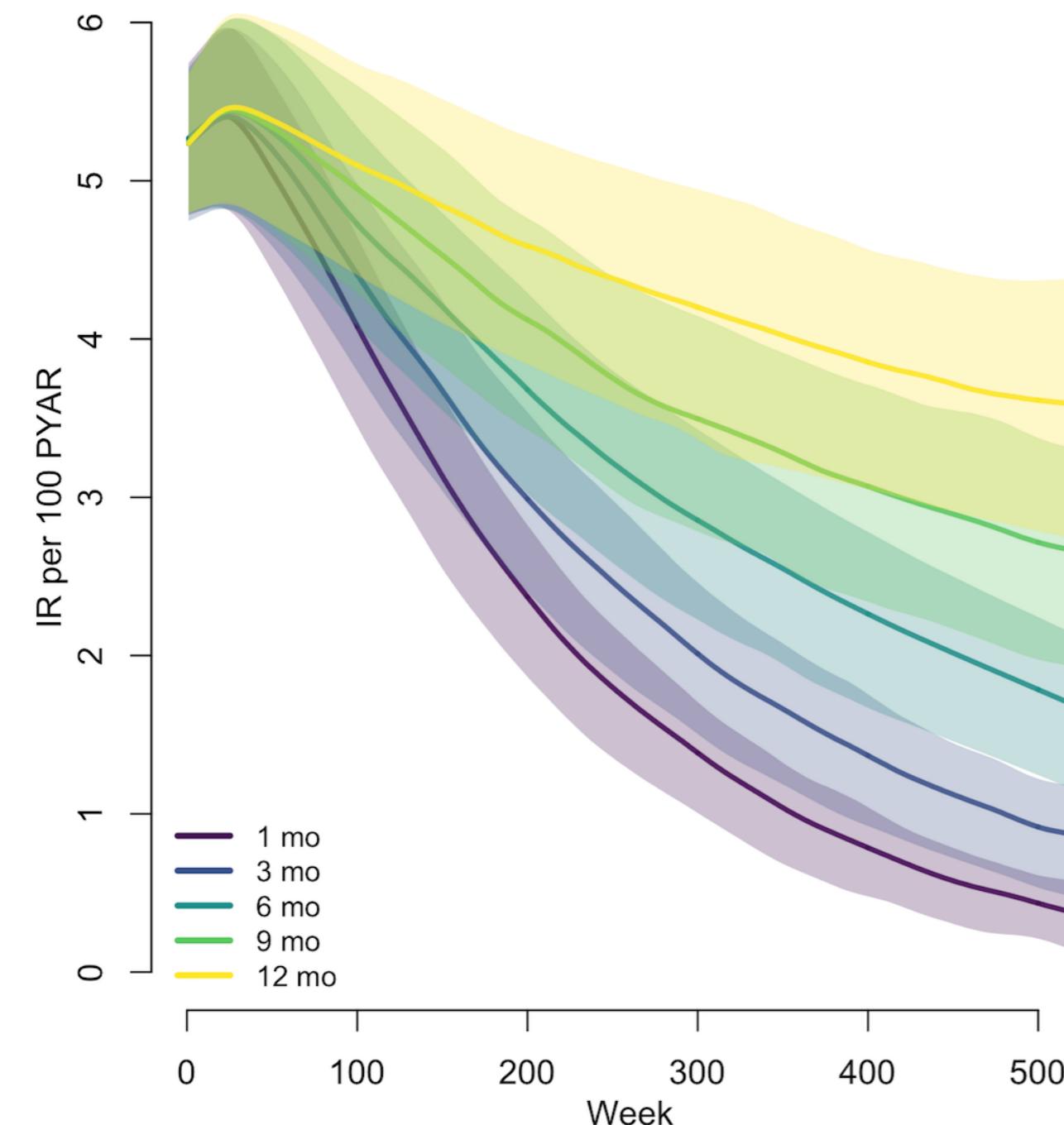
Table 2. Gonorrhea and Chlamydia Incidence Rates, Hazard Ratios, Percent of Infections Averted, and Number Needed to Treat (NNT) on PrEP, by PrEP Coverage Level and Behavioral Risk Compensation Level among Men Who Have Sex with Men in the United States

Model Scenario	Incidence (IQR)		Asymptomatic Cases Treated (%; IQR)	Rectal Cases Treated (%; IQR)
	All MSM	PrEP Users	All MSM	All MSM
Base Model (No PrEP)	5.32 (4.41, 6.38)	—	0 (0, 0)	8.2 (7.9, 8.4)
PrEP Scenarios				
<i>STI Testing Interval</i>				
1 month	0.40 (0.30, 0.58)	0.45 (0.29, 0.63)	26.4 (25.6, 27.2)	33.5 (32.5, 34.4)
3 months	0.89 (0.65, 1.18)	0.93 (0.65, 1.27)	21.3 (20.6, 21.9)	28.3 (27.6, 29.0)
6 months (ref)	1.77 (1.34, 2.16)	1.85 (1.42, 2.24)	17.3 (16.9, 17.8)	24.4 (23.7, 25.2)
9 months	2.68 (2.16, 3.22)	2.75 (2.17, 3.52)	14.9 (14.6, 15.4)	22.2 (21.7, 22.8)
12 months	3.58 (2.97, 4.25)	3.71 (3.00, 4.45)	13.3 (12.8, 13.6)	20.6 (20.1, 21.2)
<i>Proportion of Screened PrEP Users Treated</i>				
0%	13.40 (12.13, 14.62)	13.58 (12.15, 14.78)	0 (0, 0)	8.0 (7.7, 8.1)
25%	9.07 (7.87, 10.03)	9.36 (8.18 10.44)	4.7 (4.6, 4.8)	12.2 (12.0, 12.5)
50%	5.61 (4.77, 6.50)	5.80 (4.92, 6.82)	9.1 (8.9, 9.4)	16.4 (16.1, 16.9)
75%	3.23 (2.79, 3.77)	3.33 (2.84, 3.93)	13.3 (13.0, 13.7)	20.5 (20.1, 21.1)
100% (ref)	1.77 (1.34, 2.16)	1.85 (1.42, 2.24)	17.3 (16.9, 17.8)	24.4 (23.7, 25.2)
<i>Proportion Asymptomatic Randomly Screened (No PrEP-Related Screening)</i>				
0% (ref)	13.40 (12.13, 14.62)	13.58 (12.15, 14.78)	0 (0, 0)	8.0 (7.7, 8.1)
5%	10.81 (9.73, 11.99)	11.05 (10.00, 12.37)	4.2 (4.1, 4.3)	11.8 (11.6, 12.1)
10%	8.30 (7.43, 9.29)	8.37 (7.50, 9.52)	8.4 (8.2, 8.5)	15.7 (15.4, 16.0)
15%	6.22 (5.52, 7.14)	6.37 (5.57, 7.30)	12.6 (12.3, 12.8)	19.6 (19.3, 19.9)
20%	4.65 (3.96, 5.47)	4.74 (4.05, 5.56)	16.8 (16.4, 17.1)	23.4 (23.1, 23.8)

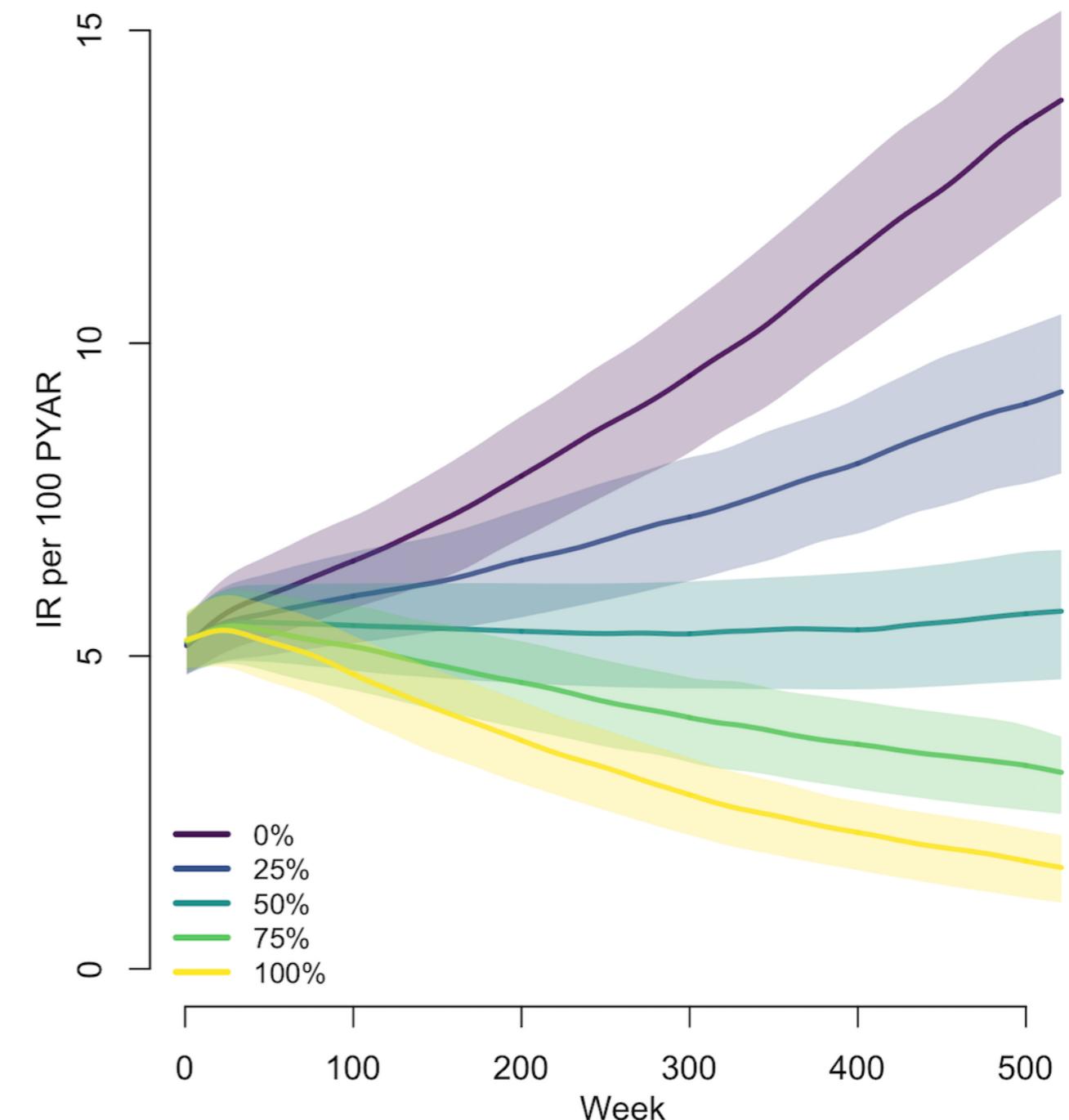
IQR = interquartile range (25% and 75% percentiles) of the simulation outcomes. Incidence expressed per 100 person-years at risk.

Incidence Curves by Screening and Treatment

STI Incidence by PrEP STI Screening Interval



STI Incidence by Proportion Treated



Partial completed treatment (50%) results in stable STI incidence

Conclusions

- HIV PrEP could result in a significant decline in STI incidence among MSM in the US
 - Attributable to recommended screening and treatment of STIs
 - HIV PrEP as a combination HIV/STI prevention package, not just meds
 - MSM indicated for HIV PrEP also at substantial risk for STIs through same sexual partnership networks and behaviors
- No levels of risk compensation could reproduce PrEP/Non-PrEP STI IR differential, suggested strong non-causal differences in cohorts
- Reducing STI screening interval from biannually to quarterly could further reduce incidence, although with complex cost implications

Github Resources

This screenshot shows the GitHub organization page for Statnet. The page features a header with the GitHub logo, 'This organization', 'Search', 'Pull requests', 'Issues', 'Gist', and a notification bell. Below the header, the Statnet logo and name are displayed, along with a brief description: 'Software tools for the analysis, simulation and visualization of network data.' and a link to <http://statnet.org/>. The main content area is titled 'Pinned repositories' and contains six repository cards:

- EpiModel**: Mathematical Modeling of Infectious Disease. Language: R. Stars: 19. Forks: 9.
- EpiModelHIV**: Network Models of HIV Transmission Dynamics among MSM and Heterosexuals. Language: R. Stars: 1. Forks: 3.
- PrEPGuidelines**: Impact of CDC's HIV Preexposure Prophylaxis Guidelines among MSM in the United States. Language: R. Stars: 1. Forks: 1.
- ndtv**: ndtv: Network Dynamic Temporal Visualizations in R. Languages: HTML, R. Stars: 12. Forks: 3.
- ergm.ego**: Fit, Simulate and Diagnose Exponential-Family Random Graph Models to Egocentrically Sampled Network Data <http://statnet.org>. Languages: R, HTML. Stars: 5. Forks: 2.
- HIV-Risk-Comp**: Modeling Risk Compensation after PrEP Initiation among MSM. Language: R. Stars: 0. Forks: 0.

Below the pinned repositories, there is a search bar, filters for 'Type: All' and 'Language: All', and a 'New' button. To the right, there are sections for 'Top languages' (R, HTML, TeX) and 'Most used topics' (agent-based-modeling, epidemiology, mathematical-modelling, network-graph, statnet). At the bottom, there are links for 'People' (26) and profile icons.

- We keep all of our ongoing software dev on Github
- Mostly in an open source way with some exceptions for new projects
- github.com/Statnet/EpiModelHIV

EpiModelHIV Branches

The screenshot shows the GitHub repository page for 'statnet / EpiModelHIV'. The top navigation bar includes links for 'This repository', 'Search', 'Pull requests', 'Issues', and 'Gist'. Below the header, there are buttons for 'Unwatch', 'Star', 'Fork', and a search bar for 'Search branches...'. The main content area is divided into sections: 'Default branch', 'Your branches', 'Active branches', and 'Stale branches'. The 'Default branch' section shows the 'master' branch as the default. The 'Your branches' section lists several branches: 'syph_ept-revis3', 'prep-sti', 'syph_ept', 'cfarc', and 'PrEPsens'. The 'Active branches' section lists 'syph_ept-revis3', 'syph_ept', 'prep-sti', 'MSM-race-disparities', and 'cfarc'. The 'Stale branches' section lists 'hivTP' and 'PrEPsens'. Each branch entry includes a status indicator (green checkmark or red X), commit counts (e.g., 44|207), and buttons for 'New pull request' and 'Delete'.

- Github Repositories = a self-contained unit of software
- Branches in Github are unique copies of a repository that diverge at a specific moment in development
- We use branches of EpiModelHIV to work on several applied modeling projects simultaneously

Modules with Current EpiModelHIV Master Branch

```
netsim(est, param, init, control)

 $t_1$  initialization module

for (at in 2 to  $t_n$ ) {

    module 1

    module 2

    network re-simulation module

    transmission module

    module 5

}

 $t_n$  Clean up and save output
```

Modules with Current EpiModelHIV Master Branch

- At t_1 :
 - Initialization
- At t_{2+} :
 - Aging, deaths, births
 - HIV testing, ART, PrEP
 - HIV stage progression, HIV viral load
 - Network resimulation (x3!)
 - HIV status disclosure
 - Acts per partnership, condom use per act
 - Risk history tracking (for interventions)
 - Sexual position for anal sex (insertive vs receptive)
 - HIV transmission
 - STI (gonorrhea/chlamydia) transmission
 - STI recovery
 - STI treatment
 - Prevalence module (summary statistics)

Initialization: initialize_msm

- Converts model fit/coefficients into t_1 network simulation
- Set up dat list and sublists (attr, epi, and related)
- Initialize attributes: demographics, risk behavior, biology, intervention-related
- Initialize summary statistics: disease prevalence, incidence, person-time on interventions...

Mortality: deaths_msm

- Simulate natural mortality based on age-race specific mortality schedule
 - Bernoulli draw for each “eligible” node with probability based on this
- Simulate disease-related mortality based on reaching a “fatal” viral load level in the AIDS stage
- Delete nodes from the network (non-trivial!)
- Remove individual node data from the attr lists

Births: births_msm

- In our population, birth = entry into the sexually active target population of interest, which is adult MSM
- Simulate an integer for the number of incoming deaths based on a Poisson distribution
- Add those new nodes to the network
- Initialize attributes for those who have entered (age, disease status, circumcision status...)

HIV Testing (test msm) and HIV treatment (tx msm)

- Randomly assign eligible (not previously HIV diagnosed) nodes a probability of testing based on race-based propensity for testing
 - Other forms of interval-based testing for HIV PrEP and other interventions
 - Record time for last test for all
- HIV ART is based on patterns of cycling on and off treatment to produce meta-level statistics for the proportion on treatment and virally suppressed in a cross-section

Network Resimulation (`simnet msm`)

- Main and casual networks are persistent (STERGMs), one-offs are cross-sectional ERGMs
- ST/ERGM formula depend on cross-network degree distributions (number of main partners influences probability of new casual partners...)
- Update all nodal covariate data
- Resimulate the network (magic!)
- Keep track of new edges (for other behavioral purposes)

Acts (acts msm), Condoms (condoms msm), Position (position msm)

- Given current edge list, act list is built by repeating rows in edge list by a factor of the act rate
 - From here on, we'll work on the act list instead of the edge list
- For each act, there is a probability of condom use (0/1)
- For each act, there is directionality (insertive/receptive)
- These act attributes are attached on the act list

HIV Transmission (trans msm)

- Let's review the code:
 - View(trans msm)

Summary

- EpiModelHIV is our current HIV/STI modeling extension that uses the current EpiModel framework and STERGM methods
- Top-down approach for answering specific questions
- Useful (hopefully) to you as a set of templates for further extension and expansion, with your knowledge of the framework and methods above
- We're here to help! Documentation and listserv on epimodel.org