BACKGROUND ON HIV MODELS FOR MEN WHO HAVE SEX WITH MEN
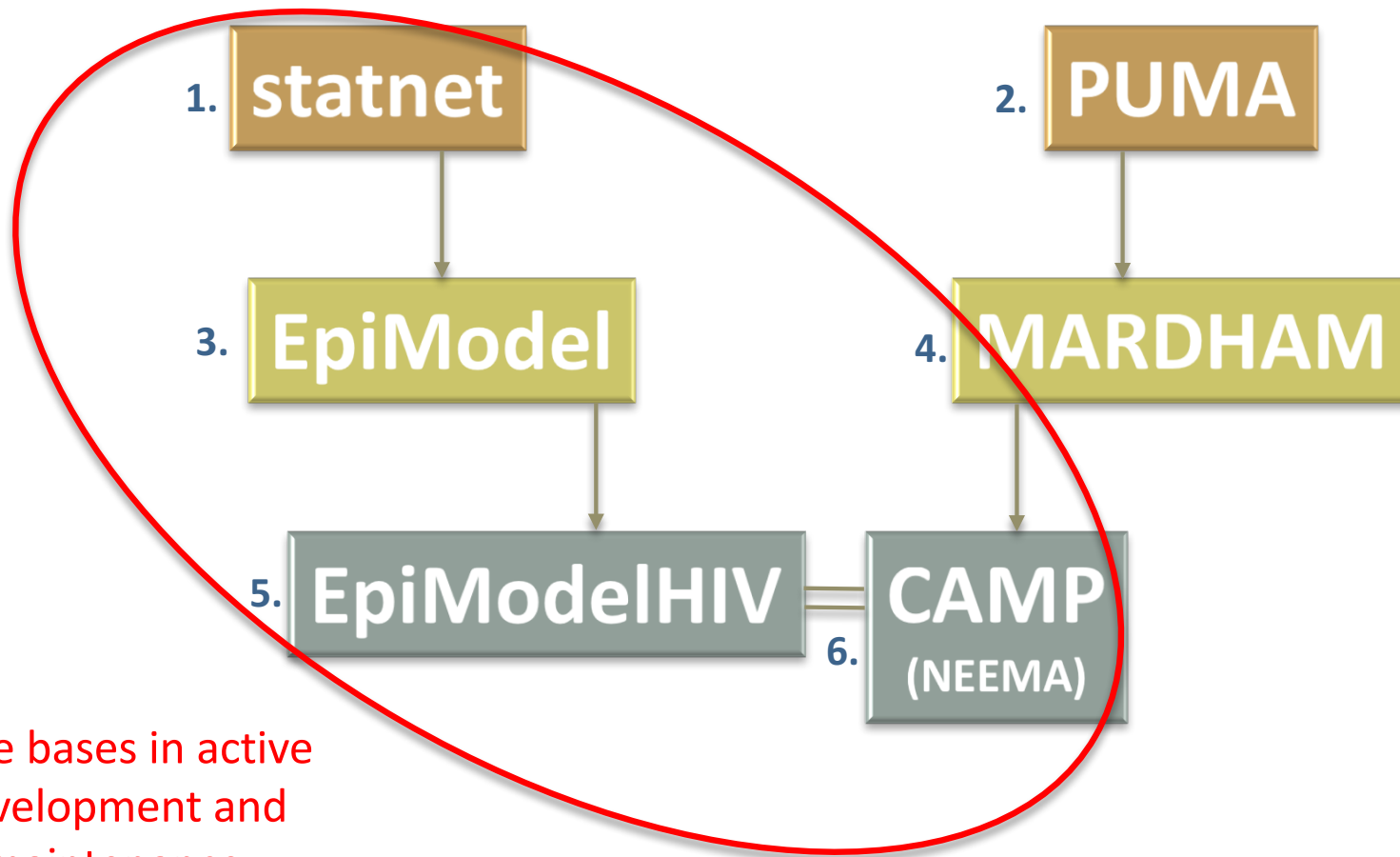
Steven M. Goodreau, Ph.D.
Samuel M. Jenness, Ph.D.
Eli S. Rosenberg, Ph.D.

Pieces overview

1. statnet
2. PUMA
3. EpiModel
4. MARDHAM
5. EpiModelHIV
6. CAMP (NEEMA)

Code bases in active development and maintenance

1. statnet

1. statnet

- 20ish-year project

- Team came together inspired by desire to have statistical models and tools for modeling HIV dynamics

- Brought a few existing packages (network, sna) into the fold along the way

- Statnet *proper* doesn't contain anything directly related to HIV (or any other infectious disease) modeling – only relational dynamics

- Widely used in many fields (e.g. sociology, political science, biology, economics, anthropology)

1. statnet

Main constituent packages

- **network** = tools for storing and managing network data
- **sna** = routines for traditional social network analysis
- **ergm** = tools for exponential-random graph models
- **networkDynamic** = dynamic extensions of network
- **tergm** = dynamic extensions of ergms
- **statnet.common** = utilities common across statnet pkgs
- *New!!* **ergm.ego** = tools to conduct egocentric network analysis (with an eye towards epidemic models)

2. PUMA

- Prevention Umbrella for MSM in the Americas (Buchbinder, PI)
- Part of NIH's MP3 program
- Focus on the US and Peru

2. PUMA

Some interesting findings:

- We estimated that about 1/3 of new infections are from main partners (in contrast to recent lit at the time)

- Capability of role versatility has large role to play in keeping HIV burden high among MSM

- PrEP has high potential to reduce HIV incidence among MSM, even with high risk compensation, but is unlikely to be a magic bullet

- PreP works best when targeted to the highest risk men ☺

- Circumcision for MSM is a mixed bag

2. PUMA

Features of the model:

- Contains two networks: "main" partnerships and all others
- Main were modeled as duration using *tergms*
- Others were all modeled as a series of one-time contacts using *ergms*, even when they were actually durational
- Calls statnet packages for the network modeling components
- All other code is custom-made and purpose-built
- Code is modular

2. PUMA

Features of the model:

- Simple homogeneous **testing** module
- **Treatment** initiation module, with two adherence levels
- **Viral load** tracked – depends on time since infection and treatment
- **Network model** includes age and race mixing, degree distributions
- **UAI acts** depend on diagnosis status (acts w/o condom use not modeled)
- **Circumcision** tracked
- **PrEP use** introduced: four adherence categories, no discontinuation

- Pops represent urban MSM in the US and in Peru
- US parameters derived from NHBS, baseline Explore, and others
- Expanded to Kenya and India for Lancet series

3. EpiModel

- Development also funded by the statnet project

- Led (understatement!) by Sam Jenness while he was a grad student

- Highly integrated with statnet, but not downloaded by default with statnet

- On CRAN and github both
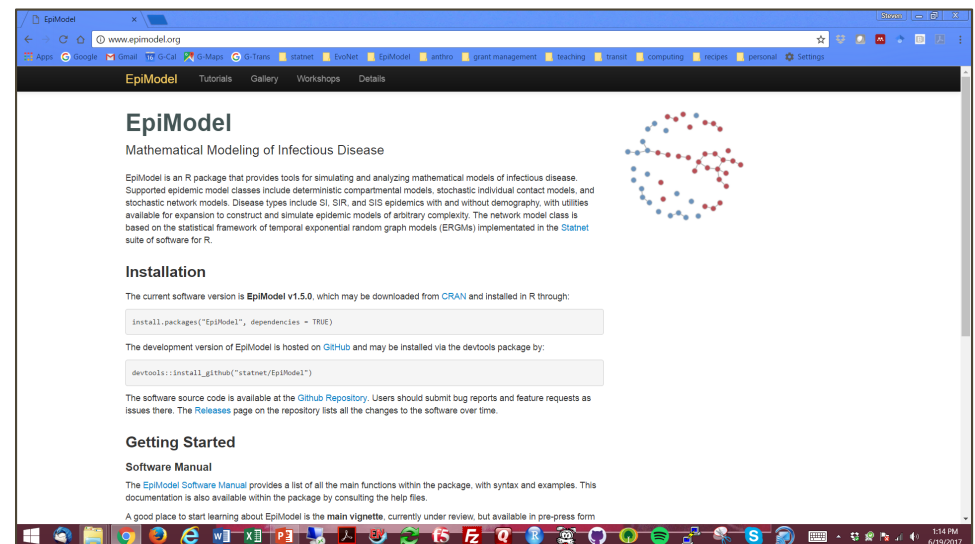
3. EpiModel

- Modeling tools for infectious disease
- Contains functions for running compartmental models and individual-based stochastic models, but real focus is network models
- Built-in tools handle models of class SI, SIS and SIR
- Built-in tools allow for web or command-line interface
- 49-page paper introducing the packages is about to come out in *Journal of Statistical Software*
- Highly modular
- Uses a strict API that allows for extensions while maintaining core functionality
- Base EpiModel has nothing specific to HIV or STIs in it per se

4. MARDHAM

- Modeling Approaches to Reduce Disparities in HIV among Atlanta MSM

- R21 (Goodreau PI)

- Specifically focused on Black and White MSM in Atlanta

- Specifically focused on understanding origins of racial disparities

- Parametrized from multiple studies by Eli Rosenberg and Patrick Sullivan and team at Emory

4. MARDHAM

Sources of racial disparities in HIV prevalence in men who have sex with men in Atlanta, GA, USA: a modelling study

Steven M Goodreau, Eli S Rosenberg, Samuel M Jenness, Nicole Luisi, Sarah E Stansfield, Gregorio A Millett, Patrick S Sullivan

Summary

Background In the USA, men who have sex men (MSM) are at high risk for HIV, and black MSM have a substantially higher prevalence of infection than white MSM. We created a simulation model to assess the strength of existing hypotheses and data that account for these disparities.

|	Prevalence of HIV infection in black MSM	Prevalence of HIV infection in white MSM	Ratio of prevalence of HIV infection in black MSM to prevalence of HIV infection in white MSM	% of disparity explained
Observed (Involvement cohort)	197/454 (43·4%, 38·9 to 48·0)	46/349 (13·2%, 9·9 to 17·0)	3·30 (2·47 to 4·40)	N/A
Null	544/5578 (9·8%, 9·4 to 10·0)	556/5605 (9·9%, 9·2 to 10·3)	0·99 (0·92 to 1·04)	−0·4% (−3·5 to 1·8)
As observed	558/5540 (10·1%, 9·5 to 10·3)	1078/5568 (19·4%, 19·1 to 20·0)	0·52 (0·50 to 0·54)	N/A
Factor groups in isolation				
Care continuum	609/5557 (11·0%, 10·6 to 11·7)	505/5630 (9·0%, 8·4 to 9·4)	1·23 (1·13 to 1·31)	10·0% (5·7 to 13·7)
CCR5Δ32	694/5523 (12·6%, 12·0 to 13·5)	490/5593 (8·8%, 8·2 to 9·1)	1·44 (1·35 to 1·54)	19·1% (15·4 to 23·5)
Stigma-associated behaviours	691/5552 (12·4%, 11·3 to 13·6)	542/5561 (9·7%, 9·1 to 10·3)	1·29 (1·17 to 1·41)	12·7% (7·2 to 17·8)
Majority of sexual behaviours	703/5591 (12·6%, 12·0 to 13·0)	1708/5381 (31·7%, 31·1 to 32·4)	0·40 (0·37 to 0·41)	N/A
Residual factors	612/5591 (10·9%, 10·6 to 11·4)	561/5596 (10·0%, 9·7 to 10·7)	1·10 (1·02 to 1·16)	4·3% (1·0 to 6·8)
Combined factor groups				
Biomedical determinants	844/5519 (15·3%, 14·4 to 16·2)	451/5630 (8·0%, 7·6 to 8·7)	1·93 (1·77 to 2·05)	40·5% (33·7 to 45·5)
Care and disclosure	696/5528 (12·6%, 12·1 to 13·2)	512/5601 (9·1%, 8·8 to 9·7)	1·38 (1·31 to 1·46)	16·4% (13·6 to 20·0)
All sexual behaviours	638/5609 (11·4%, 11·0 to 11·8)	1572/5387 (29·2%, 28·6 to 29·5)	0·39 (0·38 to 0·40)	N/A
All risk factors in black MSM	1113/5423 (20·5%, 19·4 to 21·3)	508/5600 (9·1%, 8·4 to 9·4)	2·28 (2·18 to 2·36)	55·5% (51·3 to 59·1)
Misclassification of risk behaviours	2255/5116 (44·1%, 43·9 to 44·0)	1635/5483 (29·8%, 29·2 to 30·7)	1·48 (1·45 to 1·53)	20·8% (19·7 to 22·9)

Data are n/N, unless otherwise specified. For observed values (ie, the first row), we report 95% CIs; all other data are reported with the IQR. For simulated prevalence numbers, values represent the mean (IQR) observed at the end of the 16 simulations, with initial population size of 10 000. Simulated prevalence ratios are calculated separately at the end of each of the 16 runs and are reported as mean (IQR). For percentage of disparity explained, we compared the mean (IQR) of the 16 simulated prevalence ratios with the observed point estimate, using the formula (PR$_{sim}$−1)/(PR$_{obs}$−1), where PR$_{sim}$ is the simulated prevalence ratio and PR$_{obs}$ is the observed prevalence ratio. For scenarios in which all simulations yielded a larger prevalence of HIV infection for white than for black MSM, we report the percentage disparity as N/A. The percentage disparity explained for the null model should be centered on 0, with stochasticity, by design. MSM=men who have sex with men. N/A=not applicable.

Table 4: Racial disparity in prevalence of HIV infection generated by specific measured proximal factors, alone or in combination
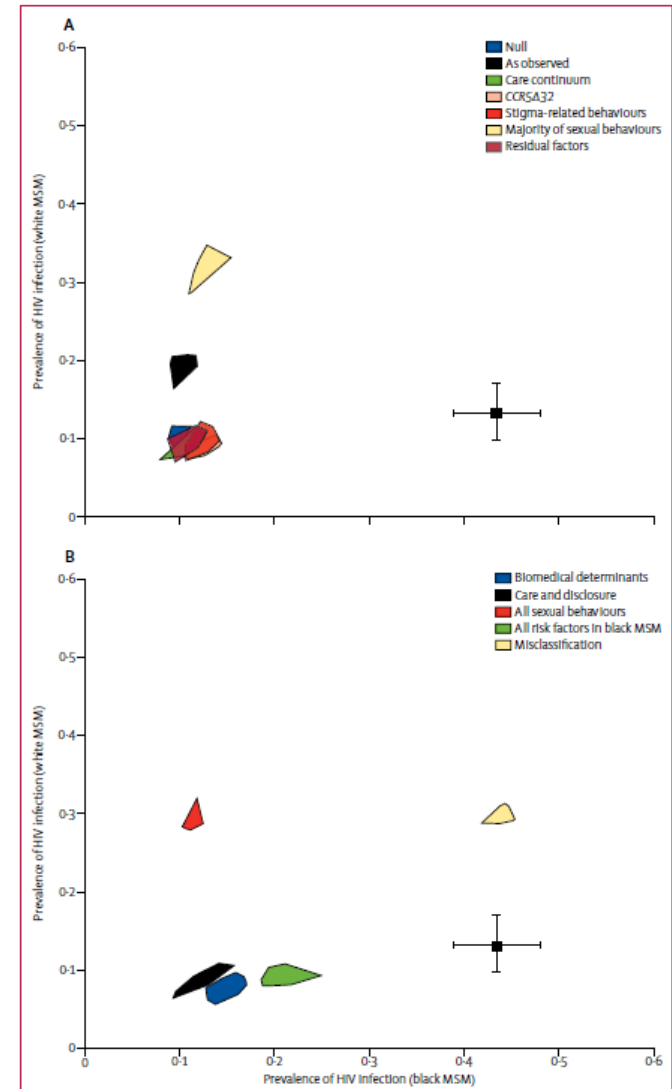
4. MARDHAM

- Code started from scratch based on lessons learned in PUMA
- Makes nearly all parameters a function of race (or race-combo in dyads)
- Adds third network (casual but persistent)
  - With two persistent networks, momentary degree is a matrix
- Adds explicit modeling of both condomless and condom-protected AI acts
- Adds in more complex treatment dynamics (going on and off)
- Adds in more complexity to disclosure
- Adds in CCR5 genotype

- Initially not coded in EpiModel, since the two were in development in parallel
- Converted over into EpiModel nomenclature and syntax by Sam

5. EpiModelHIV

- Set of EpiModel extensions modules and default parameters designed for modeling HIV (and now other STIs)

- Like everything in EpiModel, it is designed to be editable or extendable through the use of modules

- Contains separate code bases for MSM and heterosexuals

- MSM code began its life as the Mardham code converted over into EpiModel API

- Has now been extended considerably over the course of the CAMP project

- Different CAMP sub-projects create parallel versions of modules

- This yields a database of existing modules to choose from as starts

- Is continually in development

- Default parameters reflect the Atlanta mode, but are all replaceable

- Lives on github only

5. EpiModelHIV

EpiModelHIV

`build passing`

An R package for simulating HIV transmission dynamics among men who have sex with men and heterosexual populations, developed as an extension to our general network-based epidemic modeling platform, EpiModel.

`EpiModel` and `EpiModelHIV` use the statistical framework of temporal exponential-family random graph models to fit and simulate models of dynamic networks. These statistical methods have been developed and implemented as open-source software, building on the extensive efforts of the Statnet research group to build software tools for the representation, analysis, and visualization of complex network data.

These packages combine these Statnet methods with an agent-based epidemic modeling engine to simulate HIV transmission over networks, allowing for complex dependencies between the network, epidemiological, and demog changes in the simulated populations. Readers new to these methods are recommended to consult our EpiModel re including our main Vignette describe the theory and implementation.

Installation

You can install `EpiModelHIV` in R using `devtools`:

```
install.packages("EpiModel", dependencies = TRUE)
devtools::install_github("statnet/tergmLite")
devtools::install_github("statnet/EpiModelHPC")
devtools::install_github("statnet/EpiModelHIV")
```

Documentation on using this software package is forthcoming, although limited function documentation is provide the package and available with the `help(package = "EpiModelHIV")` command.

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statnet / **EpiModelHIV**

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Network Models of HIV Transmission Dynamics among MSM and Heterosexuals   Edit

hiv-transmission-dynamics   mathematical-modelling   hiv   epidemiology   network-graph   statnet   agent-based-modeling   Manage topics

467 commits   8 branches   4 releases   5 contributors   GPL-3.0

Branch: master ▾   New pull request   Create new file   Upload files   Find file   Clone or download ▾

smjenness Remove LICENSE.md from build   Latest commit 9e47fb4 5 days ago

R	Update documentation	2 months ago
data	Update built-in data to include est and st	a year ago
inst	Continue merge	5 months ago
man	Build docs	2 months ago
src	Remove RcppExports.cpp	2 months ago
tests	Continue merge	5 months ago
.Rbuildignore	Remove LICENSE.md from build	5 days ago
.gitignore	Update gitignore	2 months ago
.travis.yml	Add Travis integration to slack	5 days ago
DESCRIPTION	Update documentation	2 months ago
LICENSE.md	Create LICENSE.md	5 days ago
NAMESPACE	Continue merge	5 months ago
README.md	Update citations	2 months ago

README.md

Network Models a

6. CAMP

- Coalition for Applied Modeling Projects
- Broad name for all of the Emory/UW/JHU NEEMA projects
- Some of these (i.e. any involving Sam or Steve) use EpiModelHIV

The Journal of Infectious Diseases
MAJOR ARTICLE

Impact of the Centers for Disease Control's HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States

Samuel M. Jenness,[1] Steven M. Goodreau,[4] Eli Rosenberg,[1] Emily N. Beylerian,[5] Karen W. Hoover,[3] Dawn K. Smith,[3] and Patrick Sullivan[1,2]

Departments of [1]Epidemiology, and [2]Global Health, Emory University, and [3]Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; [4]Department of A[...] and [5]Center for Studies in Demography and Ecology, University of Washington, Seattle

RESEARCH ARTICLE

Individual HIV Risk versus Population Impact of Risk Compensation after HIV Preexposure Prophylaxis Initiation among Men Who Have Sex with Men

Samuel M. Jenness[1]*, Akshay Sharma[1], Steven M. Goodreau[2], Eli S. Rosenberg[1], Kevin M. Weiss[1], Karen W. Hoover[3], Dawn K. Smith[3], Patrick Sullivan[1,4]

1 Department of Epidemiology, Emory University, Atlanta, Georgia, United States of America, 2 Department of Anthropology, University of Washington, Seattle, Washington, United States of America, 3 Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, 4 Department of Global Health, Emory University, Atlanta, Georgia, United States of America

* samuel.m.jenness@emory.edu

Network Models a[...]

6. CAMP
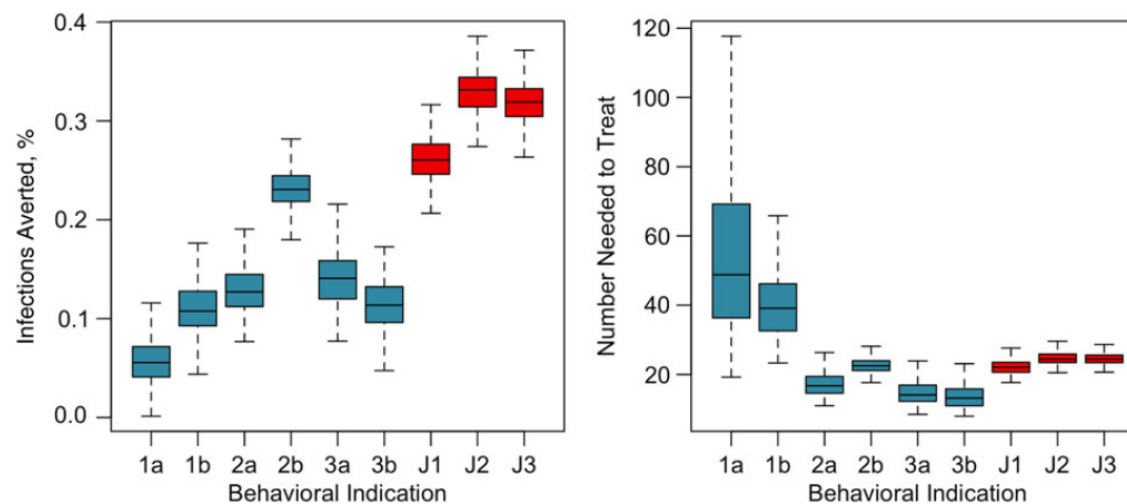
Figure 2. Box plots of the percentage of infections averted and number needed to treat to prevent 1 new infection by the individual behavioral indications (1a–3b; *blue*) and joint guideline scenarios (J1–J3; *red*) outlined in Table 1. Boxes indicate interquartile ranges; whiskers, 95% credible intervals for outcomes across all 250 simulations for each scenario.

- "Overall, taking into account the direct and indirect effects, implementing PrEP based on the indications in the CDC guidelines strikes a good balance between impact and efficiency according to our study, with 33% of infections averted and an NNT of 25."

6. CAMP

A. HIV Incidence Rate

Legend:
- Hi/Med/Low/Non Adr
- Hi/Med/Low Adr
- Hi/Med Adr
- Hi Adr
- Base (Ref)

Y-axis: IR per 100 PYAR
X-axis: Relative Increase in Risk Compensation

B. Percent of Infections Averted

Legend:
- Hi/Med/Low/Non Adr
- Hi/Med/Low Adr
- Hi/Med Adr
- Hi Adr
- Base (Ref)

Y-axis: PIA
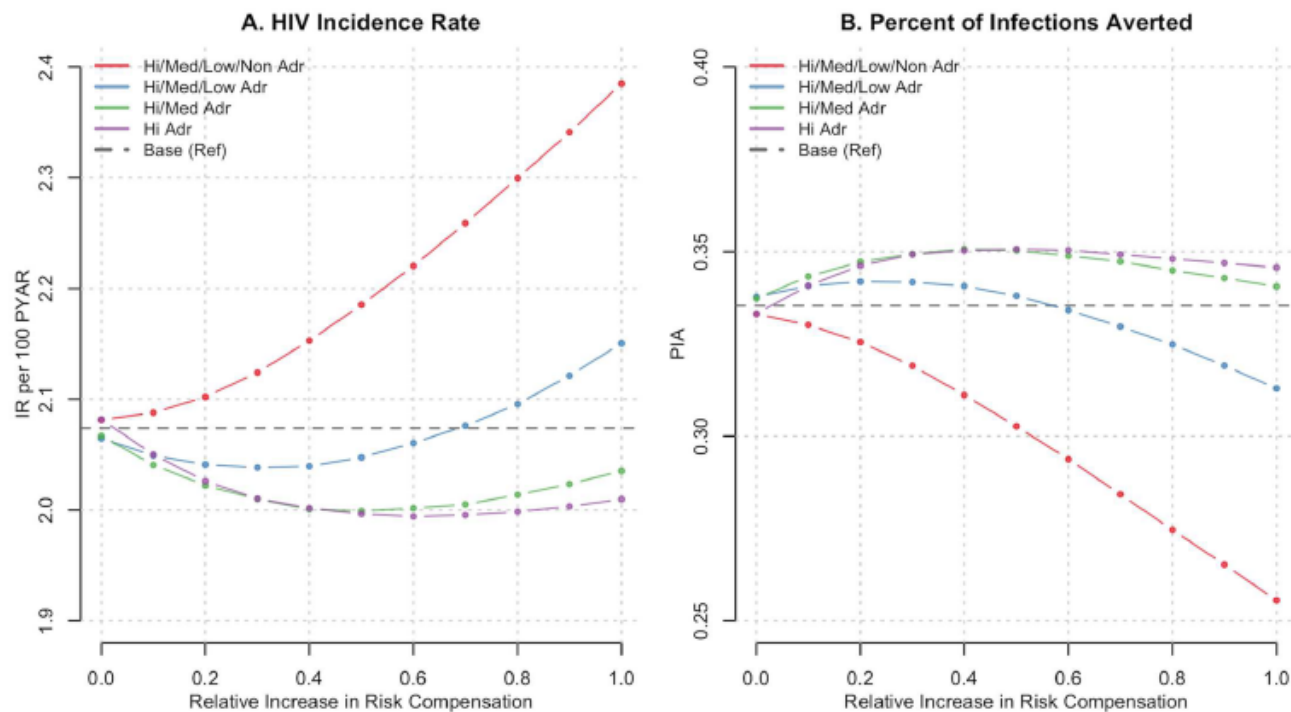X-axis: Relative Increase in Risk Compensation

Fig 1. The HIV incidence rate per 100 person-years at risk (Panel A) and percent of infections averted relative to a scenario in which no PrEP was used (Panel B), by the interaction of relative levels of condom-related risk compensation (RC) and PrEP adherence profile in which compensation occurred. The red line depicts RC in all four PrEP medication adherence profiles (high, medium, low, and non-adherent), the blue in the top three (high, medium, low) green in the top two (high and medium) and purple in the high only. The horizontal dashed lines shows a comparison of the two outcomes (incidence and PIA) if RC were not to occur (0% RC). All points summarize the empirical distribution of 250 simulations of each scenario.

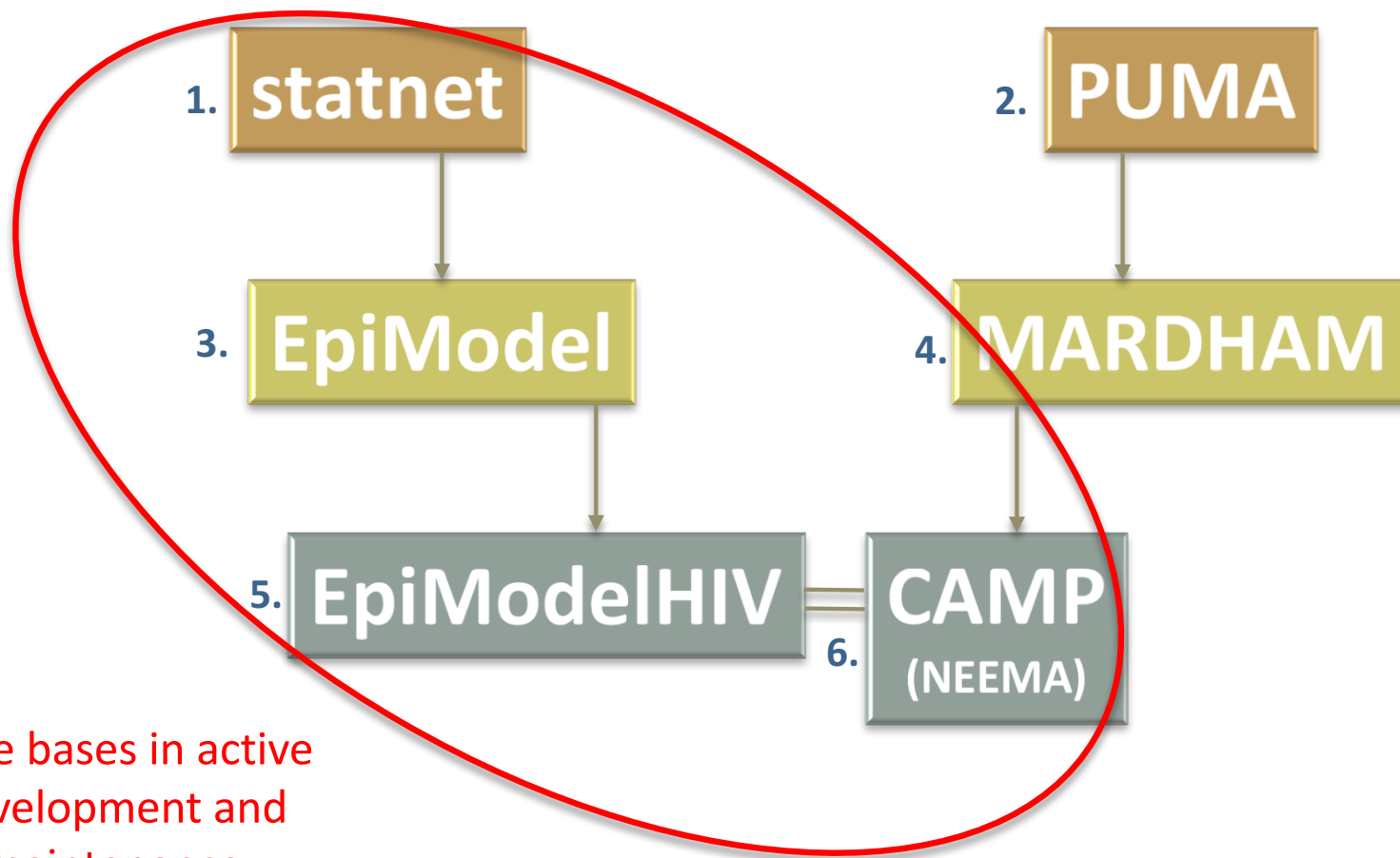doi:10.1371/journal.pone.0169484.g001

6. CAMP

- **Additional CAMP papers in press or in progress using EpiModelHIV:**

    - PrEP's impacts on STIs among MSM

    - Race-specific impacts of PrEP among adult MSM

    - PrEP among adolescent sexual minority males (ASMM)

    - Race-specific impacts of PrEP among ASMM

6. CAMP

- **Modules or features added to EpiModelHIV through CAMP:**
  - Much fancier PrEP modules (e.g. targeting based on discordant partnership status, recent partner counts)
  - Code to track these added metrics
  - Full suite of code for other STIs (gonorrhea, chlamydia, syphilis) and their interactions
  - Code for arrival at different ages (now set down to 13), and for sexual debut separate from arrival in population
  - Code to model infections from outside modeled population
  - Code for up to 5 race groups

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