INFECTIOUS DISEASE MODELING & HIV

Ron Brookmeyer
Dept of Biostatistics
UCLA

SOME QUESTIONS MODELS TRY TO ANSWER

- What is current and future scope of epidemic?
- Under what conditions does an epidemic take off?
- What interventions will reduce transmission and by how much?

HISTORY (early 1900s)

- **SIR RONALD ROSS**

  Malaria

- **LOWELL REED AND WADE HAMPTON FROST**

  The Reed Frost Model

  Susceptible, infected, & immune

  I

REED FROST EPIDEMIC MODEL

REPRODUCTIVE NUMBER *R*

Average number of new infections that one infectious person produces

At the beginning of an epidemic when nearly all are susceptible its called $\boldsymbol{R}_{o}$

Depends on biological, behavioral, social and environmental factors

WHEN DOES AN EPIDEMIC OCCUR?

- $R_0 > 1$

- If $R_0 < 1$, there could still be (small) cluster of cases, but not generally self-sustaining epidemic

REPRODUCTIVE NUMBER *R*

Kate Winslet in the movie *CONTAGION*

WHAT DOES R_0 DEPEND ON[1]?

TRANSMISSION PROBABILITY PER CONTACT

X

CONTACT RATE

X

DURATION OF INFECTIOUS PERIOD

[1] *basic case: random mixing, no heterogeneity*

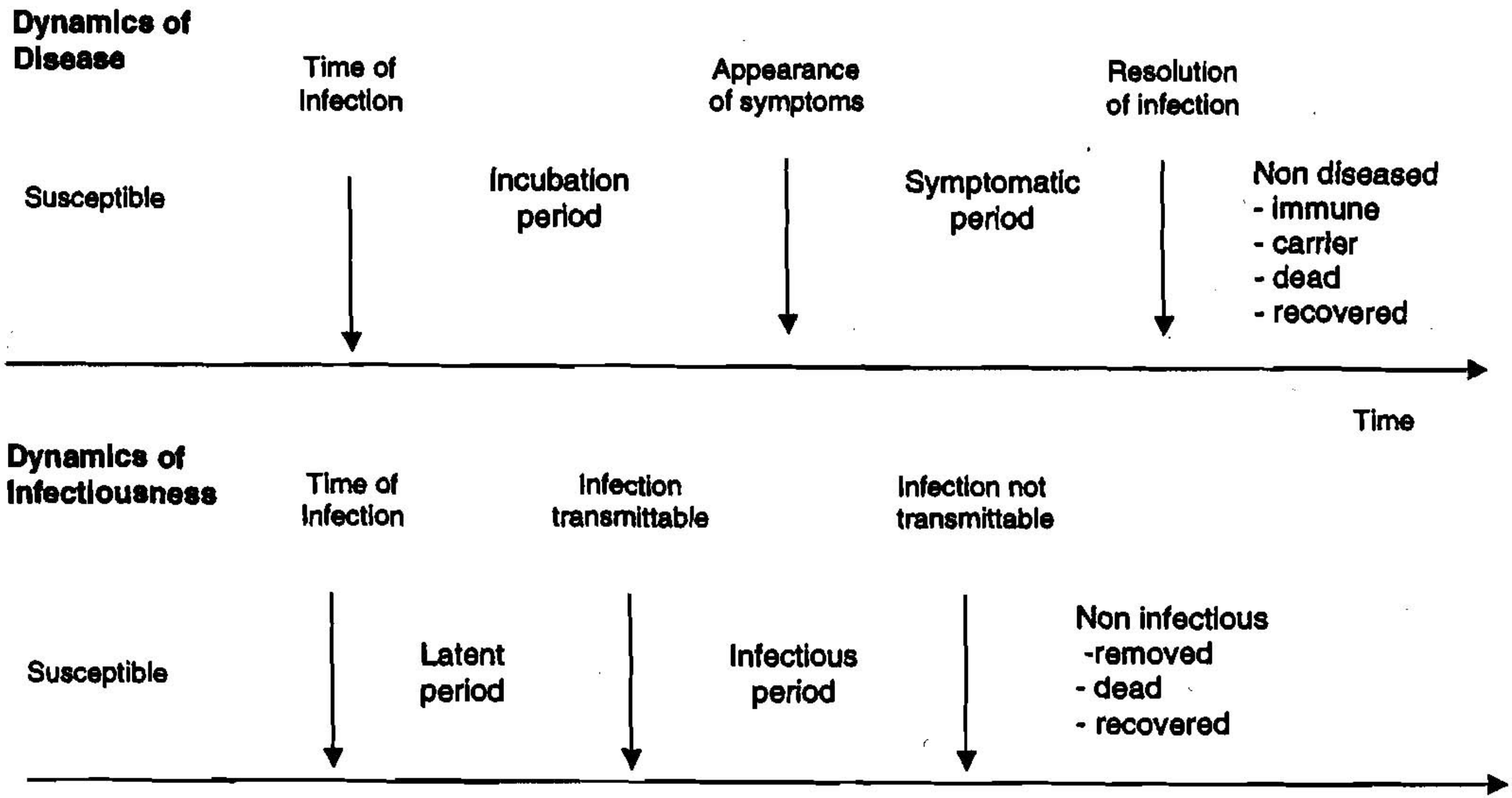


Figure 4–1. Natural history time lines for infection and disease.

GOAL: REDUCE R_O<1

- **GENITAL HERPES R_O=3**

  Decrease contact rate by factor of 4
  R_0 =1/4 x 3 =0.75

  Vaginal foam
  Reduce transmission probability by 80%
  R_0= 0.2 x 3=0.6

- **TB R_O=5**

  Active case detection and treatment
  Reduce infectious period from 52 weeks to 6
  R_0= 6/52 x 5= 0.6

R versus R_0

- ***R*** changes over the course of an epidemic (in part because the numbers susceptible decreases)

- **R**=$\boldsymbol{R_0}$ x Proportion susceptible in randomly mixing population

- Key to persistence: Continuing supply of susceptibles

- A goal of control measures is to try to reduce R<1

What fraction should be vaccinated?

What fraction should be vaccinated?

- Suppose R_0=5 (small pox)
- Suppose R_0=9 (measles).
- Suppose the vaccine is not 100% efficacious

FRACTION TO VACCINATE TO REDUCE R<1

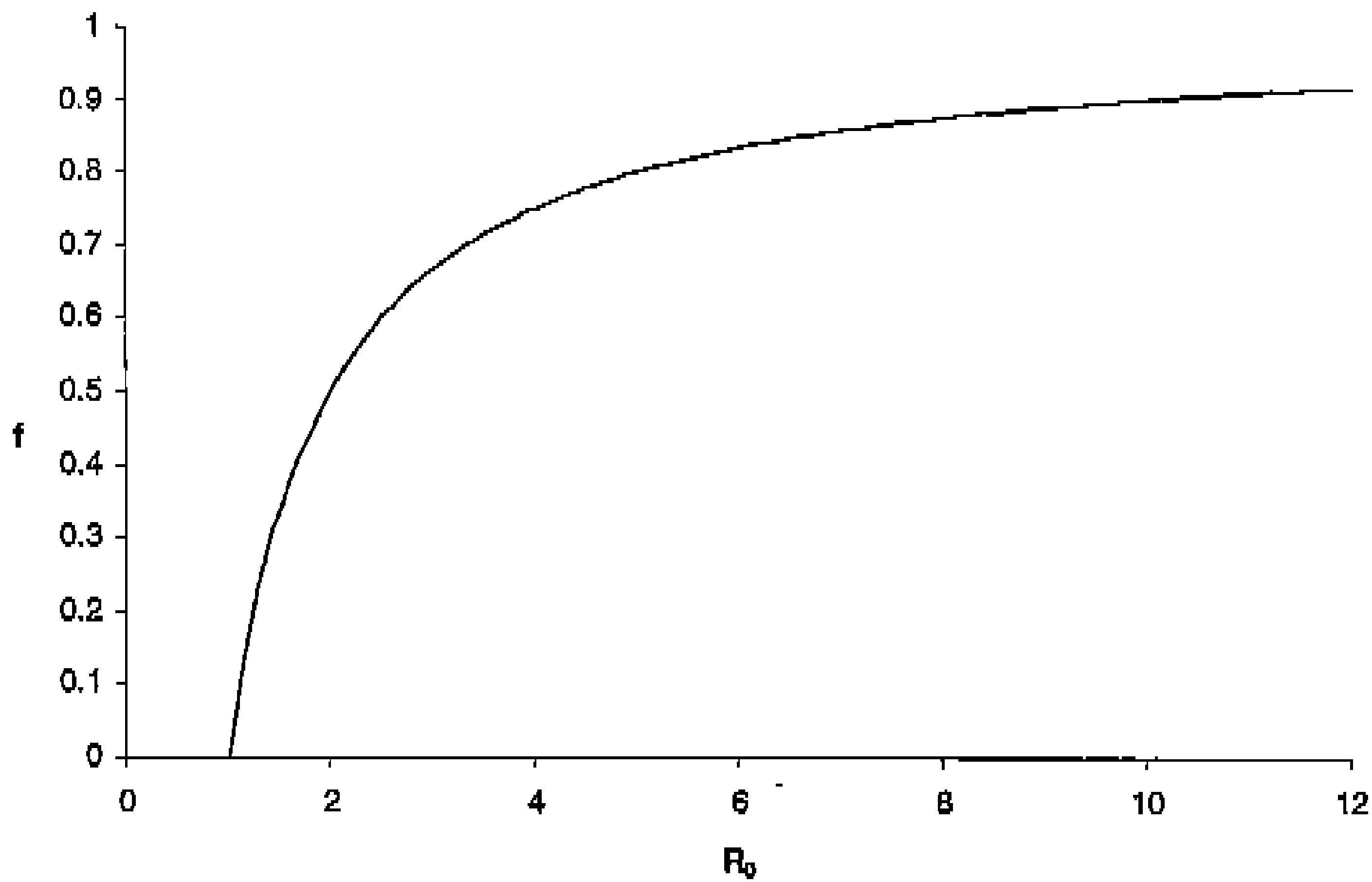
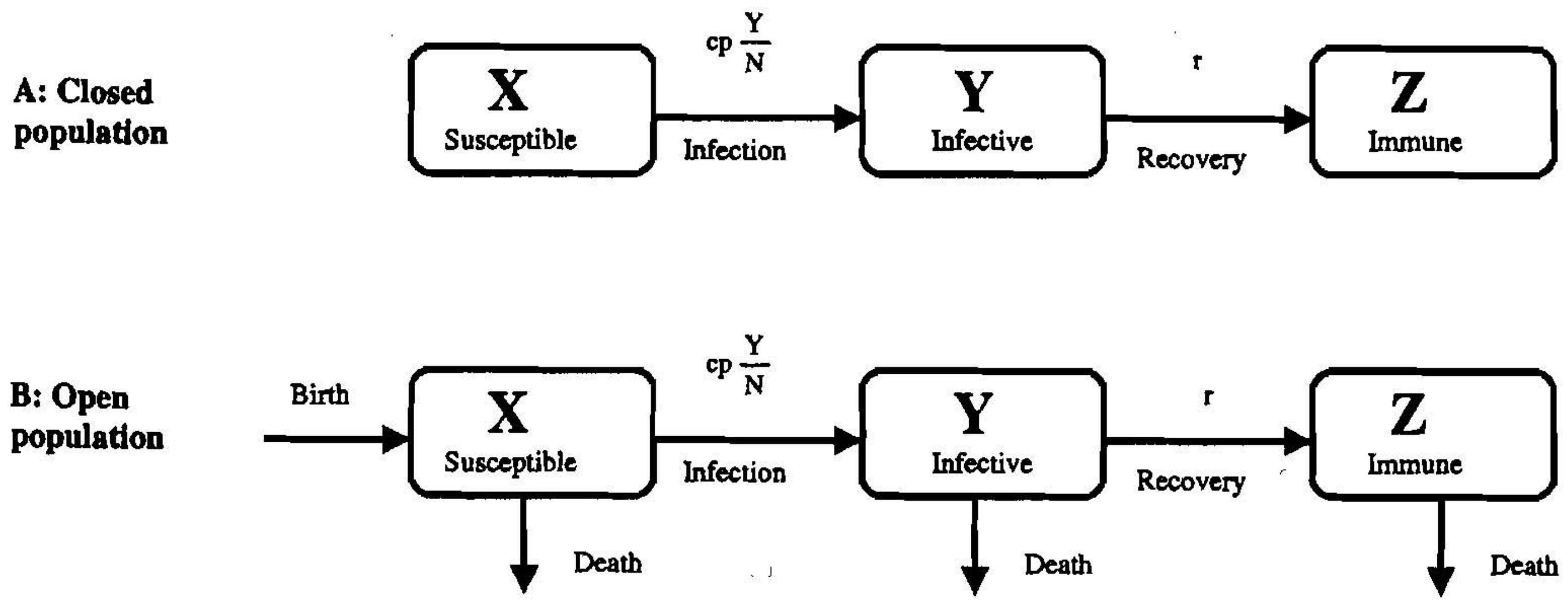
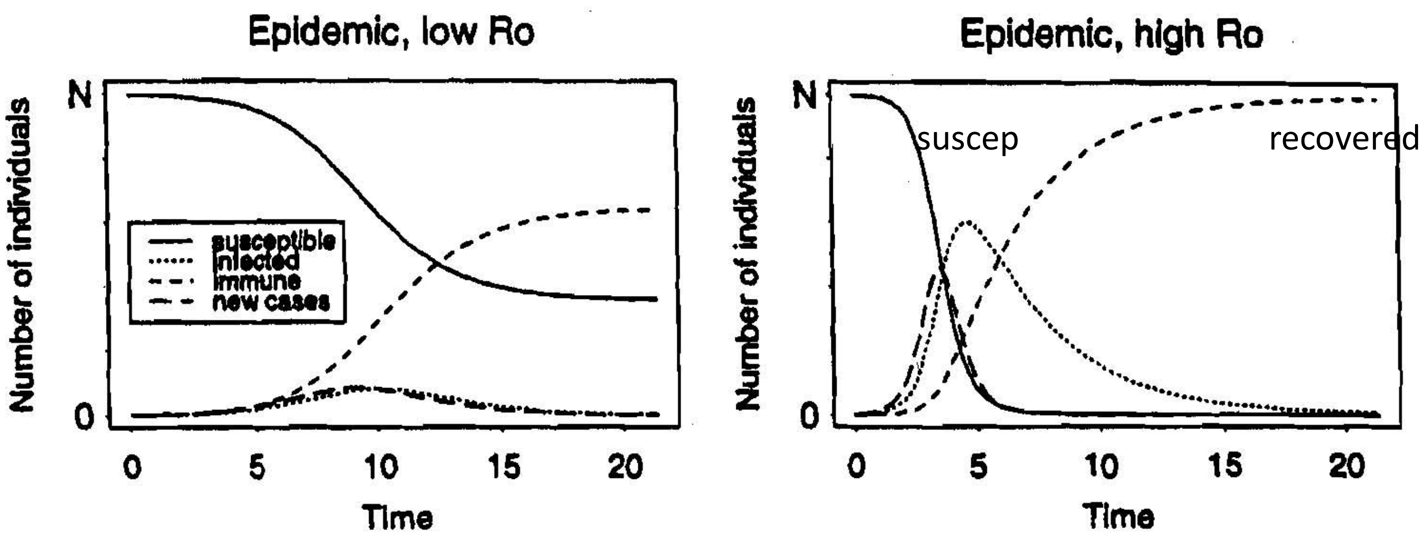


Figure 4–4. The fraction, *f*, of a population needed to be vaccinated with a completely protective vaccine to eliminate transmission as a function of R_0, the basic reproductive number.

DETERMINISTIC S-I-R MODEL random mixing



Closed population



- Epidemic begins to decrease when prop susceptible < $1/R_0$
- Not all susceptibles need to become infected before microbe dies out
- But ultimately epidemics end, one way or another, in closed populations

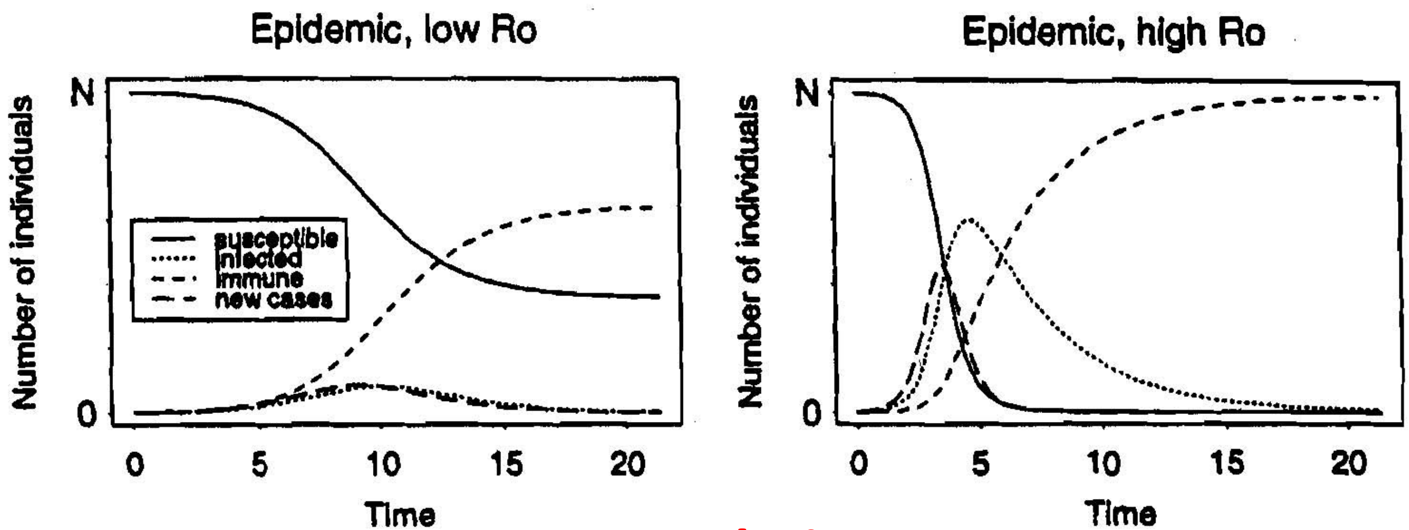
Halloran, 2001

KEY TO PERSISTENCE:

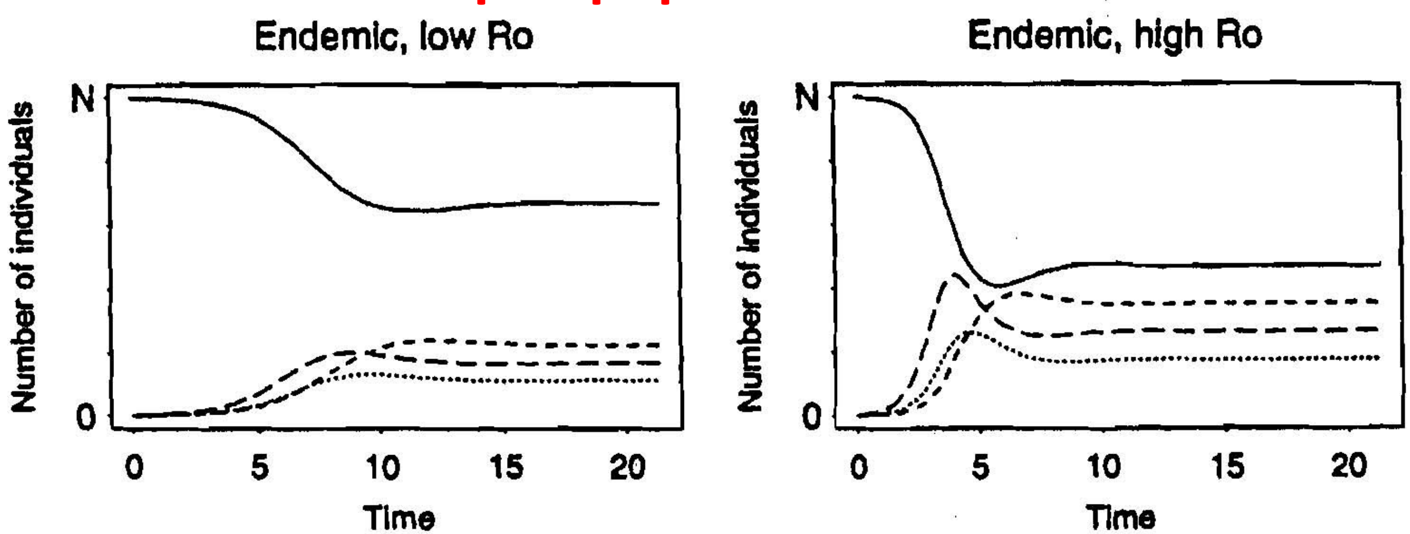
Continuing supply of susceptibles

BIRTH
IMMIGRATION
RECOVERY W/O IMMUNITY
WANING IMMUNITY

Closed population



Open population



HIV/AIDS COMPLEXITIES

TRANSMISSION PROBABILITY

CONTACT RATE

DURATION OF INFECTIOUSNESS

HIV TRANSMISSION PROBABILITY PER ACT

- Asymmetric transmission rates have different dynamics; lowers rate of spread[1] (F→M, M → F)

- Sexual roles among MSM: dual/versatile roles increases spread[2]

- Stage of disease
  Infectivity varies by stage of disease (e.g. Viral load)

- Co-infection with other pathogens may increase infectivity; e.g. Herpes simplex; genital ulcers

references:

[1]Cassels(2008)
[2] Goodreau (2005)

TRANSMISSION PROBABILITY PER ACT

PREVENTION STRATEGIES:

Circumcision- 40% reduction

Topical microbicide gel (tenofovir)-39% reduction

ART for HIV pos "treat to prevent" -92% reduction

PREP for HIV neg- 44% reduction
(depends on adherence)

DURATION OF INFECTIOUSNESS

Anti-retroviral treatment

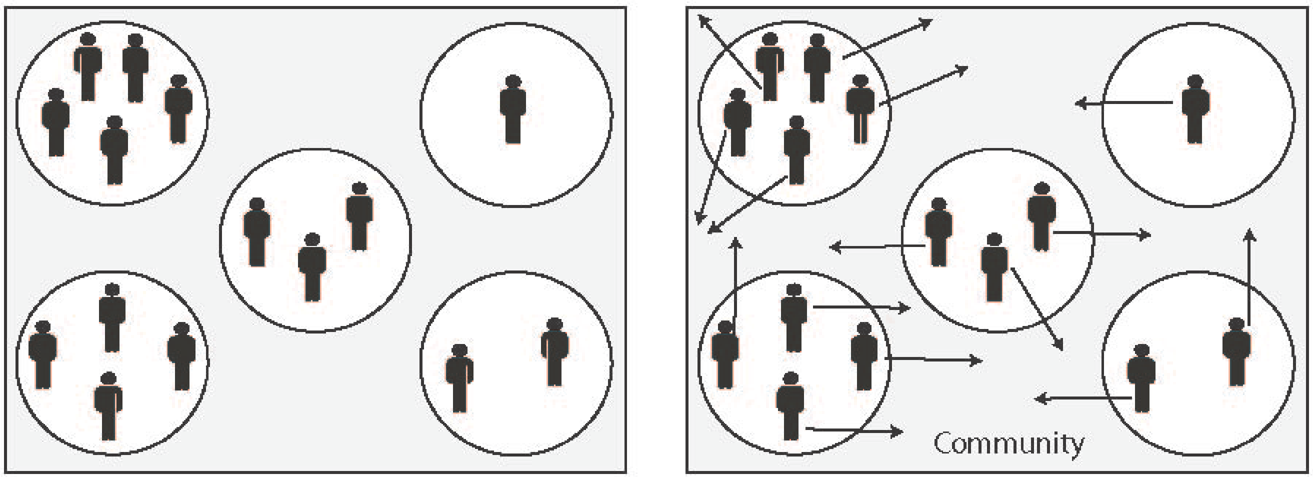
- decreases infectiousness (lower viral load)
- extending the duration of infectiousness
  (life expectancy)

CONTACT RATE

Oversimplification: random mixing with constant contact rate

(HIV) COMPLEXITIES

- **Core groups; bridging groups**
- **Networks**
- **Migration**
- **Selective/assortive mixing**
  e.g., mixing by age; Serosorting


Community

APPROACH: AGENT BASED MODEL

N persons

Interconnected

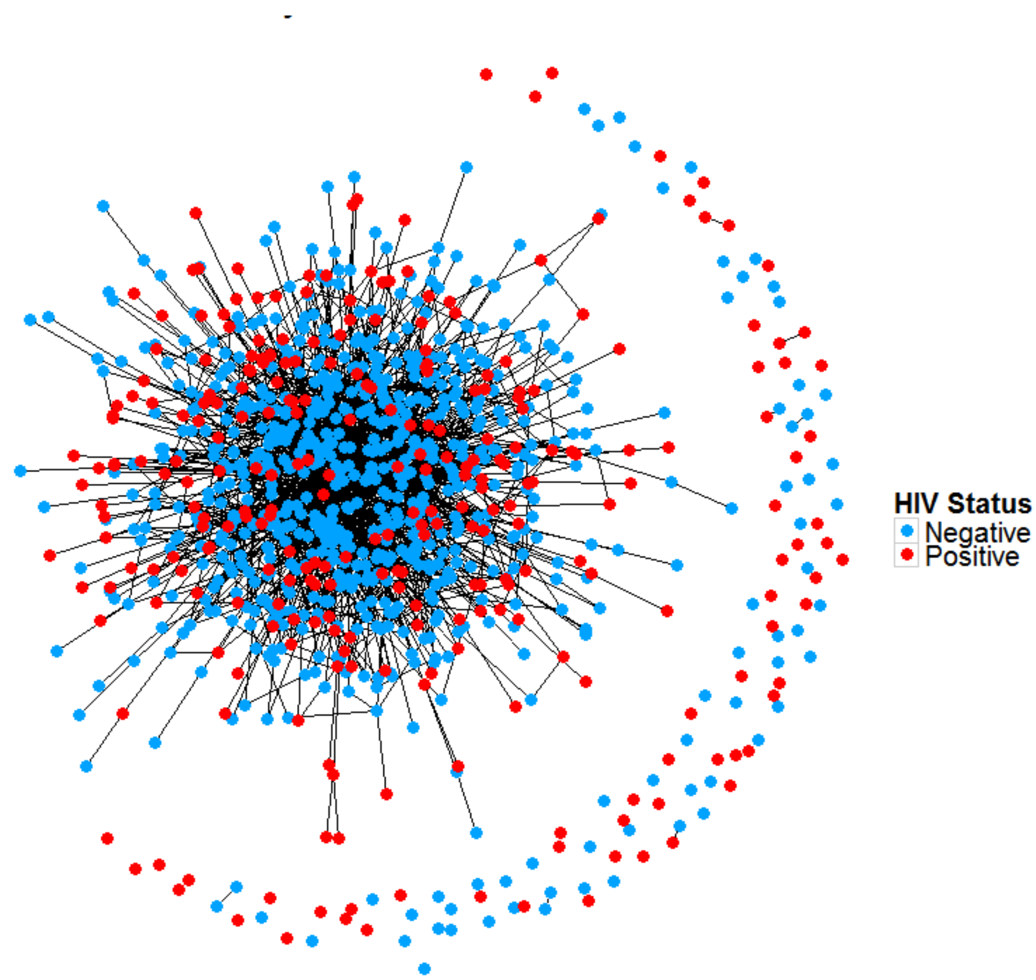
Social/sexual networks

Stochastic simulation

Computer Intensive

Daily update

NETWORKS OF SEXUAL CONTACTS



COMBINATION HIV PREVENTION MSM IN SOUTH AFRICA

AGENT BASED MODELING

GOALS

- Potential effects of combination prevention?
  interactions?

- Help design prevention trials

COMBINATION HIV PREVENTION INTERVENTIONS

ART*
PREP*
UAI reduction
HIV testing

*eligible for ART: HIV test and <350CD4

*eligible for PREP:HIV test; >12 UAI in 6 months or main partner who's infected

INPUTS

Peri-urban South Africa

literature review

sensitivity

Table 1. Main characteristics of agent based model for combination HIV prevention among MSM in peri-urban South Africa (additional information and specific parameter values are in the Supporting Information)

Attributes assigned to each person at start

Frequency of sexual activity

HIV status at start

CD4 count at start if HIV +

Knowledge of HIV status at start (yes, no)

Sexual role preference (insertive, receptive, versatile)

HIV testing frequency (3 levels: moderate, low, never)

Some assigned a main partner

Proportion of sexual contacts that are UAI (2 levels)

Sexual networks of regular partners (allowance for sero-sorting)

Daily updates

Daily sexual contacts depends on type of partnership
  Likelihood of contact (in decreasing order): main, regular, casual, have other main partners

HIV testing possible

UAI rate adjusted if learns knowledge of HIV status

CD4 levels updated for HIV positive

Infection status updated

Prevention Interventions

ART for eligible HIV positives
  Eligible: HIV test within 6 months and CD4<350
  Considered varying levels of coverage

PREP for eligible HIV negatives
  Eligible: in last 6 months had both HIV test and >12 UAIs or in sero-discordant main partnership.
  Considered varying levels of PREP acceptance with two levels of adherence (low and high)

Reduction in UAI frequency (considered varying levels)

Increase in HIV testing: convert 50% of the never testers to low frequency testers

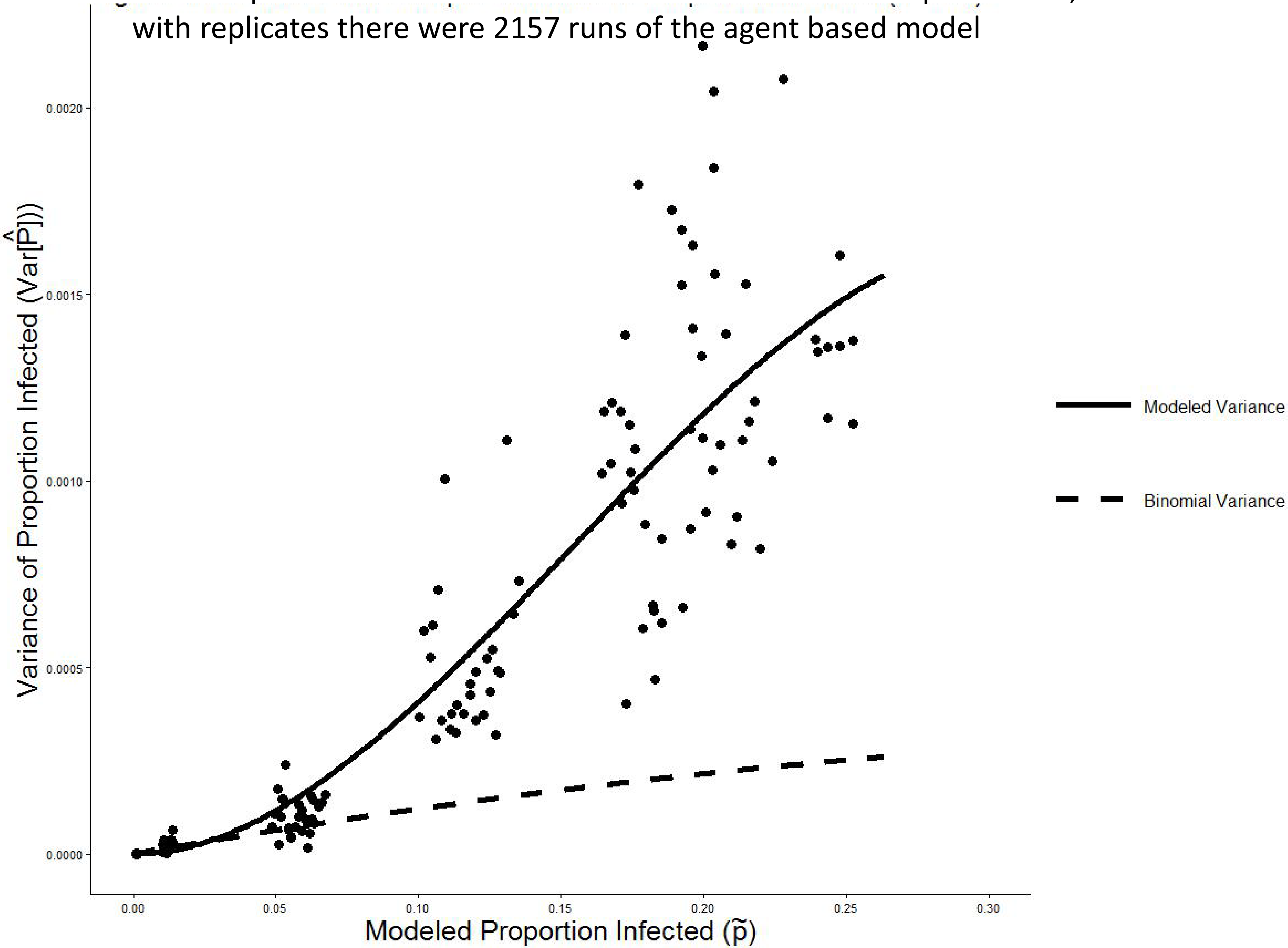
INFECTIONS AVERTED OVER 5 YEARS
Agent based model results

Prevention package component	percent infections prevented due to addition of component
ART (50% coverage of newly eligible) [incremental]	3.4
PREP (50% acceptance)	11.7
UAI reduction of 15%	21.0
HIV testing increase	4.9
TOTAL	**33.9**

HOW CAN MODELING HELP IN DESIGNING PREVENTION TRIALS?

- EFFECT SIZE
- VARIABILITY

162 data points each refers to a different combination HIV prevention;
with replicates there were 2157 runs of the agent based model



RECAP

- EPIDEMIC MODELS HAVE A LONG HISTORY
- R_O GOAL: REDUCE R<1
- KEY TO PERSISTENCE: CONTINUING SUPPLY OF SUSCEPTIBLES
- COMPLEXITIES:

  HETEROGENEITIES, NETWORKS, ASYMMETRICAL TRANSMISSION PROBABILITY, SELECTIVE MIXING (SEROSORTING)
- AGENT BASED MODELS

  MASSIVE COMPUTER SIMULATIONS
- EVALUATING COMBINATION PREVENTION; DESIGN

REFERENCES

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