Mathematical modeling: Focus on HIV/AIDS and STD's

2012 Principles of STD/HIV Research Course

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Susan Cassels, PhD, MPH

Steven M. Goodreau, PhD

University of Washington

Objectives

- Get an intuitive sense of epidemic modeling
- Basic overview of modeling types & structures of models
- Two examples
  - Compartmental model: HIV serosorting among MSM in Seattle
  - Stochastic network model: Importance of concurrency & acute stage of HIV among heterosexual young adults in Zimbabwe
  - What we do, what it takes to build each of these
- Future directions

Uses of mathematical models

- Predict population-level disease outcomes from
  - individual-level behavior
  - HIV prevention interventions

- Virtual “laboratory”
  - Identifying important components of transmission system
  - Test possible outcomes from interventions: alone or in combination
  - Explore behavioral determinants of disparities

… while being cheaper, less complicated, and avoiding ethical dilemmas

Why?

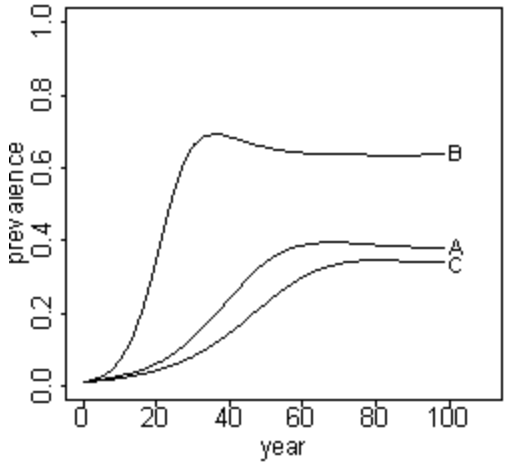
Prevalence of emerging disease

2006	0.0%	
2007	0.5%	
2008	1.2%	← Intervention 1
2009	2.6%	
2010	4.1%	
2011	5.6%	← Intervention 2
2012	5.4%	
2013	4.1%	
2014	3.9%	← Intervention 3
2015	4.0%	
2016	3.9%	
2017	4.1%	

Why?

Because non-linear dynamics are completely non-intuitive!

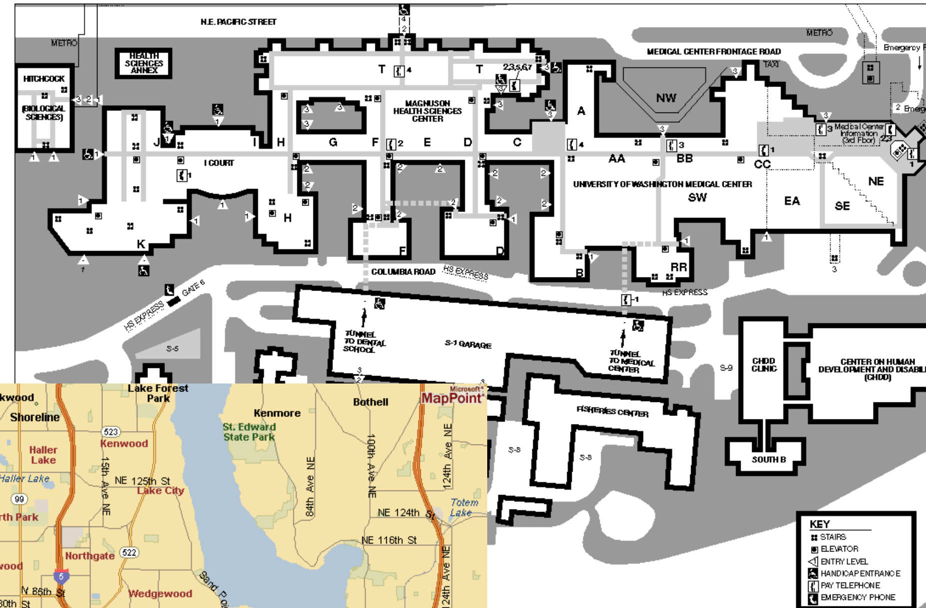
Early on provided lots of insight into basic infectious disease dynamics in general



Continues to answer questions about the predicted effects of behavioral interventions, vaccines, etc.

Maps

MapPoint
BRITISH
COLUMBIA
ALTA.
MONTANA
C A N A D A
W A S H I N G T O N
U N I T E D S T A T E S
O R E G O N
Pacific
Ocean
Vancouver
Richmond
Surrey
Victoria
Bellingham
Seattle
Tacoma
Olympia
Spokane
Yakima
Portland
Salem
Eugene
Kelowna
Penticton
Wenatchee
Kennewick



N.E. PACIFIC STREET
HITCHCOCK
HEALTH SCIENCES ANNEX
MEDICAL CENTER FRONTAGE ROAD
MAGNUSON HEALTH SCIENCES CENTER
UNIVERSITY OF WASHINGTON MEDICAL CENTER
COLUMBIA ROAD
S-1 GARAGE
FISHERIES CENTER
CHDD CLINIC
CENTER ON HUMAN DEVELOPMENT AND DISABILITY (CHDD)
SOUTH B
KEY
STAIRS
ELEVATOR
ENTRY LEVEL
HANDICAP ENTRANCE
PAY TELEPHONE
EMERGENCY PHONE

MapPoint
Shoreline
Lake Forest Park
Bothell
Kenmore
Puget Sound
W A S H I N G T O N
K I N G
Lake Washington
Kirkland
Seattle
Bellevue
Mercer Island
Ballard
Fremont
Wallingford
University District
Capitol Hill
Queen Anne
Magnolia
Belltown
Elliott Bay
Medina

How models are like maps

Like maps, models…

… are *abstractions*

… have *scale*

… must trade off *realism* with *generality*

The kind of model you use depends on the question you want to answer.

Modeling can be simple or complex

i(t) = i(0) + tc the number of infecteds at time t is a simple function of time and the linear growth rate

Assembling introductions, infections, and removals thus yields the following differential equations:

$$\frac{dn_{i-}}{dt} = (\mu_i - \gamma n_{i-}) - \frac{\beta_{ins} n_{i-} n_{r+}}{n_i n_r}\left[\bar{c}\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \bar{c}\left(\frac{n_i + n_r}{2}\right)h\right] - \left(\frac{\beta_{ins} n_{i-} n_{v+}}{n_i n_v}\right)\left(\frac{\bar{c} n_i n_v}{n}\right)(1-h)$$

$$\frac{dn_{r-}}{dt} = (\mu_r - \gamma n_{r-}) - \frac{\beta_{rec} n_{r-} n_{i+}}{n_i n_r}\left[\bar{c}\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \bar{c}\left(\frac{n_i + n_r}{2}\right)h\right] - \left(\frac{\beta_{rec} n_{r-} n_{v+}}{n_r n_v}\right)\left(\frac{\bar{c} n_r n_v}{n}\right)(1-h)$$

$$\frac{dn_{v-}}{dt} = (\mu_v - \gamma n_{v-}) - \left(\frac{\beta_{rec} n_{v-} n_{i+}}{n_v n_i}\right)\left(\frac{\bar{c} n_v n_i}{n}\right)(1-h) - \left(\frac{\beta_{ins} n_{v-} n_{r+}}{n_v n_r}\right)\left(\frac{\bar{c} n_v n_r}{n}\right)(1-h) - \left(\frac{\beta_{ins} + \beta_{rec}}{2}\right)\left(\frac{2n_{v-} n_{v+}}{n_v^2}\right)\left[\frac{\bar{c} n_v^2}{2n}(1-h) + \left(\frac{c^- n_v}{2}\right)h\right]$$

$$\frac{dn_{i+}}{dt} = (-\gamma n_{i+} - \gamma' n_{i+}) + \frac{\beta_{ins} n_{i-} n_{r+}}{n_i n_r}\left[\bar{c}\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \bar{c}\left(\frac{n_i + n_r}{2}\right)h\right] + \left(\frac{\beta_{ins} n_{i-} n_{v+} c}{n_i n_v}\right)\left(\frac{\bar{c} n_i n_v}{n}\right)(1-h)$$

$$\frac{dn_{r+}}{dt} = (-\gamma n_{r+} - \gamma' n_{r+}) + \frac{\beta_{rec} n_{r-} n_{i+}}{n_i n_r}\left[\bar{c}\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \bar{c}\left(\frac{n_i + n_r}{2}\right)h\right] + \left(\frac{\beta_{rec} n_{r-} n_{v+}}{n_r n_v}\right)\left(\frac{\bar{c} n_r n_v}{n}\right)(1-h)$$

$$\frac{dn_{v+}}{dt} = (-\gamma n_{v+} - \gamma'_{v+}) + \left(\frac{\beta_{rec} n_{v-} n_{i+}}{n_v n_i}\right)\left(\frac{\bar{c} n_v n_i}{n}\right)(1-h) + \left(\frac{\beta_{ins} n_{v-} n_{r+}}{n_v n_r}\right)\left(\frac{\bar{c} n_v n_r}{n}\right)(1-h) + \left(\frac{\beta_{ins} + \beta_{rec}}{2}\right)\left(\frac{2n_{v-} n_{v+}}{n_v^2}\right)\left[\frac{\bar{c} n_v^2}{2n}(1-h) + \left(\frac{c^- n_v}{2}\right)h\right]$$

The model is then solved for different values of $n_v(0)$ (initial prevalence of versatility), h (role assortativity), and $\bar{c}$ (contact rate), as discussed in the text (Subjects and Methods).

Epidemic potential

R_0 = the number of direct infections occurring as a result of a single infection in a "virgin" population – that is, one that has not experienced the disease before

Called the basic reproductive ratio

Tells one whether an epidemic is likely to occur or not:

• If $R_0 > 1$, then a single infected individual in the population will on average infect more than one person before ceasing to be infected. In a deterministic model, the disease will grow

• If $R_0 < 1$, then a single infected individual in the population will on average infect less than one person before ceasing to be infected. In a deterministic model, the disease will fade away

• If $R_0 = 1$, we are right on the threshhold between an epidemic and not. In a deterministic model, the disease will putter along

Epidemic potential

How many people will a single new infected person infect before they cease to be infected?

Imagine that a newly infected person is infected for **d** time units on average.

During each of these time units, how many contacts will they have? c

What is their total # of contacts while they're infected? cd

What proportion of them will be susceptible? 100%

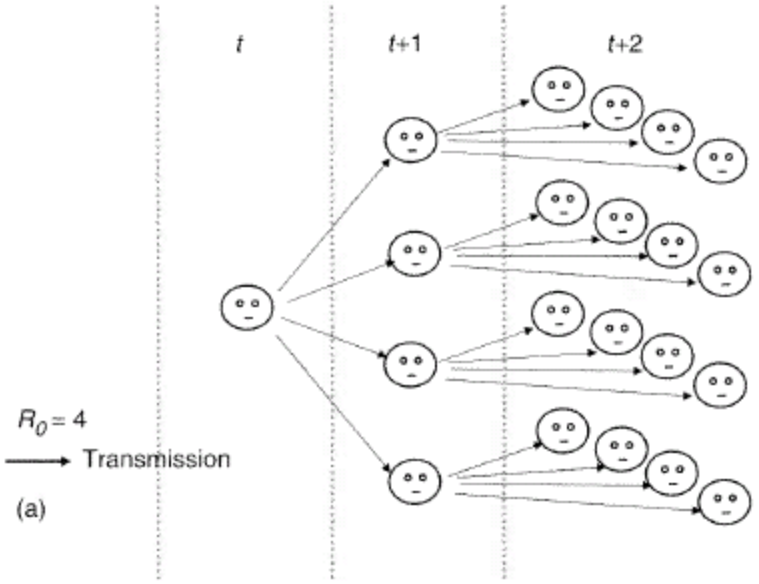
So, what is their total # of susceptible contacts while they're infected? cd

For each contact, what is the probability of transmission? β

So, what is the expected number of people a single infected person will infect? βcd

$R_0 = \beta cd$

Example: $R_0 = 4$



Epidemic modeling

- Infectious disease transmission operates within a classic *complex system*

- They exhibit feedback (how many get infected depends on how many are already infected, but in complicated ways)

- STDs in particular are transmitted on highly structured, non-random networks of *contacts*

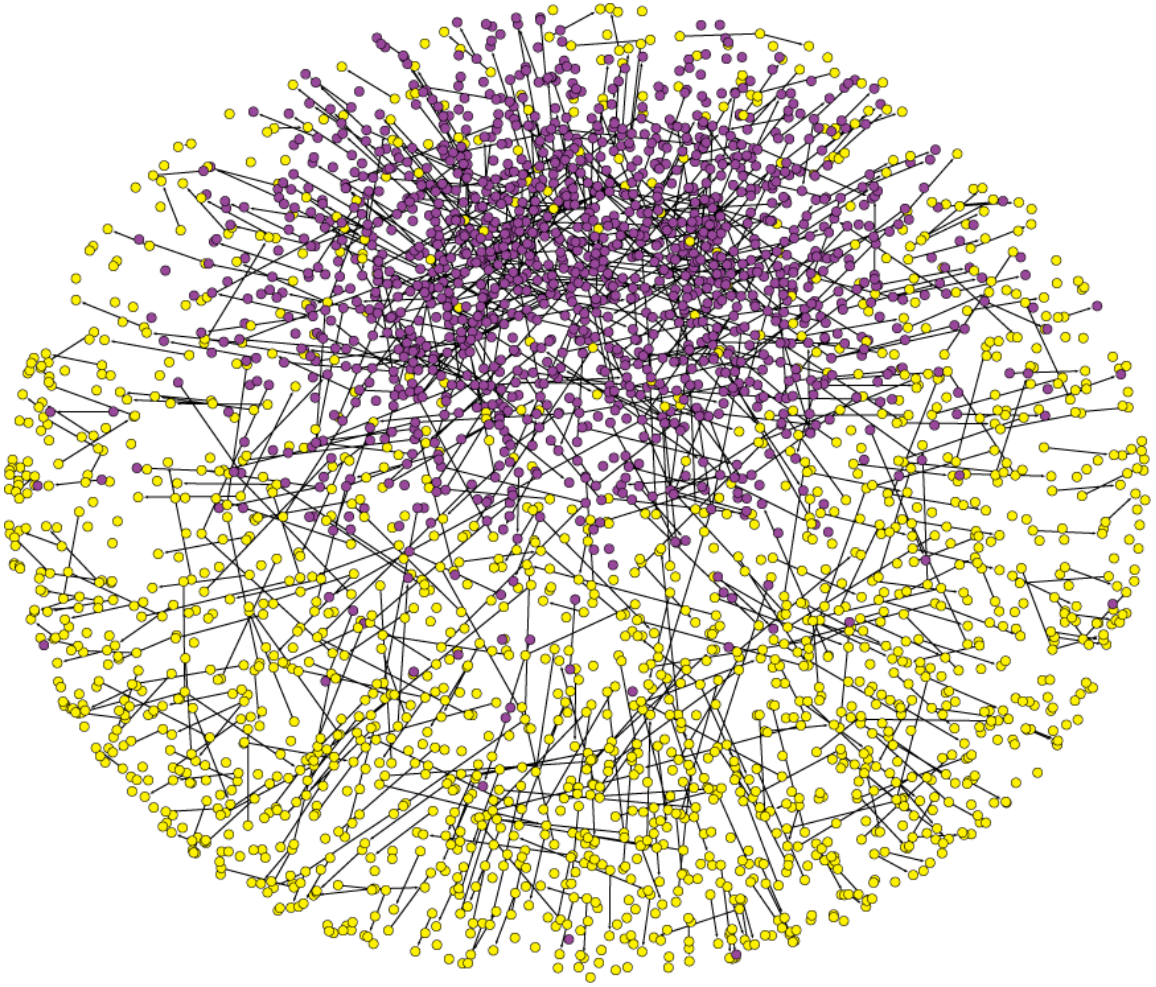
More on sexual contacts

- Contacts are usually within a partnership (i.e. multiple contacts with same person)
- The timing and sequence of partnerships matter
- Who mixes/partners with whom matters (i.e. people don’t choose partners randomly)

Daily connectivity: mixing and concurrency

Almost all components are size 2 or smaller

The largest components have 5-6 nodes



0.06%

connected

Morris et al. AJPH 2009

So, what to do?

How do we incorporate these important issues into modeling?

The answer depends on:

- the population to be modeled
- data availability
- the scientific question at hand, and
- the modeler's preferences

Let's talk about two options:

1. Deterministic, compartmental modeling
2. Stochastic, agent-based and network modeling

Models often classified by rates

- Underlying process of a model: **deterministic** or **stochastic**

- Difference is how they define the movement between states
  - ***Deterministic*** models: average *rate* of transition between states, or using the mean to predict rates of movement
  - ***Stochastic*** models: define the dynamics using the *probability* that an individual makes the transition from one state to another, or using the full probability distribution of outcomes to govern rates

- Often has implications for **states** (careful!):
  - Deterministic models: usually built on group aggregates or macro-level states (i.e. compartments),
  - Stochastic simulation models: usually built to reflect the micro-level states occupied by discrete individual persons.

Deterministic vs. stochastic

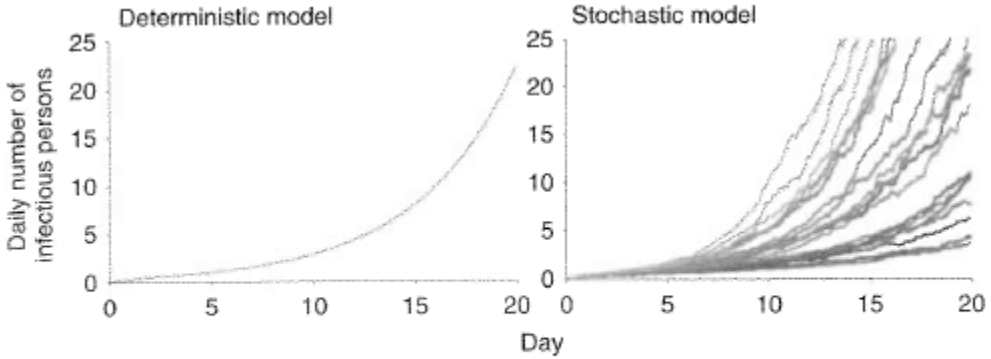


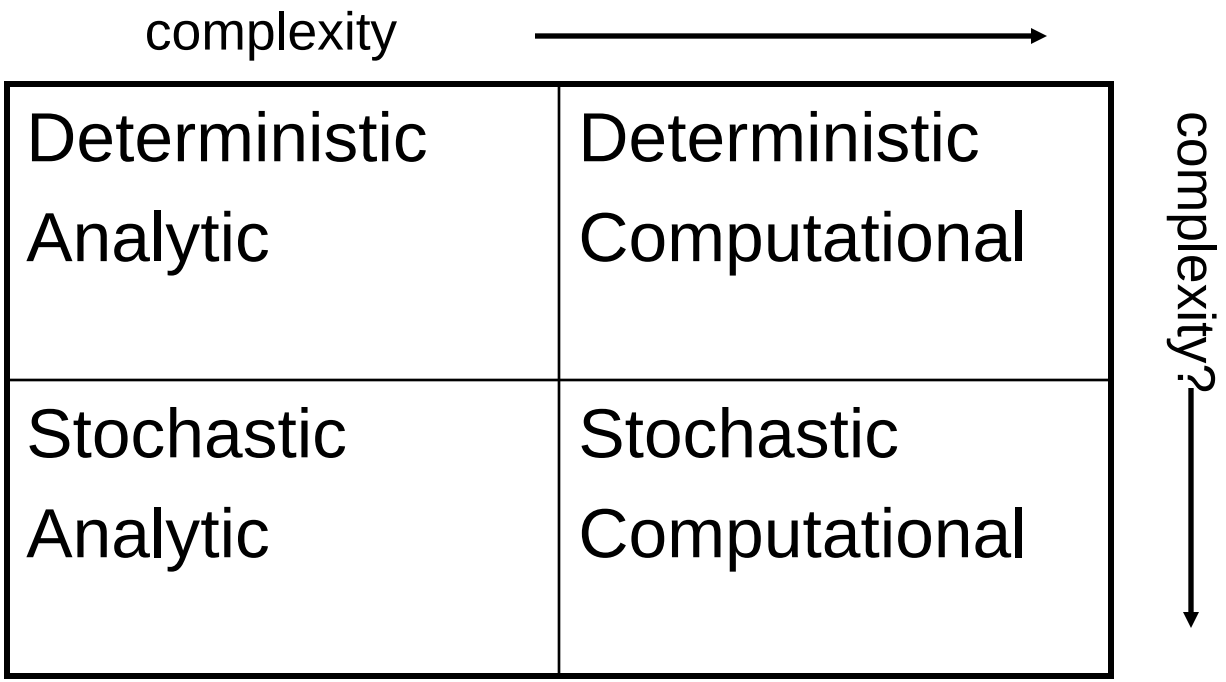
Fig. 2.4 Comparison between predictions of the number of infectious persons per day for influenza obtained using a deterministic model and a stochastic model using 20 'runs', with the rate at which individuals are infected being allowed to vary with each run.

Models can also be classified by solutions

- Dynamics over time can be solved **analytically** or **computationally**
  - Analytic, or “closed form” solutions isolate outcome on left-hand side of equation
  - Computational, or numerical, solutions need to be used if the outcome is on both sides of the equation – ex: non-trivial feedback loops
    - This happens very quickly; most models with realistic heterogeneity need to be solved this way

Model classification

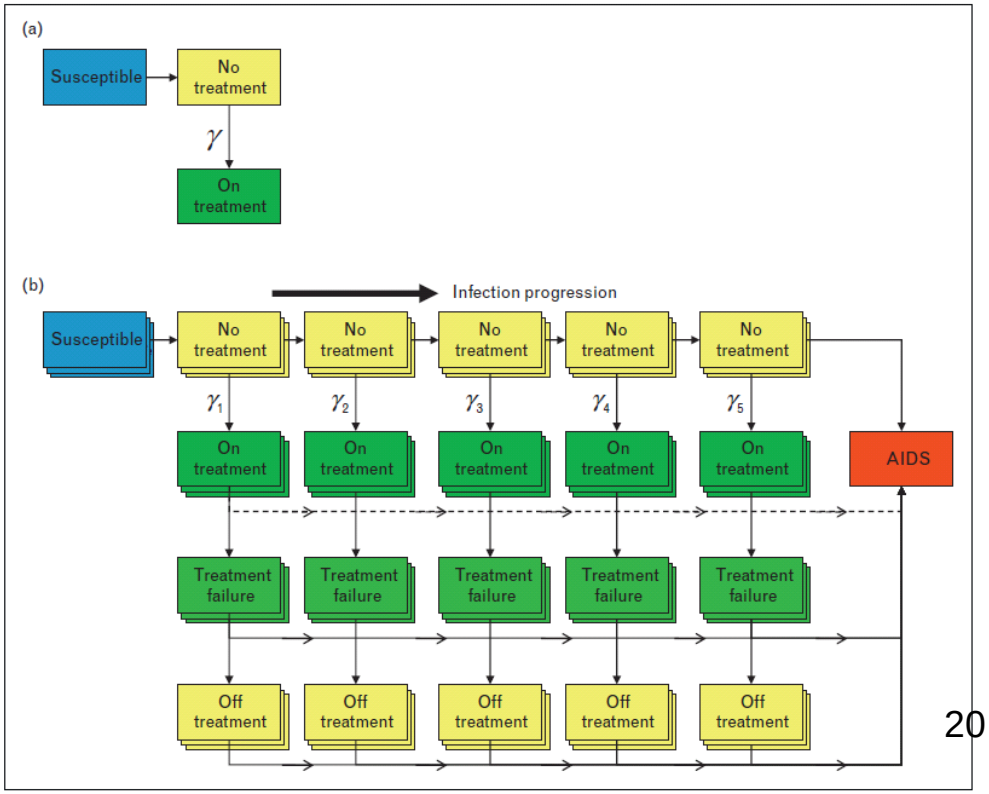
…in a simplified scheme…



Compartmental modeling

"Classic epidemic modeling": is based on differential equations that divide people into epidemiologically relevant "**compartments**" and then specify the magnitude of change on those compartment sizes at any given time

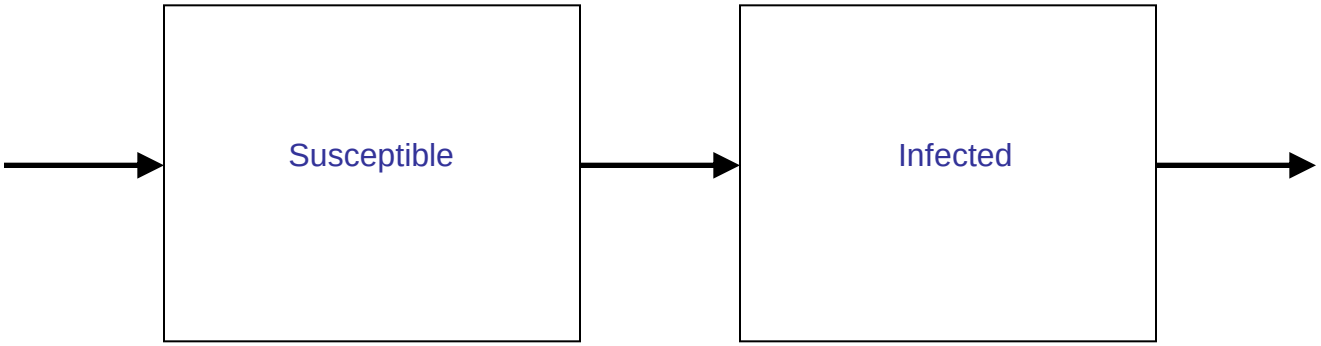
Figure 3 Schematic illustrations of the structure of HIV transmission models incorporating antiretroviral therapy



Baggeley & Fraser, July 2012 Current Opinion in HIV/AIDS, 2010

Compartmental Modeling

- People can move between compartments along “transitions,” aka “flows”.
- Transitions represent different phenomena depending on the compartments that they connect
- Transitions can also occur between a compartment and from somewhere outside of the model
- Transitions are typically a function of the size of compartments



Compartmental models: Step 1

1. **Define *compartments* and *flows***

Compartmental models: Step 1

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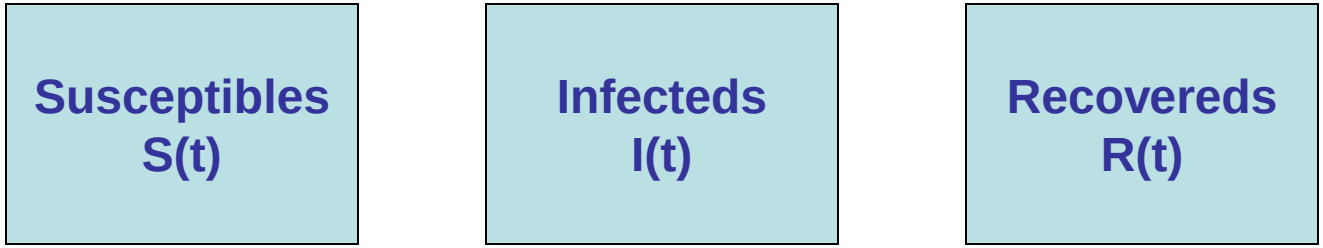
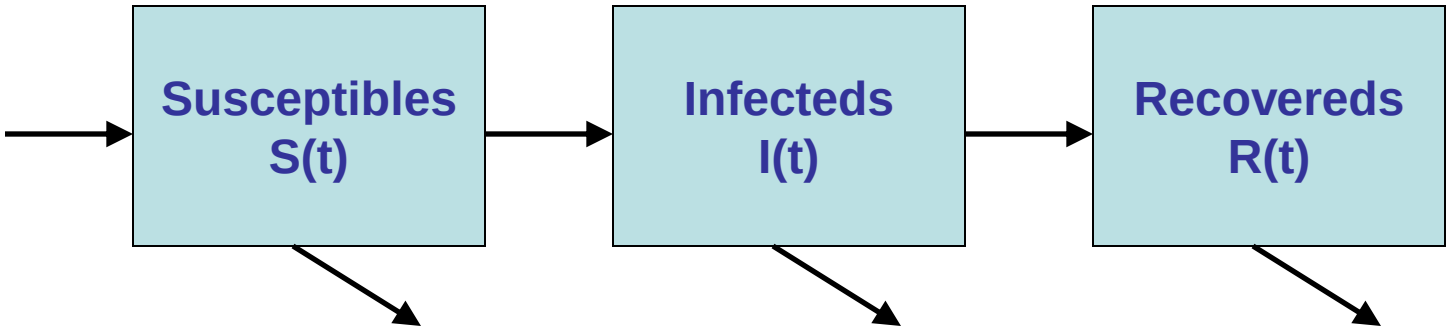


Compartmental models: Step 1

1. Define *compartments* and *flows*



Compartmental models: Step 1

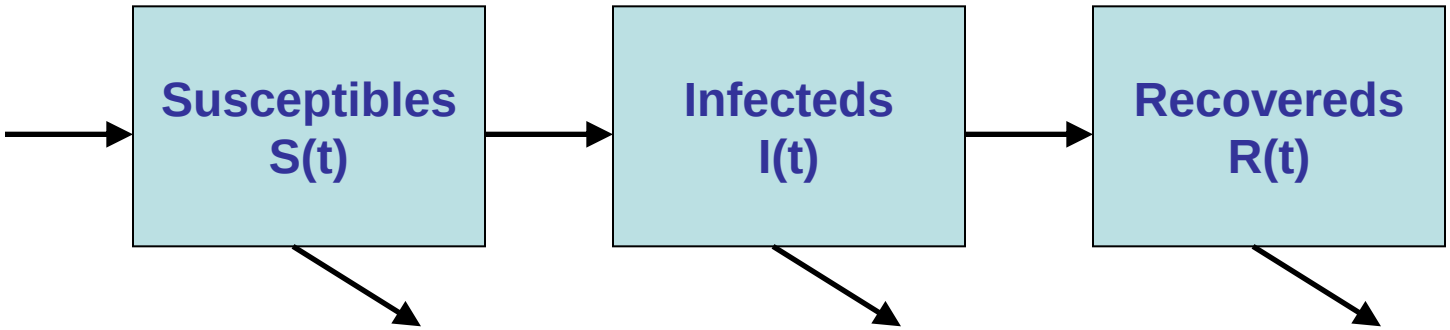
One can add additional heterogeneity (behavioral, genetic, virological, etc.) among actors in a compartmental model by defining more compartments

(e.g. undiagnosed / diagnosed / treated)

This works best when the heterogeneity comes in the form of a limited number of discrete categories.

Compartmental models: Step 2

2. Determine the initial size of each compartment



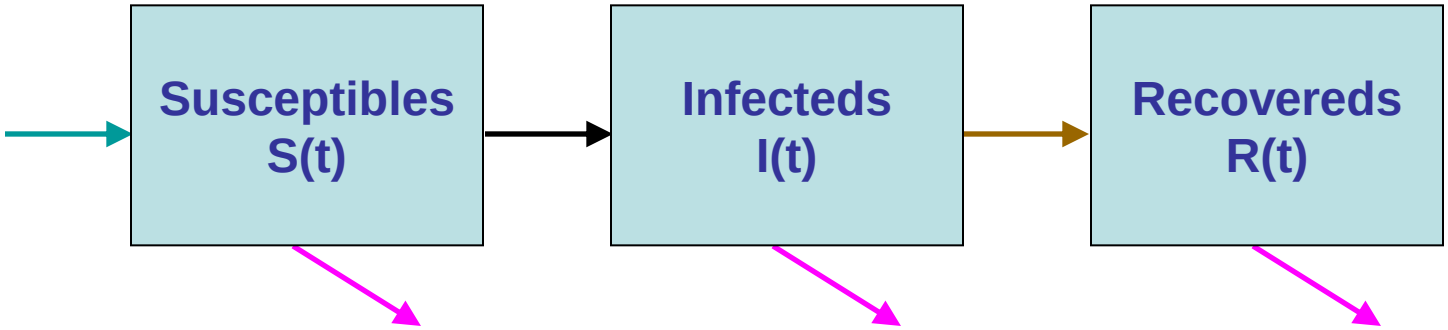
very different outcomes from initial sizes of:

S(0) = 1000 / I(0) = 0 / R(0) = 500, vs.

S(0) = 1000 / I(0) = 25 / R(0) = 25

Compartmental models: Step 3

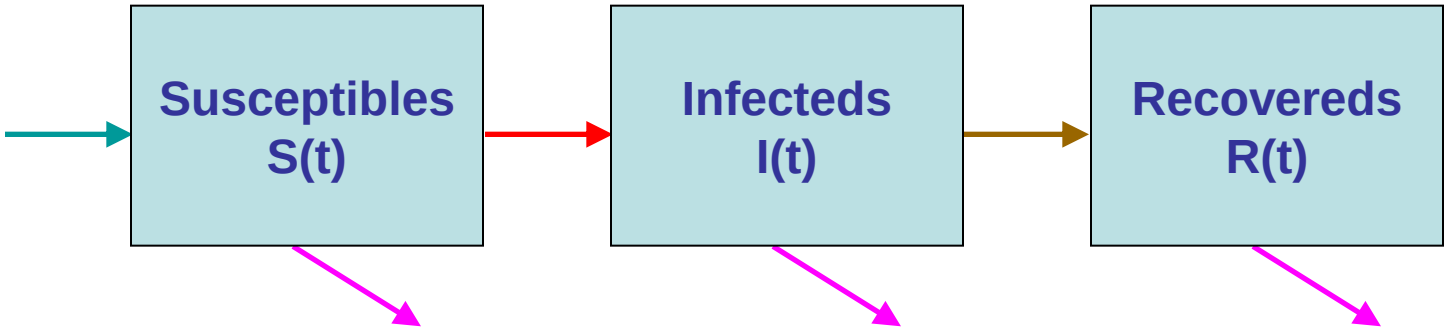
3. Determine the rates for the flows



Number of births per unit time: often modeled as a constant rate.	= b
Number of recoveries per unit time: often modeled as a constant rate *times* the size of the compartment	= k * I
Number of deaths per unit time: often modeled as a constant rate *times* the size of the compartment	= μS or μI or μR

Compartmental models: Step 3

3. Determine the rates for the flows



Number of transmissions per unit time: the interesting bit!

Compartmental models: Step 3

Transmission involves:

- Infected person
- Susceptible person
- Contact between them
- Transmission given contact

…so, one way to model transmissions is…

# of transmissions / unit time =

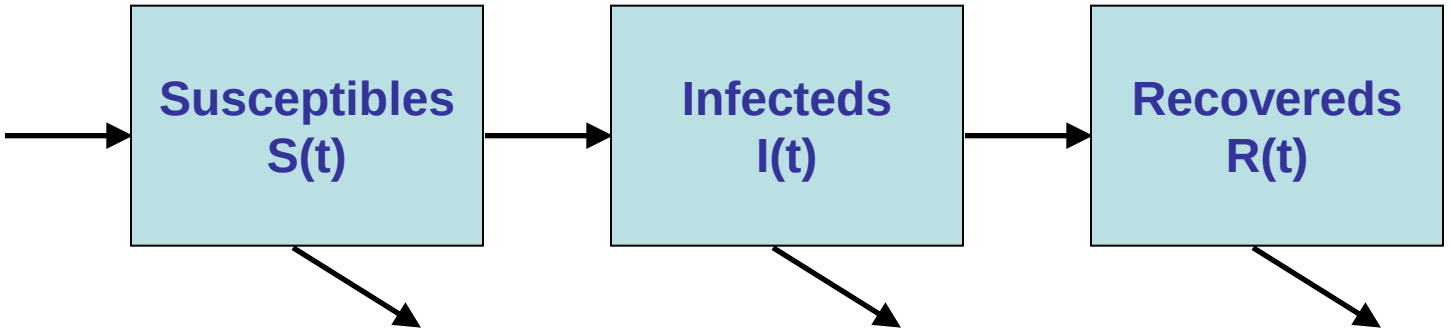
(# of susceptibles) *

(# of contacts / susceptible / unit time) *

(prob. each contact is with an infected person) *

(prob. of transmission given an SI contact)

Compartmental models: Step 3



(# of susceptibles) *
(# of contacts / susceptible / unit time) *
(prob. each contact is with an infected person)*
(prob. of transmission given an SI contact)

# of transmissions at time *t* = $S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta$

where *n(t) = S(t) + I(t) + R(t)*

Compartmental models: Step 3

How do you know what values to assign to these various quantities (c, *β*, etc.)?

1. Use data from epidemiological studies.
2. If good data don't exist, try a variety of realistic values, and if you're lucky, the results won't be very sensitive to this uncertainty.
3. If they are sensitive, then you've just identified a place where more data may be needed to adequately answer whatever important question it is you're addressing with your model.

Compartmental models: Step 4

Change in the # of susceptibles at time t = # of births – # of deaths to susceptibles – # of infections

$$\frac{dS}{dt} = b - \mu S(t) - S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta$$

Change in the # of infecteds at time t = # of infections – # of deaths to infecteds – # of recoveries

$$\frac{dI}{dt} = S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta - \mu I(t) - kI(t)$$

Change in the # of immunes at time t = # of recoveries - # of deaths to immunes

$$\frac{dR}{dt} = kI(t) - \mu R(t)$$

Compartmental models: Step 5

Change in the # of susceptibles at time t = # of births – # of deaths to susceptibles – # of infections

Incidence

$$\frac{dS}{dt} = b - \mu S(t) - S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta$$

Change in the # of infecteds at time t = # of infections – # of deaths to infecteds – # of recoveries

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Compartmental models: Step 5

Change in the # of susceptibles at time t = # of births – # of deaths to susceptibles – # of infections

$$\frac{dS}{dt} = b - \mu S(t) - S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta$$

Incidence

Prevalence → $\frac{S(t)}{n(t)}$

Change in the # of infecteds at time t = # of infections – # of deaths to infecteds – # of recoveries

$$\frac{dI}{dt} = S(t) \cdot c \cdot \frac{I(t)}{n(t)} \cdot \beta - \mu I(t) - kI(t)$$

Change in the # of immunes at time t = # of recoveries - # of deaths to immunes

$$\frac{dR}{dt} = kI(t) - \mu R(t)$$

Compartmental models: Step 5

from...

$$\frac{dn_{i-}}{dt} = [\mu_i - \gamma n_{i-}] - \left(\frac{\beta_{ins} n_{i-} n_{r+} \bar{c}}{n_i n_r}\right)\left[\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \left(\frac{n_i + n_r}{2}\right)(h)\right] - \left(\frac{\beta_{ins} n_{i-} n_{v+} \bar{c}}{n_i n_v}\right)\left(\frac{n_i n_v}{n}\right)(1-h)$$

$$\frac{dn_{r-}}{dt} = [\mu_r - \gamma n_{r-}] - \left(\frac{\beta_{rec} n_{r-} n_{i+} \bar{c}}{n_i n_r}\right)\left[\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \left(\frac{n_i + n_r}{2}\right)(h)\right] - \left(\frac{\beta_{rec} n_{r-} n_{v+} \bar{c}}{n_r n_v}\right)\left(\frac{n_r n_v}{n}\right)(1-h)$$

$$\frac{dn_{v-}}{dt} = [\mu_v - \gamma n_{v-}] - \left(\frac{\beta_{rec} n_{v-} n_{i+} \bar{c}}{n_v n_i}\right)\left(\frac{n_v n_i}{n}\right)(1-h) - \left(\frac{\beta_{ins} n_{v-} n_{r+} \bar{c}}{n_v n_r}\right)\left(\frac{n_v n_r}{n}\right)(1-h) - \frac{(\beta_{ins} + \beta_{rec})}{2}\left(\frac{2n_{v-} n_{v+} \bar{c}}{n_v^2}\right)\left[\left(\frac{n_v^2}{2n}\right)(1-h) + \left(\frac{n_v}{2}\right)(h)\right]$$

$$\frac{dn_{i+}}{dt} = [-\gamma n_{i+} - \gamma' n_{i+}] + \left(\frac{\beta_{ins} n_{i-} n_{r+} \bar{c}}{n_i n_r}\right)\left[\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \left(\frac{n_i + n_r}{2}\right)(h)\right] + \left(\frac{\beta_{ins} n_{i-} n_{v+} \bar{c}}{n_i n_v}\right)\left(\frac{n_i n_v}{n}\right)(1-h)$$

$$\frac{dn_{r+}}{dt} = [-\gamma n_{r+} - \gamma' n_{r+}] + \left(\frac{\beta_{rec} n_{r-} n_{i+} \bar{c}}{n_i n_r}\right)\left[\left(\frac{n}{2} + \frac{n_v^2}{2n} - n_v\right)(1-h) + \left(\frac{n_i + n_r}{2}\right)(h)\right] + \left(\frac{\beta_{rec} n_{r-} n_{v+} \bar{c}}{n_r n_v}\right)\left(\frac{n_r n_v}{n}\right)(1-h)$$

$$\frac{dn_{v+}}{dt} = [-\gamma n_{v+} - \gamma' n_{v+}] + \left(\frac{\beta_{rec} n_{v-} n_{i+} \bar{c}}{n_v n_i}\right)\left(\frac{n_v n_i}{n}\right)(1-h) + \left(\frac{\beta_{ins} n_{v-} n_{r+} \bar{c}}{n_v n_r}\right)\left(\frac{n_v n_r}{n}\right)(1-h) + \left(\frac{\beta_{ins} + \beta_{rec}}{2}\right)\left(\frac{2n_{v-} n_{v+} \bar{c}}{n_v^2}\right)\left[\left(\frac{n_v^2}{2n}\right)(1-h) + \left(\frac{n_v}{2}\right)(h)\right]$$

…to…

Number of new cases at a given time
Number of people infected at any given time
Number of people not infected at any given time…

And therefore, prevalence at any given time

(As well as most other epidemiological measures you can think of)

Compartmental modeling: strengths

- General framework well understood (and studied for many decades now)
- Relatively easy to implement using existing software
- Because it has been the standard for decades, it is what most modelers are most familiar with
- It is thus relatively easy to communicate to others (other investigators, reviewers, grantees, etc.)

A Tale of Two Futures: HIV and Antiretroviral Therapy in San Francisco

S. M. Blower,[1]* H. B. Gershengorn,[1] R. M. Grant[2]

Declines in HIV prevalence can be associated with changing sexual behaviour in Uganda, urban Kenya, Zimbabwe, and urban Haiti

T B Hallett, J Aberle-Grasse, G Bello, L-M Boulos, M P A Cayemittes, B Cheluget, J Chipeta, R Dorrington, S Dube, A K Ekra, J M Garcia-Calleja, G P Garnett, S Greby, S Gregson, J T Grove, [illegible] Ismail, S Kassim, W Kirungi, L Kouassi, A Mahomva, L Marum, [illegible]tover, N Walker

Sex Transm Infect 2006;**82**(Suppl I):i1–i8. doi: 10.1136/sti.2005.016014

No HIV stage is dominant in driving the HIV epidemic in sub-Saharan Africa

Laith J. Abu-Raddad[a,b,c] and Ira M. Longini Jr[a,b,d]

HIV serosorting as a harm reduction strategy: evidence from Seattle, Washington

Susan Cassels[a], Timothy W. Menza[b], Steven M. Goodreau[c] and Matthew R. Golden[b]

Objective: We sought to estimate how serosorting may affect HIV prevalence and individual risk among men who have sex with men in Seattle, Washington, and how the results vary under different assumptions of HIV testing frequency, heterogeneity in sexual behavior, and condom use.

Methods: We developed a deterministic mathematical model of HIV transmission dynamics. Data from the 2003 random digit dial study of men who have sex with men conducted in Seattle, Washington ($n = 400$) are used to parameterize the model.

Research aims

1. To evaluate the population and individual-level effects of HIV serosorting among MSM in Seattle

2. To define factors that might influence how serosorting affects HIV transmission dynamics

*Punchline: serosorting is protective in the context of MSM in Seattle, but might not be elsewhere. Testing is key.

Thus recognition of serosorting's importance should prompt more frequent HIV testing and more sensitive assays

Compartments (x2)

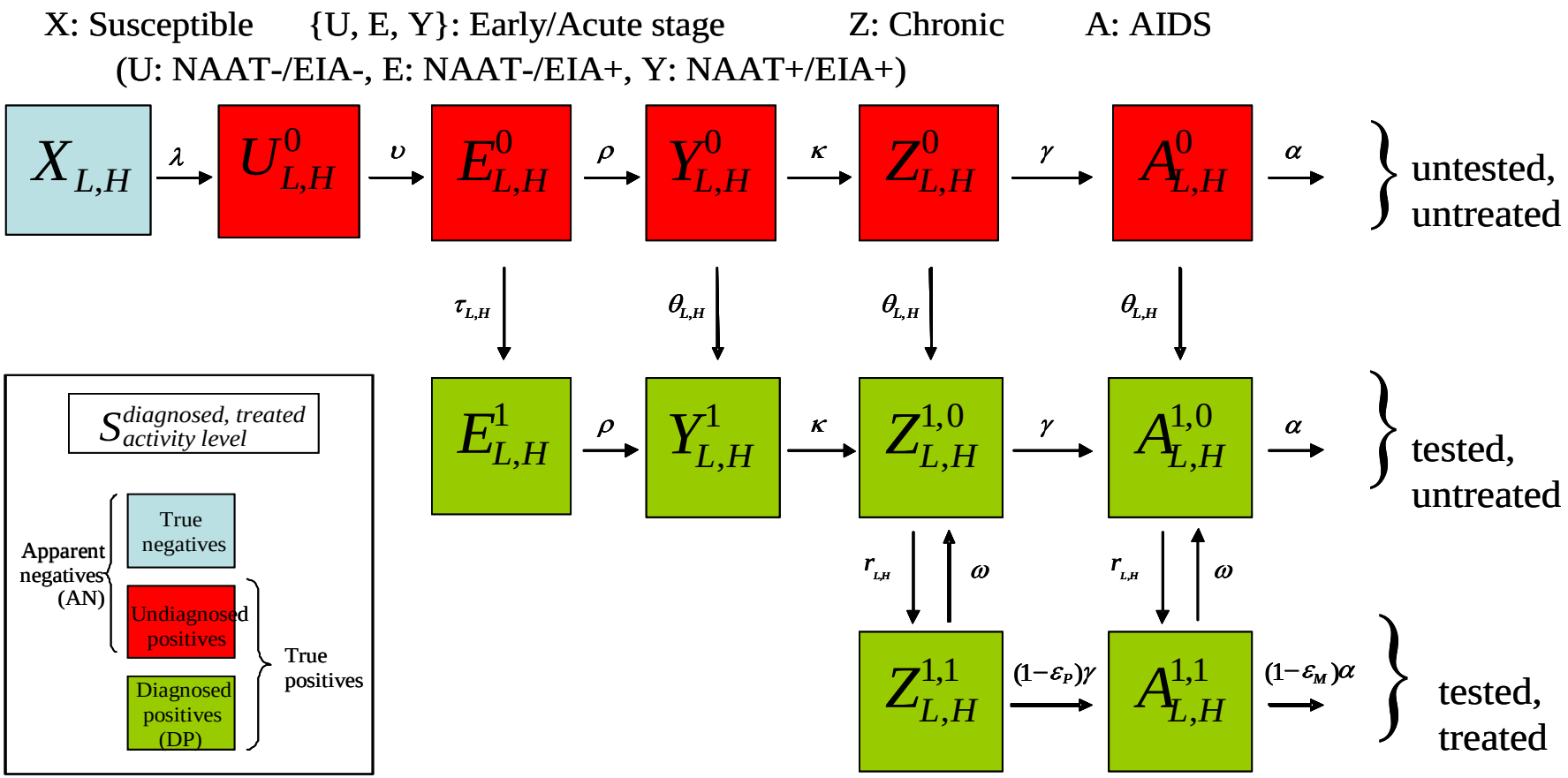


Figure 1. Model structure: compartments and flows. There are 12 compartments for each activity class, Low (L) and High (H).

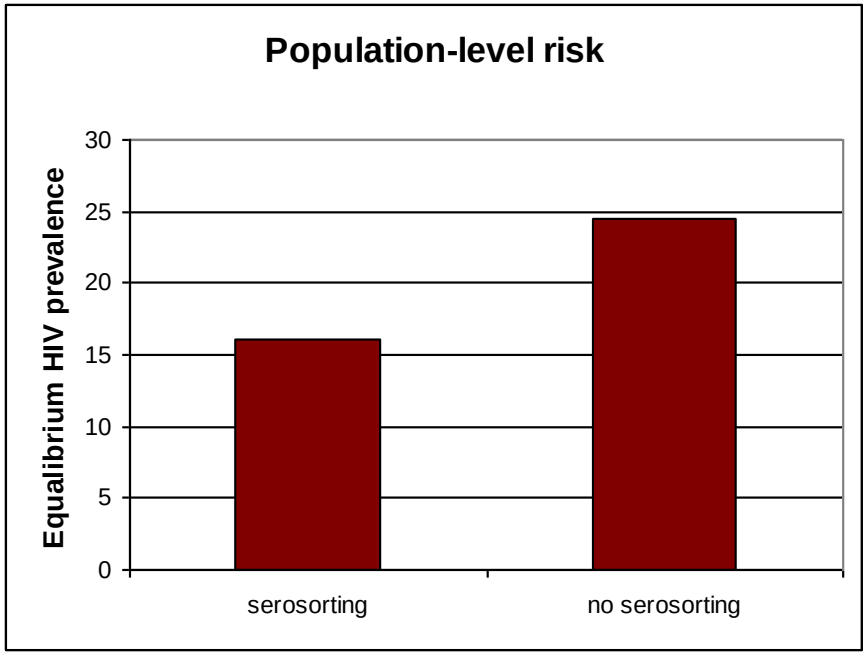
Key social/behavioral assumptions

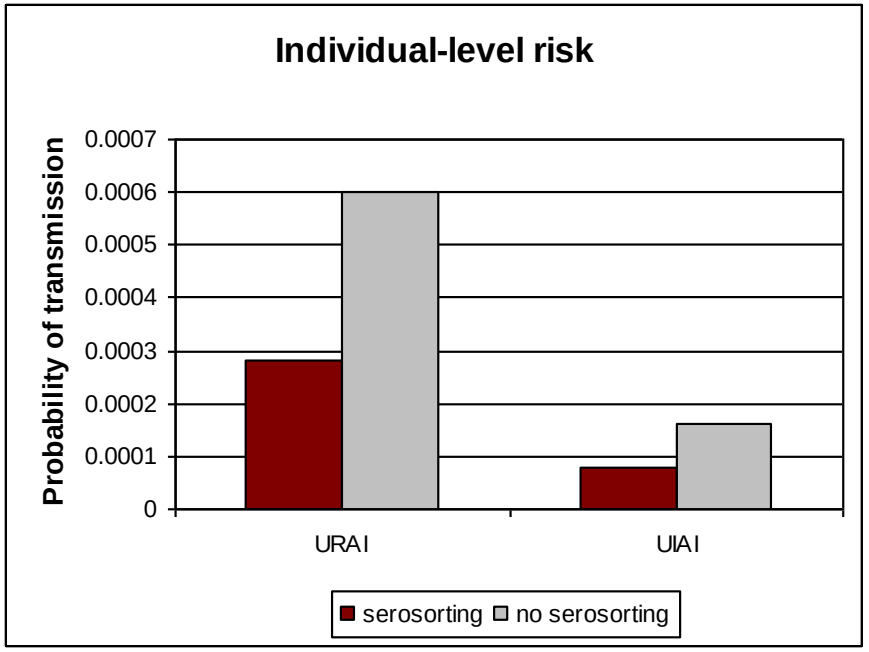
- Men choose partners based on serostatus
- Men proportionally choose partners based on “sexual activity class”

Transmission is a function:

- diagnosed or undiagnosed positive
- high/low sexual activity class
- stage of HIV disease
- # contacts within partnership
- sexual position
- condom use

Results: baseline

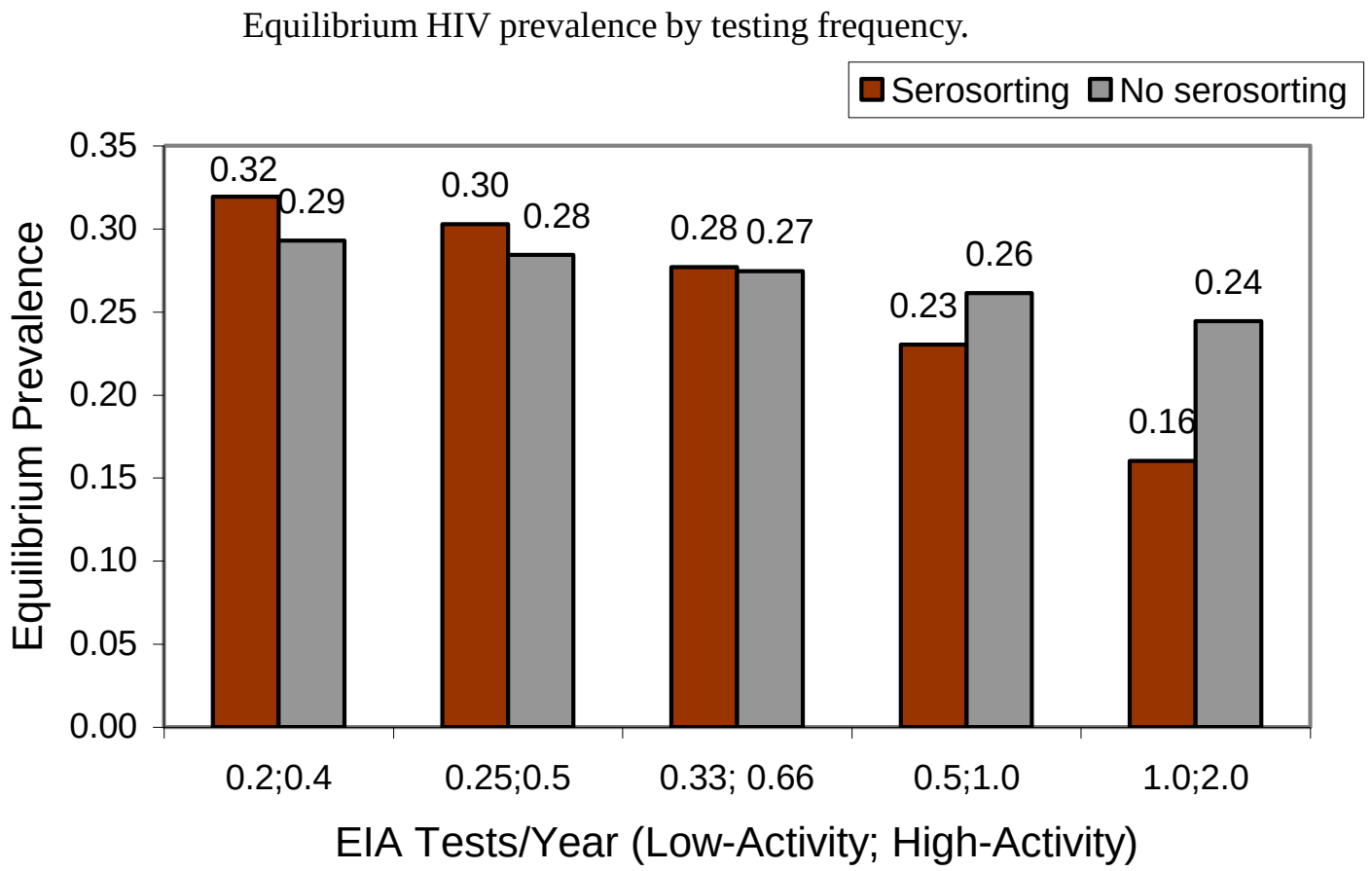




Probability of transmission during unprotected anal sex with a randomly chosen *apparent negative*.

**URAI/UIAI: Unprotected receptive/insertive anal intercourse

Results: testing



Summary

1. HIV prevalence among MSM in Seattle would be higher if men did not serosort.
2. Serosorting may be detrimental if men do not test often.

thus recognition of serosorting's importance should prompt more frequent HIV testing and more sensitive assays.

Compartmental models: limitations

At least four important limitations.

1. Because the approach is usually implemented deterministically, it is hard to get a sense of the possible range of outcomes for a scenario.
2. Does not easily handle continuous variation, or variation that comes in a form with many possible values.
3. Some phenomenon of key interest are (next to) impossible to represent in the compartmental modeling framework
4. Model complexity grows exponentially with phenomenon complexity

The elephant in the room

- Compartmental models have worked to simulate reasonable epidemics among MSM in the U.S.

- Many published compartmental models for heterosexual epidemics in sub-Saharan Africa posit absurdly high rates of partner accumulation
  - E.g. One widely cited study has to assume that the average male and female in the population of Yaounde´, Cameroon has 221 lifetime partners, and 7%have an average of 2,870 partners, each relationship at least 1 week long, over 35 sexually-active years (Abu Raddad, AIDS 2008).

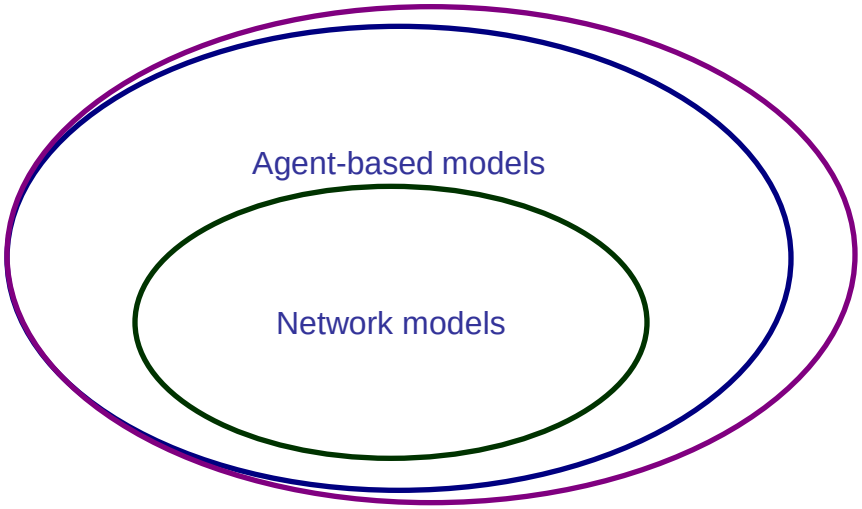
- Why? Concurrency might be more important for sustaining ongoing transmission in heterosexual epidemics.

Stochastic agent-based & network modeling

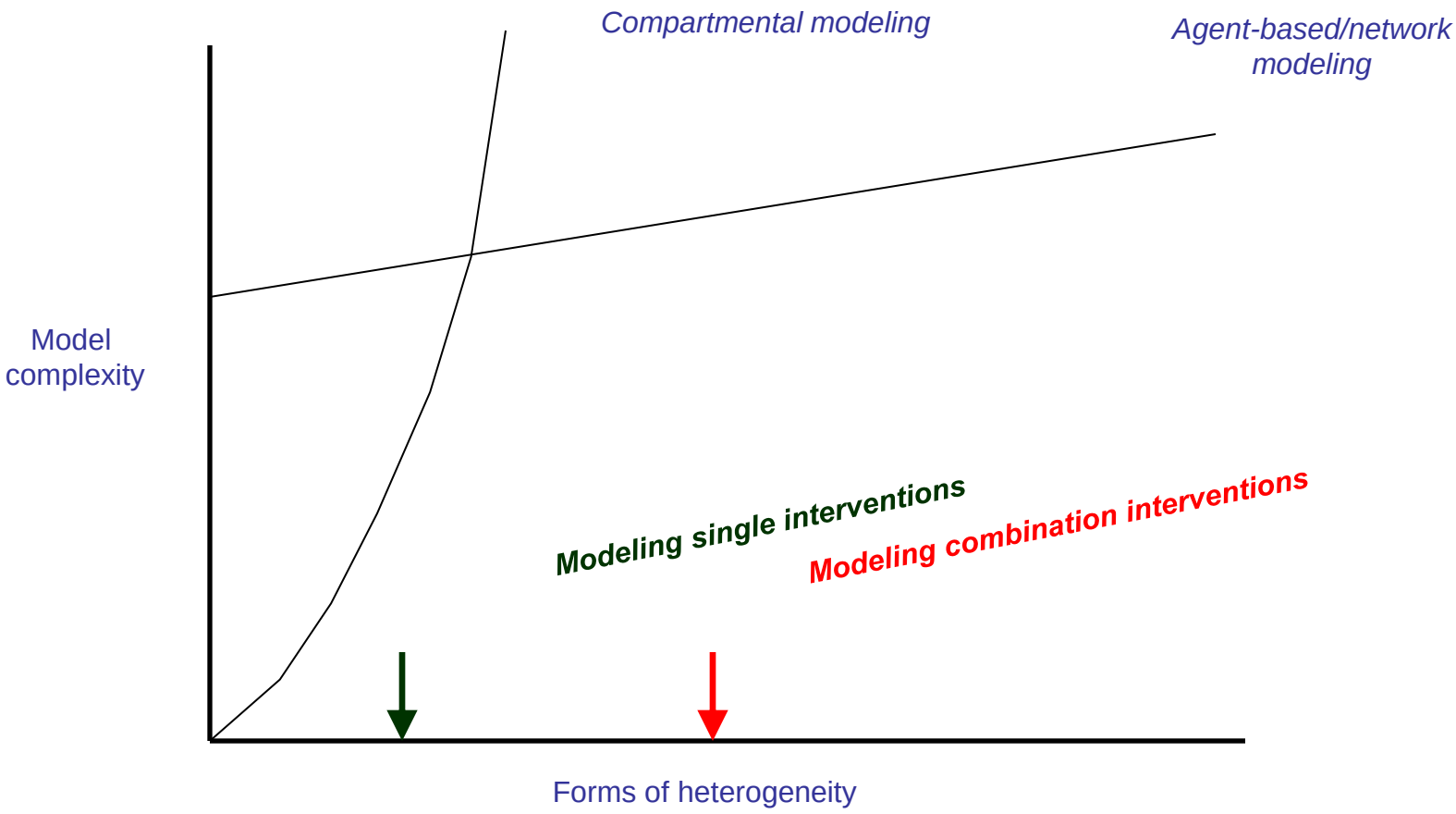
Agent-based model = a model representing each member of the population explicitly, typically in some sort of large matrix of individuals and their attributes

Network model = a model representing individual contacts explicitly (whether they be persistent relationships or one-time contacts)

Stochastic model = a model in which multiple runs of the same scenario can produce different results



Effort required…



Agent-based models: benefits

- These models can incorporate much more individual heterogeneity
- E.g.: Goodreau et al. (PAA 2011): HIV among MSM

Age	Race/ethnicity	Circumcision status	Treatment status
PrEP status	Viral load	Sexual role preference	Diagnosis status
Time since infection	Time since last negative test	Enrolment in interventions	Etc. etc.

Network modeling: Step by Step

1. Represent each member of the initial population explicitly, typically in some sort of matrix or data frame of individuals and their attributes

```
>
> mypop
   sex age inf treatment
1    F  53   0        NA
2    F  23   1         1
3    F  34   0        NA
4    F   1   1         0
5    F  21   0        NA
6    F  42   1         0
7    F  29   0        NA
8    F  48   1         0
9    F  29   0        NA
10   F  43   1         1
11   M   9   0        NA
12   M  37   1         0
13   M  12   0        NA
14   M  22   1         1
15   M  11   0        NA
16   M  26   1         1
17   M  56   0        NA
18   M   3   1         0
19   M  20   0        NA
20   M  60   1         1
>
```

- Major positive: data storage and method complexity increases only linearly with number of attributes
- Minor negative: it also increases linearly with population size

Network modeling: Step by Step

2. Develop a model for relational structure, derived from data

    • What predicts which individuals will or will not form a relationship? (e.g. sex, race, disease status, age, etc., etc.)

    • What structural features tend to be present in the relational network beyond simply attribute mixing? (E.g. particular degree distributions, triangles, etc.)

    • How long do relationships last, and what sources of heterogeneity are there?

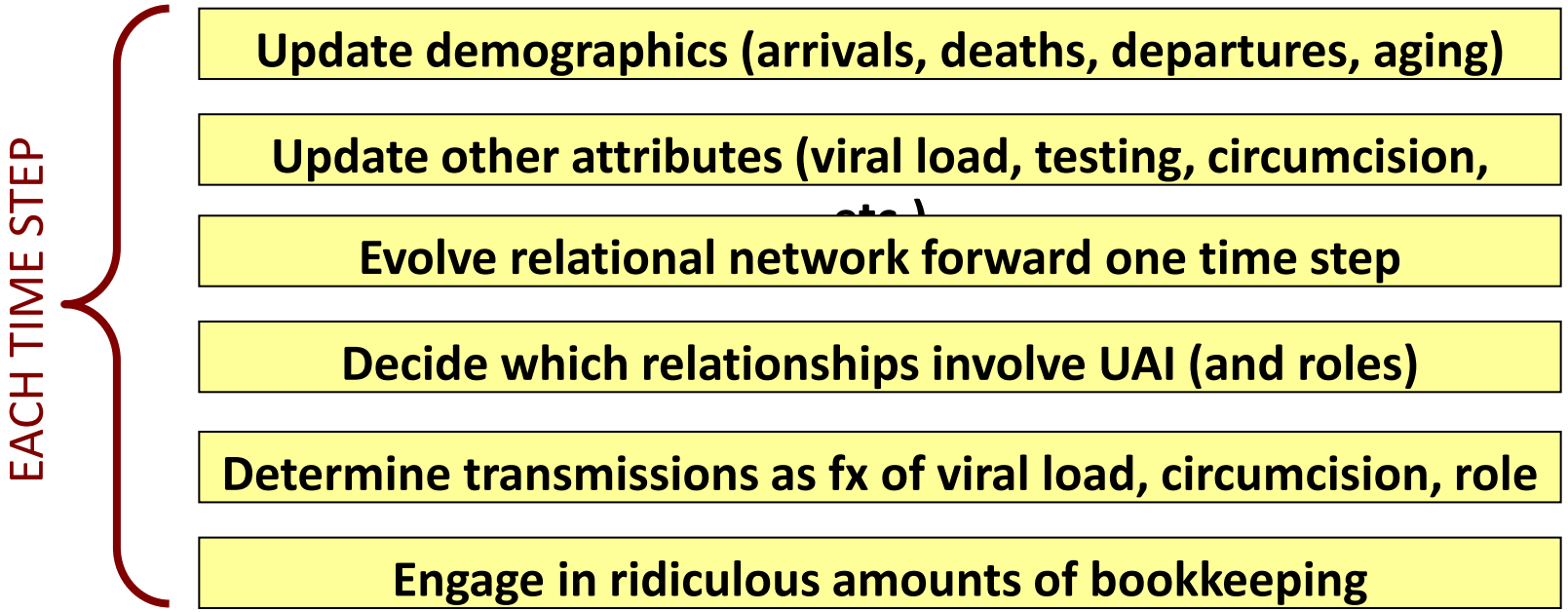
3. Estimate that model using a statistical framework built for estimation and simulation of dynamic social networks

    • We use exponential random graph modeling, although other frameworks exist.

Network modeling: Step by Step

4. Build the initial network for the initial population.

5. Develop modules for the various phenomena that the population experiences moving forwards in time



Update other attributes (viral load, testing, circumcision, etc.)

```
msm.update.attributes <- function(pop,curr.time,
        testcutoff=testcutoff,
        circum.healingtime=circum.healingtime,
        active.v,
        treatment.starttime.by.race
        ) {

    # Intro
    newpop <- pop
    activenodes <- active.v
    uncirc <- which(pop %v% "circum.status" == 0)
    neg.or.undiag <- union(which(pop %v% "diag.status" == 0),which(pop %v% "inf.status" == 0))
    notonprep <- which(pop %v% "prep.status" == 0)
    onprep <- which(pop %v% "prep.status" == 1)

    # Non-intervention circumcision (presumably zero but worth including)
    nointerv <- which(pop %v% "circum.interv.status" == 0)
    active.uncirc.nointerv <- intersect3(activenodes,uncirc,nointerv)
    circumcisers <- active.uncirc.nointerv[(runif(length(active.uncirc.nointerv)) <
        (pop %v% "prob.circum.nointerv")[active.uncirc.nointerv])]
    newpop <- set.vertex.attribute(newpop,"circum.status",9,circumcisers)
    newpop <- set.vertex.attribute(newpop,"circum.time.bp",0,circumcisers)

    # Non-intervention testing
    nointerv <- which(pop %v% "testing.interv.status" == 0)
    active.neg.or.undiag.nointerv <- intersect3(activenodes,neg.or.undiag,nointerv)
    testers <- active.neg.or.undiag.nointerv[(runif(length(active.neg.or.undiag.nointerv)) <
        (pop %v% "prob.test.nointerv")[active.neg.or.undiag.nointerv])]
    apparentpos <- which(newpop %v% "inf.time.bp" > testcutoff)
    apparentneg <- union(which(newpop %v% "inf.time.bp" <= testcutoff),which(pop %v% "inf.status" ==
    testpos <- intersect(testers,apparentpos)
    newpop <- set.vertex.attribute(newpop,"diag.status",1,testpos)
```

HIV & Concurrency in Zimbabwe

AIDS Behav (2012) 16:312–322
DOI 10.1007/s10461-010-9858-x

ORIGINAL PAPER

Concurrent Partnerships, Acute Infection and HIV Epidemic Dynamics Among Young Adults in Zimbabwe

Steven M. Goodreau · Susan Cassels · Danuta Kasprzyk · Daniel E. Montaño · April Greek · Martina Morris

Our aim: Develop a generalized modeling approach for sexual networks and HIV spread that incorporates sexual network characteristics, and apply it to questions of acute infection

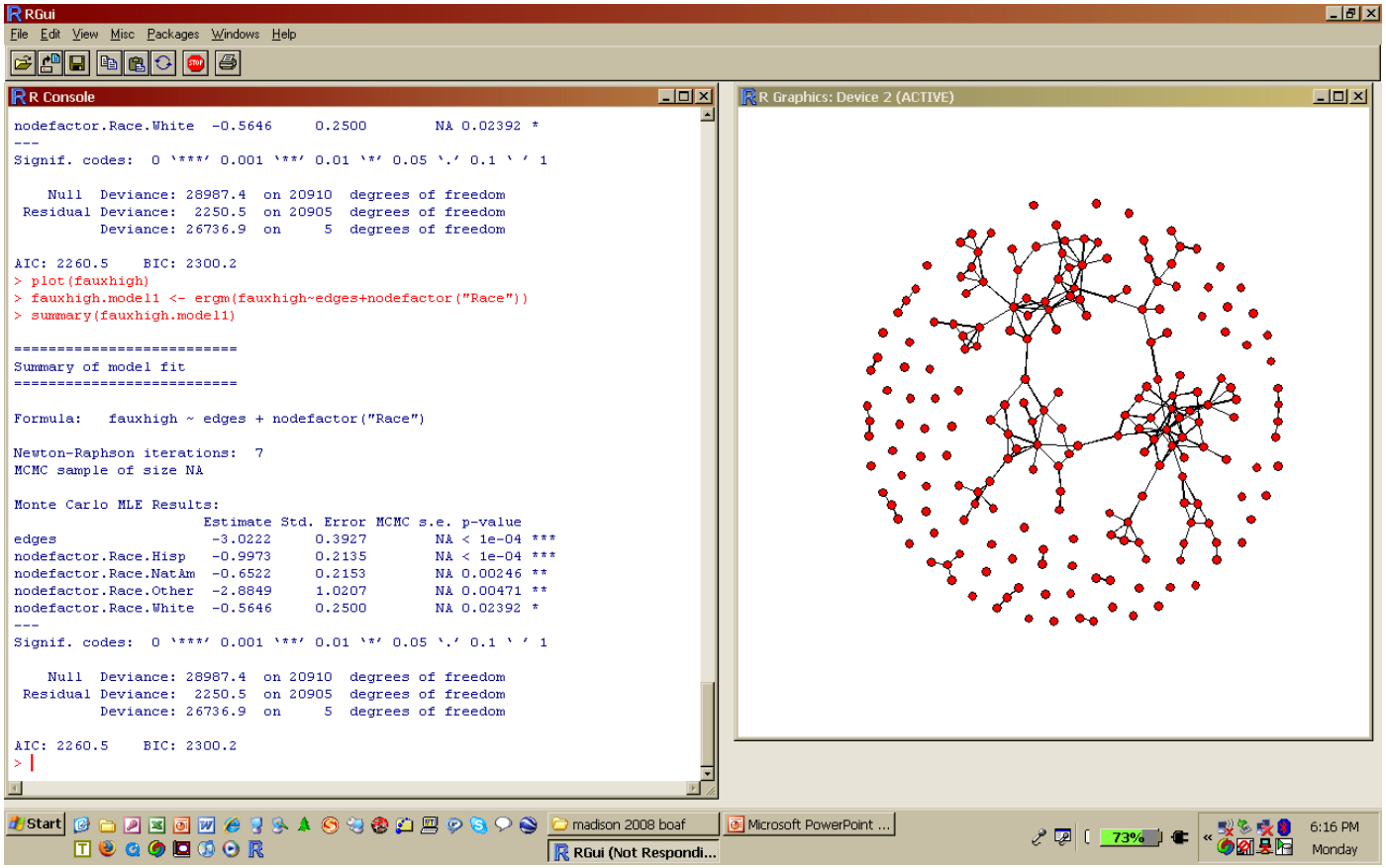
Key social/behavioral components

- Explicitly model sexual network, including:
  - rates of concurrency for men and women
  - partnership type (marriage/live-in vs. casual)
  - durations of partnerships

This paper was one of the first to do so (thanks to the University of Washington *statnet* team)

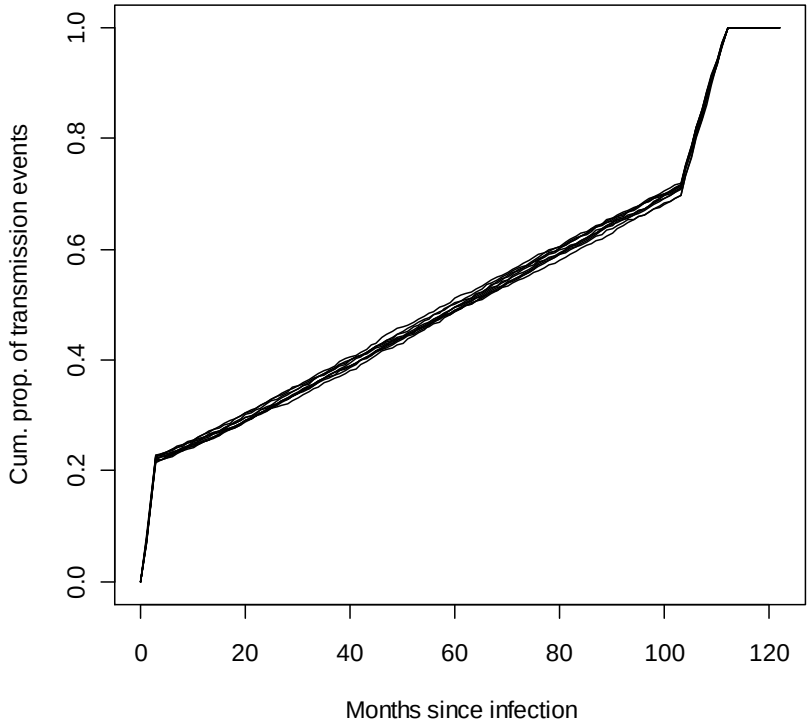
Methods: Exponential random graph modeling (ERGM)

www.statnetproject.org



Results: Proportion of infections by stage

Cumulative proportion of infection events, by time since infection of index partner



Alternative models:

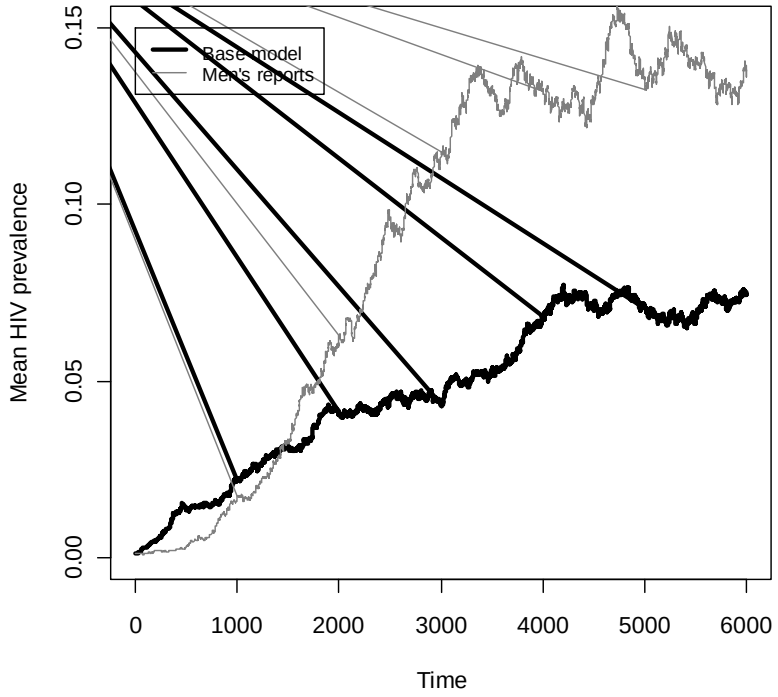
1. Male reports instead of mid-point

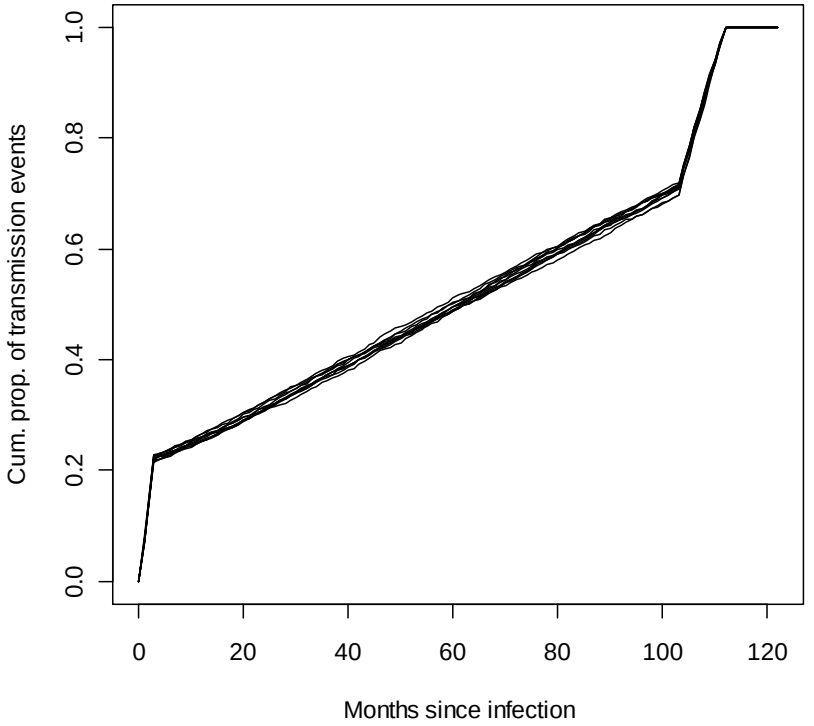
   Males reported an average of 0.08 more partnerships than females did; a small difference, but one which must be dealt with. Rather than assuming the midpoint is correct, here we assume male reports are correct.

2. No concurrent relationships (same # of relationships; same mean duration; but forced to be sequential)

   How much does concurrency drive the epidemic here? What would be the effect of changes in concurrency?

Male reports instead of mid-point





No concurrent relations

Epidemic dies out every time….

Final thoughts

- Important for non-modelers to understand assumptions behind models (a look under the hood), and do not necessarily accept conclusions on blind faith

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings

Peter J. Dodd, Geoff P. Garnett and Timothy B. Hallett

Final thoughts

- Effectiveness of interventions: account for
  - Coverage
  - Impact
  - Duration
  - Trade-offs

- Connections between modelers and behavioral scientists
  - Realism of social and behavioral assumptions: not a “throw away” parameter
  - Collaboration from the beginning

Final thoughts

- Long-term outcomes, sustainability?
- Unexpected consequences
- Unintuitive population-level impact – not a direct scale-up of individual actions