Using mathematical models for health economic analyses

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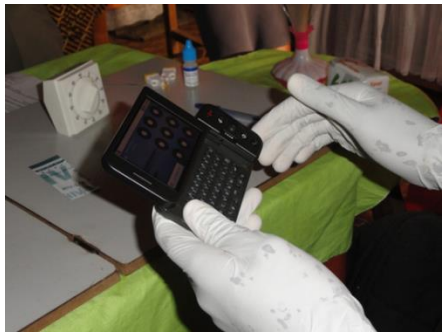

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Outline

- Introduction to modeling
- Infectious disease modeling
  - Introduction; R_0
- How models can be used to estimate health outcomes
  - Example: Potential impact of ART for prevention
  - What study data can you use to parameterize models
- When to use which model

An introduction to Mathematical Models

- Framework for understanding and communicating infectious disease*
- Explicit assumptions help delineate which parameters are based on evidence
- Quantitative or qualitative results are compared with observed or experimental data
- Validated models can be used to estimate the potential impact of interventions (e.g. ART for prevention) on health outcomes
  - HIV incidence cases
  - HIV associated death
  - HIV associated disability adjusted life years (DALYs)

*Garnett, G. P. (2002). Sex Transm Infect 78(1): 7-12.

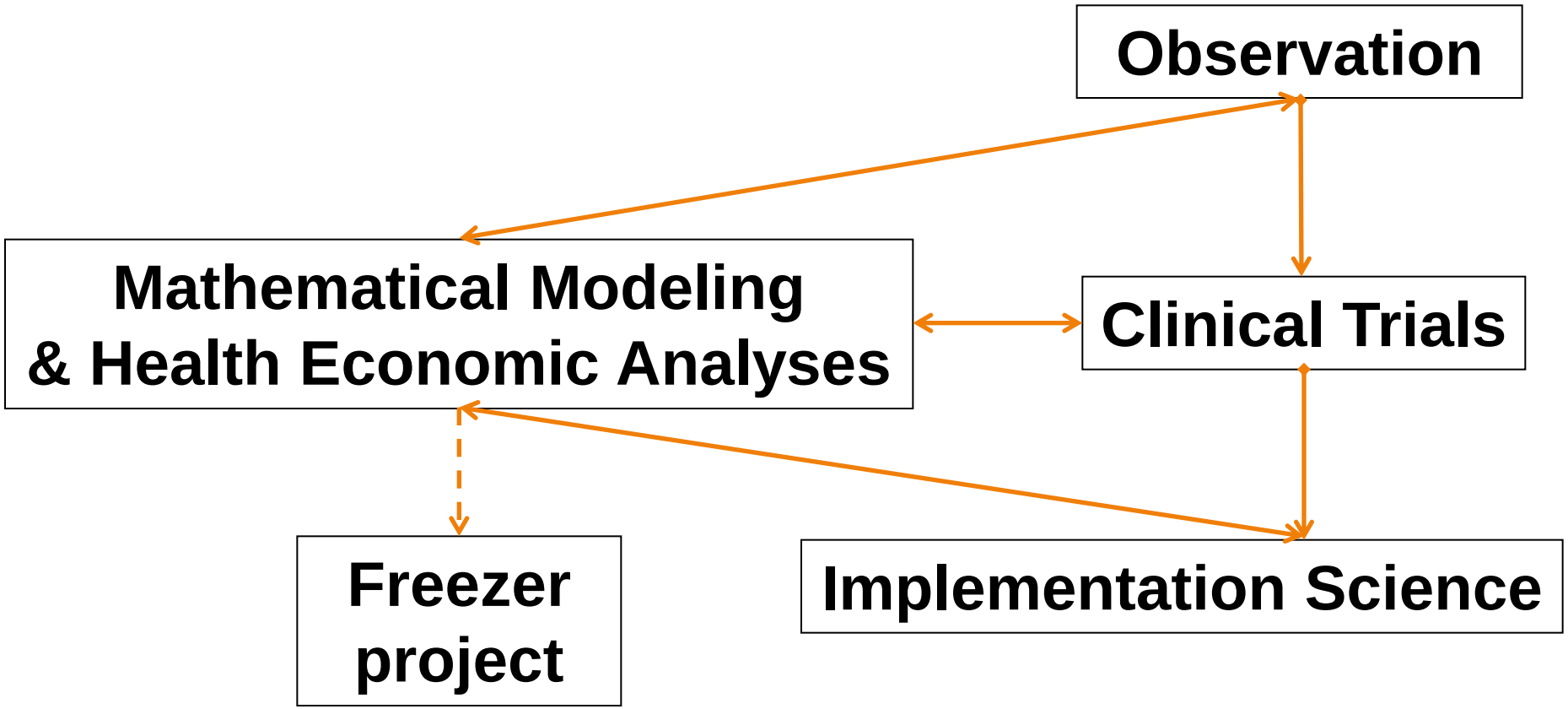
Models in health economic analyses

- Used to structure the economic question and compare all relevant alternatives
- Extrapolate beyond observed data
- Link intermediate and final endpoints
- Generalize results to other settings/patient groups
- Synthesize evidence to simulate comparisons where RCTs don't exist
- Indicate the need for further research

Types of models

- Static models – equilibrium (time-invariant)
- Dynamic models – time dependent change
  - Force of infection can change over time
  - Includes herd immunity
- Both static and dynamic models can be either deterministic or stochastic (constrained random variables)
- Choice of model depends on scientific question

Where do models fit in the path from discovery to implementation?



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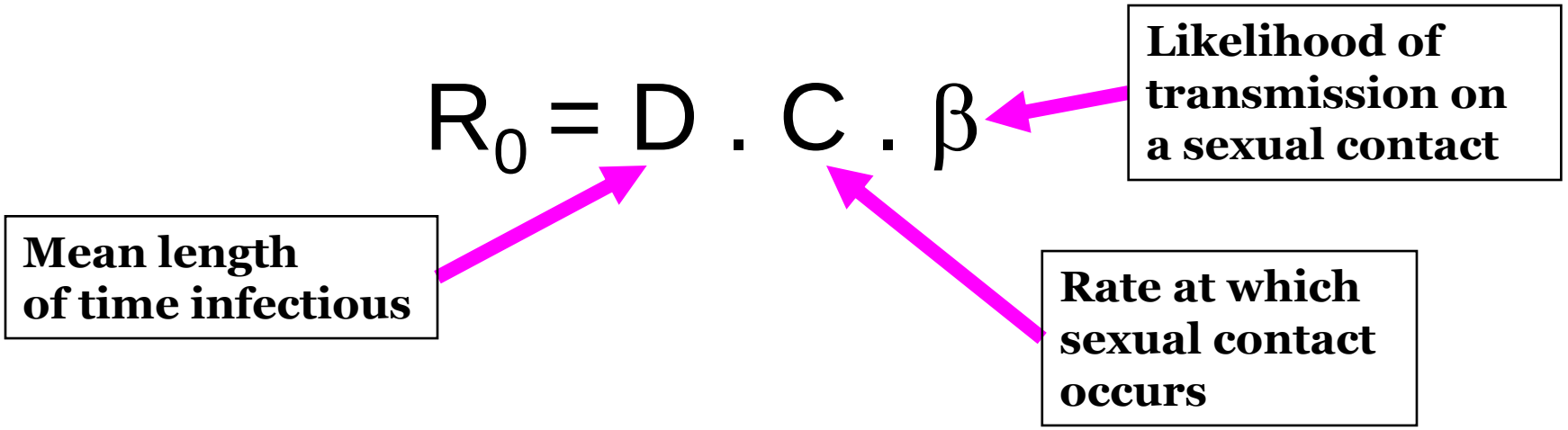
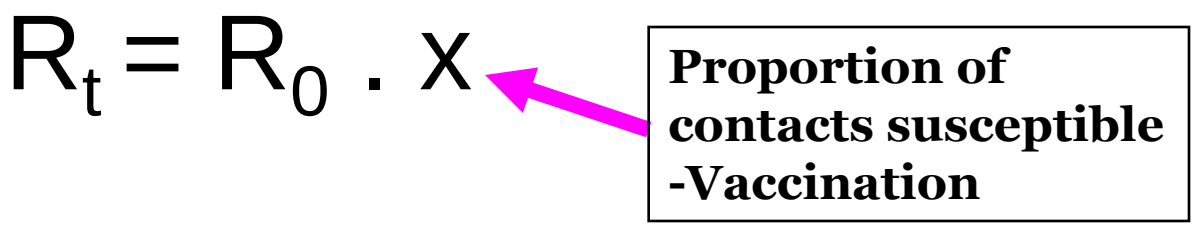
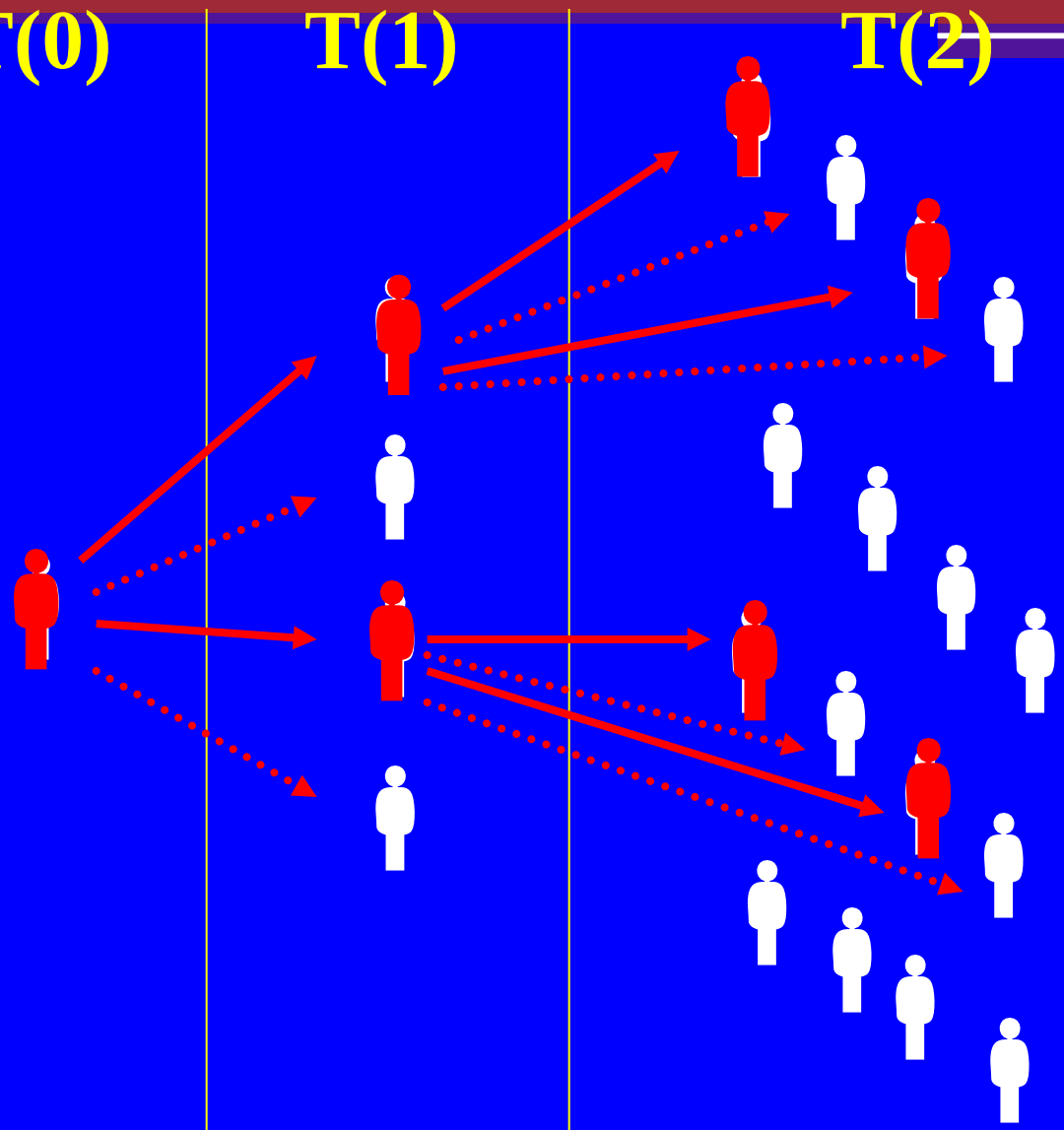
The basic and effective reproductive numbers

R_o The Basic Reproductive Number - The number of new infections caused by one infection in an entirely susceptible population

R_t The Effective Reproductive Number - The number of new infections caused by one infection at a given time







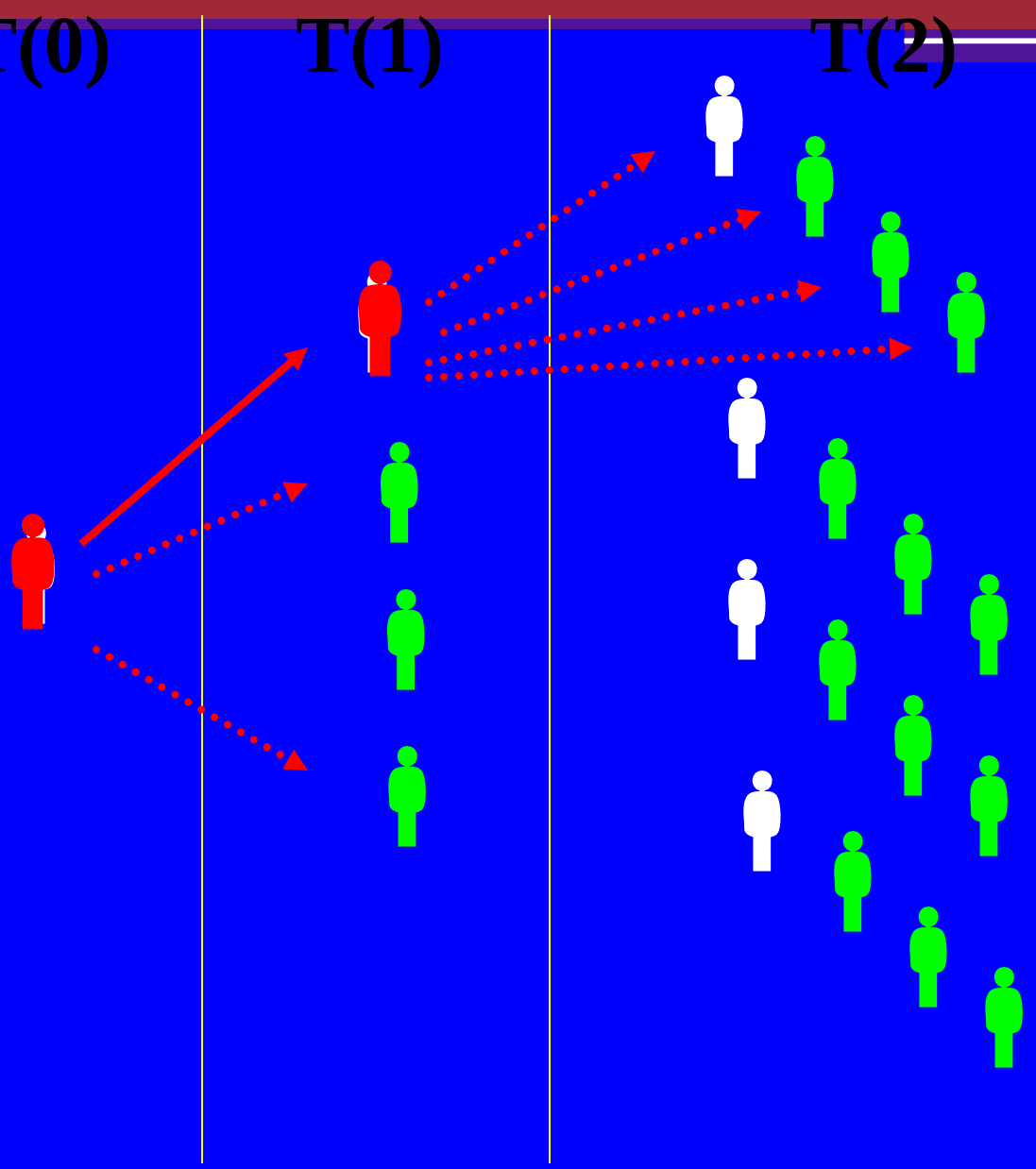
$R_0 = 2$

Transmission

No Transmission

Infectious

Susceptible



$R_0 = 2$

$R_t = R_0.\text{prop susceptible}$

$=0.5$

Transmission

No Transmission

Infectious

Susceptible

Immune

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Models demonstrate potential impact of interventions

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

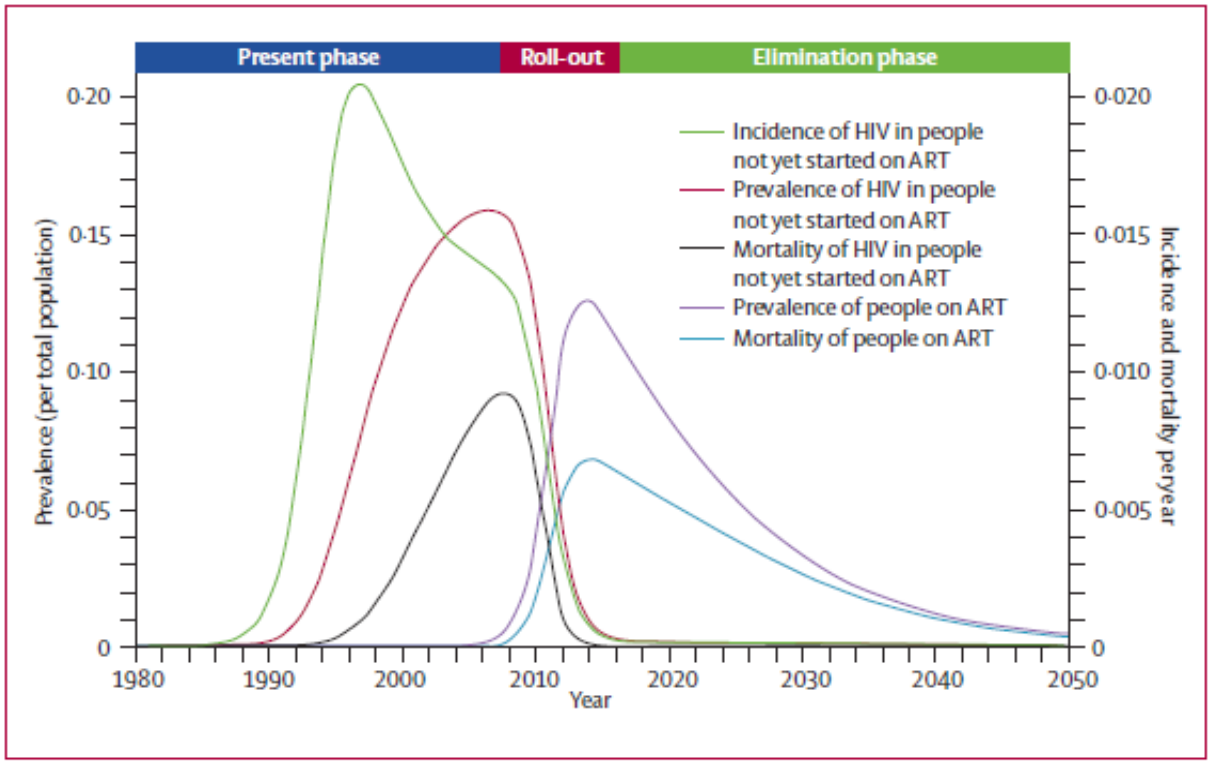


Figure 5: **Time trends resulting from application of universal voluntary HIV testing and immediate ART strategy for people who test HIV positive, in combination with other adult prevention interventions that reduce incidence by 40%**

The programme implementation start date is arbitrarily set as immediate, with coverage increasing logistically to 50% by 2012 and 90% by 2016.

ART implementation

Models can estimate potential impact of health programs

Treating our way out of the HIV pandemic: could we, would we, should we?

*Geoffrey P Garnett, Rebecca F Baggaley

- "HIV prevention is easy in theory – the practice is hard."
- Need intensive HIV testing and robust linkages to care, even among people who feel well
- Strategies need to be effective and cost effective

Community wide HCT & Linkage to care in South Africa

IMPLEMENTATION AND OPERATIONAL RESEARCH: EPIDEMIOLOGY AND PREVENTION

High HIV Testing Uptake and Linkage to Care in a Novel Program of Home-Based HIV Counseling and Testing With Facilitated Referral in KwaZulu-Natal, South Africa

Heidi van Rooyen, PhD, Ruanne V. Barnabas, MD, DPhil,†‡§ Jared M. Baeten, MD, PhD,†‡‖*
Zipho Phakathi, Philip Joseph,* Meighan Krows,†‡ Ting Hong, MD, PhD,†‡*
Pamela M. Murnane, MPH,‖ James Hughes, PhD,§‖ and Connie Celum, MD, MPH †‡‖

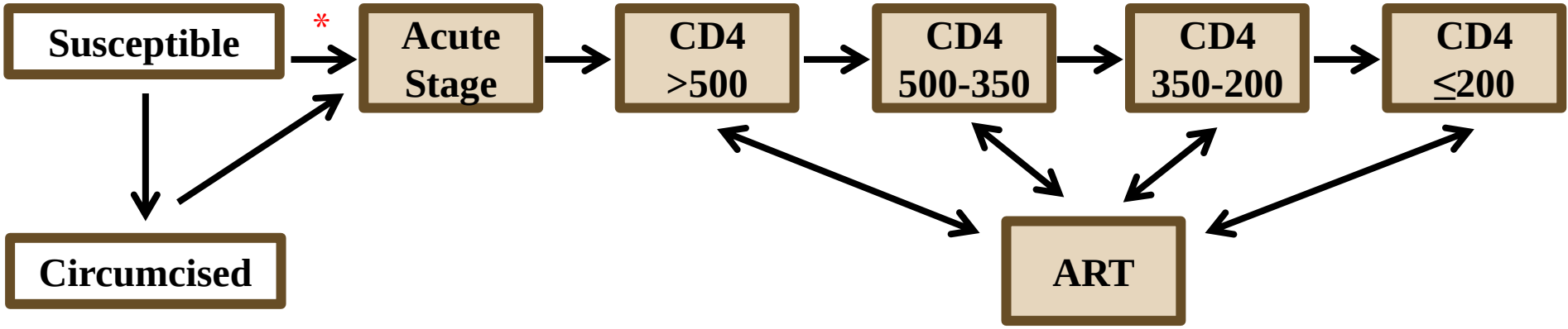
	South Africa: N (%)*
HIV testing coverage	671 (91%)
HIV prevalence	201 (30%)
Median CD4 count	425 cells/μL

Results 6 months after HCT

	N (%)
Visited an HIV Clinic	195 (97%)
ART uptake among those eligible	15 (80%)
MC uptake in Uganda	-
Proportion with viral load <1,000 copies/mL among ART eligible participants	Increased from 20% at baseline to 80% at 6 months*
Change in mean viral load over 6 months among ART eligible participants	-2.46 $\log_{10}$ copies/mL*

*p ≤0.01

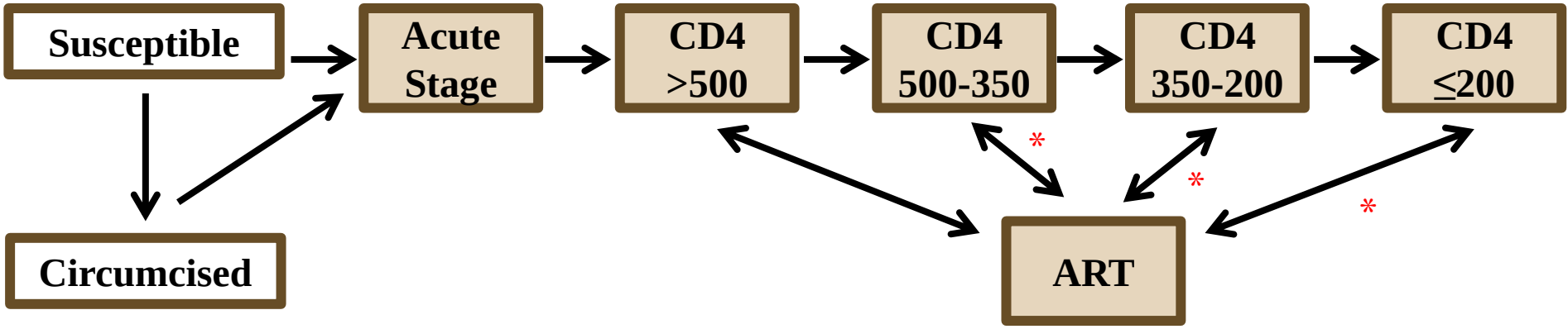
ART Model: Structure



- Compartmental, deterministic model for HIV - population level
- Stratified for gender, age, sexual activity classes
- Includes births, HIV-associated deaths & all-cause mortality
- *Force of infection – per susceptible risk of acquiring HIV (fxn – sexual mixing, HIV prevalence, transmission probability)
- Validated for KZN, South Africa

Roger Ying, ISSTDR, 2013

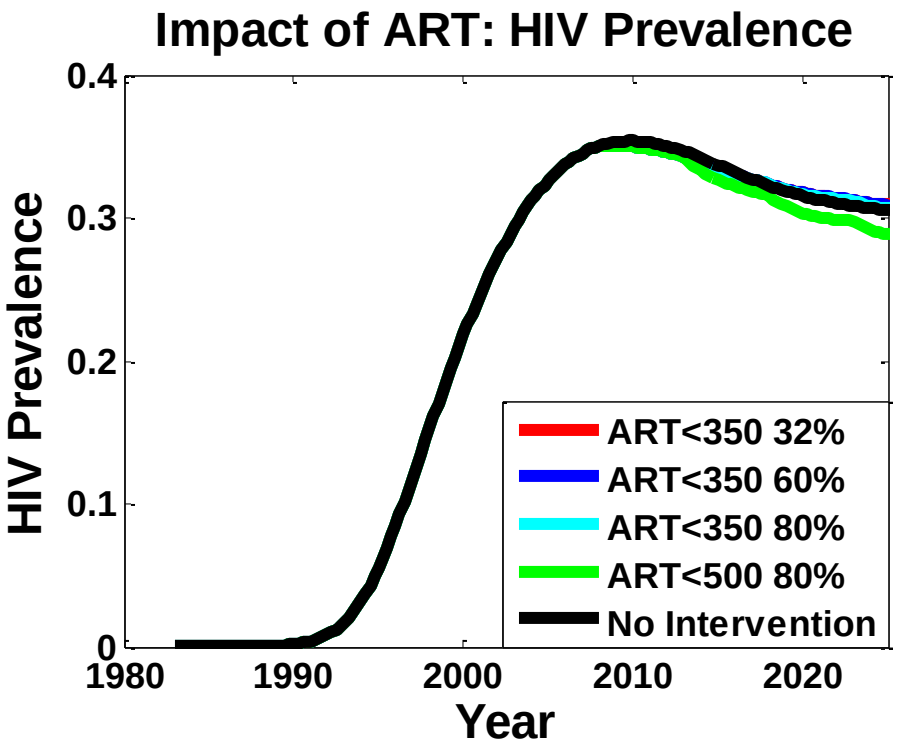
ART Model: Structure

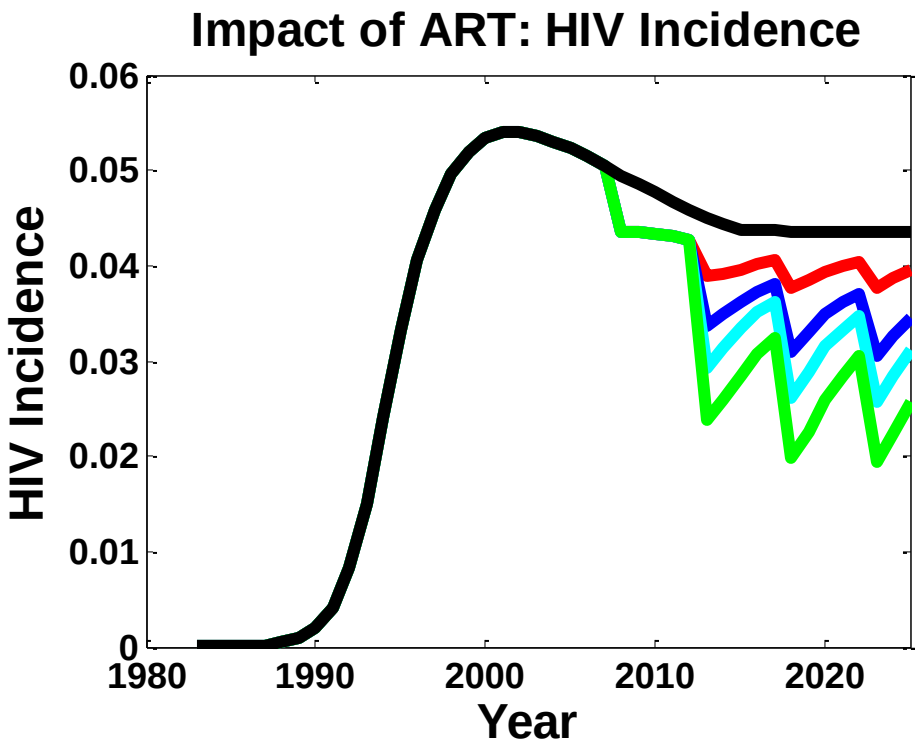


- Mathematical model to evaluate ART scale-up
- Realistic assumptions for ART coverage
  - *32% CD4 ≤ 350 (baseline counterfactual)
  - *80% CD4 ≤ 350 (efficacy)
  - *60% CD4 ≤ 350 (effectiveness)
  - *80% CD4 ≤ 500 (WHO recommendations)

Roger Ying, ISSTDR, 2013

ART Model: Results





Roger Ying, ISSTDR 2013

ART Model: Cost-effectiveness

ART Coverage	Costs per Infection Averted from 2013 to 2025
	Overall Cost
1) 32% for CD4≤350 cell/µL	$44,104
2) 60% for CD4≤350 cell/µL	$34,691
3) 80% for CD4≤350 cell/µL	$32,072
4) 80% for CD4≤500 cell/µL	$27,606

Roger Ying, ISSTDR 2013

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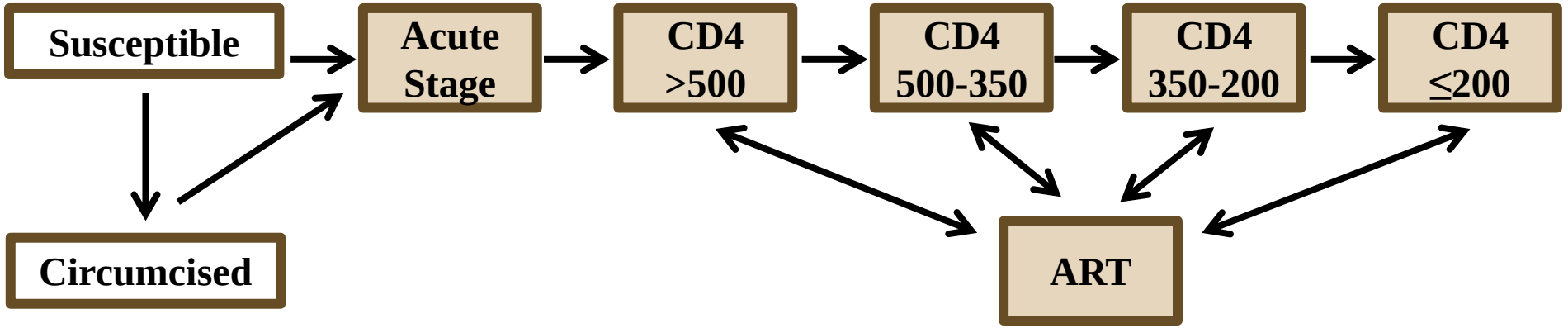
What data do we need for models?

- Demographics
- Mixing patterns
- Natural history
- Transmission probability
- Factors that change susceptibility
- Factors that change infectiousness
- Effectiveness of interventions
- Engagement in health care

What study data can you use to parameterize models?



- Country specific demographics
- Distribution of CD4 count and viral load
- Intervention (including treatment) coverage and efficacy – capture cascade of care
- Factors that impact on HIV transmission: viral load, gender, circumcision status, co-infection status

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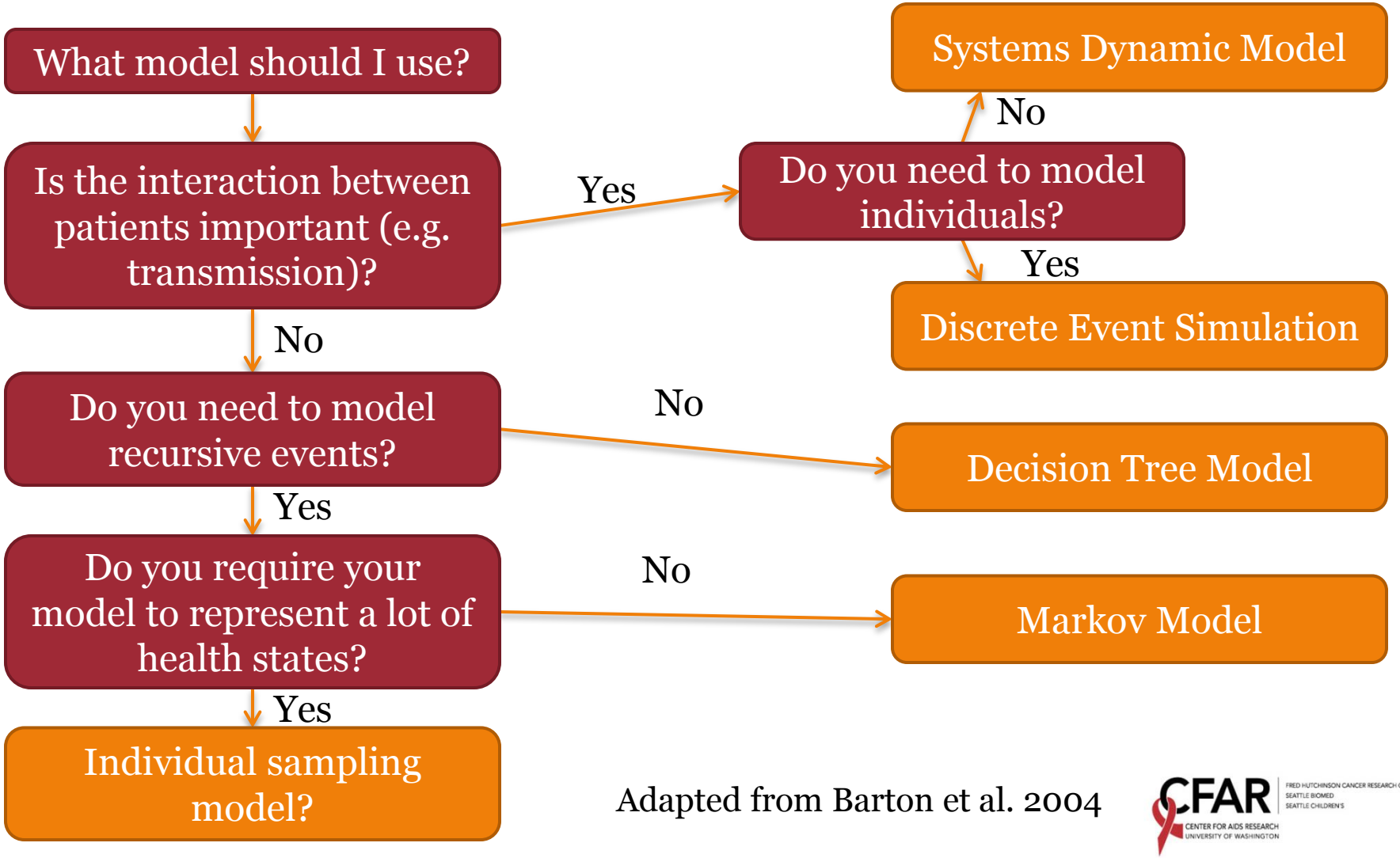
How to choose the appropriate model for health outcomes



Adapted from Barton et al. 2004

Summary

- Infectious disease modeling is a useful tool – assumptions are explicit, characterize uncertainty
- Study data can be used to parameterize models
- Models can be used to estimate health outcomes
- Consult with a health economist and/or modeler to choose an appropriate model to answer your question

- Contact: rbarnaba@uw.edu

Thank you

Study Participants

ICOBI and HSRC Staff

Connie Celum, Carol Levin, Jared Baeten, Roger Ying, Aditya Khanna, Monisha Sharma, Sarah Roberts, Susie Cassels, Jim Hughes, Geoff Garnett, Meighan Krows, Hilton Humphries, Bosco Turyamureeba, Katherine Murray, Elioda Tumwesigye, Heidi van Rooyen & Judy Wasserheit

Funding

NIH NCRR Grant 5 KL2 RR025015

NIH CFAR Grant P30 AI027757

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PreventionRX Study