CMPT 858

Nathaniel Osgood

Lecture 1

CMPT 858 Focus: Systems Simulation Models for Public Health

- **Purpose of models**
- **Model strength & limitations**
- **Diversity of classes of models available**
- **How models are built, refined & analyzed**
- **Software & analytic tools for working with models**
- **How models mesh with traditional techniques**
  - **Linkage databases**
  - **Real-time data collection (EMA)**
  - **Biostatistics**

Class Objectives: To Help Students

- Learn to appreciate and critique existing models
- Understand the proper limitations and limitations of such models
- Understand the mathematical foundation on which models are based
- Gain familiarity with modeling software
- Learn how to conceptualize, formulate, and analyze dynamic models (regardless of application area)
- Gain experience in applying such models in the public health context
- Understand some open areas of modeling research

Class will Be…

- Highly interactive
- Informal
- Adapted to student interests
- Aimed for accessibility to diverse audience
  - Some material presented in additional sessions for certain backgrounds

Anticipated Class Coverage

- Motivations
- Basics of systems thinking
- Causal loop diagrams
- Stock & Flow Diag.
- State equations
- Focused discussion of particular areas
  - Chronic
  - Infectious
  - C&I Interactions
- Individual-based vs. aggregate
  - Tradeoffs
  - Network models

Class Coverage Cont'd

- Modeling process
  - Scoping
  - Formulation
  - Parameterization
  - Calibration
  - Validation & Confidence building
  - Model analysis tools & techniques
- Possible: Uncertainty & Stochastics

Class Diversity

- **Our class is expected to be diverse in many ways**
  - **Students/Faculty observers**
  - **Student backgrounds in CH&E/MPH/Biostats/Computer Science/Economics**
  - **Participant interests**
  - **Participant background in particular subject**
- **The instructor will make efforts to address diverse backgrounds & interests**
- **Please be respectful of those from all backgrounds**

Extra Resources for Students

- Office hours
- Focused Tutorials
  - Providing extra background & context
  - Providing more advanced material (upon student interest)
- Likely topics
  - Software basics/Epi terminology/Calculus intuitions/Elements of of differential equations/Analysis techniques

What is Expected of You

- Attendance & Participation
- Reading papers before class
- 2 modeling exercises
- Project (with instructor guidance)
- End-of-Term Presentation

Classroom Exercises

- Interactive modeling exercises on laptops will be a key component of the course
- We will have (pre-installed) laptops delivered to the classroom for students who need them
- Please speak with the instructor if you'd like a laptop

Administrative Info

- Good Reference: Sterman, J. Business Dynamics. Boston: McGraw-Hill Higher Education. 2000.
- Office Hours: Friday 3-4:30pm (Thorv 280.6) & by appointment
  - Especially important b/c of diversity of backgrounds & limited time
- Course website at webct6.usask.ca

Project Information

- Multi-person projects
- Project can be
  - Modeling application (in area for which data is readily available)
  - Paper review & critique
  - Methodological study
- Instructor can help facilitate
- Talk with instructor about any ideas of strong personal interest
- Meet early with the instructor to discuss possibilities

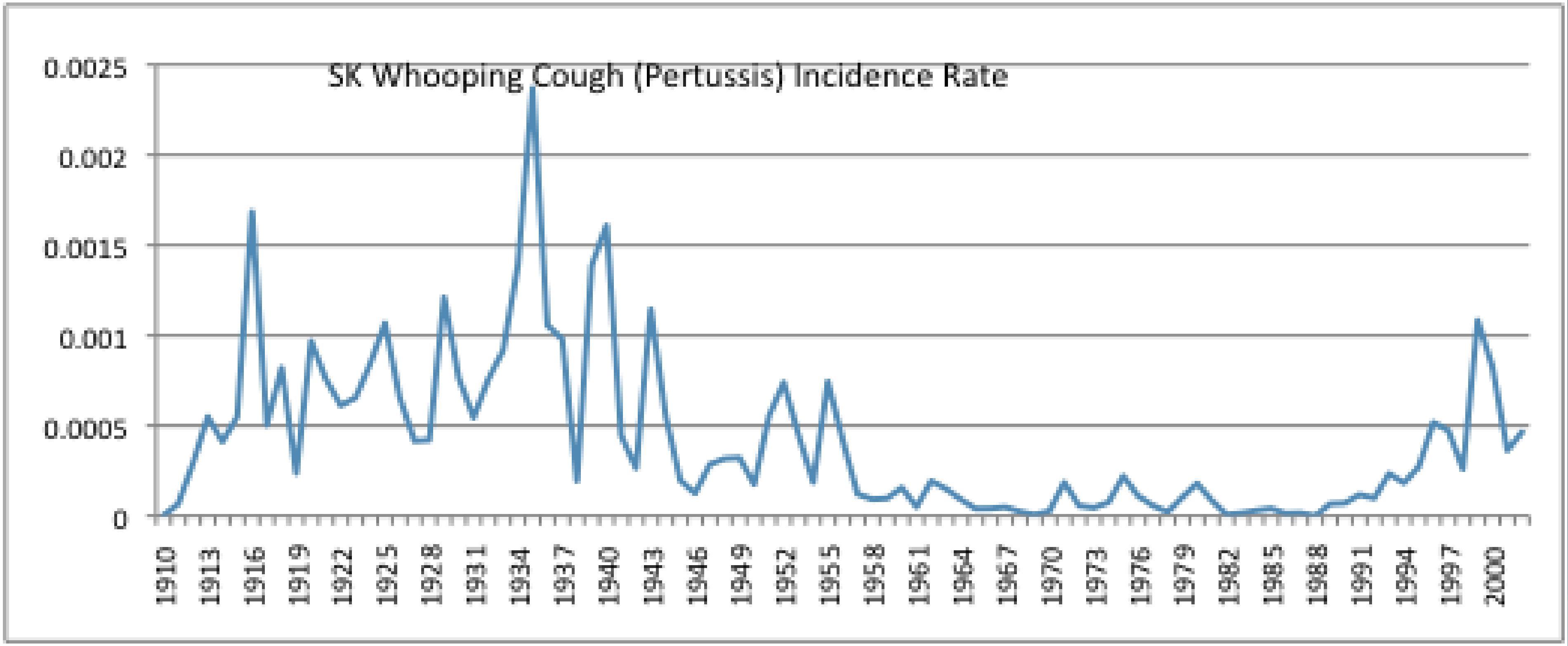
Resources

- Vensim Download
  - http://www.vensim.com/freedownload.html
- Vensim is also installed on lab computers & laptops provided by dept
- WebCT
  - http://www.webct6.usask.ca

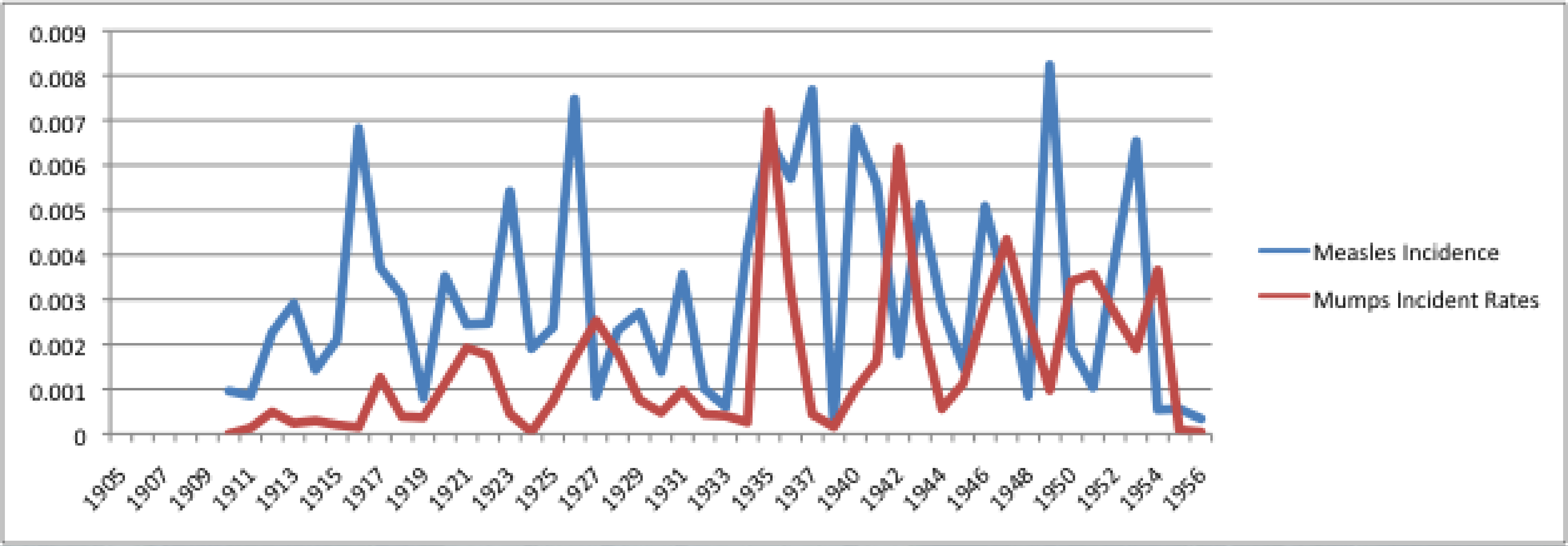
Motivation: Assisting Management of Complex Situations

- Serve as "what if" tool for
  - Counterfactuals:Identifying desirable policies
    - Cost-effective
    - High-leverage
    - Robust
  - Prioritizing research/data collection
- Help make sense of interaction of diverse information, processes
  - Understanding drivers for trends
- Communication (e.g. "learning labs" for stakeholders)

Complexities & Regularities



Measles & Mumps in SK



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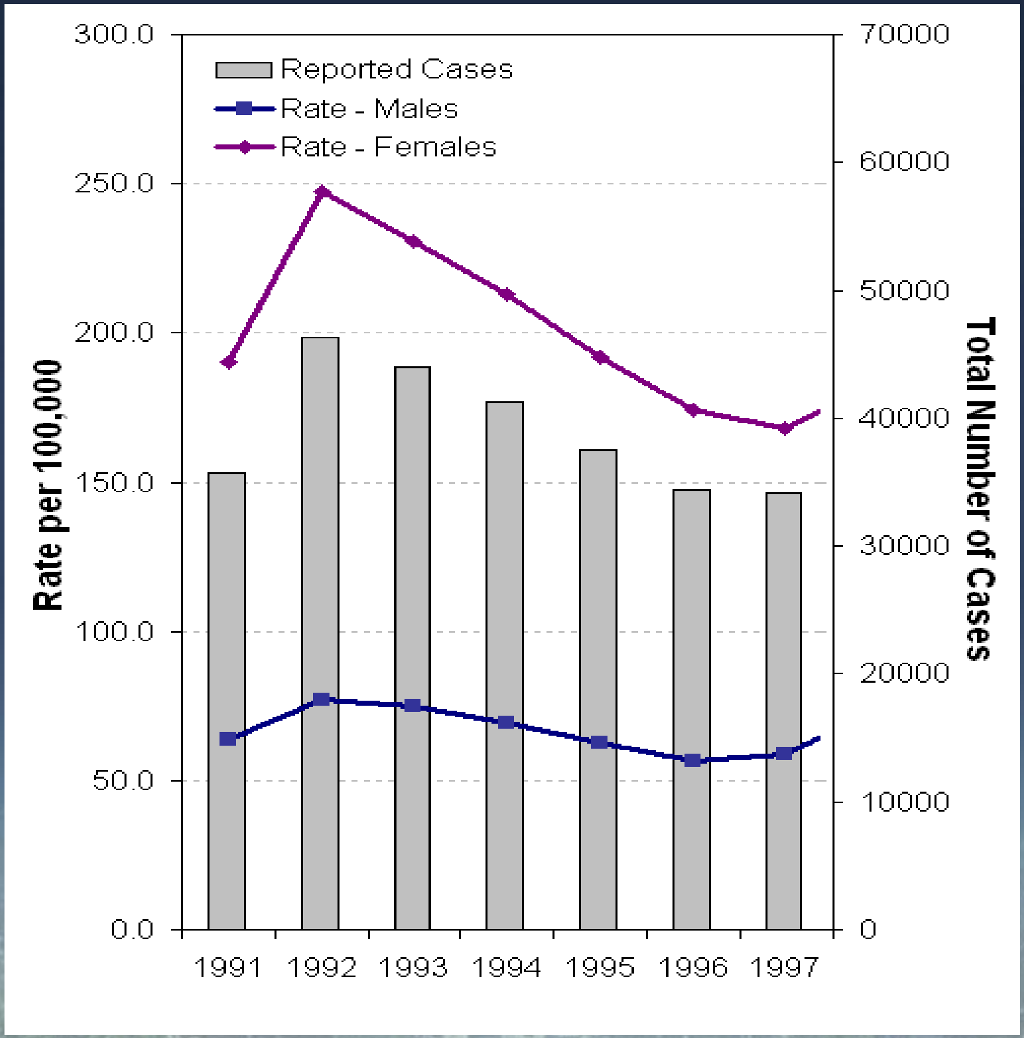
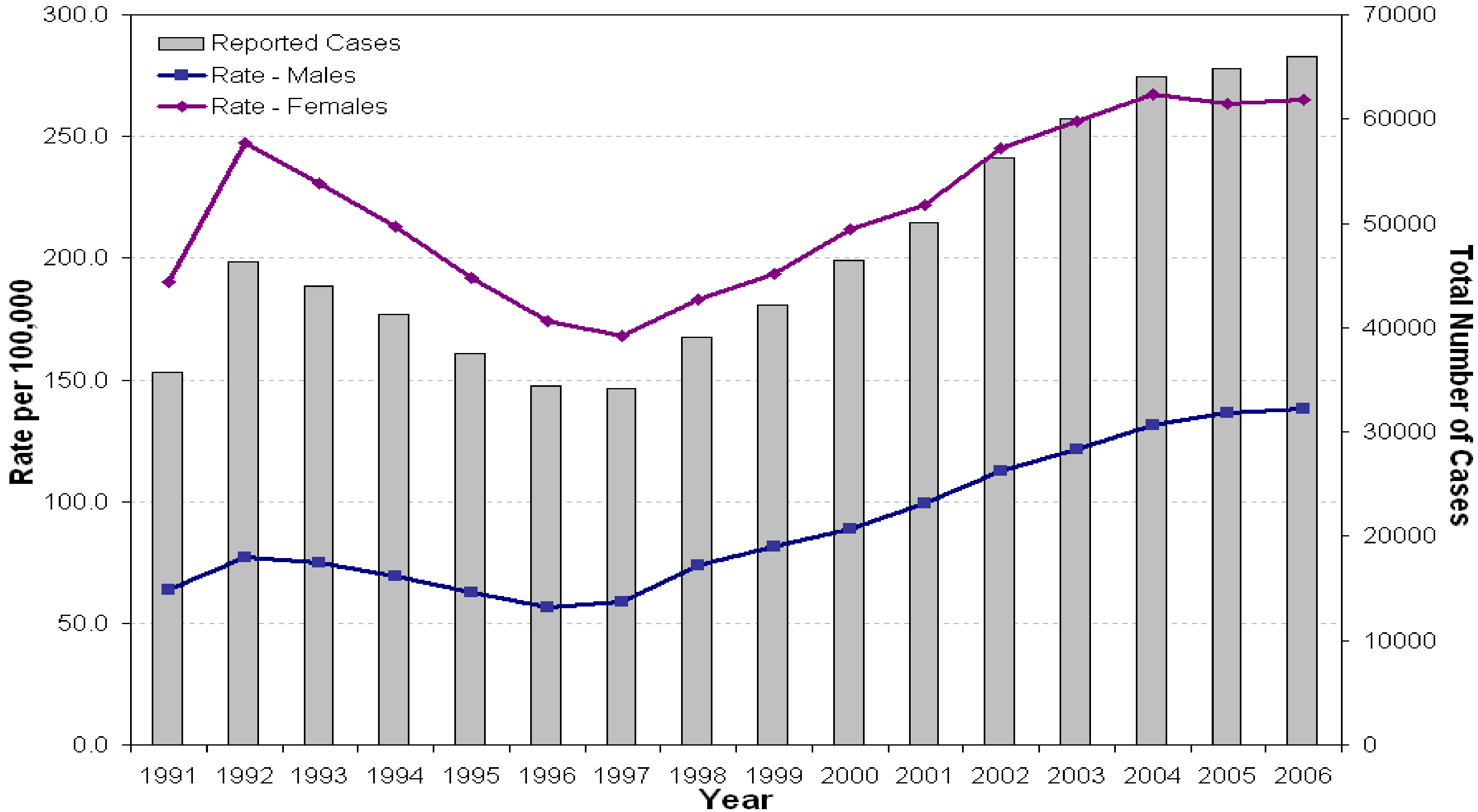
Public Health as "Redirecting the Course of Change"



- **Adapted from Tom Wong, 2007**
- Data for 2005 and 2006 are preliminary and are anticipated to change
- Source: Surveillance and Epidemiology Unit, Community Acquired Infections Division, PHAC

Public Health as “Redirecting the Course of Change”



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Complexities

- Delays
  - Presentation of symptoms/Contact tracing/Identification of asymptomatic
- Interactions (e.g. STIs & HIV, HCV&HIV, Chronic & Infectious illness)
- Feedbacks
  - Intergenerational/social network mediated
  - Immune system
  - With healthcare system
  - Behavior change after knowledge of health status
  - Risk perceptions
- Nonlinear: Risk, cost, intervention synergies
- Heterogeneity in progression, behaviour

Complexities Matter for Intervention Selection

- **Blowback, multiplier effects**
- **Presence of "tipping points"**
- **Tradeoffs of prevention vs. screening vs. contact tracing & treatment**
- **Interaction between infections, with chronic d.**
- **Evaluation of focused intervention on**
  - **Presenting Individuals? *(Risk perception)***
  - **Youth (*Risk attitudes & social network effects*)**
  - **Sex workers? (*Social network effects*)**
  - **Centrality in social network *(peer effects?)***
  - **Immuno compromised**
- **Evaluation of intervention portfolios**

Common Phenomena In Complex Systems

- **Snowballing: When things go bad, they often go *very* bad very quickly**
  - **“Vicious cycles” lead to “cascading” of problems**
  - **“Path dependence”: Different starting points can lead to divergence in project progress**
- **Lock-in, Policy resistance: Situation can be unexpectedly difficult to change**

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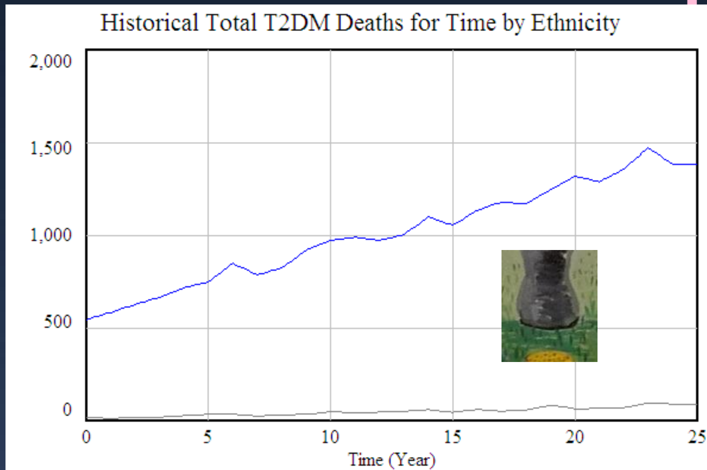
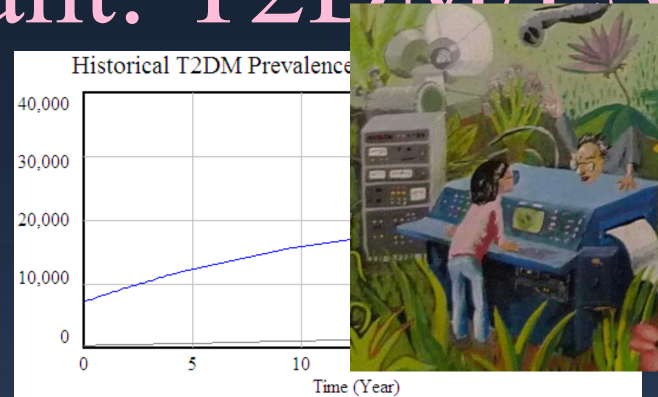
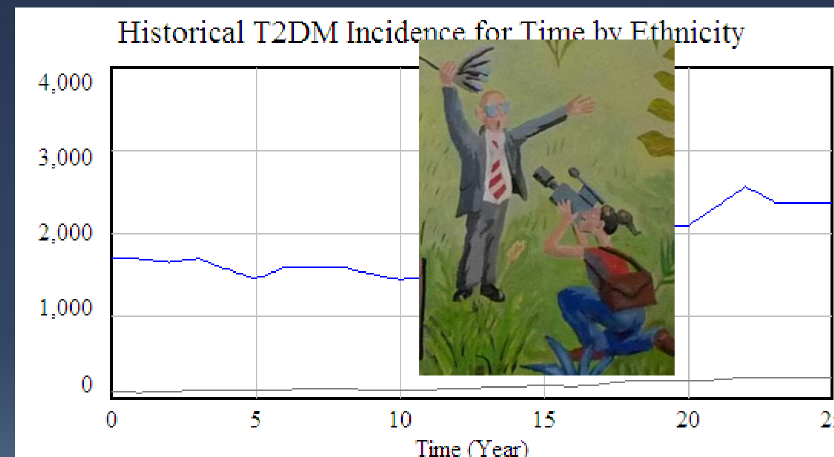
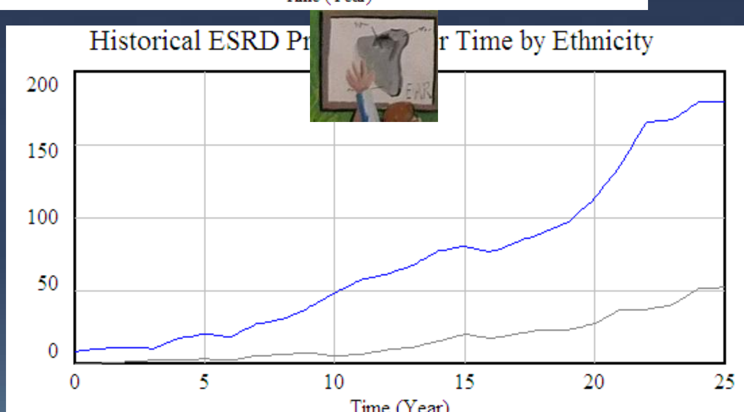
A Metaphor for Scientific Exploration

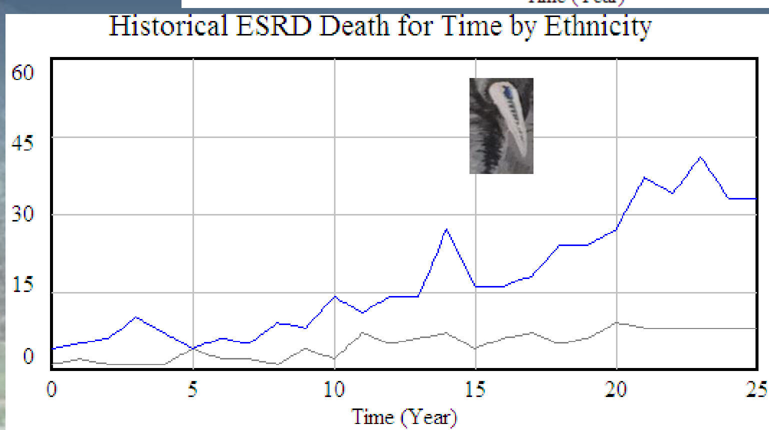
Pieces of the Elephant: T2DM/ESRD











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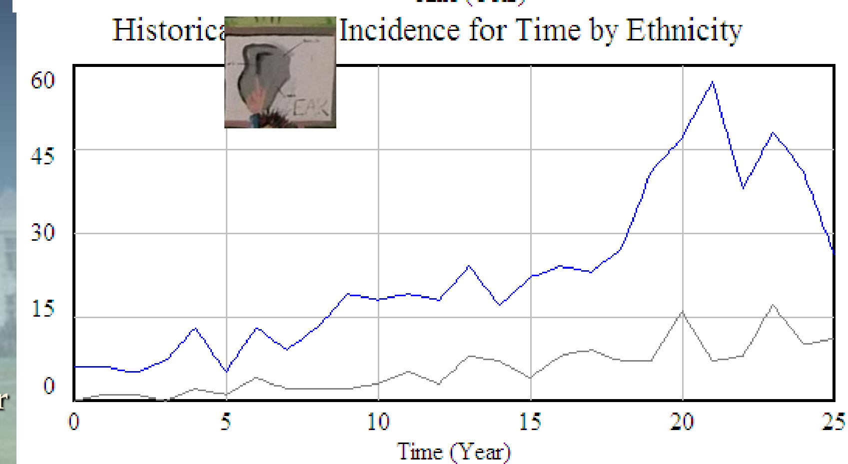
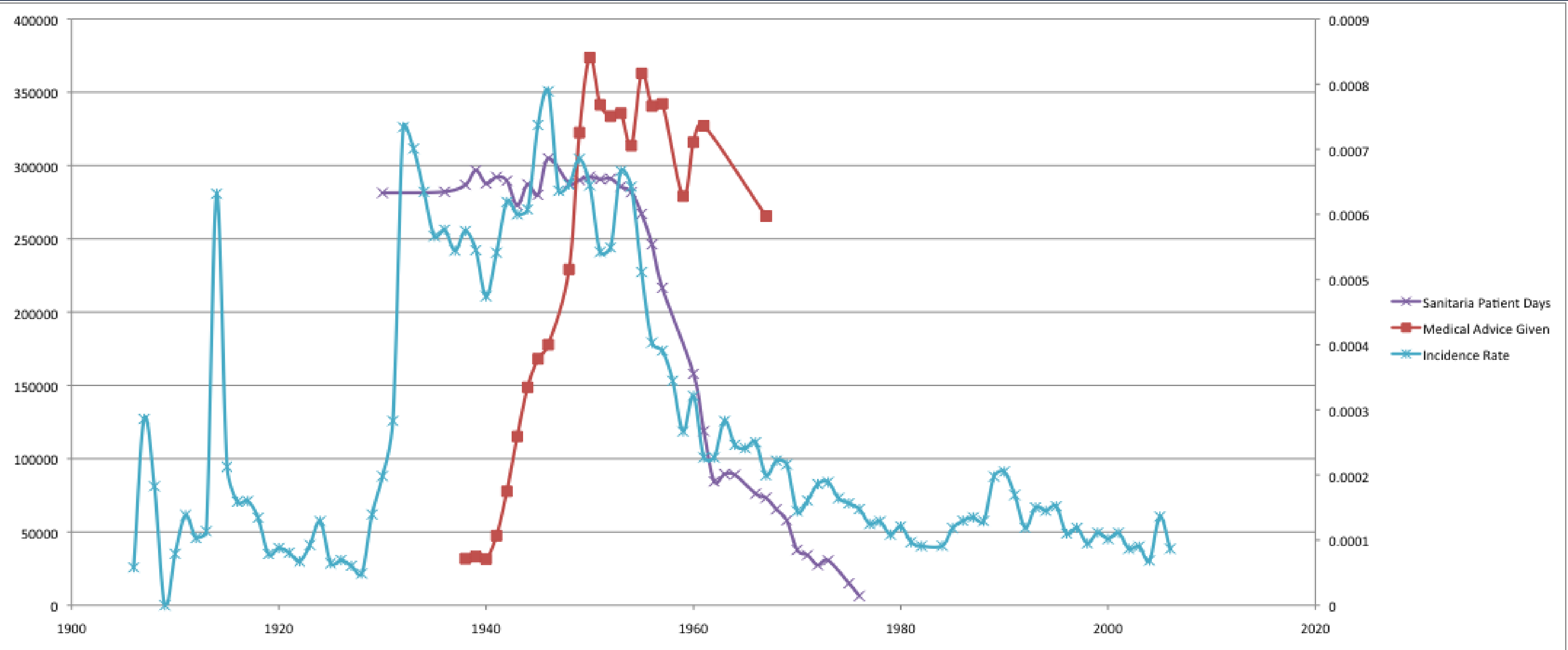
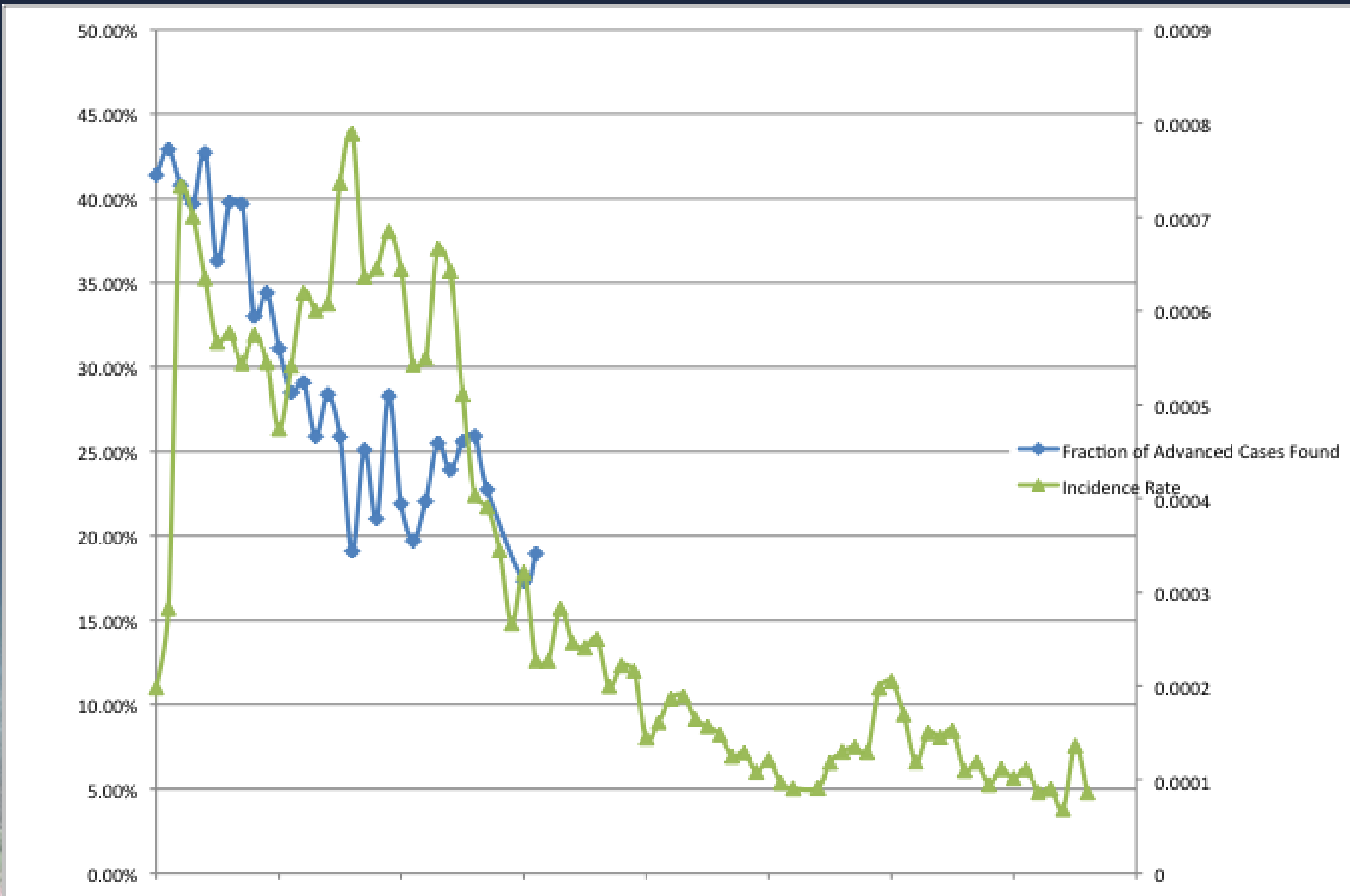


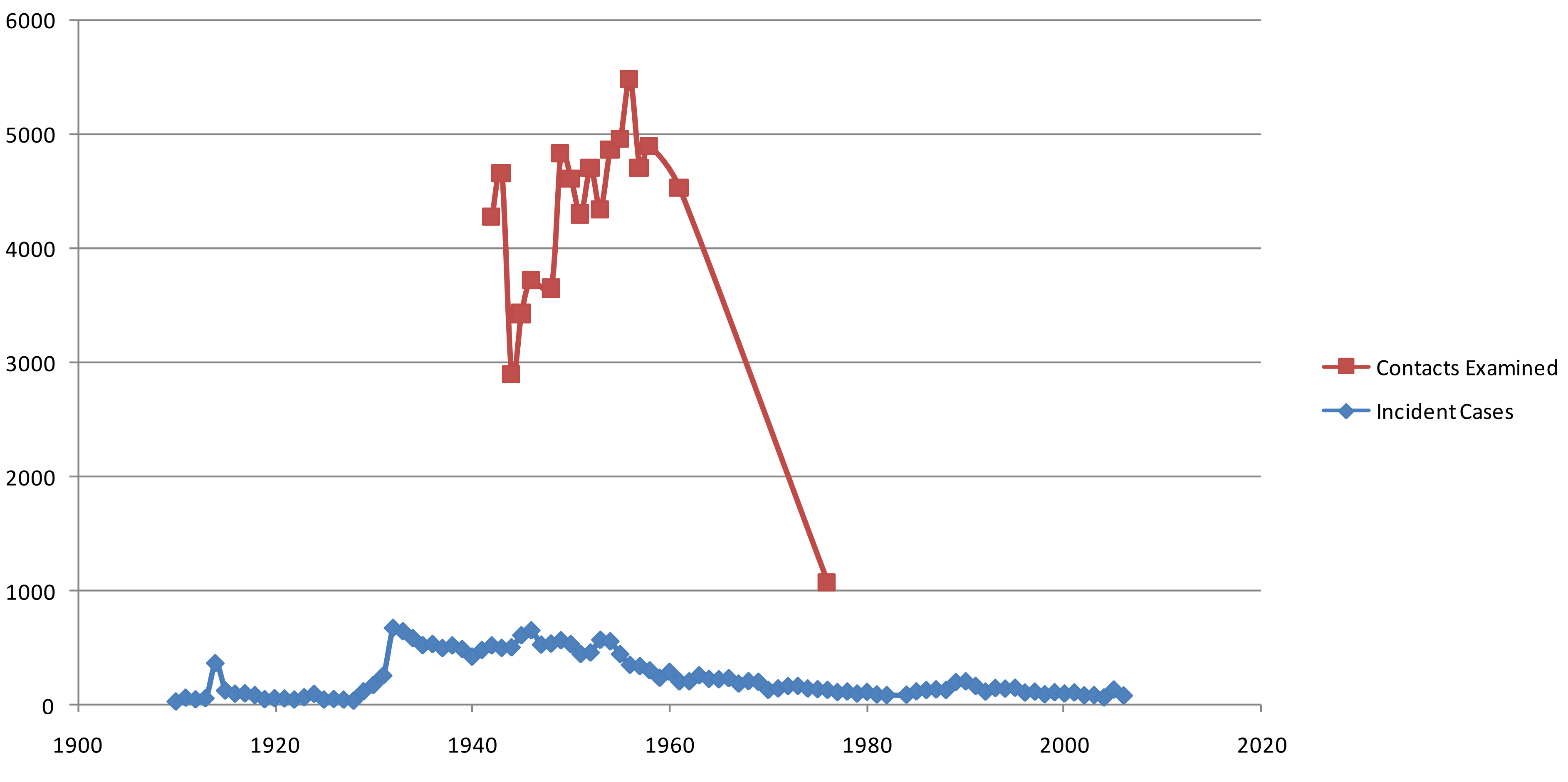
Pieces of the Elephant: TB Saskatchewan's War on "White Plague"



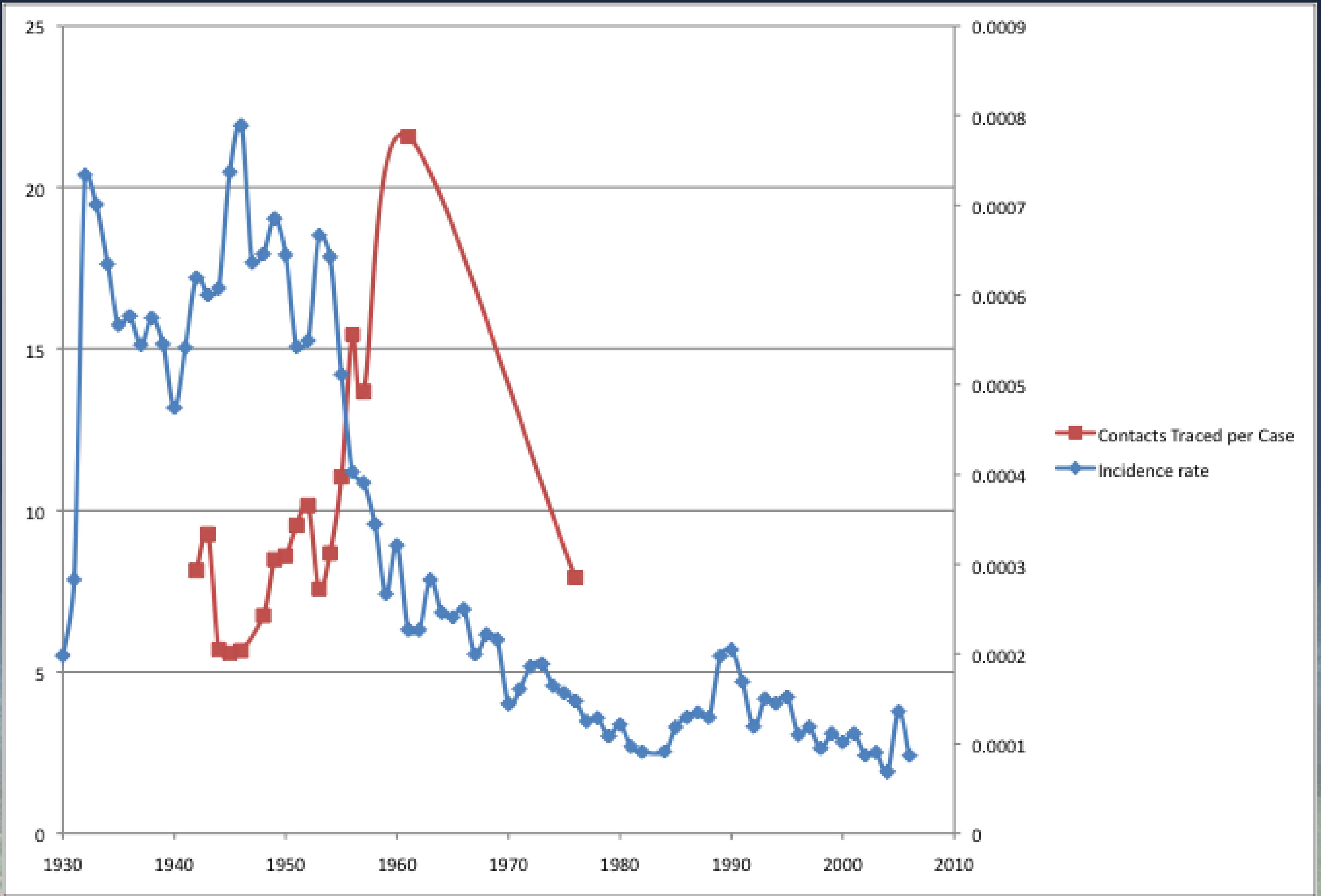
Level of Progression of Cases



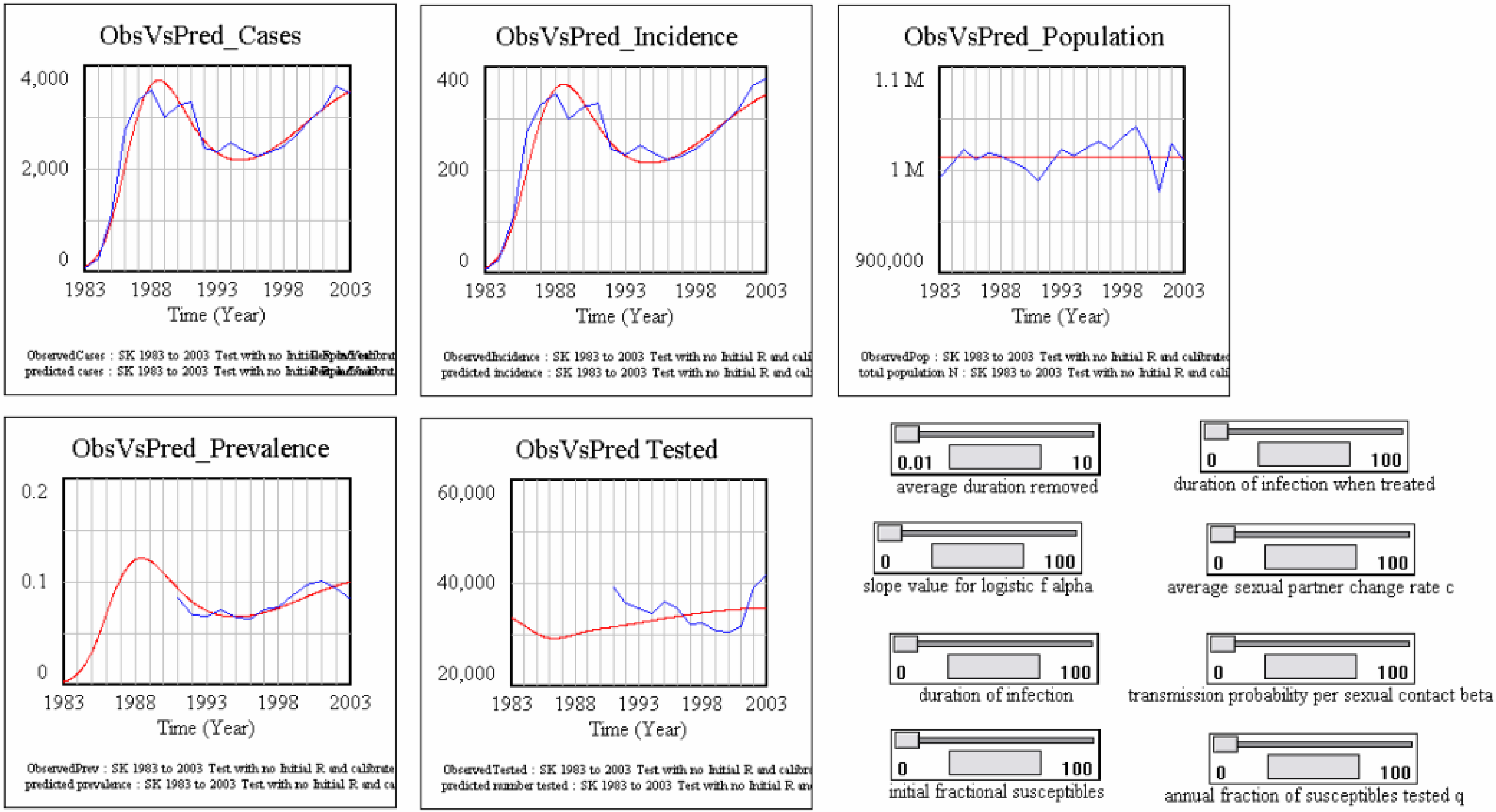
Cases and Contact Tracing



Contact Tracing Effort per Case



Pieces of the Elephant: STI



Regularities Arise from Underlying *Processes*

- **The time series shown are tightly interrelated, not independent**
- **Many of the features of the time series are driven by the same underlying processes**
  - **Natural history of infection/**
  - **Demographic change of the population**
  - **Mechanisms of infection transmission**
  - **Risk behaviour & risk perception**
  - **Health system response**
- **Simulation seeks insight from characterizing *causal structure* of those**

Systems Simulation Models

- Simulation models can be viewed as *dynamic hypotheses* concerning the causal structure underlying observed patterns
- We need to understand causal structure to understand *counterfactuals* – how patterns would change if we were to change X
- All simulation models are computational realizations of a mathematical process
  - There are many dynamic mathematical frameworks for defining simulation models
    - All of these frameworks characterize *processes*

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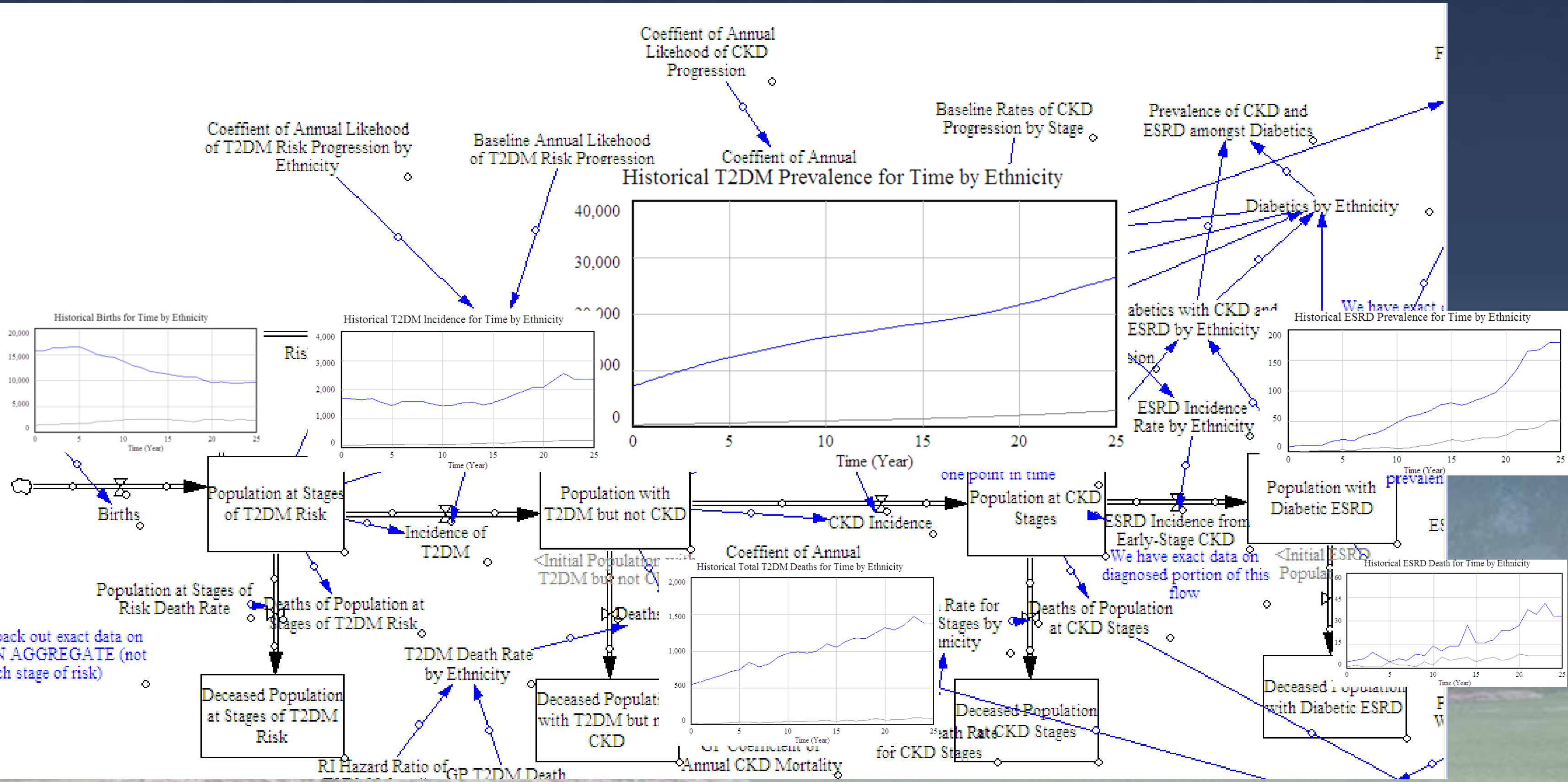
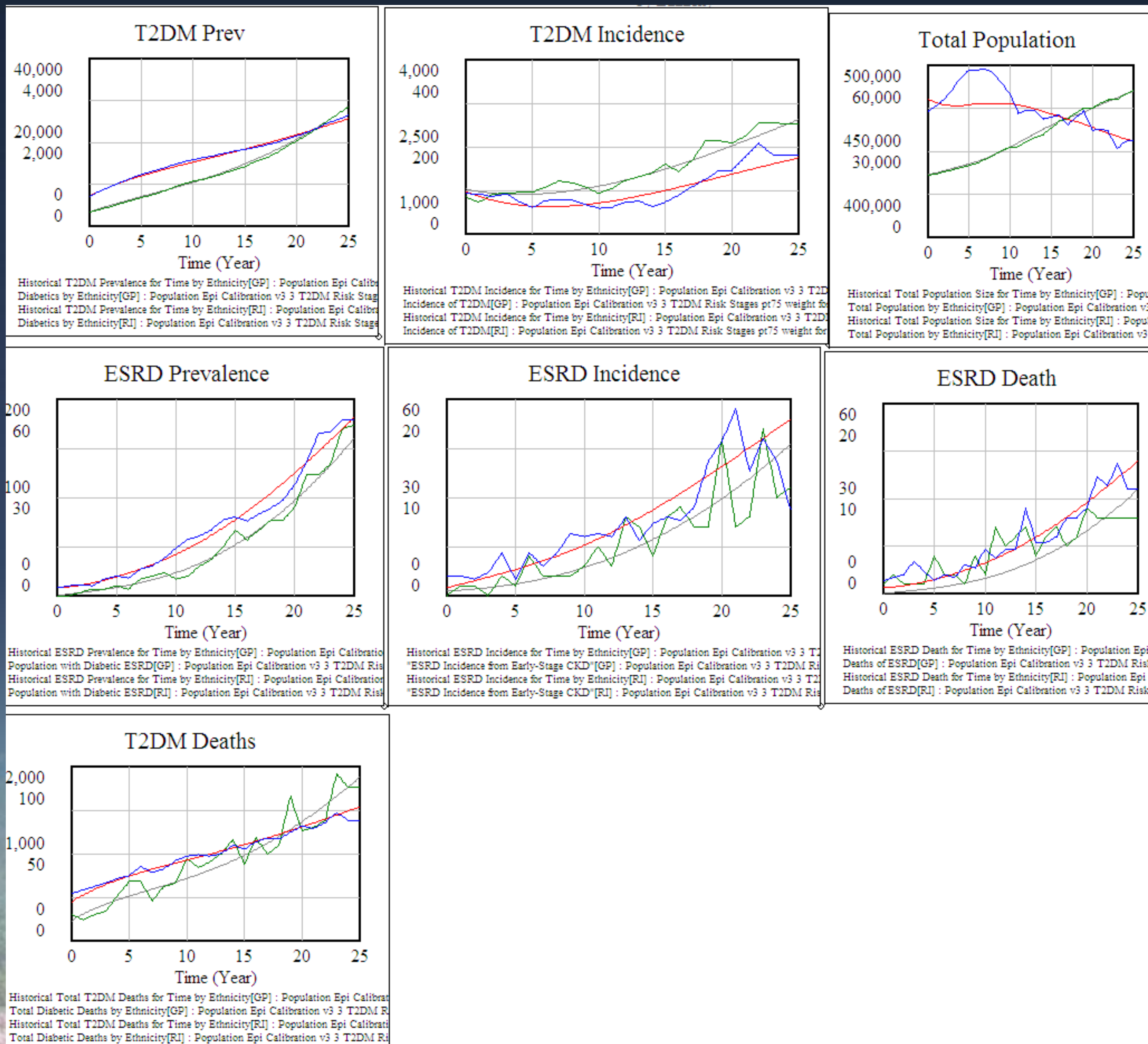
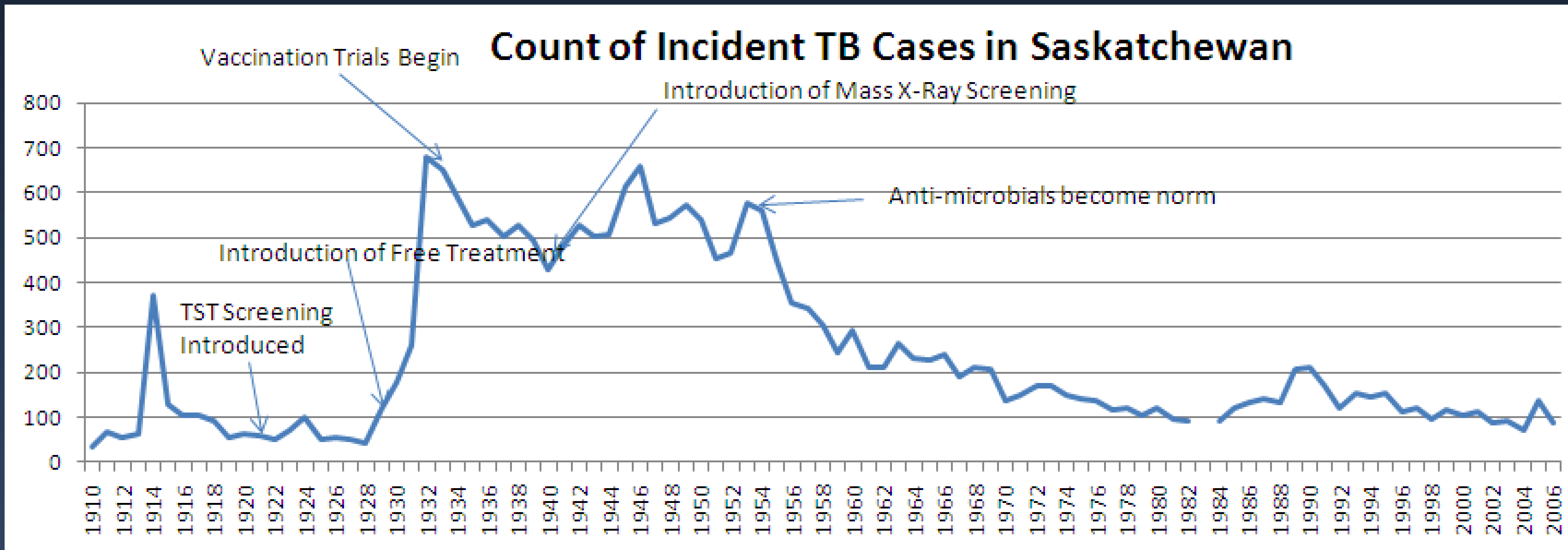
The Pieces of the Elephant Example Model of Underlying Process & Time Series It Must Match

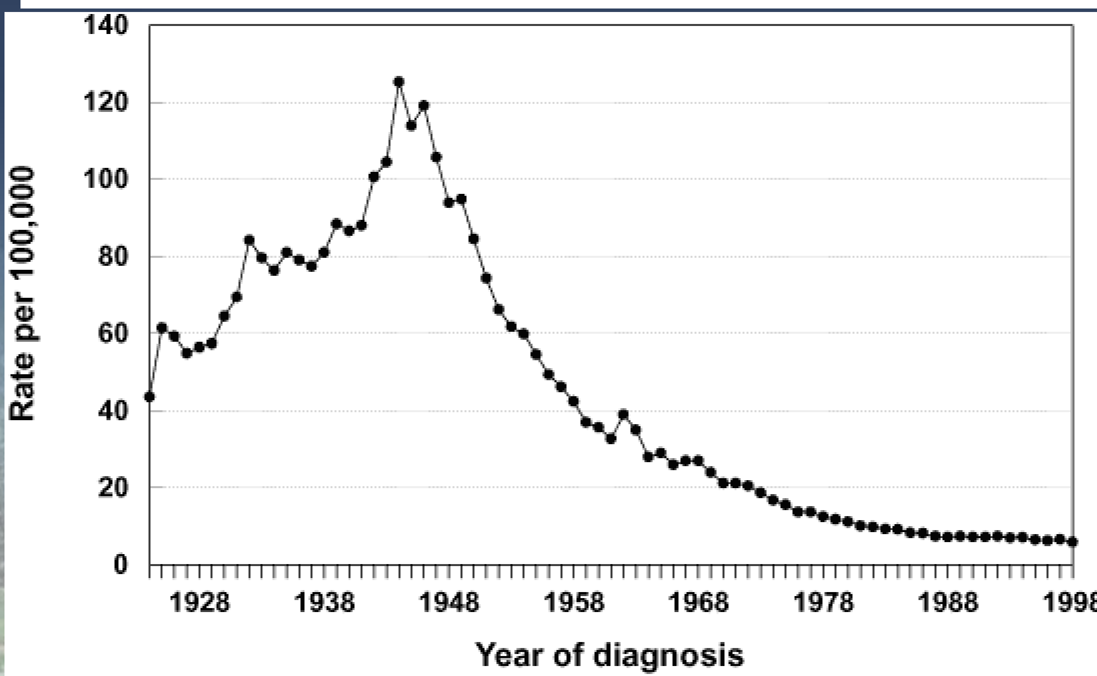


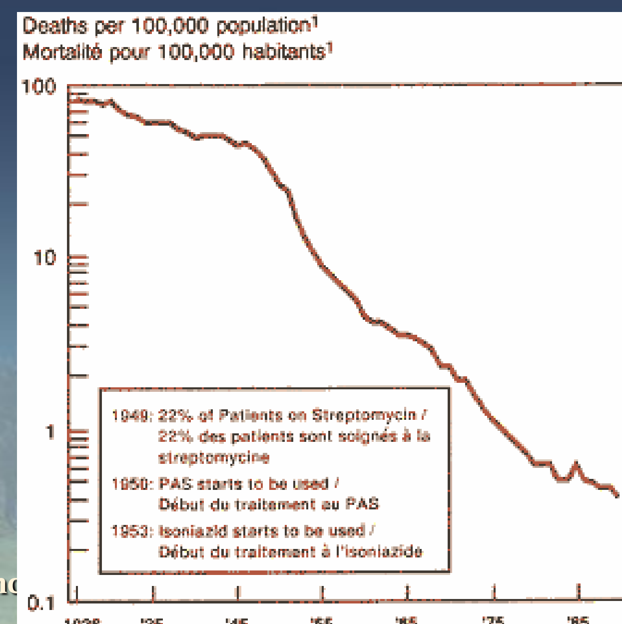
Single Model Matches Many Data Sources



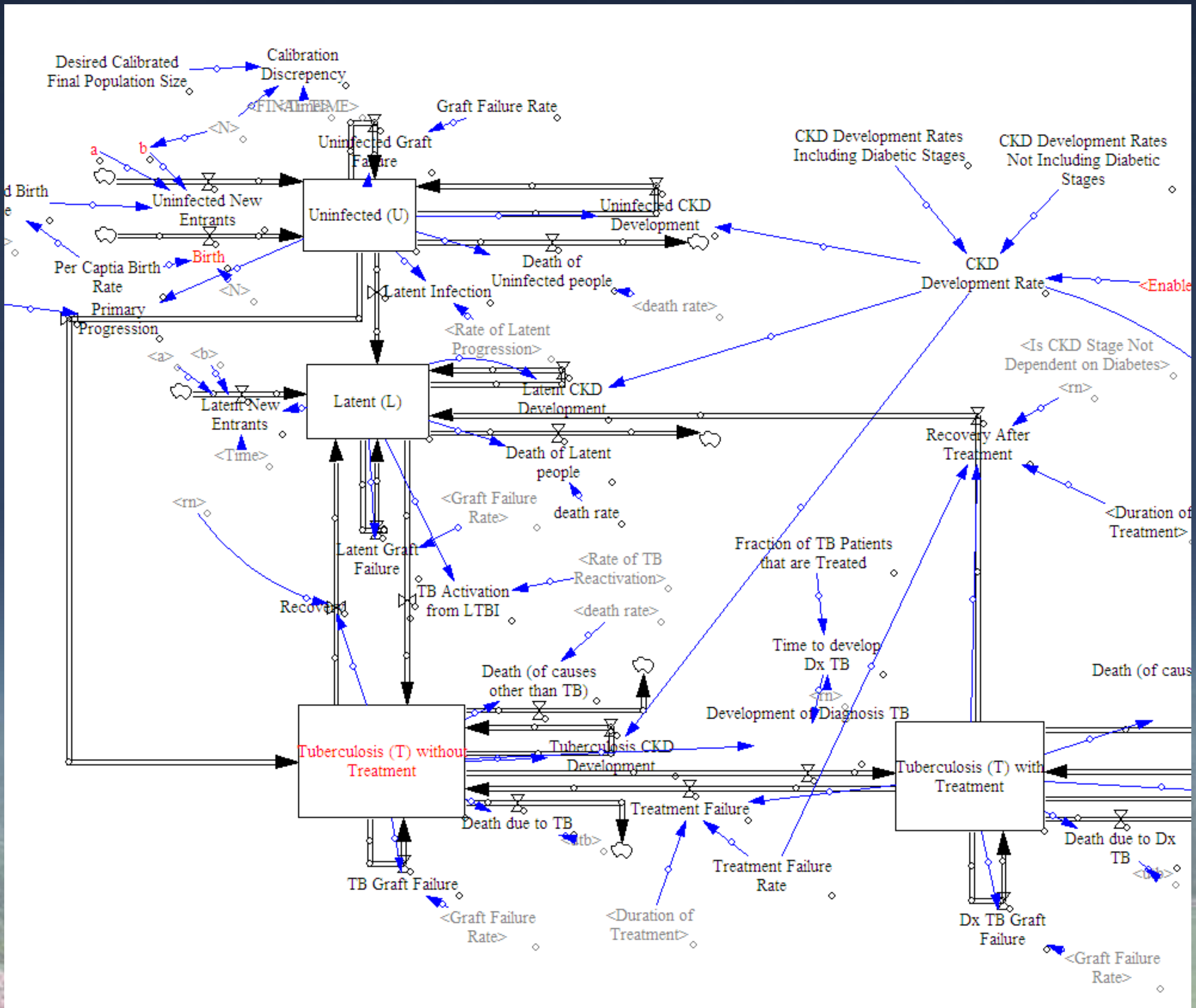
Tuberculosis



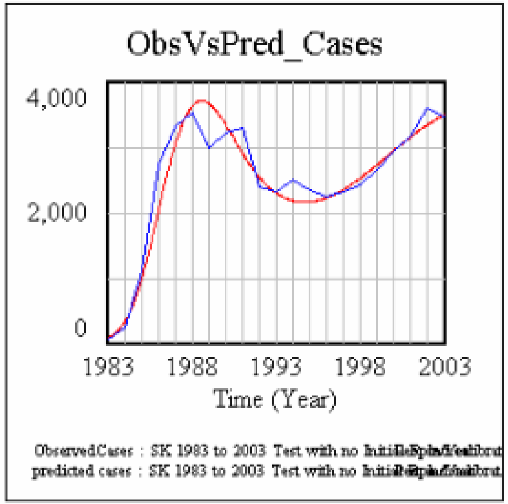


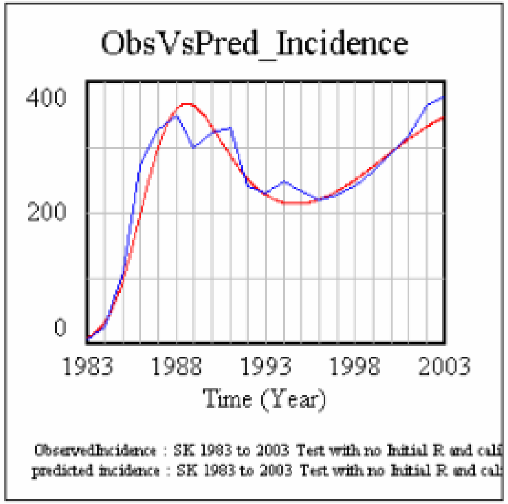


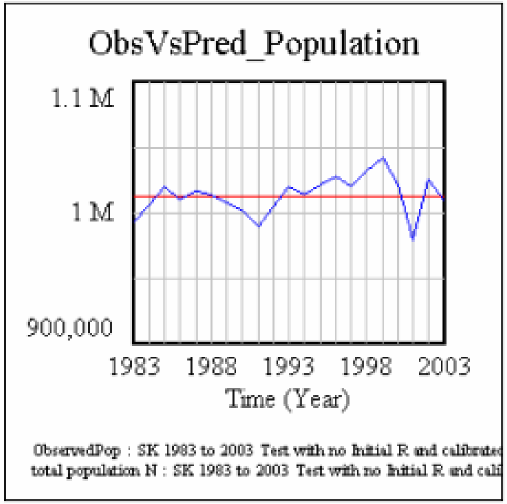
Aggregate Simulation Models (TB)

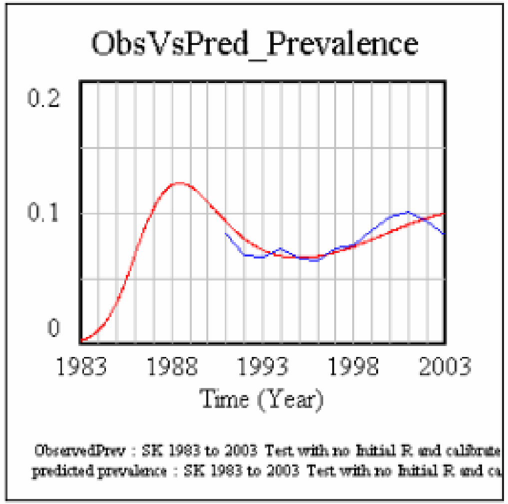


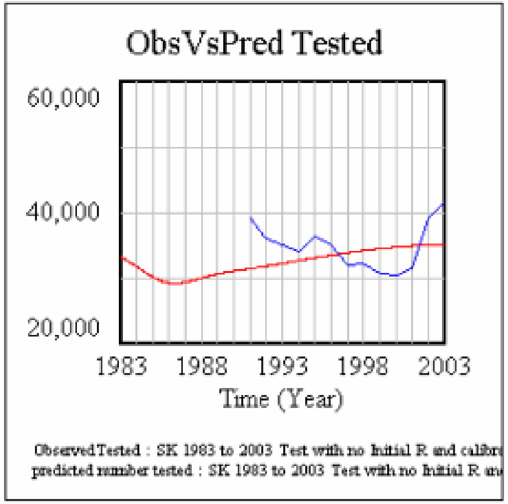
Pieces of the Elephant: STI

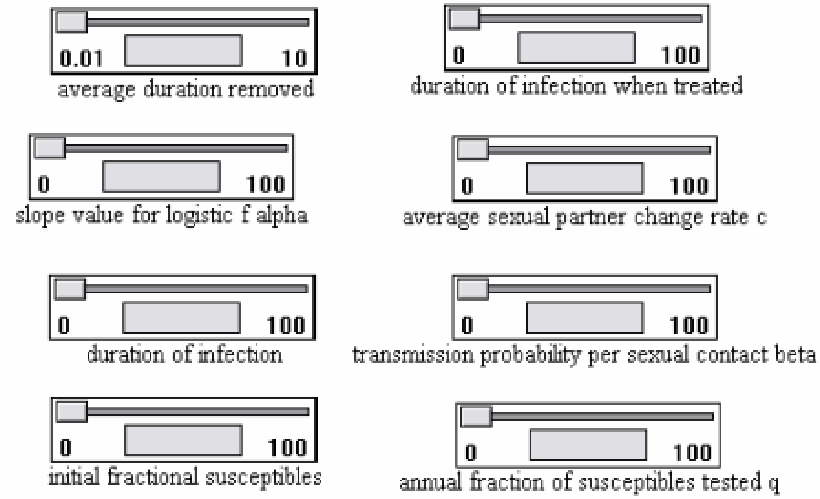




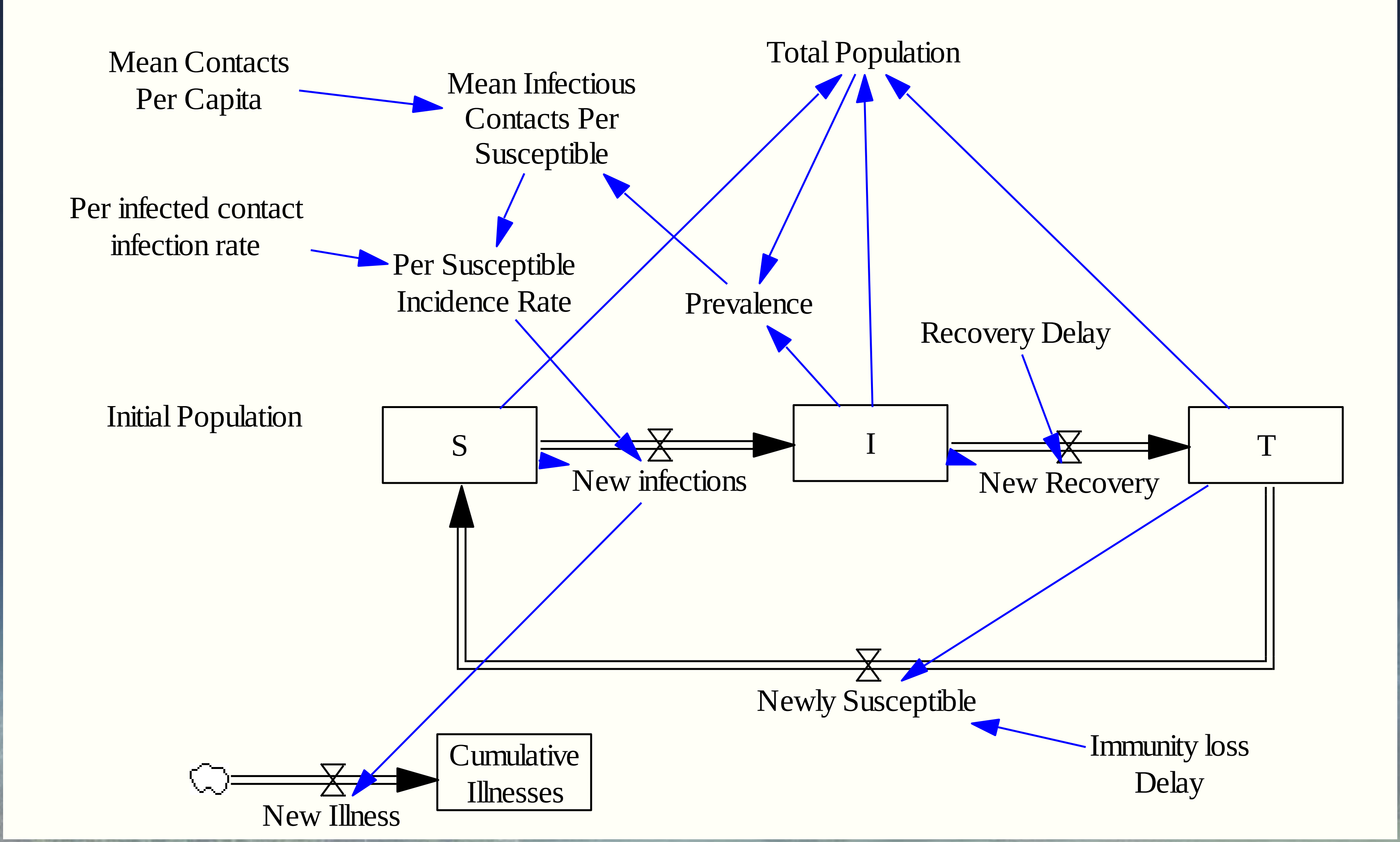




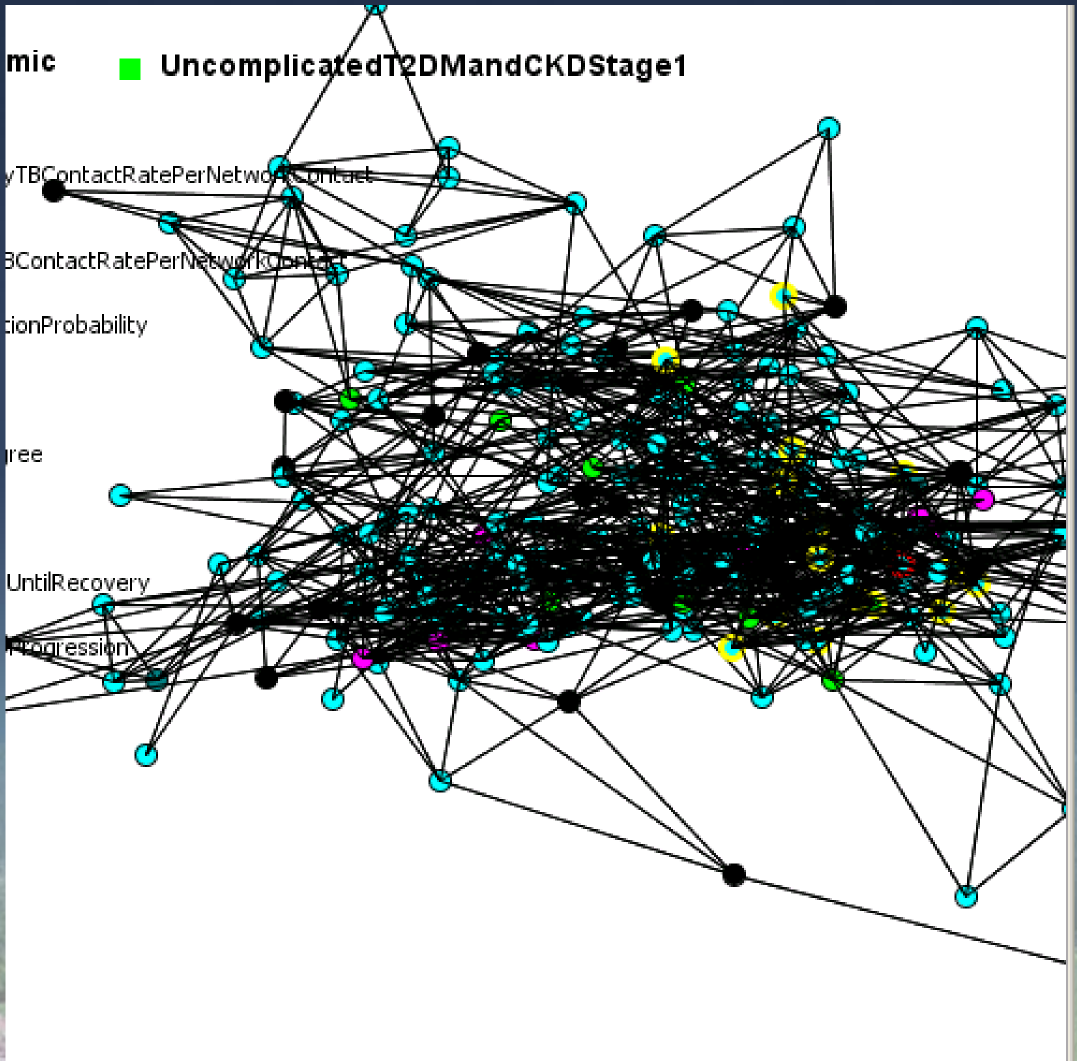




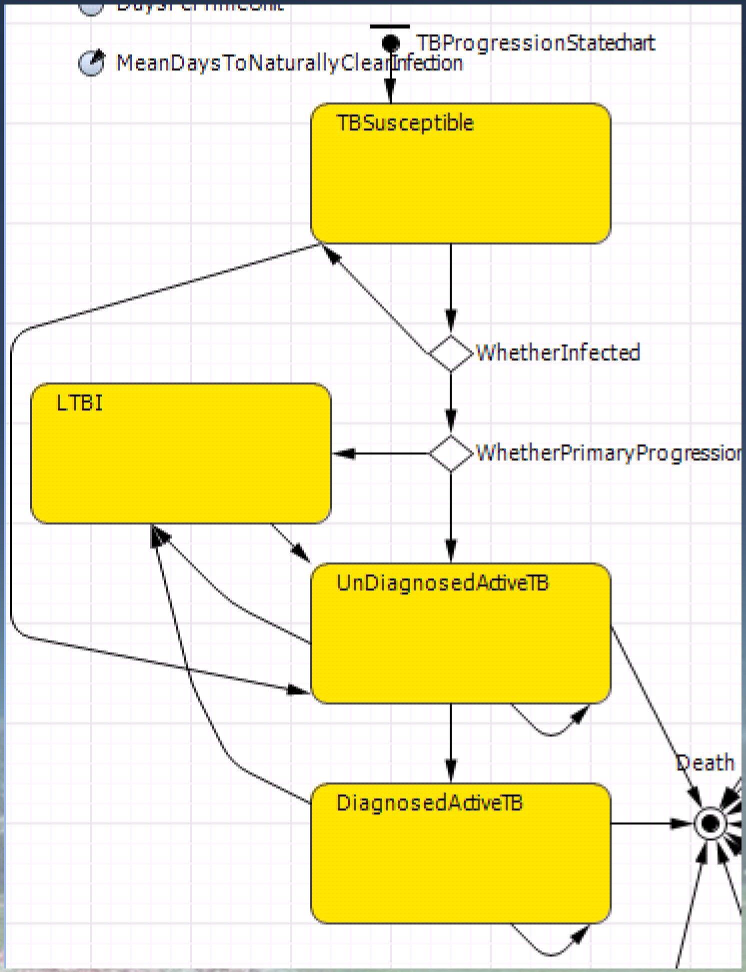
An Example STI Model



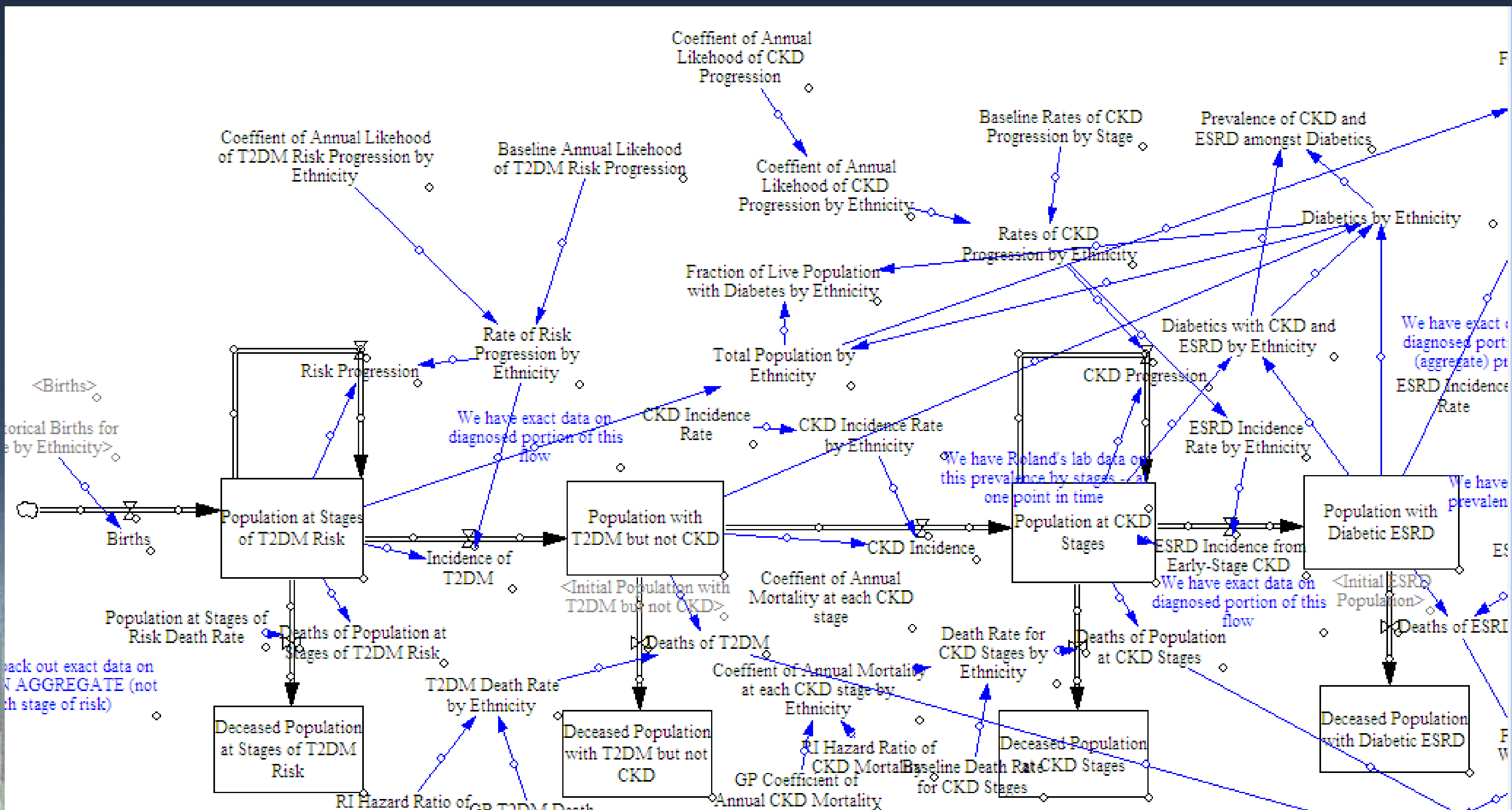
Individual-Based Modeling Simulation Models



State Transitions (Agent-Based IBM)



Aggregate Simulation Models (T2DM/ESRD)



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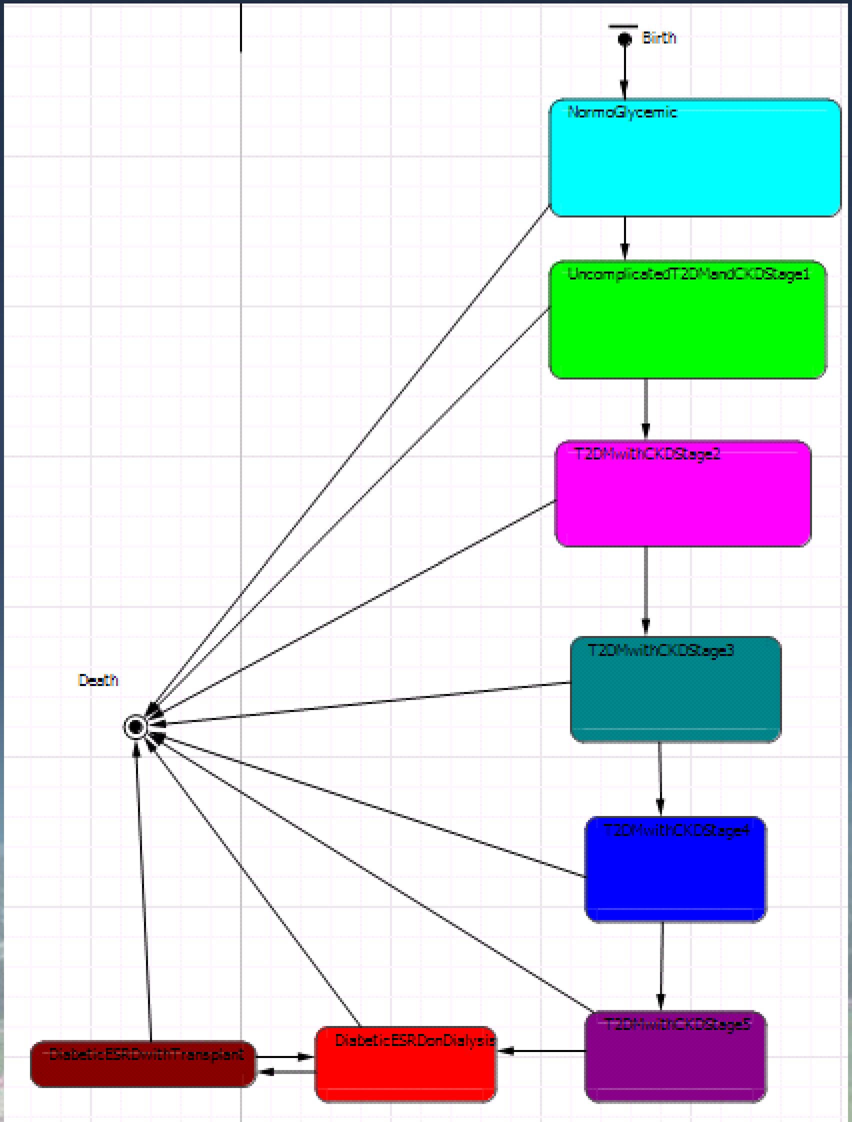

Deleterious Feedbacks

- **Cutting cigarette tar levels reduces cessation**
- **Cutting cigarette nicotine levels leads to compensatory smoking**
- **Targeted anti-tobacco interventions lead to equally targeted coupon programs by tobacco industry**
- **Charging for supplies for diabetics leads to higher overall costs by increases costs due to reduced self-management, faster disease progression**
- **ARVs prolong lives of HIV carriers, but lead to resurgent HIV epidemic due to lower risk perception**
- **"Saving money" by understaffing STI clinics, leads to long treatment wait, greater risk of transmission by infectives & bigger epidemics**
- **Antibiotic overuse worsens pathogen resistance**
- **Antilock breaks lead to more risky driving**
- **Natural feedback: Intergenerational "Vicious Cycles"**

Examples of High-Profile Simulation Modeling Projects

- CDC Diabetes Model
  - Influenced health goals
  - Adapted to 7+ States
- SimSmoke
  - US National tobacco policy
  - ~15 Countries

Outline

- Motivation for systems modeling concepts
- Model Vignettes
  - Aggregate
    - Type 2 & Gestational Diabetes Mellitus Models
  - Individual-Based
    - HIV Spread in Papua New Guinea
    - Multi-scale immune/viral transmission model
- Concluding Remarks

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Common Misconceptions about Causality

- **Focus on single events**
- **Focus on proximal causes (close in time and space)**
- **Focus on one-way chains of cause and effect**
- **Assume unchanging strength of cause-effect links**

Such narrow framing of issues overlooks the importance of cumulative effects, delays, feedback loops, and nonlinearities

Richmond B, Peterson S, High Performance Systems Inc. *An introduction to systems thinking*. Hanover NH: High Performance Systems, 1997.

Adapted from Homer & Milstein

Complex System Characteristics

- Feedbacks
- Nonlinearities
- Delays
- Path dependence & Lock-in
- Behavior a result of internal structure ("The enemy is us")
- Result: Emergent behavior ("Whole greater than the sum of its parts")

Common Phenomena In Complex Systems

- **Snowballing: When things go bad, they often go *very* bad very quickly**
  - **"Vicious cycles" lead to "cascading" of problems**
  - **"Path dependence": Different starting points can lead to divergence in project progress**
- **Lock-in, Policy resistance: Situation can be unexpectedly difficult to change**

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Deleterious Feedbacks

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- Antibiotic overuse worsens pathogen resistance
- Antilock breaks lead to more risky driving
- Natural feedback: Intergenerational “Vicious Cycles”

COMPLEXITY of SYSTEMS

- *Dynamics:* Dynamic problems are harder than static problems. There are time delays involved between causes and effects; between actions and reactions.

- *Feedback:* The problem is further complicated when dynamics are created by operation of feedback loops. It means that which way the system will move is not easily predictable; the evolution path unfolds gradually and continuously determines its own path into the future. (Path-dependent dynamics).

- *Non-linearity:* Most system dynamics problems are non-linear. This means that the cause-effect relations between variables are not proportional. Non-linear effects are subtle, because a certain effect observed in a one range may not be valid at all in another range. Non-linearity furthermore often means that there are “interaction effects” between variables.

- *Cause and effect separated in time and space:* In a non-linear dynamic feedback model with several variables, the cause-effect relations become detached in time and space.

- *Scale:* As the number of variables increases, the complexity of the problem increases nonlinearly. Even “small size” policy problems involve tens of variables. At this scale, a non-linear feedback problem immediately becomes impossibly hard to track –analytically and intuitively.

- *Human dimension:* Typical system dynamics problems involve human actors. So we must model not only the physics of the system (including information flows), but also how people react to situations, make decisions, set goals, make plans, etc.

Adapted from Barlas, 2007

PRINCIPLES/LAWS of SYSTEMS

- ***Principle: Meaningful macro behavior emerging from the interactions of micro components.*** **The macro dynamics is not built into the behavior of individual components nor is it obviously predictable from the action rules of these agents.**
  - **Dividing an elephant in two does not produce two small elephants**

- ***Principle: Counter-intuitive nature of systems.*** **We human beings are naturally equipped only to deal with cause-effect relation close in time and space. The baby touches the stove with his index finger; his index finger burns and it burns now and he learns. Our intuitive ability is further impeded by delays, errors, omissions and bias in data/information that we use in real life.**
  - **Systems may exhibit better-before-worse dynamics (or vice versa)**

- ***Principle: Systemic misperceptions, biases and omissions are typical in decision making in a dynamic feedback environment.*** **Experiments show that we are poor decision-makers in dynamic, non-linear feedback environments. Our intuitive time and space-constrained notion of causality cannot cope with systemic complexities. We ignore, distort or misperceive feedbacks, time delays and non-linearities in making decisions.**
  - **Yesterday's "solutions" can be today's problems**

- ***Principle: Learning by experience is difficult and flawed in complex systems.*** **Perhaps the most critical of all, learning is not natural/intuitive in complex dynamic environments. Experimental evidence shows that, with our reductionist intuition of causality, we make incomplete or plain wrong causal inferences about effectiveness of actions/decisions**
  - **There is no "enemy out there"**
  - **Faster is slower**

Barlas, 2007

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Linked Communities of Scholars & Research

- Biomathematics
- Complex systems
- System Dynamics
- Operations research
- Public health informatics

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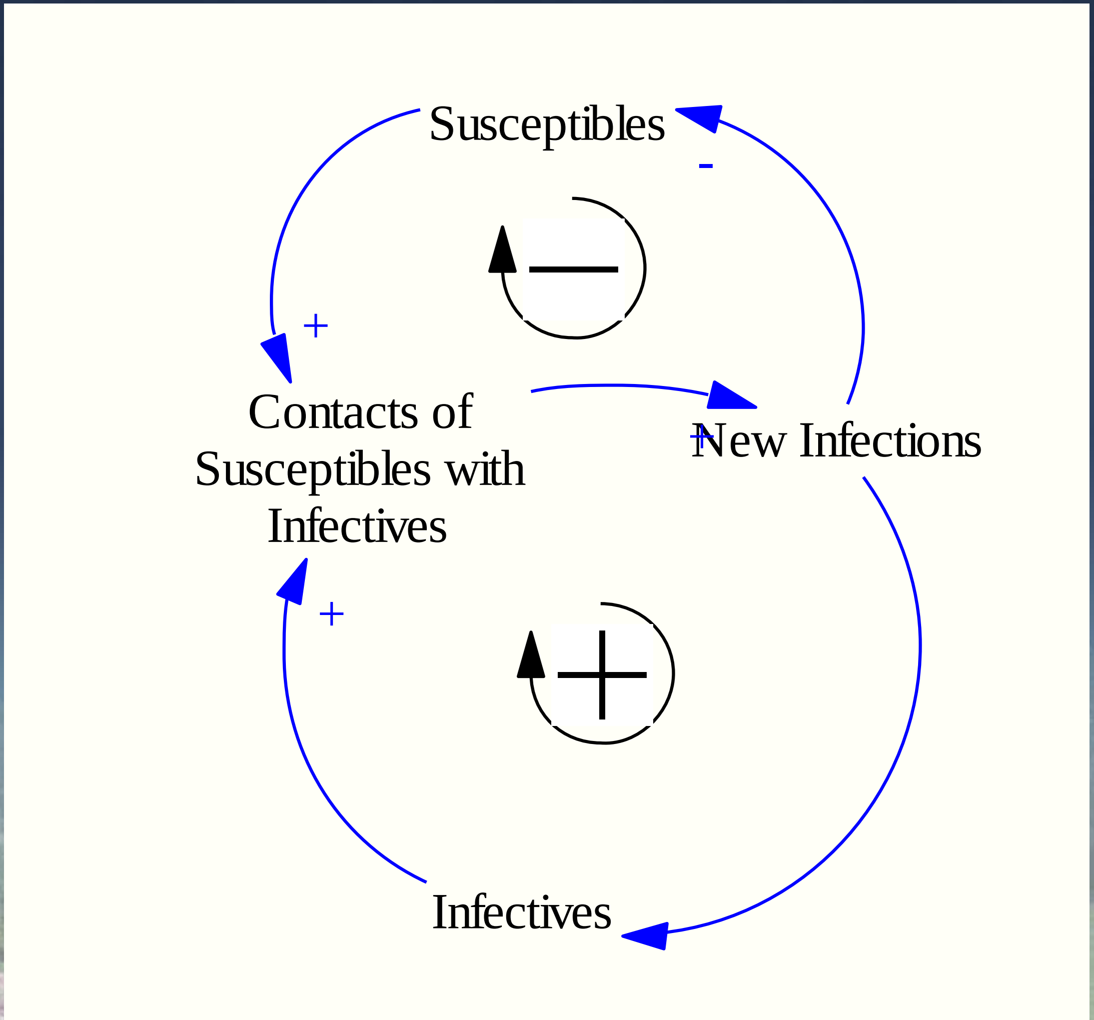
Outline

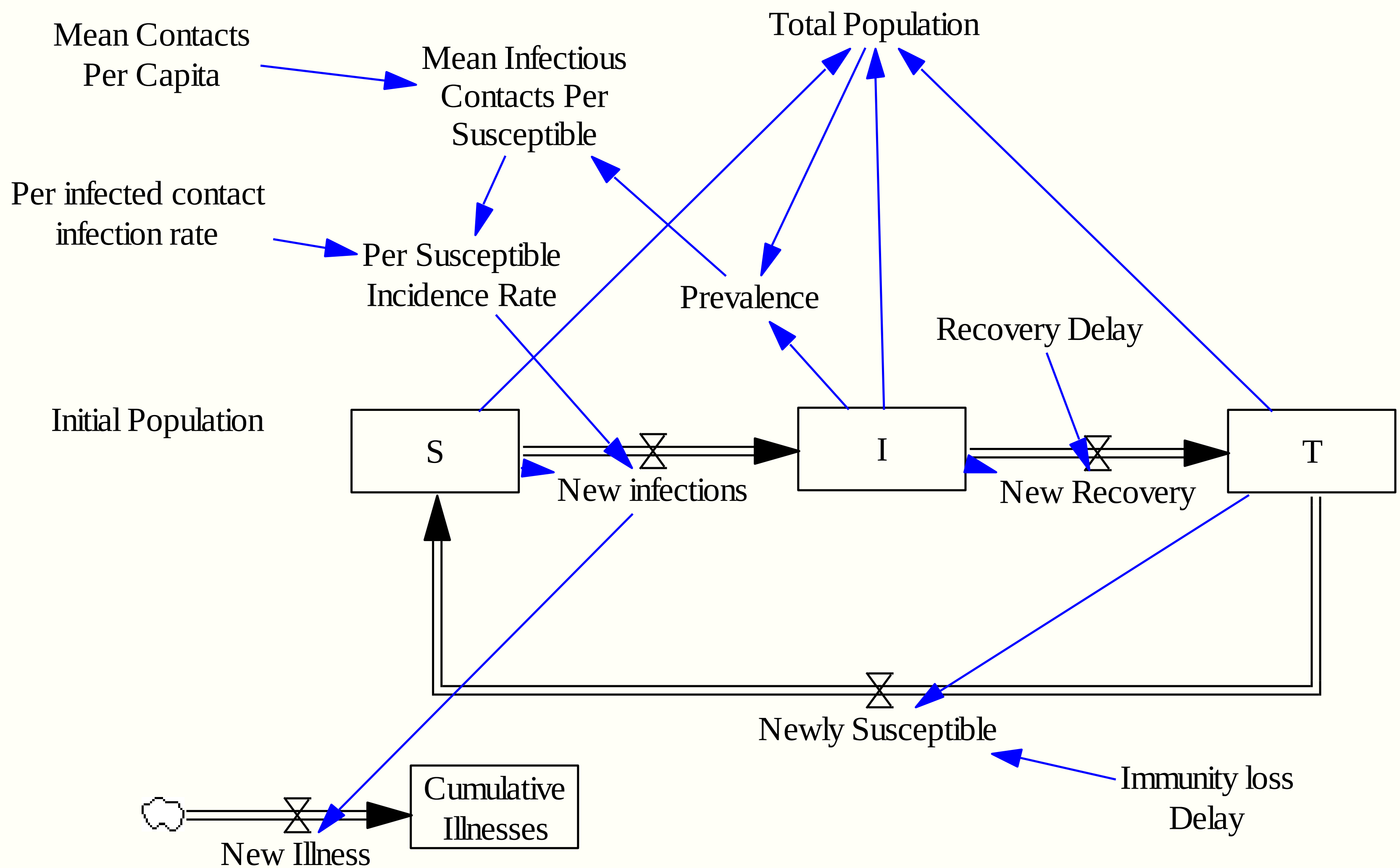
- ✓ Motivation
- Model Vignettes
  - Aggregate
    - Infectious Disease models: Broadening classic compartment model formulations
    - Emerging Type 2 & Gestational Diabetes Mellitus Model
  - Individual-Based
    - HIV Spread in Papua New Guinea
  - Multi-scale
    - Immune/viral transmission model

Feedbacks

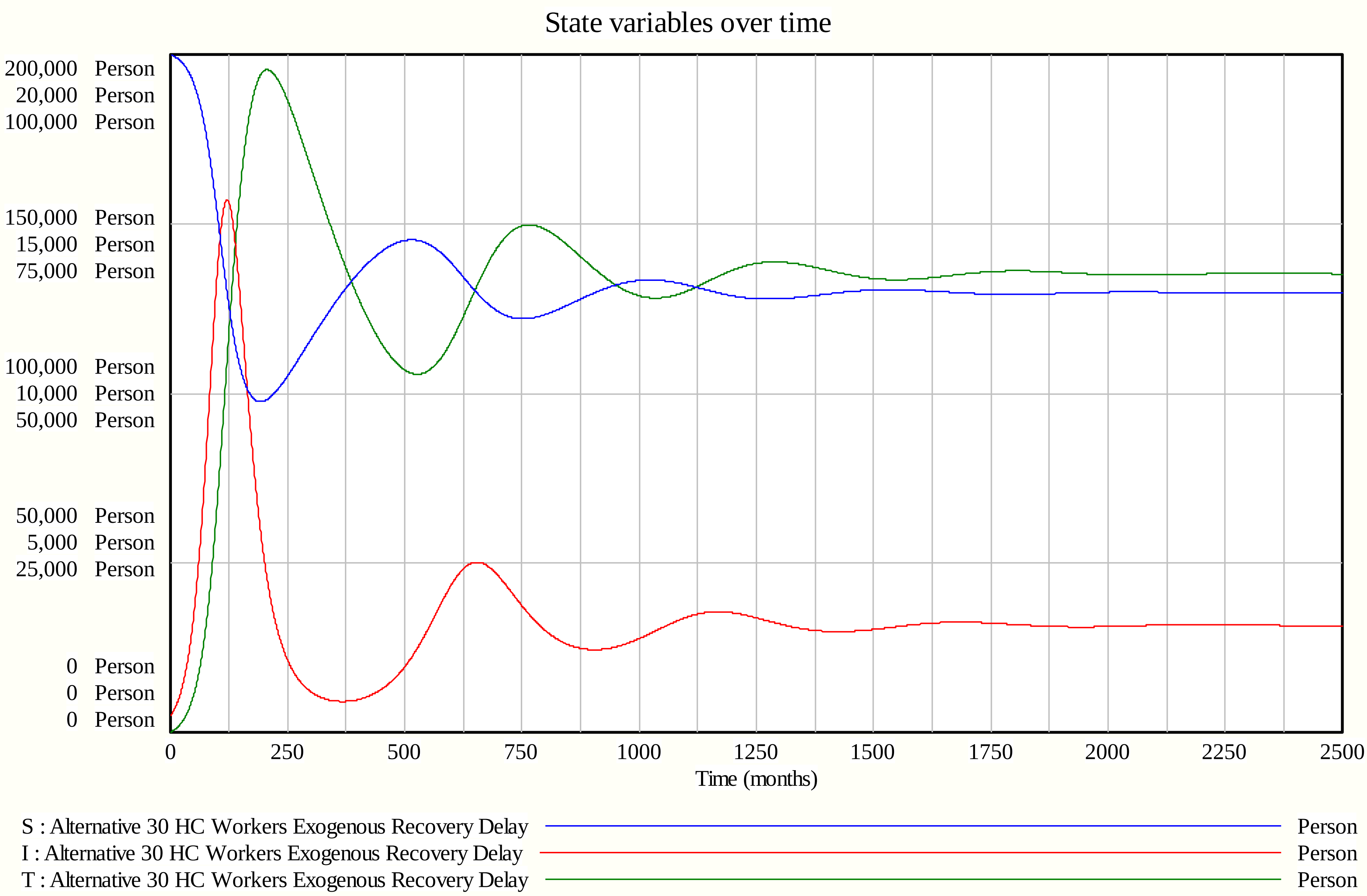


Susceptibles
-
+
Contacts of Susceptibles with Infectives
+
New Infections
+
Infectives

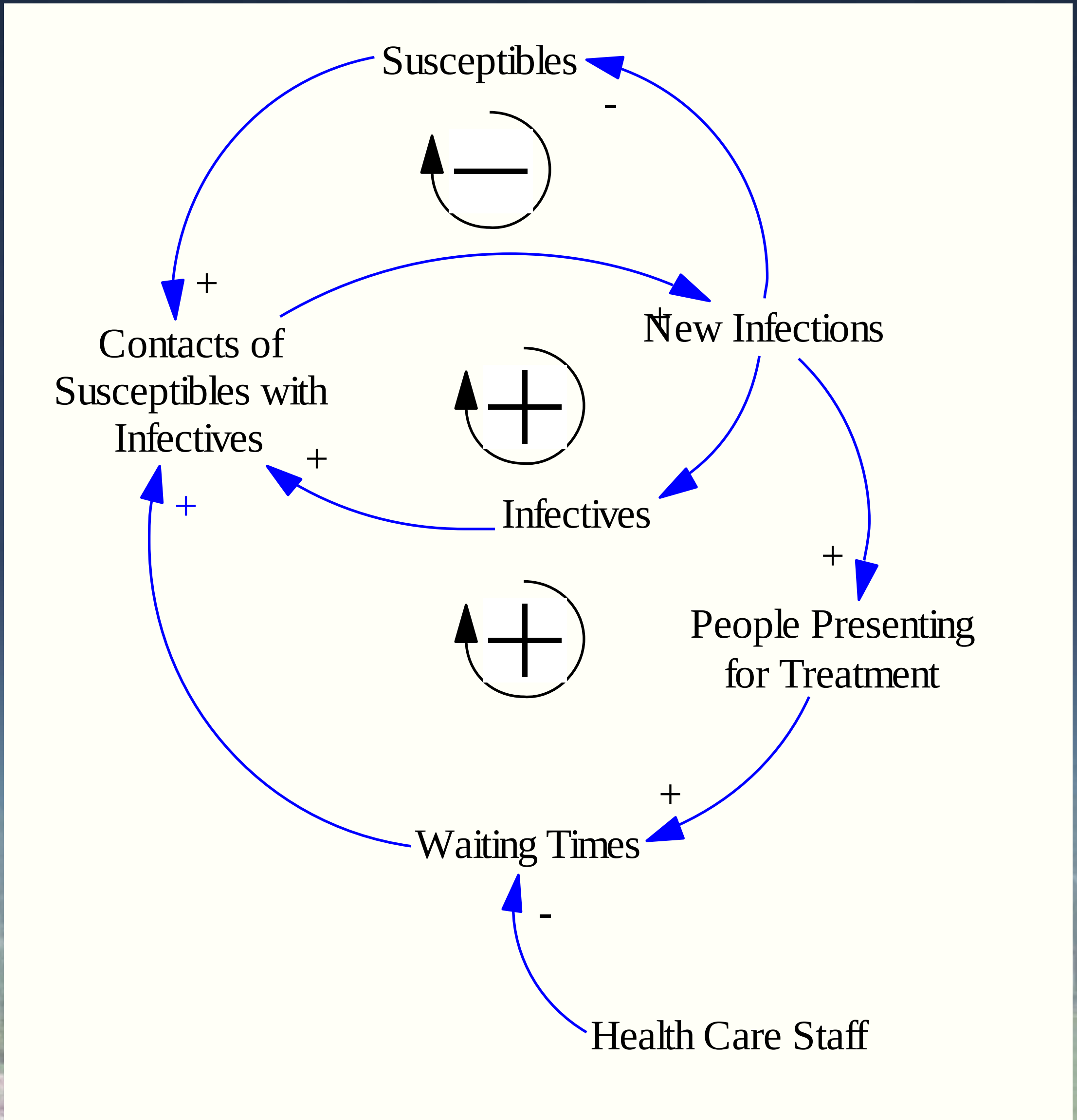
Simple SIT Model



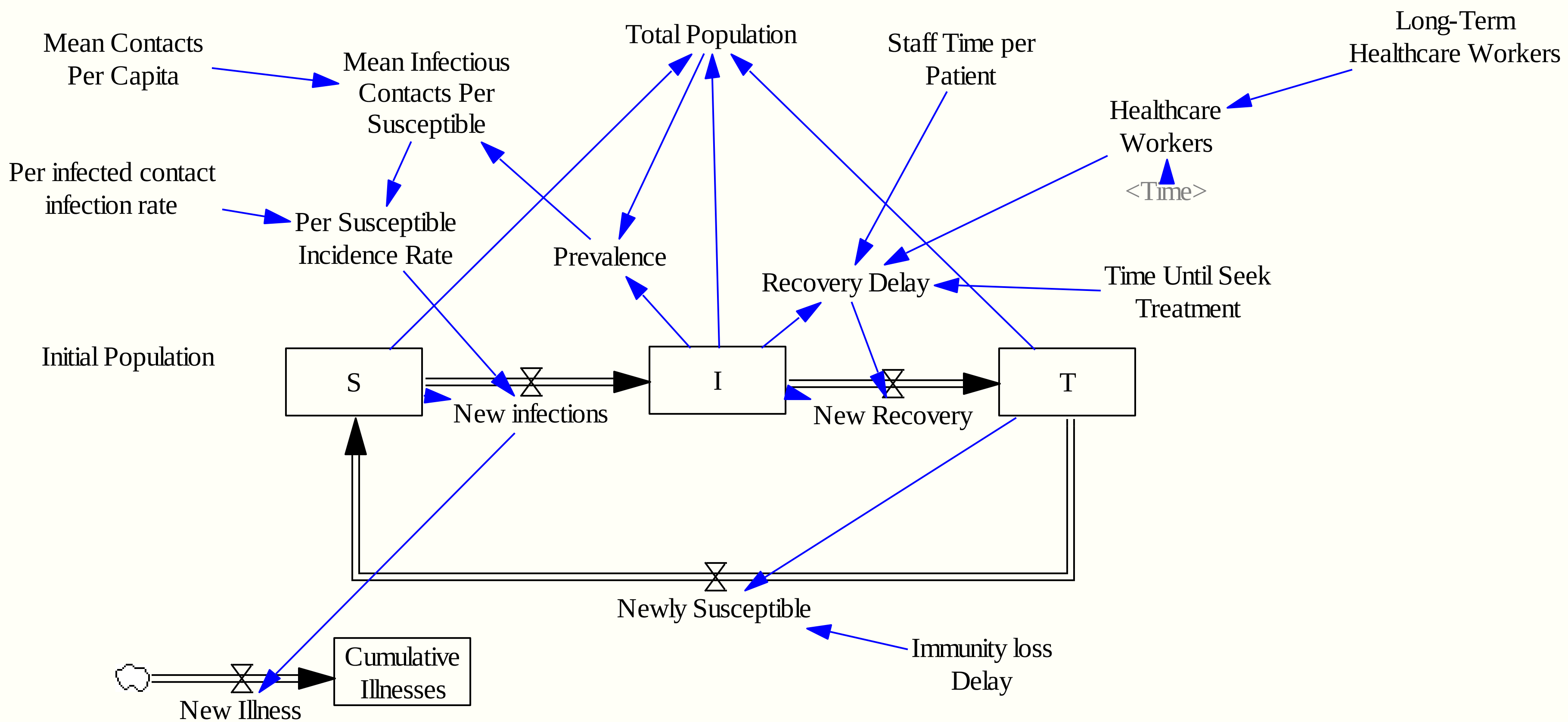
Stocks?


State variables over time
200,000 Person
20,000 Person
100,000 Person
150,000 Person
15,000 Person
75,000 Person
100,000 Person
10,000 Person
50,000 Person
50,000 Person
5,000 Person
25,000 Person
0 Person
0 Person
0 Person
0
250
500
750
1000
1250
1500
1750
2000
2250
2500
Time (months)
S : Alternative 30 HC Workers Exogenous Recovery Delay
Person
I : Alternative 30 HC Workers Exogenous Recovery Delay
Person
T : Alternative 30 HC Workers Exogenous Recovery Delay
Person

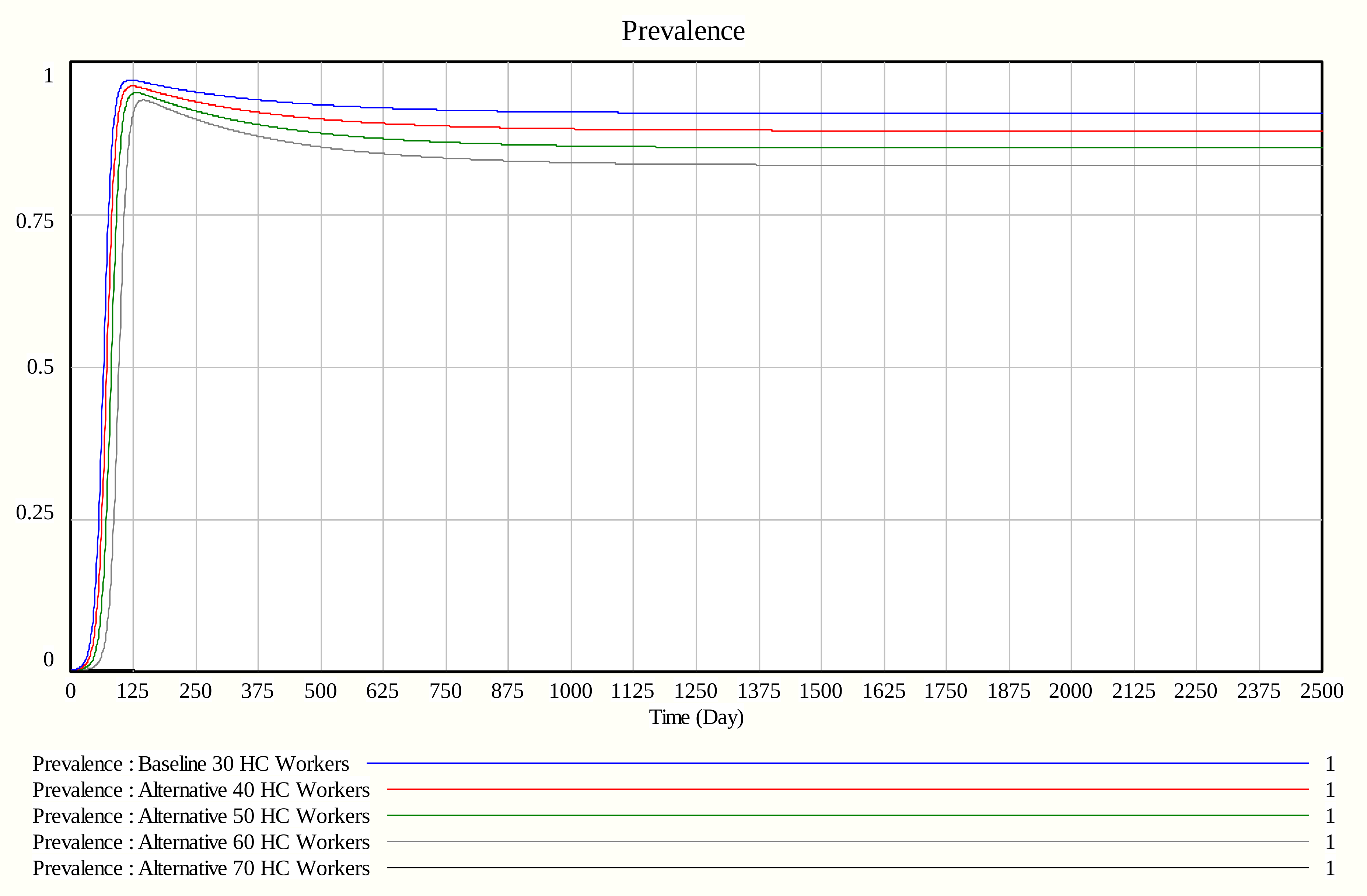
Broadening the Model Boundaries: Endogenous Recovery Delay



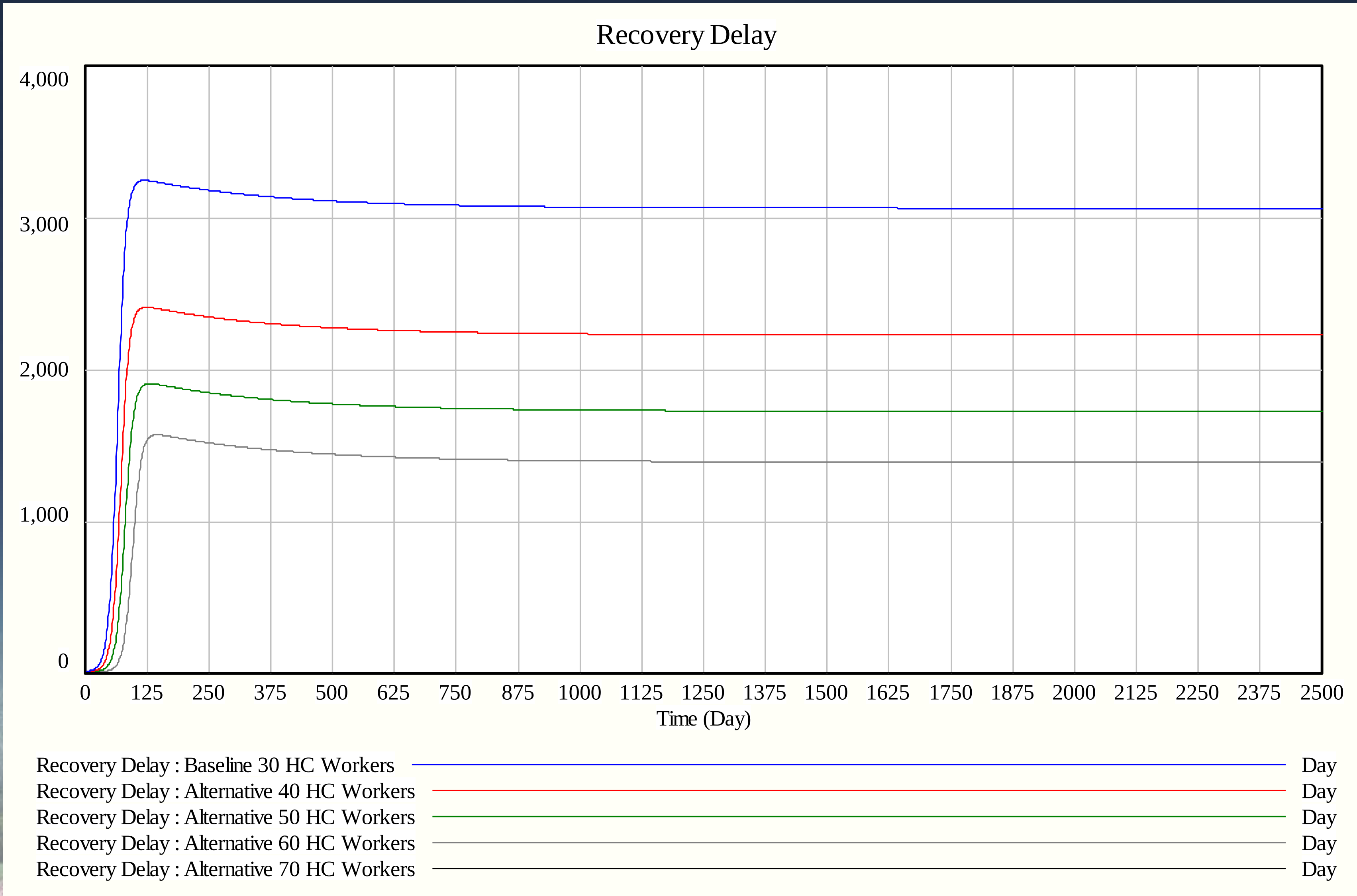
Broadening the Model Boundaries: Endogenous Recovery Delay



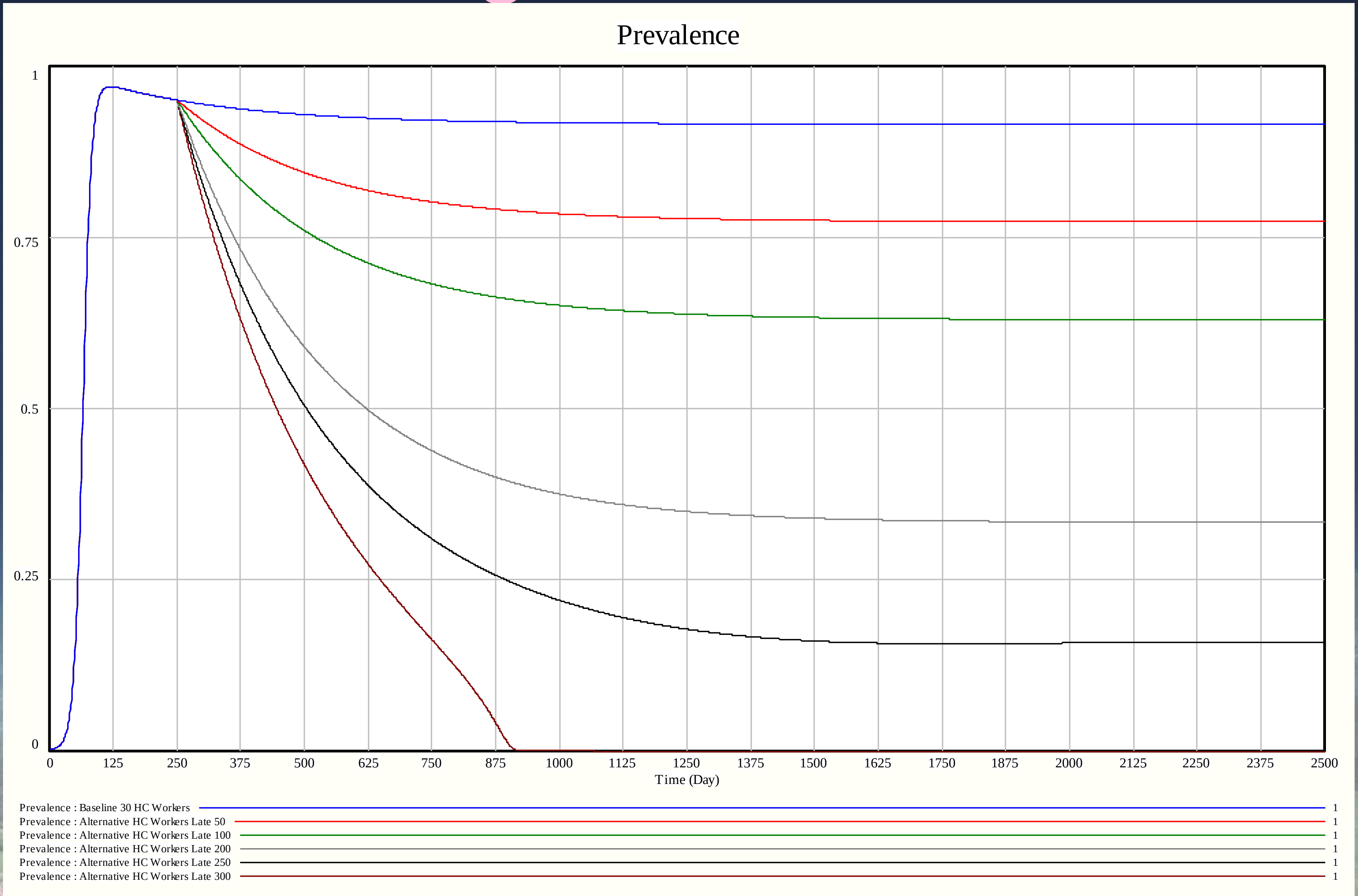
Prevalence Implications?



How Does Count of Health Care Workers Affect Treatment Delay?

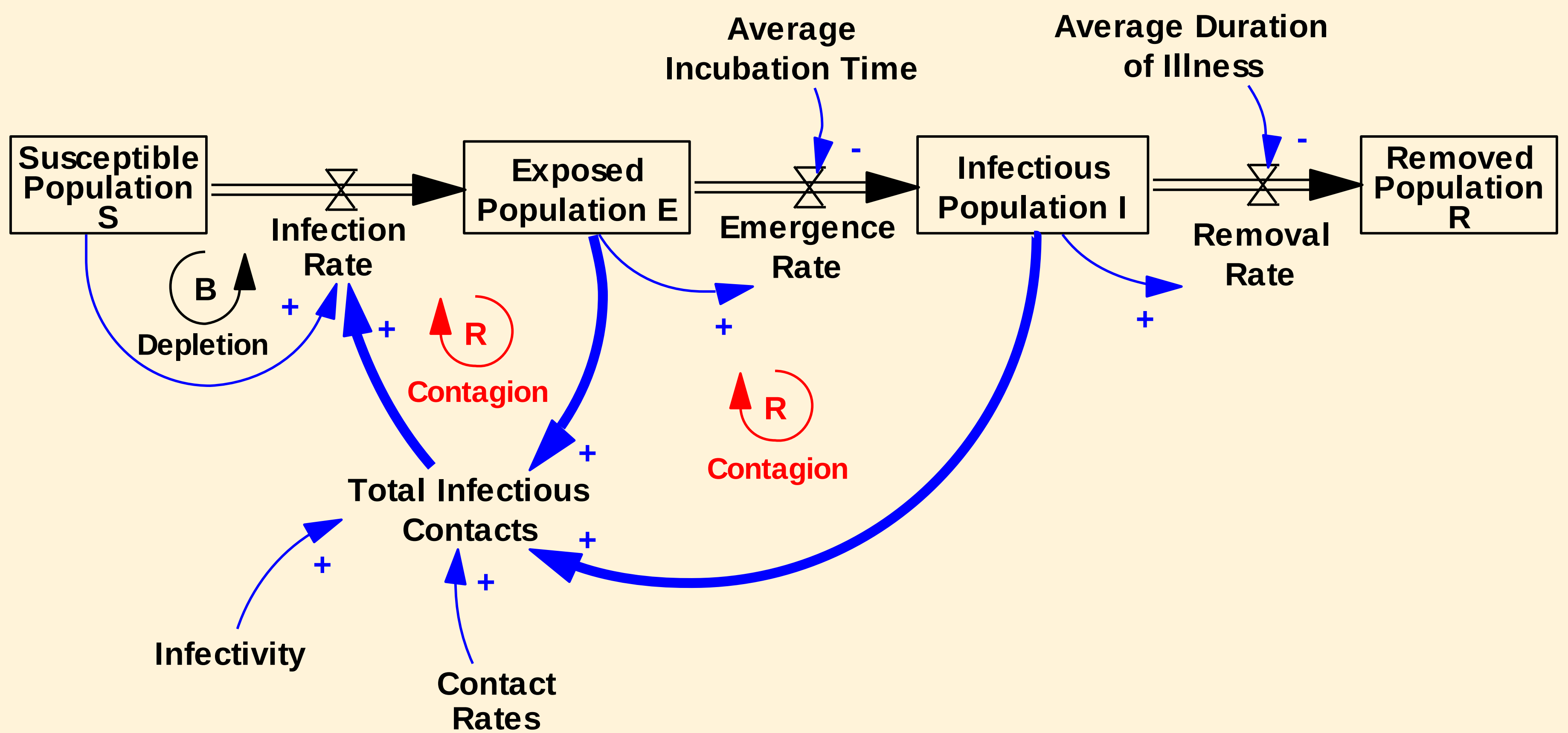


Oops!
Late Hiring of 70 HC Workers?



Lock-In Effect (Path Dependence)

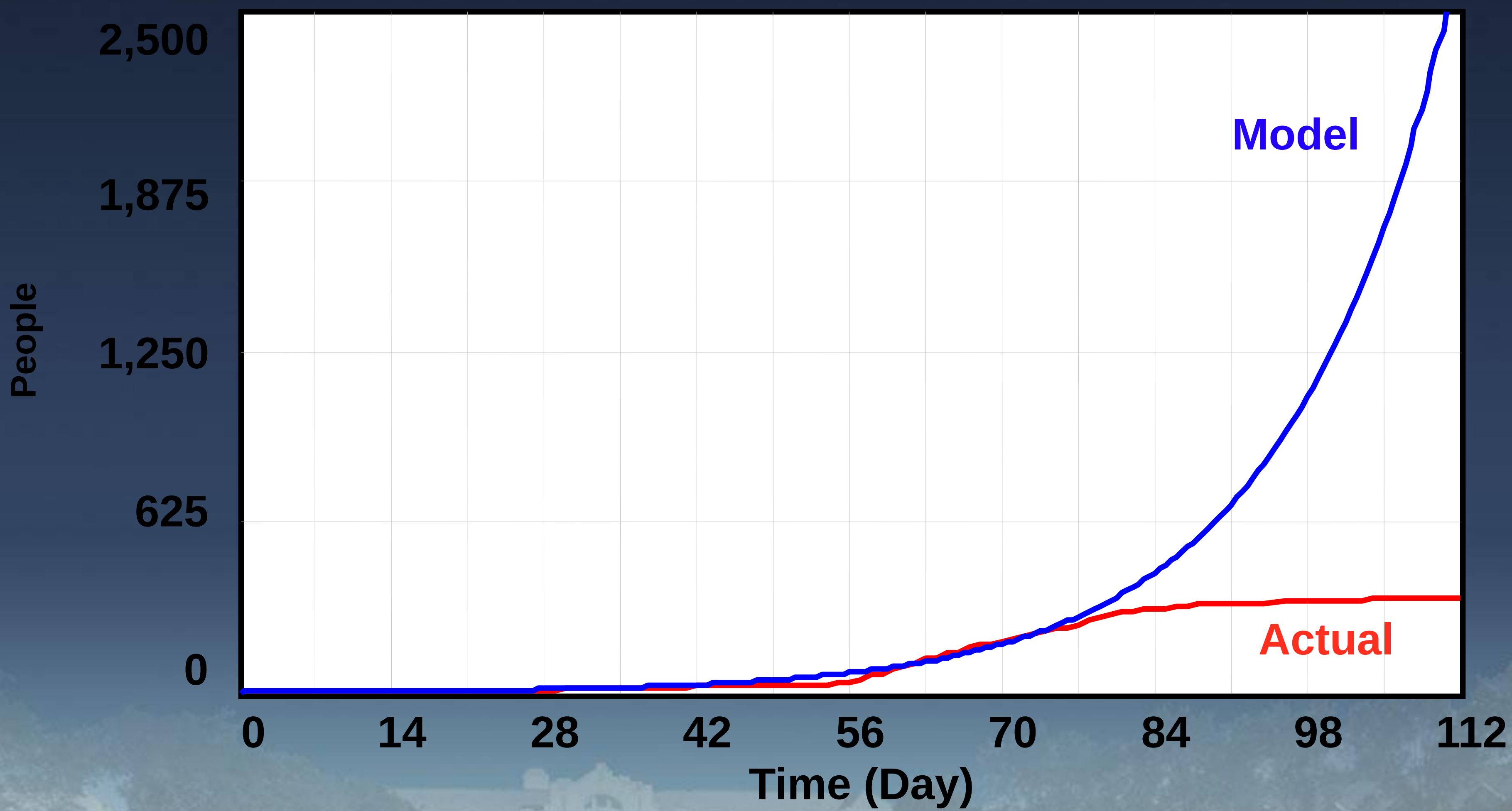
- Investing Early in HC workers ⇒Small Prevalence ⇒ Fewer HC workers needed to maintain low prevalence
- Limited # of HC workers ⇒ High Prevalence ⇒ More HC workers needed to achieve low prevalence



Average Incubation Time
Average Duration of Illness
Susceptible Population S
Infection Rate
Exposed Population E
Emergence Rate
Infectious Population I
Removal Rate
Removed Population R
B
Depletion
R
Contagion
R
Contagion
Total Infectious Contacts
Infectivity
Contact Rates
+
-

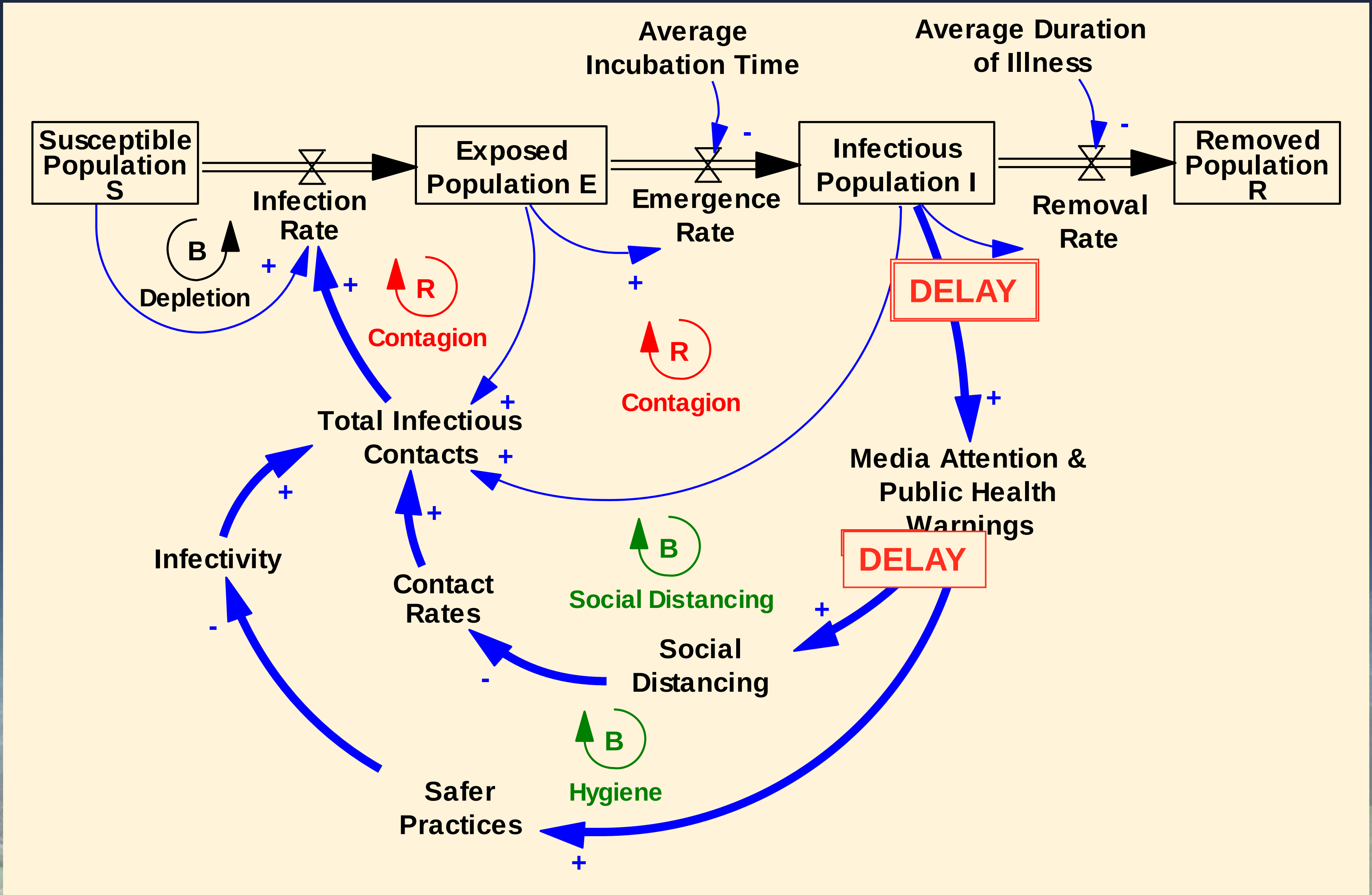
SEIR Model vs. Data, Taiwan

Cumulative Cases, No Behavioral Response



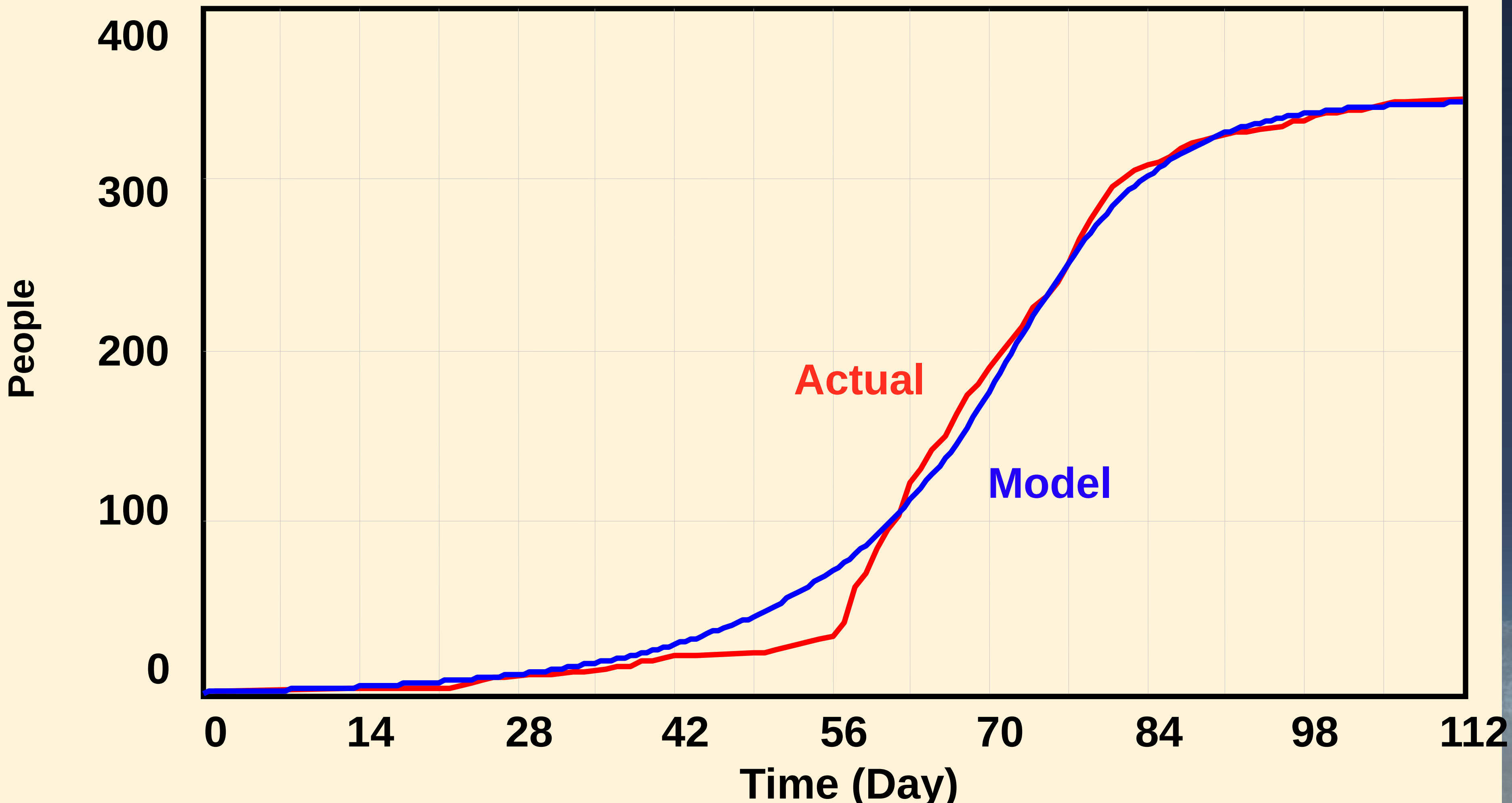
Insert Source

Expanding the Boundary: Behavioral Feedbacks

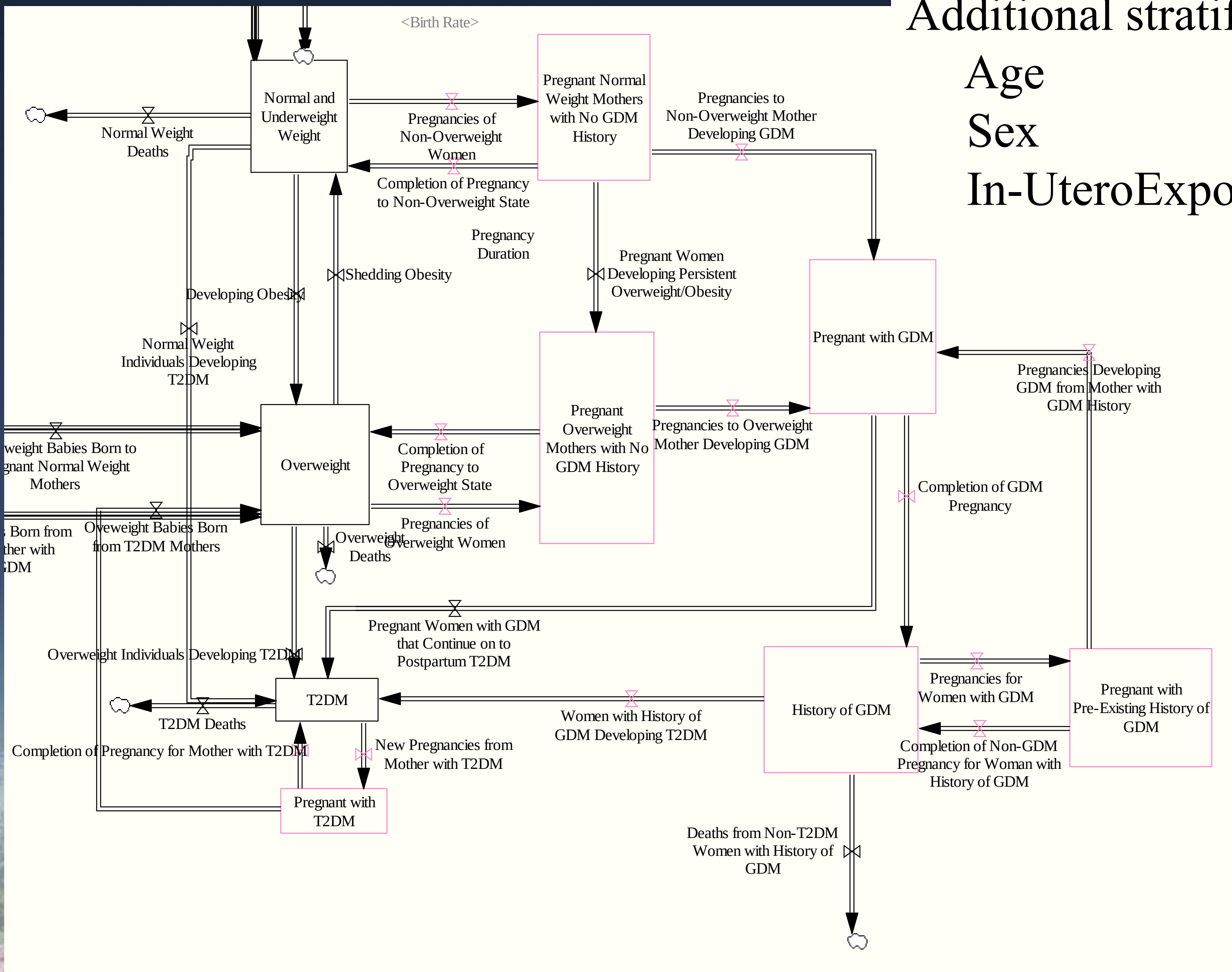


Model vs. Data with Behavioral Feedback

Cumulative Cases



Overall Model Structure



Additional stratifying:

- Age
- Sex
- In-UteroExposure

Outline

- ✓ **Motivation**
- **Model Vignettes**
  - ✓ **Aggregate**
    - ✓ **Infectious Disease models: Broadening classic compartment model formulations**
    - ✓ **Emerging Type 2 & Gestational Diabetes Mellitus Model**
  - **Individual-Based**
    - **HIV Spread in Papua New Guinea**
  - **Multi-scale**
    - **Immune/viral transmission model**

Complicating Factors

- **Co-morbidities**
- **Influences of parents, peers on risks**
- **Heterogeneity**

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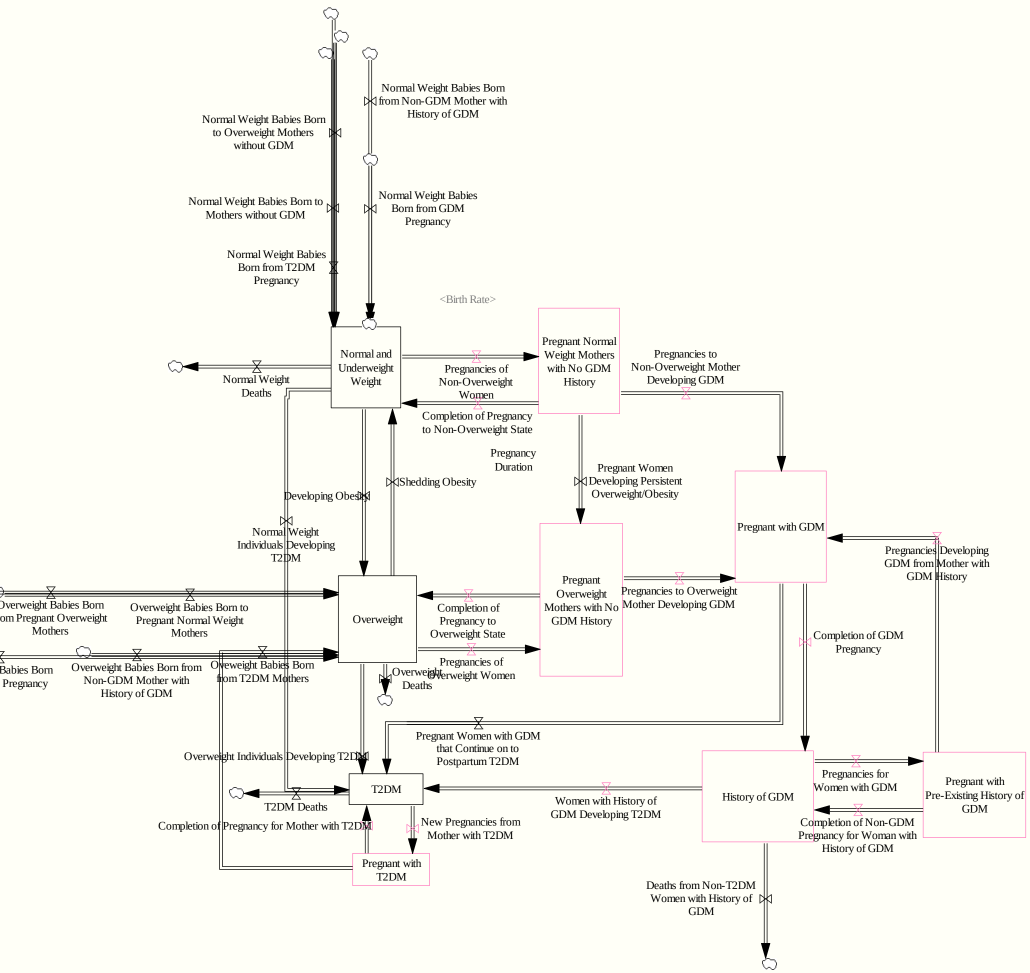
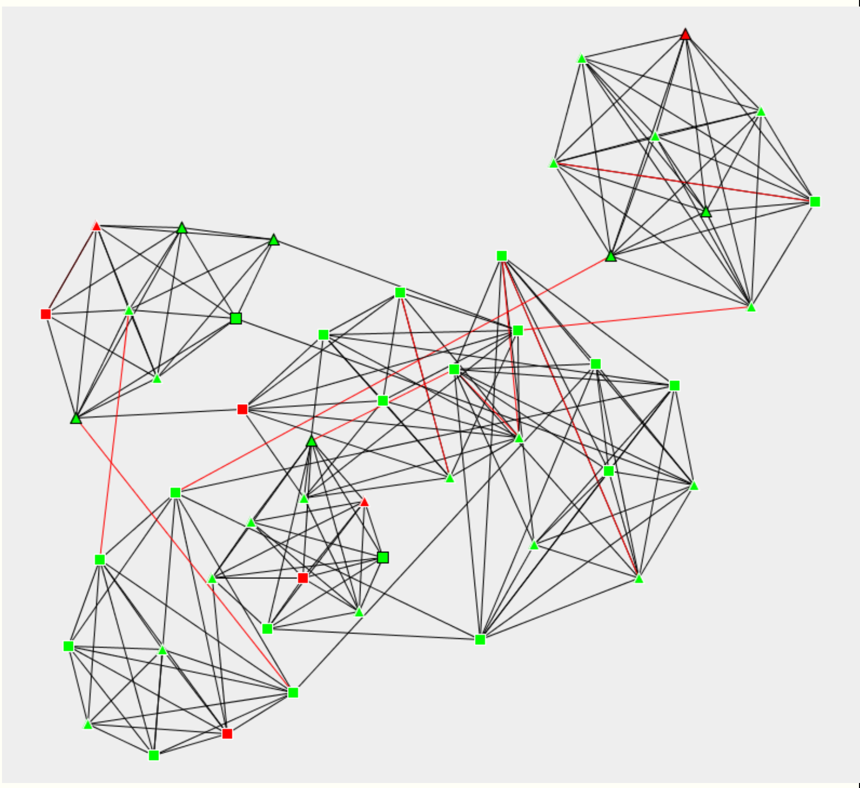
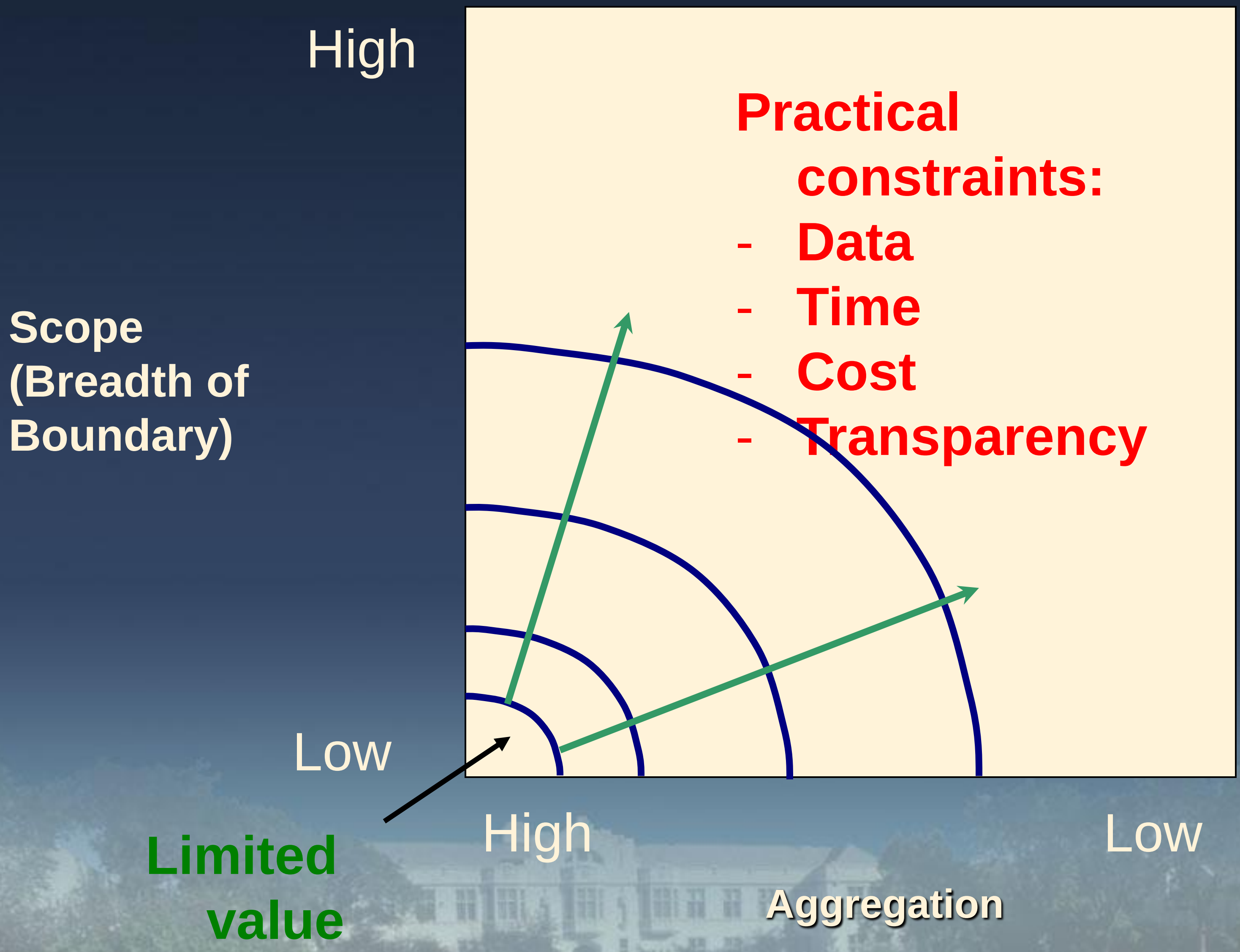
Contrasting Model Granularity





Inevitable Tradeoffs



Slide adapted from Geoff McDonnell

Contrasting Benefits

Aggregate Models

- Easier
  - Construction
  - Calibration
  - Parameterization
  - Analysis & Understanding
- Performance
  - Lower baseline cost
  - Population size invariance
- Less pronounced stochastics
  - Less frequent need for Monte Carlo ensembles
- Quicker construction, runtime ⇒More time for understanding,refining

Individual-Based Models

- Examining finer-grained consequences
  - Network spread
  - e.g. transfer effects w/i pop.
- Learning, bounded ration.
- Fidelity to some dynamics
- Support for highly targeted policy planning
- Better heterogeneity flexibility
- Simpler description of some causal mechanisms
- Better understanding by some clients

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Areas of Advantage of Individual-Based Modeling

- Examining finer-grained consequences
  - Network spread
  - Transfer effects within population
  - Detailed spatial dynamics
  - Effects of population heterogeneity
  - Effects of highly targeted policies
  - Local risk perception
  - Effects of individual-level synergies (e.g. multiple risk factors)
- Simple individual-based description of causality
- Sufficient individual-level (distributional) data are available for policy modeling beyond exploratory models

Agent State Chart

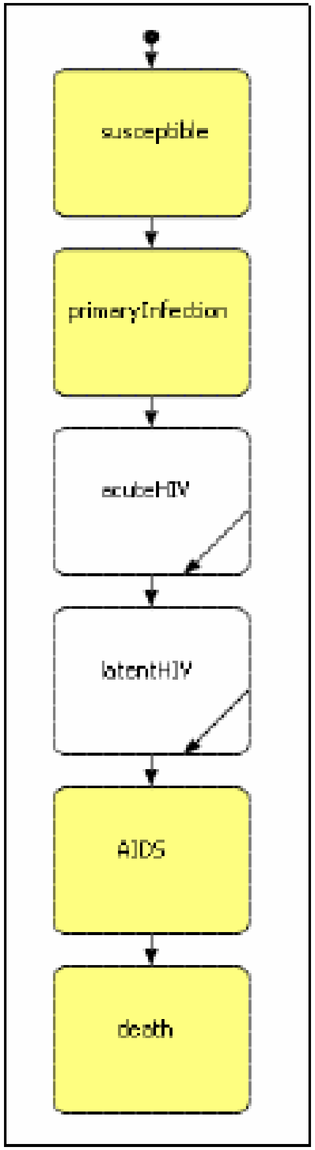

Figure 6.6 Agent State Chart

HIV and AIDS Progression Time	
Primary Infection	26 Days
Acute HIV	2 Weeks
Latent HIV	9 Years
AIDS	1 Years
Probability of Transmission	0.001 per Day

Table 7.2 HIV and AIDS Progression Time used in Model

Model Parameters	
Population Size	2000
Pair Formation Probability	0.01 per Day
Pair Separation Probability	0.005 per Day

Table 7.1 Model Parameters from Kretzschmar and Morris

Agent Attributes			
Name	**Type**	**Values**	**Description**
Networks			
Partners	Vector	Agent	Vector which maintains current partnerships
Friends	Vector	Agent	Vector which maintains current friendships
Partner Data			
totalPartners	Integer	varies	Counts total partners for the execution of the model
partnersDuration	Vector	Time steps	Vector which maintains the length of current partnerships
Demographics			
province	Integer	1-100	Represents region in which agent resides
beliefGroup	Integer	1,2	Type of belief system of the agent: Christian, Animist
educLevel	Integer	1,2	Level of Education received: primary, secondary
dwelling	Integer	1,2	Urban/rural
age	Integer	1,2	Age group: 20-30, 30-40
sex	Integer	1,2	Female/Male
Idea Spread			
idea	Integer	0,1	Determines whether agent is a non-transmitter or vulnerable
isAdvocate	Boolean	false,true	True if agent is an advocate
isIDeaFromAdvocate	Boolean	false,true	True if agent received idea directly from advocate
goodIdeaReceived	Boolean	false,true	True if agent has ever received idea

Table 6.2 Agent Attributes

Outline

- ✓ Motivation
- Model Vignettes
  - ✓ Aggregate
    - ✓ Infectious Disease models: Broadening classic compartment model formulations
    - ✓ Emerging Type 2 & Gestational Diabetes Mellitus Model
  - ✓ Individual-Based
    - HIV Spread in Papua New Guinea
  - Multi-scale
    - Immune/viral transmission model

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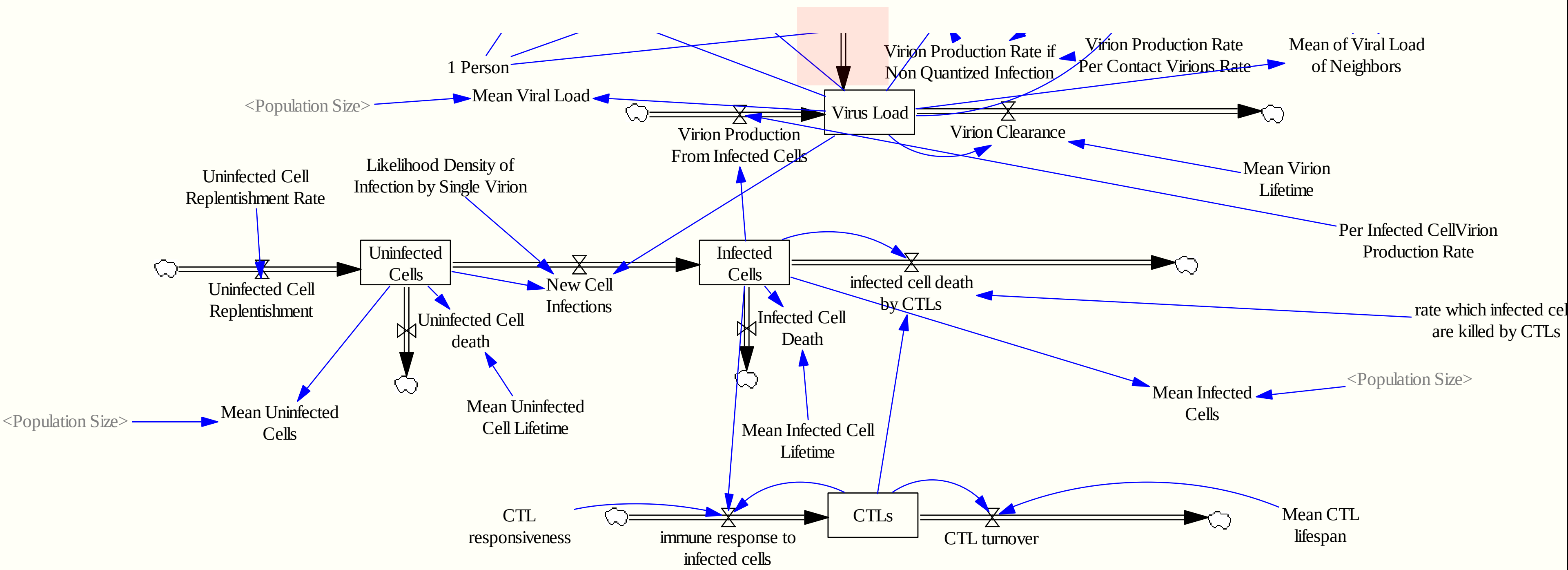
Multi-scale Model

- Conceptual model
- Network structure, dynamics
- Continuous condition (state)
- Model presently being generalized, parameterized for specific disease (w/ B. Sahai)

Individual Model Structure



Governing Equations for Individual

$$\dot{x}_i = \lambda - x_i\left(d + \beta v_i\right)$$

$$\dot{y}_i = \beta x_i v_i - y_i\left(a + p z_i\right)$$

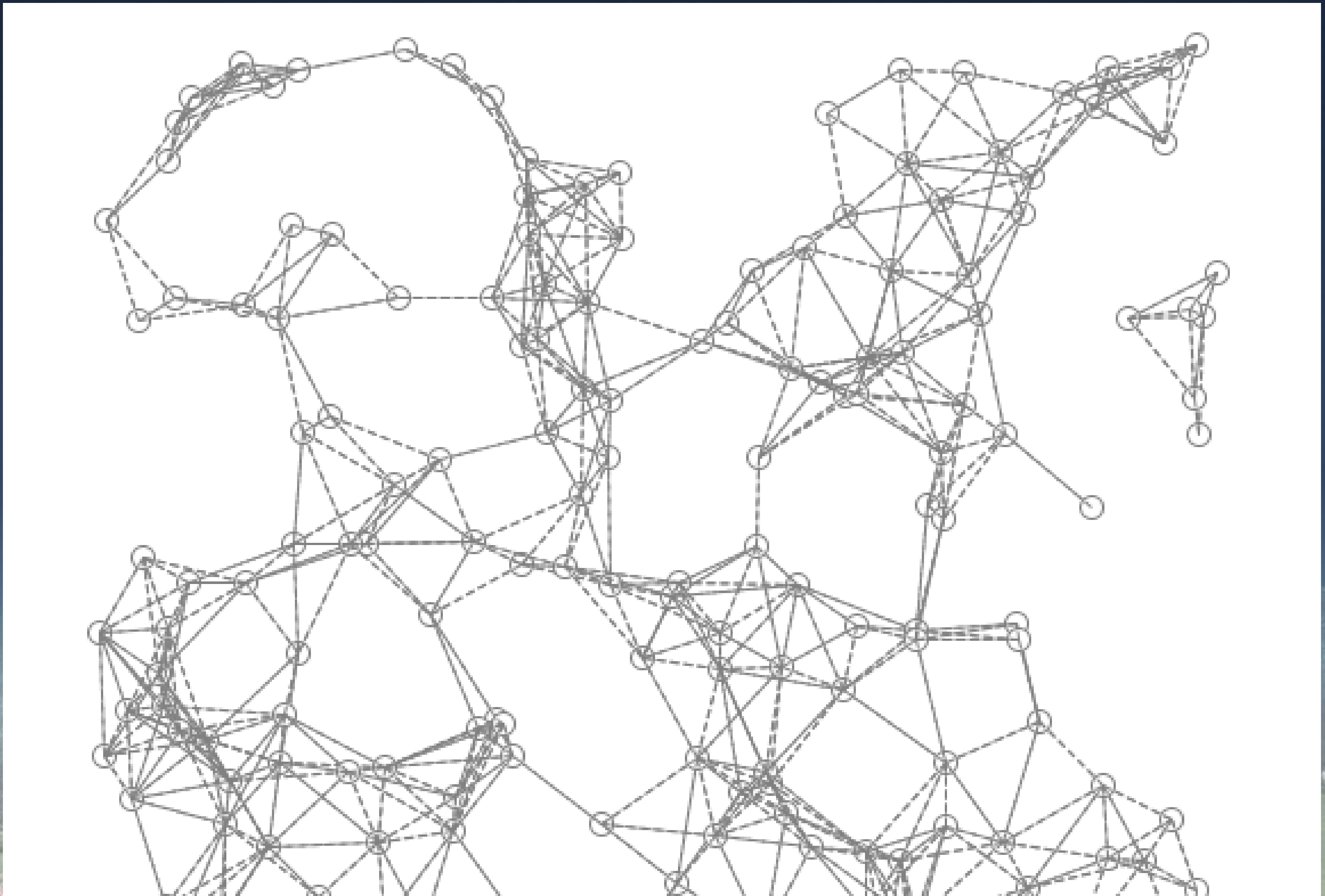
$$\dot{v}_i = k y_i + \omega_i \sum_{j \in P} \mathbf{A}_{ij} v_j - u v_i$$

$$\dot{z}_i = c_i y_i z_i - h z_i$$

Individual Model Parameters

Parameter	*Description*	*Value (units)*
λ	Production rate of uninfected cells	10 (cells/day)
d	Rate of uninfected cell die-off	0.1 (day^{-1})
β	Rate infected cells are produced from uninfected cells and free virus	0.001 $(virion \cdot day)^{-1}$
a	Infected cell death rate (due to virus)	0.5 (day^{-1})
p	Rate that infected cells are killed by CTL_E cells	1 (cells/day)
h	Rate of CTL_E die-off	0.1 (day^{-1})
k	Rate at which free virions are produced from infected cell death	3 $(virion/(cell \cdot day))$
u	Viral decay rate	3 (day^{-1})

Network Embedded Individuals



Outline

- ✓Motivation & basic systems modeling concepts
- Model Vignettes
  - ✓Aggregate
    - Emerging Type 2 & Gestational Diabetes Mellitus Model
  - Individual-Based
    - ✓HIV Spread in Papua New Guinea
    - ✓Multi-scale immune/viral transmission model
- Concluding Remarks

Concluding Remarks

- Simulation modeling complements existing methodologies for insight into health issues
- Different simulation modeling approaches offer insight into different aspects of obesity challenge
- Model design is specific to questions & context
- Models require significant investment to build, provide ongoing insight