How Sensitive are My Conclusions to Model Assumptions: Insights from Health Care Models

Professor Stephen Chick
INSEAD
Technology and Operations Management Area
Fontainebleau, France
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Type of Model

“keeping models simple enhances understandability and theoretical utility but that using models for disease control decisions often requires realism that adds considerable complexity.”
– Roy Anderson

Factors for choosing a model

Why Patient Level Simulation?

- Need patient-level information from model
- Sufficiently heterogeneous populations (many risk groups, many stages of natural history, geography)
- Constrained resources (queuing and health outcome)
- Patient interaction (e.g. infectious disease transmission)

- Purpose: understand one system (sensitivity) or select best of finite set or optimize
- Estimand: Mean? Variance? Distribution?

Factors for choosing a model

- Also:
  - Stationary versus transient
  - Time invariant versus time varying parameters
  - Continuous time versus discrete time versus untimed
  - Deterministic versus stochastic
  - Large or small population

- The simplest model to answer a question is preferred (Occam’s razor)
- Different model types can give different conclusions
- Goal: Understand how models relate, and what systematic implications are due to model choice

Roadmap

Model Type

- System dynamics; Markov chain; discrete event simulation at patient level
- Independence and system dynamics
- Water treatment policy for the E.P.A.
- Stochastic versus deterministic
  - Infectious disease control: NTH
- Patient-level, discrete-event simulations
  - Structure, time-oriented social dynamics, resource constraints
- Call for model transition sensitivity analysis
- Open Questions

Some Models

(Some details not visible in the image)
Some Models

Decision Tree

Waterborne Transmission of Infection and Risk of Infectious Disease

Model Hierarchy

Roadmap

Microbial Risk Assessment
Comparative Analysis: Milwaukee in Retrospect

- HIV community more susceptible? Did suffer more serious outcomes
- Chemical Risk: Filter (local) vs. Ozone (global)
  - Contaminated water → exposure to HIV community
  - $100 Million question
  - Assessment: Filters 10x more effective than ozone
- Microbes: Secondary transmission
  - Even with 100% effective filters, human-human transmission might continue infection!
  - Can ozone be more effective than filters?

Simplified Transmission System:
ODE Infection Transmission Model

- Natural history of infection
- Susceptible-Infectious-Susceptible (SIS)
- Infection dynamics
- Water contamination

Microbes: Secondary transmission
- Even with 100% effective filters, human-human transmission might continue infection!
- Can ozone be more effective than filters?

SIDRS-W model for Heterogeneous Populations

- More complex natural history of infection
- Subpopulations
- Human-human & human-water-human loops

Summary: Independence and System Dynamics

- Current U.S. water treatment policy for microbes based on invalid risk assessment
- Lives of many and hundreds of millions of $£€
- Dynamics of risk account for dependent outcomes
- One issue: Unknown transmission parameters

- System dynamics (aka ODE or PDE or compartmental models) embody risk dynamics
- Question: Are conclusions sensitive to the type of model (ODE versus stochastic dynamics)?

Ozone/Filter Policy Regions

- Ozone pretreatment: centralized, entire population
- Filters: targeted, in homes of HIV subpopulation
- Criterion: “better” = fewer crypto infections in HIV subpopulation

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ODE ⇔ Markov Chain

\[ \frac{dI}{dt} = -\frac{1}{N} + r_{pw}W + c\beta \frac{S}{N} (N - I) \]

<table>
<thead>
<tr>
<th>I</th>
<th>S</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>I_0</td>
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Infection

Recovery

ODE and MC give different mean prevalence if...

…most contacts are local

ODE and MC give different mean prevalence if...

…or local groups are small

ODE Compartmental Models

Many have unique attractor

Markov chain on lattice

"Shadow": count # individuals (people, microbes) in compartment.

Pushing the model:

Local and disseminating contact

Different agents transmitted differently

Local:

Family unit, classroom, small office, geographic "word of mouth"

Disseminating:

Contaminate source water, random mixing in street, "mass marketing"

What if we have 2 groups, and vary the fraction of "local" contacts?

ODE and MC give different mean prevalence if...

Proof: Math Biosci 2002

<table>
<thead>
<tr>
<th># per subgroup</th>
<th>Fraction of local contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.500 0.500 0.500 0.500 0.500</td>
</tr>
<tr>
<td>0.25</td>
<td>0.490 0.492 0.493 0.494 0.495</td>
</tr>
<tr>
<td>0.5</td>
<td>0.480 0.483 0.485 0.487 0.491</td>
</tr>
<tr>
<td>0.75</td>
<td>0.470 0.473 0.475 0.477 0.480</td>
</tr>
<tr>
<td>0.90</td>
<td>0.460 0.462 0.464 0.466 0.468</td>
</tr>
</tbody>
</table>

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Summary: Stochastic versus deterministic model types
- **ODE**: large population limit of MC for some models
  - (Ethier and Kurtz, Whitt, ...)
- **MC** behavior differs on two levels
  - Random outcomes
  - Long-run averages may differ (local die-out of infection).
- **Prevention**:
  - Disseminating: municipal water treatment, SARS masks
  - Local: hygiene in families, behavioral
  - 10% decrease in disseminating transmission reduces prevalence more than at 10% decrease in local
  - Vaccination: target to individuals \(\Rightarrow\) hits both local & global

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  - Open Questions

How Sensitive are the Conclusions to the Assumptions?
- **Partnership Concurrency and STDs**
  - ODE models typically assume one long-term partner, several independent short-term contacts (e.g. Dietz, ...)
  - Prevalence depends strongly upon potential of multiple long-term partners (Adams Chick Koopman, Math Biosci 2000)
- **Smallpox preparedness**
  - ODE says mass vaccination more effective than contact tracing, model with service capacity constraint (Kaplan, et al. PNAS 2002)
  - Patient-level simulation with social structures (family, neighborhood, age, etc.) gives a better picture of infection prevalence, tracing as effective (Longini et al. 2002; capacity/variable simpler)
- **Local versus disseminating**
  - Critical fraction of 'random contacts' leads to infection outcomes that are more similar to random mixing versus (Soocharath, Chick Koopman 2003; social references)
- **Service constraints and delays**
  - Breast cancer screening not as sensitive to delays in a stochastic system as to oher effects of service delivery program (e.g., frequency of screening, quality/volume, Gunes et al. HCMS 2004 – an ODE is sufficient)

Summary: Patient-level models
- **Outcomes and conclusions** may depend upon the type of model, not just to input parameters
  - Many patient-level models are ‘black boxes’; little information given for verification
  - No names given/no blame/too many ‘special cases’
  - Reasonable values if assumptions simplified?
- **Question**:
  - How to calibrate conclusions from one model relative to conclusions of another, if both model types can be used?
  - How to dissect the effect of various modeling assumptions at each level, in order to account for the side-effects of modeling in our conclusions?

Roadmap
- **Model Type**
  - System dynamics; Markov chain; individual (patient) level spreadsheets; discrete event simulation
- **Independence and system dynamics**
  - Water treatment policy for the E.P.A.
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MTSA/ModelSeer with BioMedware
- **GERMS**: implemented DEDS, validated with ODE separately
- **MTSA**: assess effect of model on decisions regarding the analysis, surveillance, and control of infectious diseases.
  - Sensitivity to changes in parameter values, model type, (e.g. ODE vs. MC vs patient-level) and model complexity (e.g., mixing, natural history)
- **Progress**:
  - **Phase I**: Prototype for NTHi mixing in patient setting done
  - **Phase II**: In progress
Individuals flow through ‘cross product’ of compartments, some combinations ‘illegal’

Example of cross-product

ODE Trajectory

Markov Chain Sample Path

Patient-Level Event History

Model Hierarchy

<table>
<thead>
<tr>
<th>Aggregate level</th>
<th>Patient level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deterministic continuous state</td>
<td>Stochastic discrete counts</td>
</tr>
<tr>
<td>Stochastic discrete counts</td>
<td>Stochastic Markov model (queue, …)</td>
</tr>
<tr>
<td>Decision tree</td>
<td>Stochastic decision tree</td>
</tr>
<tr>
<td>Finite difference model</td>
<td>Stochastic decision tree with covariates</td>
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</tbody>
</table>

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Summary: Model Type Sensitivity

- Models can be handed to different simulation engines may / may not give similar results (output or decision), but some differences are predictable
  - Large numbers
  - Discrete or continuous time
  - Multiple types of models: useful for ‘debugging’
  - Some models might only be handed to one type of simulation engine
  - People trained to model in system dynamics may approach problems differently than those trained in discrete-event simulation versus decision diagrams

Modeling is part of the understanding

Viva la difference!

Conclusions

- No models are right, some models are useful
- All model types make assumptions: Awareness
- Implied conclusions may depend upon model type
- Which model type to choose?
  - Basic question needs to trace individuals data on patient level (clinical trial, contact tracing, 
  - Interactions (infection, constrained resources) ⇒ don’t use ‘untimed’ model (e.g. decision tree)...
  - “Curse of dimensionality”: Much patient/natural history heterogeneity ⇒ patient level simulation
  - Tightly constrained resources + waits affect health outcomes ⇒ patient level simulation
  - “Law of small numbers”: Interactions + small numbers per compartment ⇒ stochastic models
  - Need to explore variability ⇒ stochastic model
- Simulation for visualization and communication
- Simulation runtimes and uncertainty analysis

Professional Resources

- Institute for Operations Research and Management Science (INFORMS)
- Health Applications
- Simulation [www.informs cs.org]
- Winter Simulation Conference
  - [www.wintersim.org]

Related Works


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