Assessing Infection Risks and Control Options when Transmission is Person-to-Person via Multiple Routes across Diverse Venues

Jim Koopman, Joe Eisenberg, Ian Spicknall, Sheng Li, Josep Pujol, Nottasorn Plipat

University of Michigan Dept. of Epidemiology & Center for the Study of Complex Systems

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CAMRA
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CAMRA Modeling Project Goals

- Develop analytic tools & methods to assess the:
  - infection transmission effects of environmental conditions, human hygiene behaviors & movement patterns, cleaning & decontamination, flows of air & food & water & fomites
  - roles of modes of transmission in circulating infection
- Use environmental agent measurements & sequences to analyze transmission systems
- Identify key venues and control actions at those venues to stop transmission

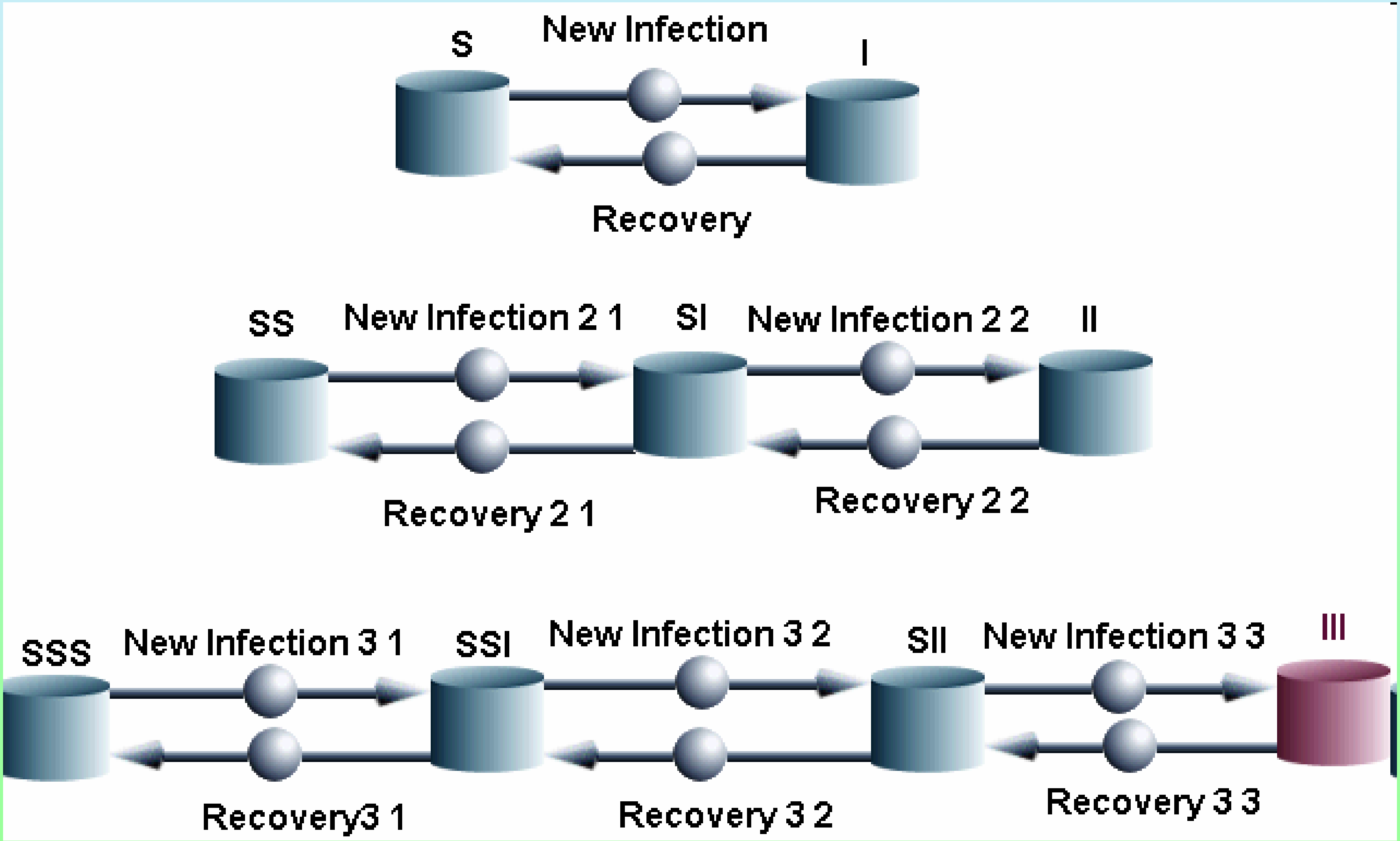
Outline

- Transmission system modeling
- Issues arising from our initial work
- New research directions

Transmission System Models

- Environmental risk assessment models ignore the human transmission system
- Deterministic compartmental
  - Mass action or pairs & small groups
- Fixed network individual models
  - Percolation theory & new derivatives
- Individual (Agent) Based Models
- Environmental transmission system models
- Different forms should work together

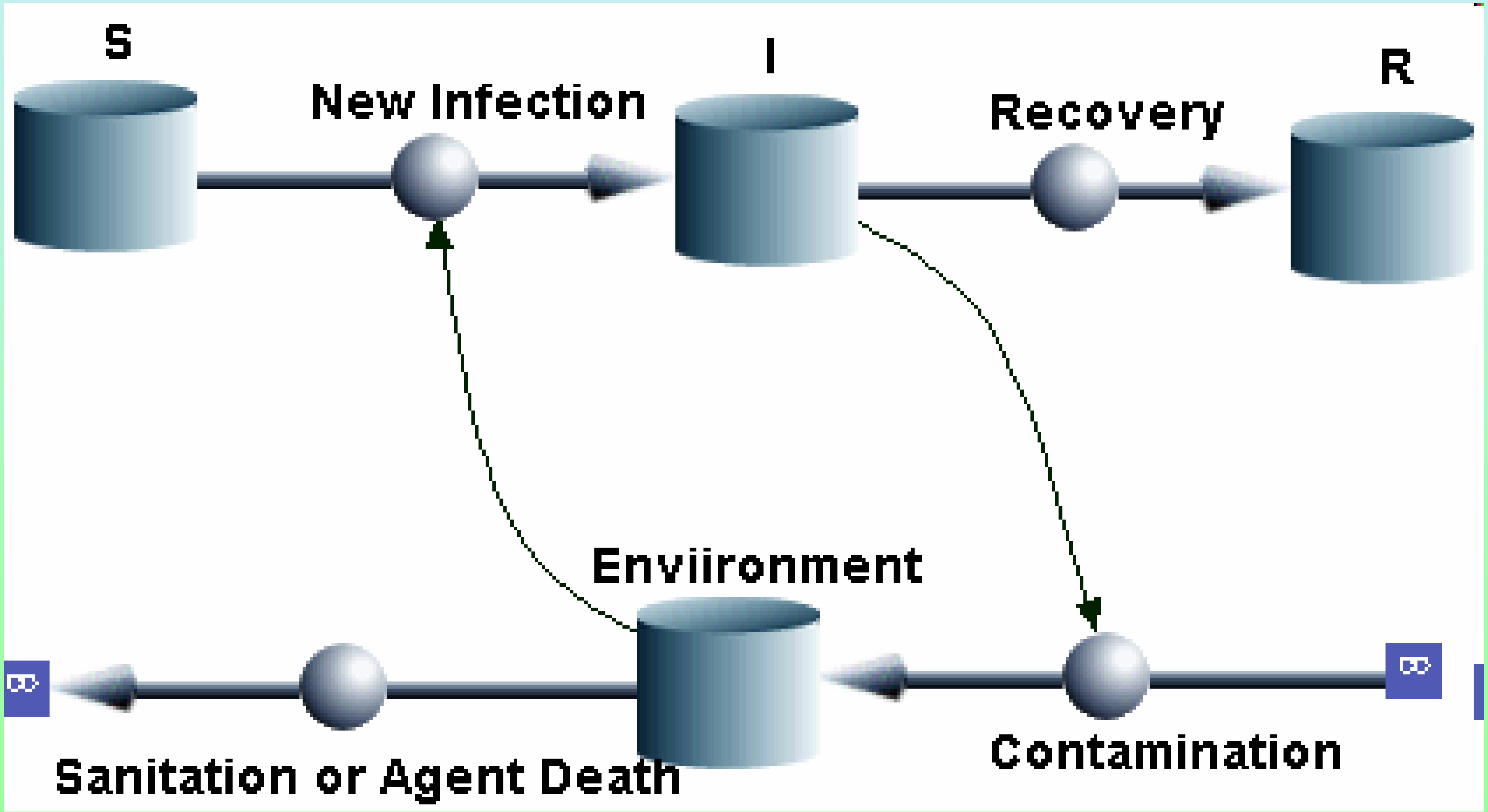
Deterministic Compartmental Models



Deterministic Compartmental Models

- Mass action approach of Hamer in 1906
  - Focus on insights into transmission dynamics
  - Assumes instantaneous symmetric contact with thorough mixing after each contact
  - Mid 1980s focus on macro-network contact patterns
- Pair & small group compartments
  - Dynamic linkages address micro-network patterns
  - Separate contact from linkage process
- Environmental compartment approach relaxes symmetric contact assumption

Environmental Transmission System Models



Deterministic Compartmental Mass Action Model Limitations

- Microparasite agent levels not modeled
- Mode (route) of transmission ignored
  - Airborne (Aerosol)
  - Direct large droplet or respiratory hand-fomite mediated
  - Fecal hand-fomite mediated
- Effect of contact assumptions ignored
- Erroneous conception that simpler models make fewer assumptions
  - Deficient inference robustness assessment tradition

Deterministic Compartmental Pair & Small Group Models

- Slows & changes shape of dynamics
  - More realistic for childhood & other infections
  - Captures key aspects of STDs like HIV
- Difficult to capture macro-network patterns
- Limited individual variability
- Ignores microparasite agent levels & modes (routes) of transmission

Fixed Network Models

- Capture both micro & macro network patterns
- Can specify transmission venues
- New analytic potential from physicists
- Ignores routes of transmission and microparasite levels
- Ignore contact dynamics

Individual (Agent) Based Models

- Capture micro & macro network patterns with dynamic linkages
- MIDAS program at NIH
  - Symmetric mass action models with 286 million discretely modeled individuals
  - EpiSims models transport determined contact
  - Computationally intensive analysis leads to insufficient inference robustness assessment
  - Have ignored contact tracing data, routes of transmission, & microparasite levels

Traditional Microbial Risk Assessment Models

- Follow the path of infectious particles through the environment
- Good for or non-transmissible agents (anthrax) or transmissible agents from common sources with low direct transmission
- Ignore nonlinear transmission system linkages between individuals
- Focus on dose-response relationships but not cumulative dose effects

Environmental Transmission System Models

- Venue based like MIDAS models
- Capture micro & macro network patterns without need for contact tracing data or for assuming instantaneous symmetric contact
- Follow infectious agent levels in air, on surfaces & fomites, and on individuals

Environmental Transmission System Models

- Our Aims
  - Determine roles that different routes of transmission play in the transmission system
  - Assess the effects of actions at specific venues intended to interrupt separate routes of transmission on population infection levels
    - Handwashing, masks, cleaning, decontamination, air exchange, UV irradiation,
  - Use environmental agent identification and sequencing to analyze the transmission system

Environmental Transmission System Models

- OUR APPROACH
  - Agent based models of venues with spatially explicit air, surfaces, fomites, agent levels, human movement, pathogen deposit & pickup by humans, pathogen die off, cleaning, decontamination, & air exchange effects
  - Venues within venues: Communities, complexes, buildings, rooms, hotspots
  - Find model abstractions consistent with detailed model behavior
  - Use both detailed and abstracted models in inference robustness analyses

Inference Robustness Assessment Analyses

- Use multiple models jointly to conclude that inferences made from any model analyses are robust to realistic violation of assumptions made by a particular model
  - Some models are more suited for rapid exploration of parts of parameter space (e.g. deterministic ODE)
  - Some models are better suited for assessing effects of relaxing assumptions (e.g. IBM or ABM)

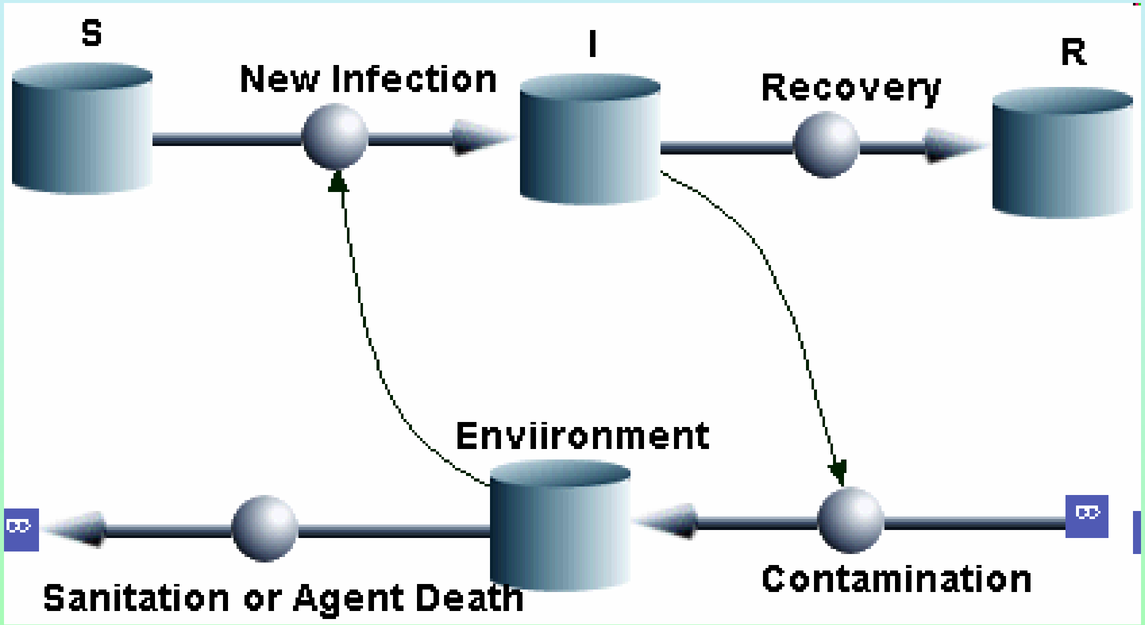
Outline

- Transmission system modeling
- **Issues arising from our initial work**
- New research directions needed

Agent Level Variability

- Across a wide range of parameters on human movement, agent pick up, and deposit, time to equilibrium is very long
  - Non-equilibrium analyses are essential
- Cost effectiveness of qualitative vs. quantitative agent identification varies
  - Need more data & analyses to specify these
  - Value of any environmental sampling scheme is not yet demonstrated

DC Environmental Transmission System Models



Equilibrium and homogeneity assumptions will be problematic but perhaps new infection functions can be written based on human movement patterns at specific venues

Dose-Response Issues

- Air and fomite transmission system models are extremely sensitive to time effects on accumulating doses
- No experimental studies on such time effects are known to us
- Physiologically based dose-response models will be essential for environmental transmission system modeling

Large Droplet vs. Aerosol Spread Influenza

- Recent models cite large droplet spread
- Recent reviews cite work demonstrating airborne transmission
- Fomite role uncertain
- Aerosolization of settled droplets uncertain
- Role in transmission system of either droplet or aerosol is undefined for any pathogen

Roles of Routes of Transmission in the Transmission System

- Most frequent transmissions may not be the ones on which to focus control
- Peripheral or dead end transmissions
- Redundant transmissions
- Key transmissions sustaining chains
- Disseminating transmissions starting new transmission trees

Initial Findings

- The amount of transmission via aerosol or large droplet and the role of each type of transmission in the system is sensitive to
  - Cumulative dose-response behavior
  - Human movement patterns at different venues

Outline

- Transmission system modeling
- Issues arising when integrating the environment into transmission system models
- **New research directions**

New Research Opportunities

- Agent identification and quantification costs are dropping
  - Accumulated dead agent detection provides better data than isolation of pathogens from people for fitting transmission models
  - Should facilitate venue & route of transmission role determinations
- Computational power is expanding
- Sequencing costs dropping dramatically

Research Directions

- Explore what is required for more abstract models to validly capture phenomena identified in detailed models
  - Can frequency-density dependent symmetric mixing scales capture human movement and environmental transmission effects?
  - Venue metapopulaton vs. statistical mechanics approaches
  - Small group deterministic approaches to better capture large venue effects

Research Directions

- What processes need modeling to evaluate inference robustness to model assumptions?
  - Physiological & immunity effects on cumulative dose-response behavior
  - Human deposition & pickup of pathogens
  - Agent transfer from different surfaces
  - Human movement
  - Human linkage processes & patterns
- What parameters need more precise measurements to make valid inferences

Research Directions

- Using data to fit models
  - Cost effectiveness of environmental pathogen vs. human infection surveillance data
  - Quantitative vs. qualitative agent identification
  - Use of sequence data reflecting infection flow
  - MCMC vs. curve fitting estimation methods

Summary & Conclusions

- Analyzing transmission routes & effects of venue and/or route specific interventions needs environmental transmission system models working jointly with other transmission system models
- Venue and route specific analyses are facilitated by new agent detection & computer analysis technologies
- Major needs are physiological based dose-response models & ways to abstract detailed model complexities so as to better apply an inference robustness assessment strategy