Disease Modeling and Simulation

---Literature Review

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Outline

- **Study Focuses**
  - Evaluate the contribution of different factors in the emergence and transmission of infectious diseases
  - Develop transmission models of the spread of infectious diseases
  - Simulate the process of infectious disease transmission: Discrete-Event Simulation, Agent-based Simulation Model (ABSM)
  - Evaluate the effects of interventions (i.e., vaccination, social-distancing)

Introduction

- Levels of Infectiousness:
  - Sporadic: occasional occurrence
  - Endemic: regular cases often occurring in a region
  - **Epidemic:** an unusually high number of cases in a region
  - **Pandemic:** a global epidemic

- Typical Infectious Diseases:
  - Influenza
  - Respiratory Infections
  - Measles
  - Smallpox: eradicated in 1979
  - The Black Death
  - HIV/AIDS

Introduction

- **Factors in the emergence of infectious disease:**
  - **Kenrad E.Nelson *et.al*., Infectious Disease Epidemiology,2006**
    - Population growth
    - Speed and ease of travel
    - Expansion of human population into previously uninhabited forested and suburban areas
    - Relocation of animals
    - Global climate change

Introduction

- **Population Growth**
  - The most important factor globally in the emergence of infectious diseases
  - The human population had been stable for several centuries, then increased gradually with the urbanization and concentration of the labor force required for industrialization

    Yong Yang, *et.al*., Individual space-time activity-based modeling of infectious disease transmission within a city,2007

    <u>Urbanization:</u> by 2020, 55% of the world's population is projected to live in urban areas

    - The epidemiological environment can be improved by urbanization.
    - Large density of population in urban areas increases the probability of intimate contact between people

Introduction

- **Speed and Ease of Travel**
  - In the last several decades, dramatic changes occurred in the ability and ease of travel, which make it possible for people to travel anywhere in the world with modern airplane
  - It has facilitated the introduction and spread of diseases from one area to another
  - Food supply has become very international

Introduction

- **Factors in transmission of infectious diseases**
  - The transmissibility of the pathogen responsible for the infection
  - Population heterogeneity
    - Many types of host heterogeneity influence host/pathogen interactions at the scale of individual
    - Socio-demographic structure: generics, age, location
    - Human mobility: typical movement patterns

Introduction

- Transmission of pathogens
  - An infectious disease is transmitted from some sources
  - Transmission may occur through several different mechanisms
  - Means of Transmission of Infectious Disease and Their Characteristic Features **(Kenrad E.Nelson *et.al*., 2006),** which play an important part in understanding the biology of an infectious agent, in addressing the disease it causes, and furthermore, in developing proper interventions of disease control

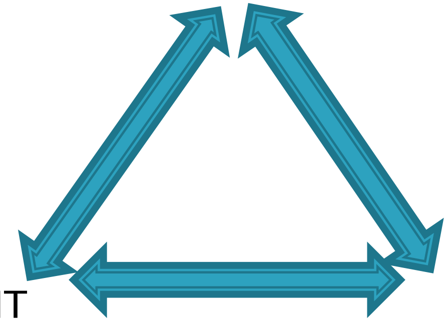
Transmission	Characteristic
Contact	Require direct or indirect contact
Food-or water-borne	Ingestion of contaminated food
Airborne	Inhalation of contaminated air
Vector-borne	Dependent on biology of the vector

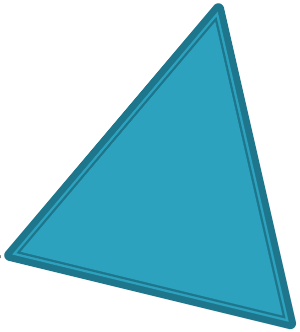
Introduction

(Kenrad E.Nelson *et.al*., Infectious Disease Epidemiology,2006)

Conceptual Framework: *Epidemiologic Triangle*

- Used to describe the relationship between the host (i.e., the diseased person), the agent (i.e., infecting virus), and the environment (i.e., the setting in which transmission occurs)
- Useful in modeling the transmission dynamics of an infectious disease





Disease Transmission Models

- **SIR Model**
  - The original and simplest SIR model was first formulated by Lowell Reed and Wade Hampton Frost in the 1920s
  - The basic theory for the dynamics of transmission describes a population which is divided into three classes or states: *Susceptible(S)*, *Infectious(I)*, and *Recovered(R)*
  - Assumptions:
    - The population is closed, no one enters or leaves the population
    - Permanent immunity

Disease Transmission Models

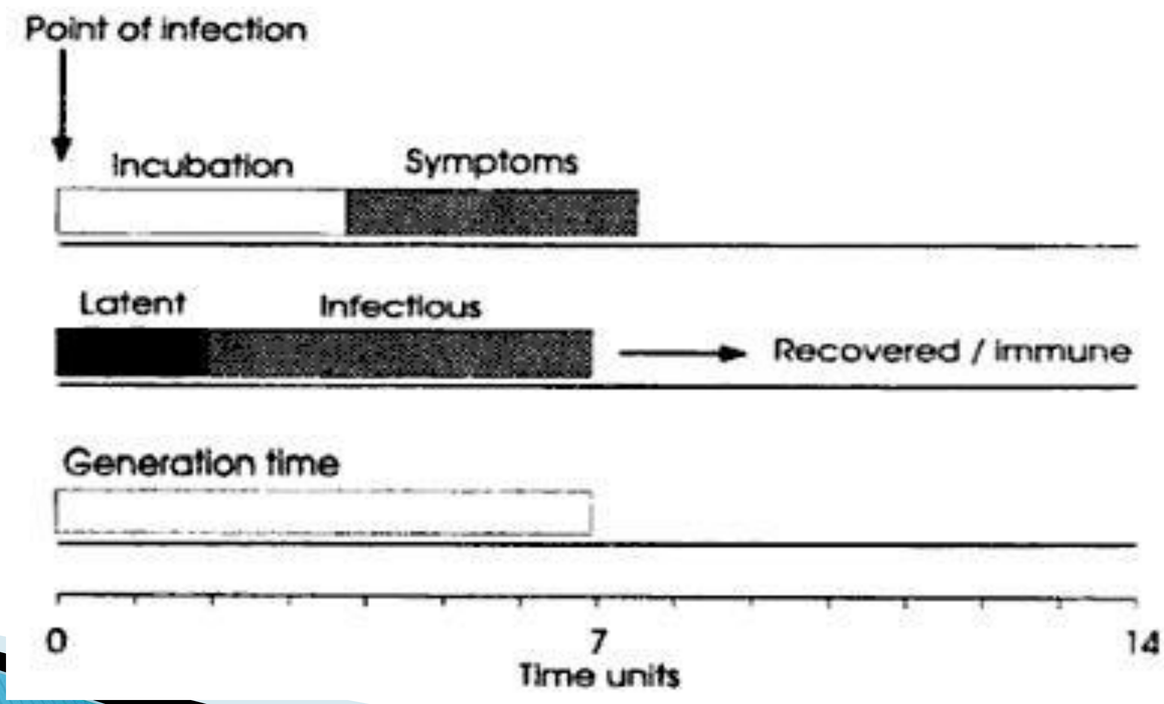
- SIR Model

$$S \xrightarrow{\beta SI} I \xrightarrow{\gamma I} R$$

$$\frac{dS}{dt} = -\beta SI, \frac{dI}{dt} = \beta SI - \gamma I, \frac{dR}{dt} = \gamma I$$

Disease Transmission Models

- **Incubation period**
  - Time from infection to the development of symptoms
- **Latent period**
  - Time from infection until the virus can be passed to others, that is, become infectious



Disease Transmission Models

- **The process of disease transmission:**
  - Occurrence of contact
  - Infection

- **Contact Groups**

  Longini Jr.*et.al*., Containing pandemic influenza at the source, 2005

  - Close contact groups: households, households clusters, preschool groups, schools, and workplaces
  - Casual contact groups: other social settings (markets, shops, and temples) and hospital

Disease Transmission Models

- **Contact rate:**
  - The average number of individuals are contacted with an infectious person in a certain period of time
  - Frequency and Intensity (Yang,2007)

Table 1. Distance rules (Hall 1966).

distance type	value (m)	meaning
public	>3	the range of non-involvement
social	3–1.5	the range in which most public interactions are observed. This is a comfortable distance for people who are standing in a group, but maybe not talking directly with one another. People sitting in chairs or gathered in a room will tend to prefer this distance
personal	1.5–0.6	this is a protected area, where strangers would not be welcomed. At its inner limit it holds other people 'at arm's length'
intimate	<0.6	this range is reserved for lovers, family, small children and very close friends

Disease Transmission Models

Transmission rate:

- Defined as the product of the contact rate times the probability of transmitting the infection
- Unknown for a new epidemic

Transmission Probability:

- Every susceptible individual who contacted an infectious individual have a probability of contracting the disease
- For airborne infectious disease, it is assumed that transmission probability is inversely related to the distance between the infectious and susceptible individuals, and also directly related to the duration of the contact

Disease Transmission Models

- Bruce Y. Lee, *et.al.*, A computer simulation of employee vaccination to mitigate an influenza epidemic, 2010

Transmission parameters			
Contact group	**Infected**	**Susceptible**	**Transmission probability[a]**
Household	Adult	Adult	0.4
Household	Child	Adult	0.3
Household	Adult	Child	0.3
Household	Child	Child	0.6
Elementary school	Student	Student	0.0435
Middle school	Student	Student	0.0375
High school	Student	Student	0.0315
Workplace	Adult	Adult	0.0575
Hospital	HCW	HCW	0.0575
Hospital	HCW	Patient	0.01
Hospital	Patient	HCW	0.01
Community	All	Child	0.00255
Community	All	Adult	0.00480

Disease Transmission Models

- **Basic Reproduction Ratio (R_0)**
  - The basic reproduction ratio, R_0, is the number of secondary cases generated from a single infective case introduced into a susceptible population.
  - A disease can spread if $R_0 > 1$, but if $R_0 < 1$, chains of transmission will inevitably die out.
  - Plausible transmissibility scenarios: range from 1.6 to 2.4

Disease Transmission Models

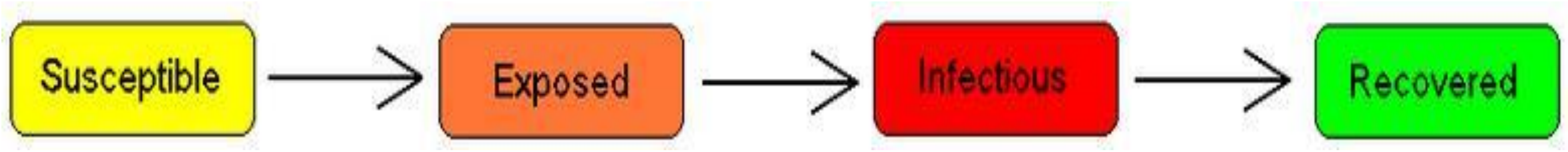
- **Extensions of the SIR Model**
  - Age differences in contact rates
  - Latent period
  - Demographic effects
  - Spatial effects
  - Stochastic effects

Disease Transmission Models

- **Age differences in contact rates**
  - Simple SIR model assumes that everyone in the population has the same contact rates, regardless of age
  - More realistic: different contact rates among different age groups

Disease Transmission Models

- **Latent period** (SEIR Model)
  - For an analysis of latency, an exposed but latent class E transforms the model from SIR to SEIR
  - Latency does not affect the basic reproduction ratio
  - However, latency always affects time-dependent phenomena, i.e., the speed of the epidemic

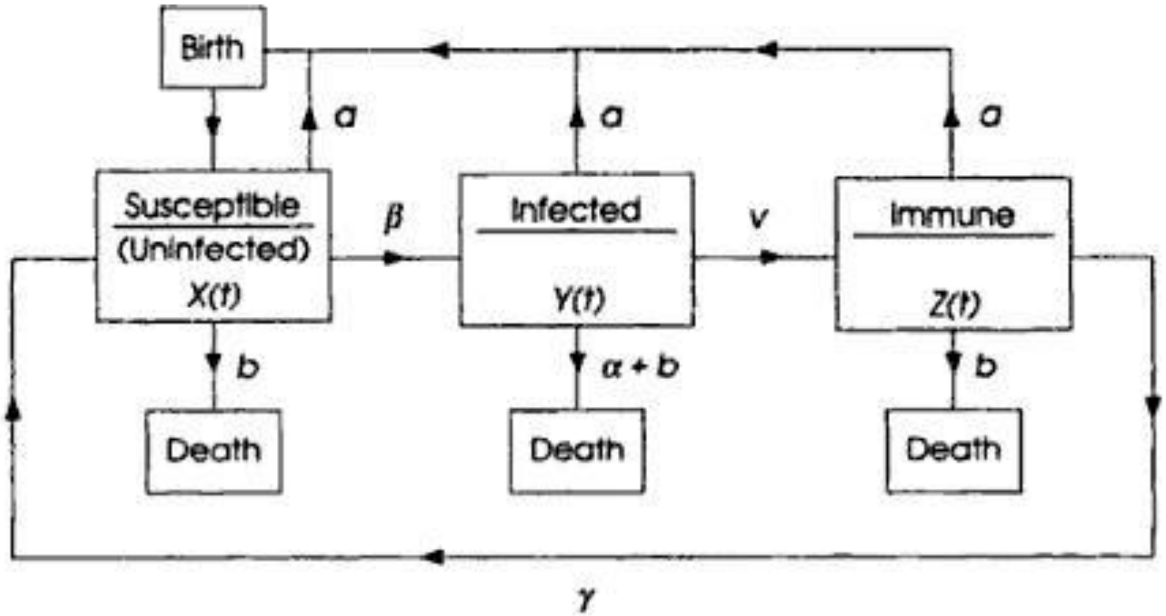


Disease Transmission Models

- **Demographic effects**
  - Epidemiological models usually assume a fixed population size for diseases
  - Differences between crude birth rates and crude death rates in many developing countries is large enough to affect the population dynamics of infection
  - Introduce substantial additional complexity

Disease Transmission Models

- **SIR Model** (Roy M. Anderson & Robert M. May, Infectious disease of humans, 1991)
  - Schematic representation of the flow of hosts between S, I and R
  - Records the dynamic interaction between a directly transmitted agent and its host population



Disease Transmission Models

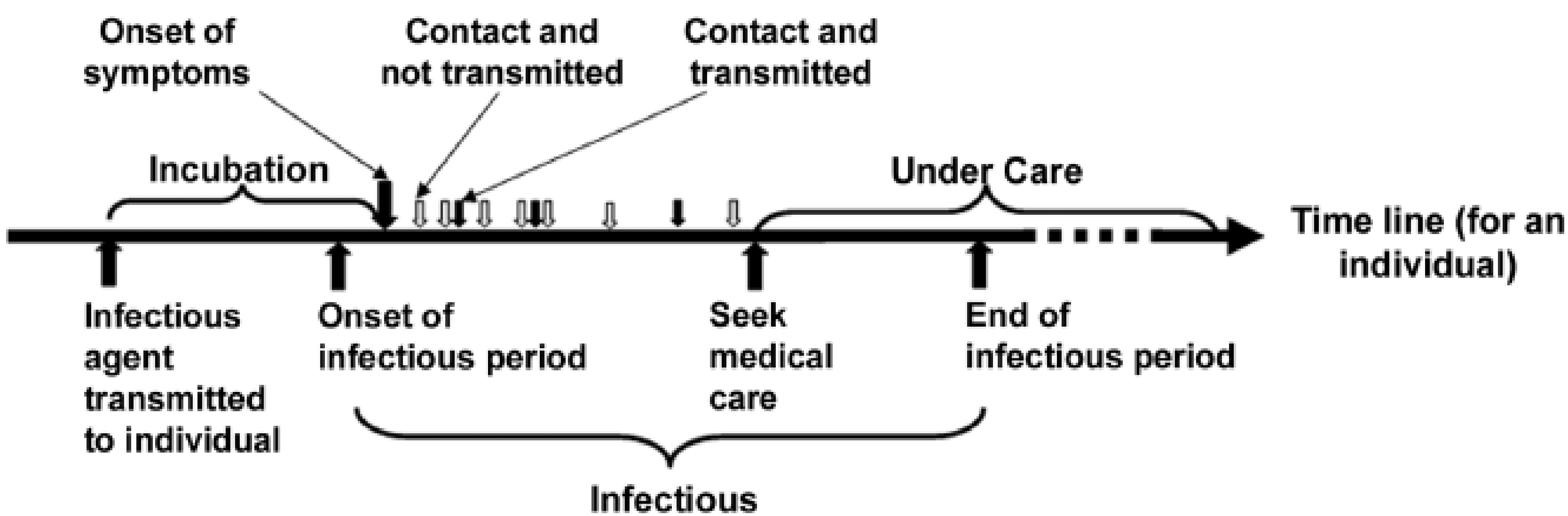
- **Spatial effects**
  - Populations are geographically dispersed
  - Explicit representation of a collection of populations permits joint analysis of characteristics of individual populations, i.e., birth rate and population size, and contacts between populations in a region
  - Important implications for the spread of disease and design of disease control programs

Disease Transmission Models

- **Stochastic effects**
  - Deterministic models have fixed rules for change, given the same initial conditions, a deterministic model will produce the same result
  - More realistic to consider stochastic effects in the spread of disease due to dynamics of host population

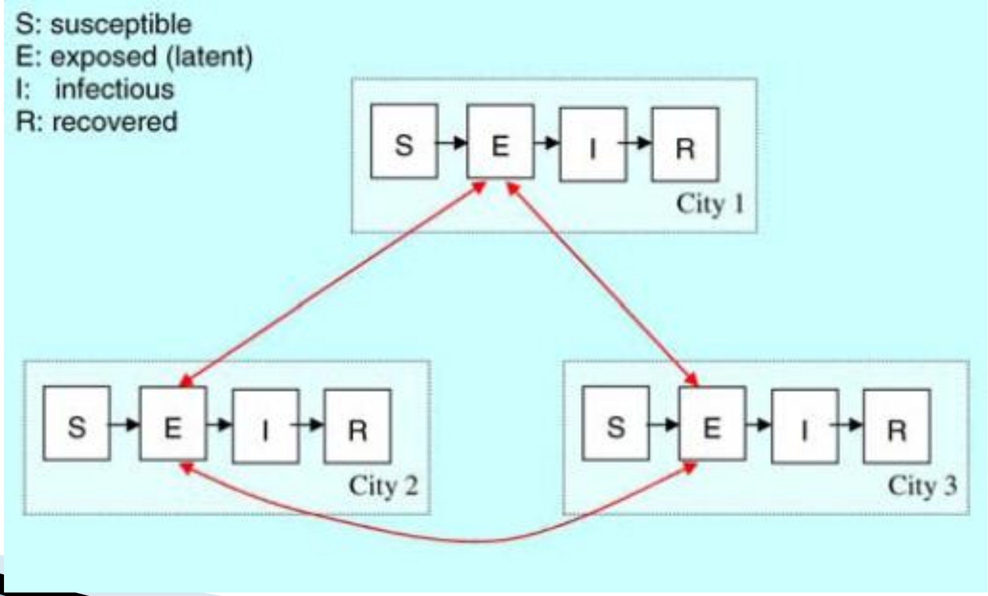
Disease Transmission Process

- **George Miller, Responding to simulated pandemic influenza in San Antonio, Texas, 2008**
  - Generic-disease timeline, which simulates the activities of a patient from the time of transmission of the disease agent to the end of the infectious period
  - A new timeline is created for each contact to whom the disease agent is transmitted



Disease Transmission Process

- **Ben S. Cooper et.al., Delaying the international spread of pandemic influenza, 2006**
  - Each component model represents one city and tracks the progression of individuals through four classes: susceptible to infection (S); exposed to the virus but not yet infectious (E); infectious (I); and recovered and no longer susceptible (R).



Disease Transmission Models

- Spatial-Transmission Model

(Steven Riley, Large-Scale Spatial Transmission Models of Infectious Disease, 2007)

Spatial models of infectious disease transmission provide the ***only*** plausible experimental system in which knowledge of the **location** of hosts and their **typical movement patterns** can be combined with quantitative description of the infection process and disease natural history to investigate observed patterns and to evaluate alternative intervention options.

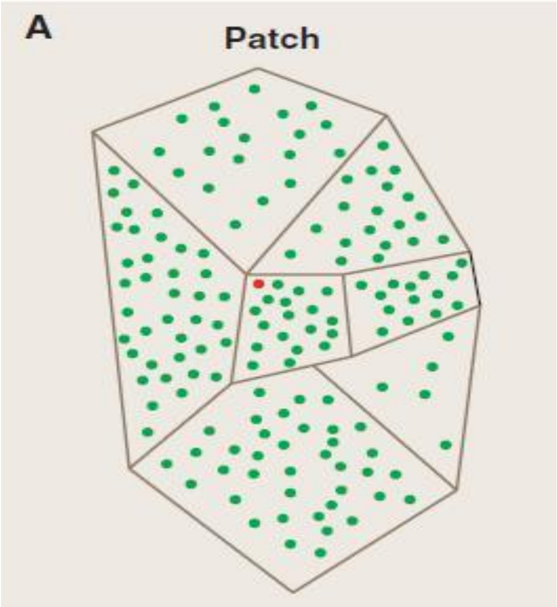
Disease Transmission Models

- **Spatial-Transmission Models**
  (Steven Riley, 2007)
  - Four models were reviewed for four infectious diseases
    - Patch models ----- Measles
    - Distance-transmission models ----- foot-and-month disease
    - Multi-group models ----- pandemic influenza
    - Network models ----- smallpox

- **FOI: Force Of Infection**
  - The hazard of infection experienced by susceptible individuals
  - Location-specific

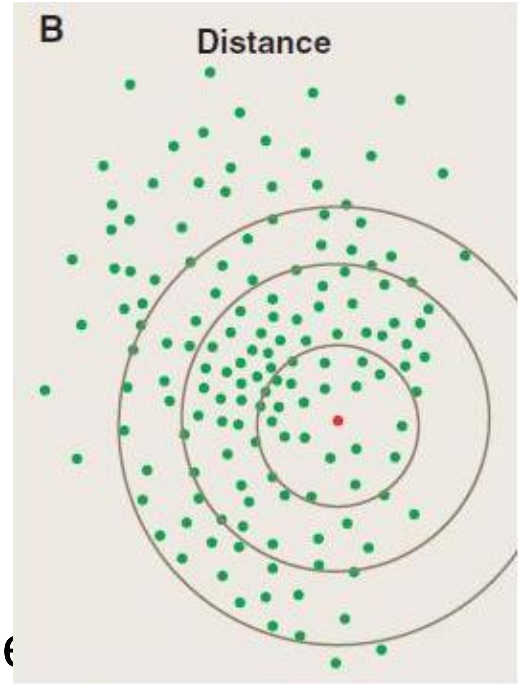
Spatial-Transmission Models

- **Patch Models** (spatial metapopulation models)
  - All members of the same patch receive the same FOI, which is a function of the distance from their home patch to other patches and of prevalence of infection in all patches
    i.e., residents of a town



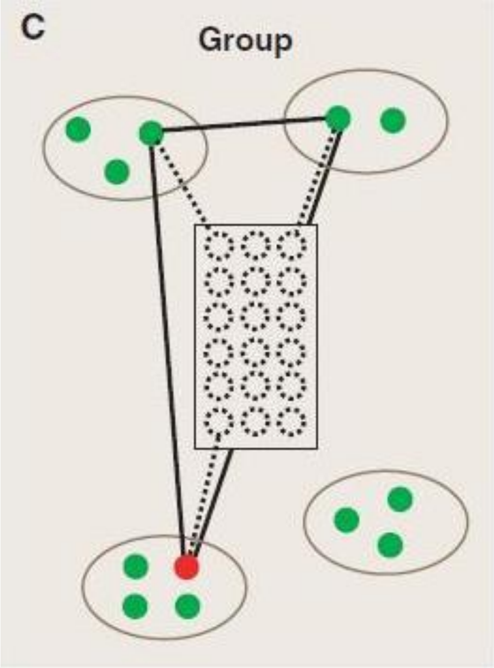
Spatial-Transmission Models

- **Distance-transmission Models**
  - Individual-based: each farm is assigned a precise location
  - Assuming that any given infectious individual can infect all susceptible individuals within range
  - Probability of infection is usually a monotonically decreasing function of distance, and the absolute FOI experience by each susceptible individual



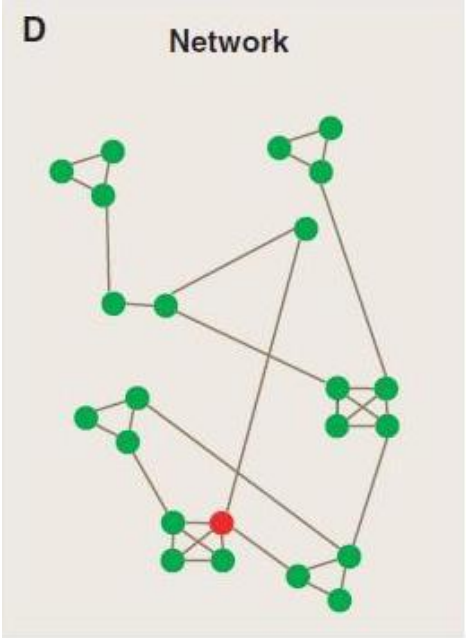
Spatial-Transmission Models

- **Multi-group Models**
  - FOI is determined entirely by group membership
    i.e., if an infectious individual shares a household with a susceptible individual, there is a high probability of transmission occurring between the two
  - Spatial patterns of spread are determined by the locations of households and workplaces/schools and by the typical distribution of journeys between them



Spatial-Transmission Models

- **Network Models**
  - FOI experienced by susceptible individuals is zero, unless they share an arc with an infectious individual



Disease Transmission Models

- **Stefano Merler & Marco Ajelli, The role of population heterogeneity and human mobility in the spread of pandemic influenza, 2010**
  - Examine how different levels of population heterogeneity and different patterns of human mobility affect the course of pandemic influenza in terms of timing and impact

  - Two factors affect the spread of an infectious disease:
    - Transmissibility of the pathogen responsible for the infection
    - **Characteristics of the host population: complexity of modern human society**

Disease Transmission Models

- Heterogeneity and Mobility in Epidemics (Merler, 2010)
  - **Population heterogeneity** (census data)
    - Frequencies of household type and size
    - Age structure
    - School size
    - The rates of school attendance and employment by age
    - …
  - **Human mobility** (air and railway transportation data)
    - International trips
    - Internal commuting

Agent-Based Model

- **Basic idea:** to expand traditional simulation to include entities whose behavior can change over time

- **Technology:**
  - SWARM: the first widely available computer package designed for ABM
  - REPAST: REcursive Porous Agent Simulation Toolkit
  - These packages offer the ability to specify entities – agents – within the system, program them with rules to govern their behavior, program the overall system with rules by which agents interact, and then analyze the simulated results

Agent-Based Model

- **Agent**
  - Capable to make independent decisions
  - A set of characteristics and rules governing its behavior and decision-making capability
  - Additional rules that modify its rules of behavior
  - Function independently in its environment and in its dealings with other agents
  - goal-oriented
  - Flexible and has the ability to learn and adapt its behaviors over time based on experience

Agent-Based Model

- **Maciej Borkowski *et.al*., 2009**
  - An Agent-based Model offers considerable flexibility in extending the study of the phenomena before, during and after an outbreak and catastrophe.
- **Prietula *et.al*., 1998**
  - Agent-based Models can provide insights into different organizational scales that are not possible using other modeling approaches, by representing complex social and physical systems through faithful modeling and model space exploration.
- **Epstein and Axtell, 1996**
  - Agent-based modeling entails the construction of a landscape, populated with a heterogeneous group of agents who move and interact in ways that more closely resemble human behavior that is possible in most modeling techniques.

Agent-Based Simulation

- **Connie Carpenter and Lisa Sattenspiel The design and use of an Agent-Based Model to Simulate the 1918 influenza epidemic at Norway House, Manitoba, 2009**
  - **Advantages of using ABSM over traditional models**
    - An epidemic can be introduced into a dynamic and detailed **social context.**
    - ABSM is the stochastic nature of the modeling technique which allows randomness involved.
    - ABSM is a historical population and landscape can be simulated and experiments performed that allow for the examination of contributing factors to specific outcomes.
  - Five basic steps of simulation (Gilbert, 1999)
    - model design, model construction, verification, validation and publication

Agent-Based Simulation

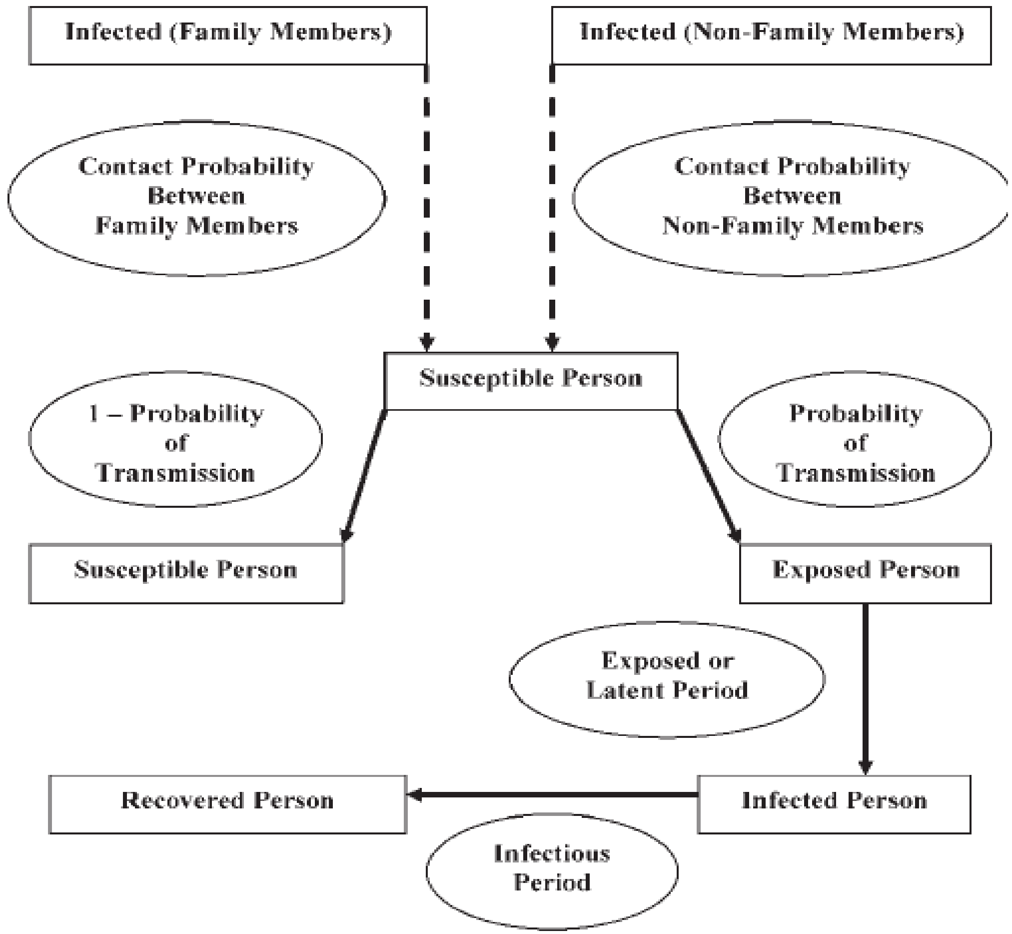
(Carpenter, 2009)

- **Model design**
  - Use existing archival and ethnographic information to design a landscape
  - Determine the structure of the epidemic component: SEIR model
  - Determine demographic attributes for the agents: age-sex groups

- **Model construction**
  - Heterogeneity population of agents
  - An environment for interaction (landscape)
  - Established rules of behavior for agents and the environment

Agent-Based Simulation

(Carpenter, 2009)



Epidemiological Component of Model

Agent-Based Simulation (Carpenter, 2009)

- Four major types of parameters in simulation
  - **Population**

    i.e., total number of people in the community
  - **Contact**

    i.e., probability of contact between family/nonfamily members
  - **Movement**

    i.e., distance between each camp and post
  - **Disease**

    i.e., probability of infection upon contact
- Other variables:
  - Number of days per simulation
  - Number of simulations performed for each parameter change

Agent-Based Simulation
(Carpenter, 2009)

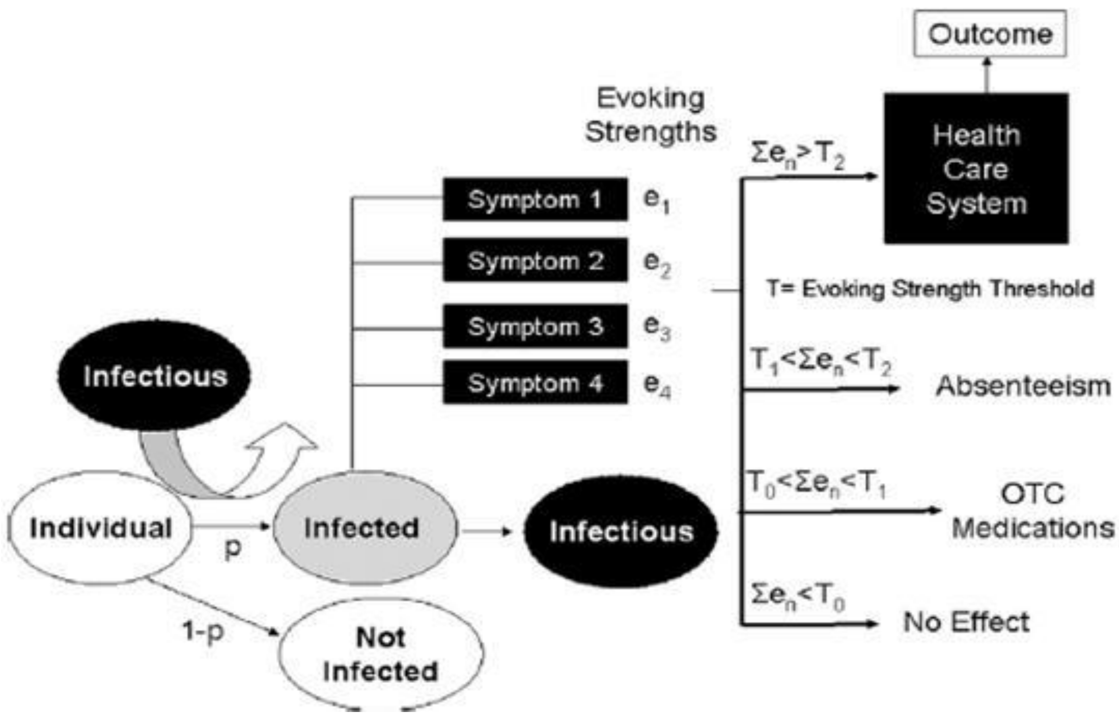
- **Measurements**
  - The number of susceptible (S), exposed (E), infected (I) and removed (R) for each day of the simulation
  - The duration of the epidemic
  - The peak number of infected people during epidemic
  - The day when the peak number of people are infected
  - The total number of people infected during the epidemic
  - The percent of the population infected during the epidemic

Agent-Based Simulation

- **Bruce Y. Lee, *et.al.,* Virtual epidemic in a virtual city: simulating the spread of influenza in a US metropolitan area, 2008**
  - A wide variety biologic, physiologic, clinical, social, economic, and geographic factors may affect the transmission, spread, and impact of influenza
    - City: Norfolk, VA, moderate-sized city.
    - Time: 1 year, 4-h “ticks” with decision, agent movement, and all other actions and changes occurring at each “tick”
    - Population heterogeneity: Agent characteristics, Agent movement, Agent’s social network, Agent interactions
    - Influenza infection: 2 days incubation period, 11 days illness duration, 50% transmission rate, evoking strength score for each symptom

Agent-Based Simulation (Bruce Y. Lee, 2008)

- Health-care system: the sum of an agent's evoking strength scores determines its health-care-seeking behavior. Score of 0 means that the agent is completely asymptomatic and does not seek any medications or medical attention.



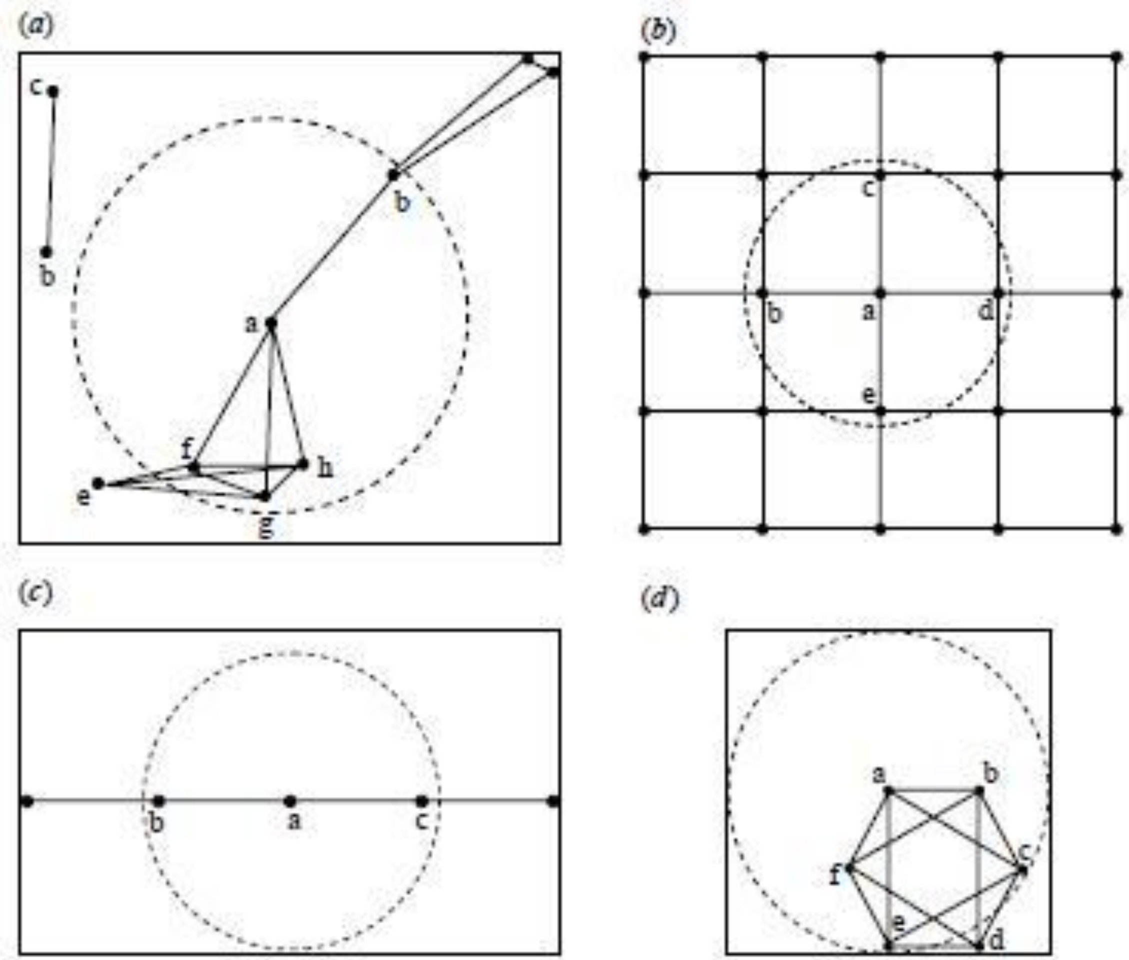
Disease and health-care system model

Agent-Based Simulation

- **Yong Yang, *et.al*., Individual space-time activity-based modeling of infectious disease transmission within a city,2007**
  - Activity-based models are rooted in time geography, which provides a framework for describing and defining how individuals perform activities under the constraints of time of space
  - **Activity Bundle**
    - defined as semantic space where contact probability varies as a function of the dynamics of humans inside the bundle
  - **Role-based AB simulation**
    - the interaction between individuals depends strongly on the different roles that the individuals play

Agent-Based Simulation (Yang, 2007)

- Spatial patterns of individuals within groups



Agent-Based Simulation
(Maciej Borkowski *et.al.*, 2009)

- **Discrete-Space Scheduled Walkers**
  - Basic tenets:
    - The extraction of spatial (topologies) from maps
    - The extraction of agent behavior primarily derived from crude demographics and heuristics
  - **Model** (data-driven)
    - **Where**: institutional locations
      - Topological data, or Physical "network" data – ***where*** we are attempting to apply the study of epidemic spread.
      - Primarily real places: homes, institutions, businesses, industry, schools, hospitals and transportation hubs.
      - "Google-like" mapping: repository for location various institutions where people meet or come into contact with one another.

Agent-Based Simulation

(Maciej Borkowski *et.al.*, 2009)

- **Who**: who are being infected and capable of infecting
  - Census data: not technical issues but rather political or policy issues
  - Statistical data: sampling a statistically significant percentage of the population
- **When:** agents' schedules
  - Data is typically inferred rather than explicitly available
  - Prior research: the assumption that majority of an agent's daily activities take place within a given radius of one's home and workplace. (i.e., fairly routine weekday schedules and more flexible weekends)
- **What:** a disease
  - Communicated by physical human-to-human contact, and carrying a probability of infection when in contact with an infectious agent
  - Parameters are adjustable (sensitivity analysis)

Agent-Based Simulation

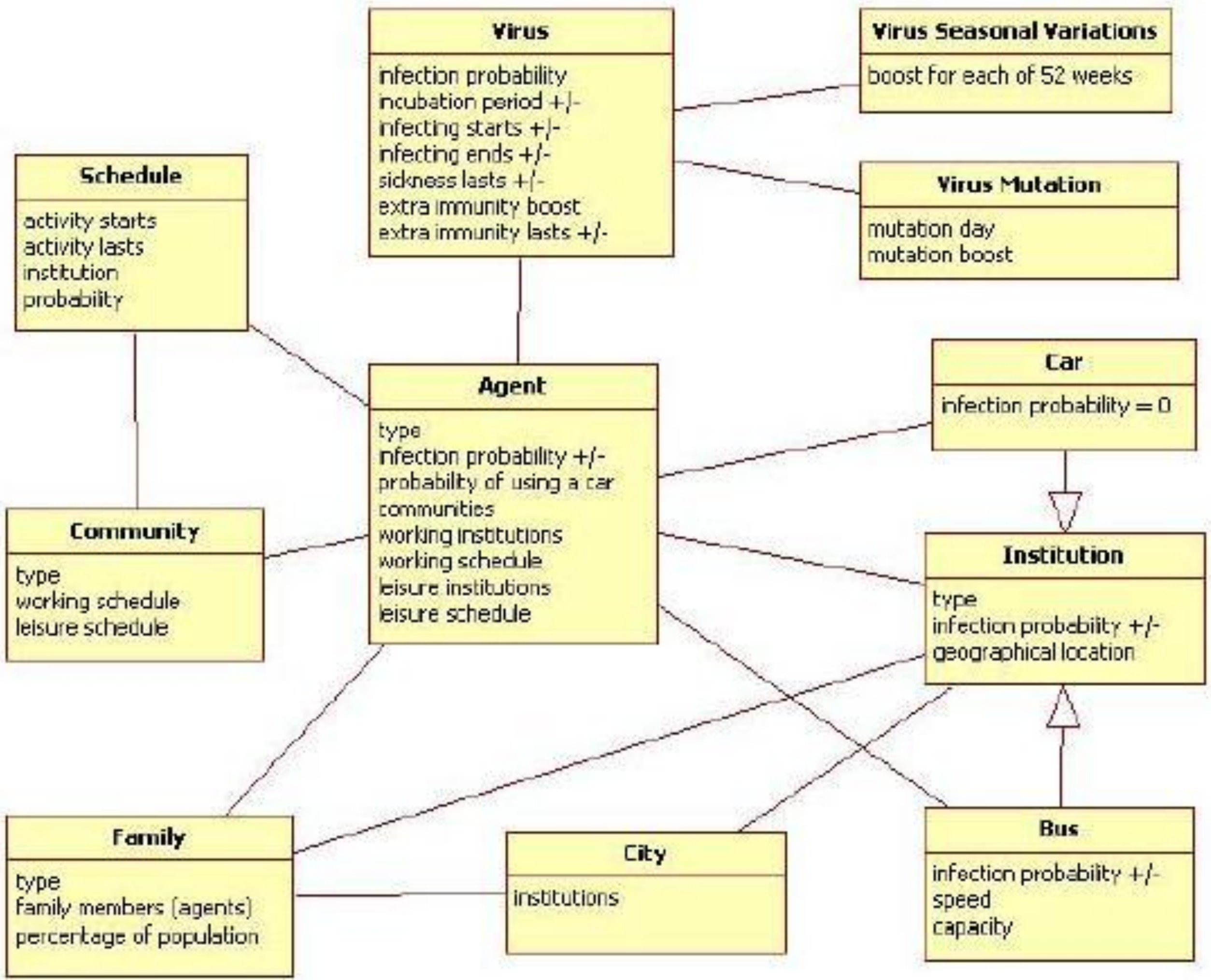
(Maciej Borkowski *et.al.*, 2009)

- Some other considerations in the model
  - Each of the simulation aspects (where, who, when, what) can be extended to a multitude of cities, coupled by institutions such as planes, trains, cars and buses supporting agent movement
  - Seasonal variation:
    - Can be incorporated in the model to account for variability in travel schedules and activities
    - Seasonal prevalence of particular diseases (i.e., influenza)

- Model is developed to capture the most important aspects of real-people networks.

Agent-Based Simulation
(Maciej Borkowski *et.al.*, 2009)

- System overview



Agent-Based Simulation

- **General Questions**
  - How to build the whole population in terms of the demographic, social and economic properties?
  - How to assign daily activity patterns to each individual?
  - How to simulate individual activities?

Intervention

George Miller, 2008

Evidence shows that a successful outcome for the community must be achieved by reducing demand through early and effective public health intervention to drastically reduce the overall attack rate

Strategies

Neil M. Ferguson, Strategies for containing an emerging influenza pandemic in Southeast Asia, 2005

- Reduce contact rates in the population
  - Social distance: household quarantine, school or workplace closure, restrictions on travel
- Reduce the infectiousness of infected individuals
  - Treatment or isolation
- Reduce the susceptibility of uninfected individuals
  - Vaccination or antiviral prophylaxis

Intervention

- **Social-distancing** **(Neil M. Ferguson, 2005, 2006)**
  - Isolation and household quarantine could have a significant impact on reducing of attack rates
  - School closure during the peak of a pandemic can reduce peak attack rate, but has little impact on overall attack rates
  - Travel restrictions are unlikely to delay spread by more than 2-3 weeks unless more than 99% effective.
  - Air Travel restrictions are likely to be of surprisingly little value in delaying epidemics (Cooper, 2006)

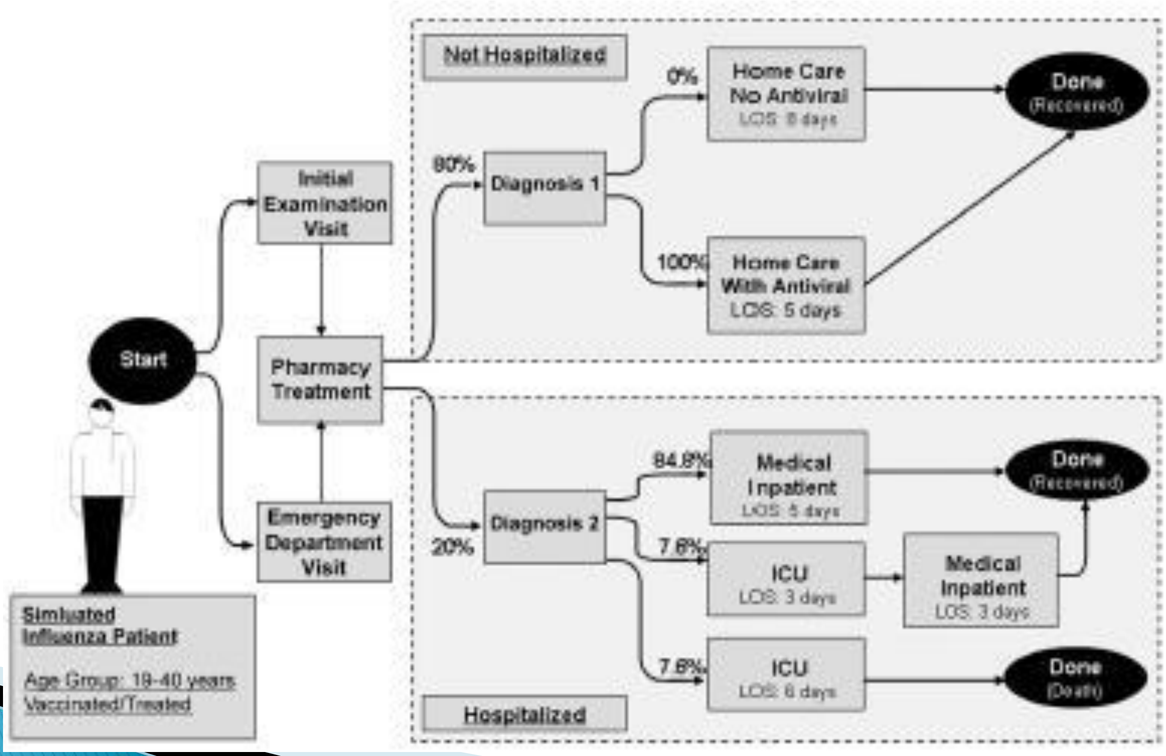
  - Measures to increase social distance have been used in past pandemics and remain important options for responding to future pandemics.
  - However, predicting the effect of policies such as closing schools and workplaces is difficult, as potentially infectious contacts may be displaced into other settings.

Intervention

- **Treatment**
  - **Neil M. Ferguson, Strategies for mitigating an influenza pandemic, 2006**
    - Clinical cases are clearly the first priority for any more-targeted approach, as prompt treatment with antivirals reduces clinical severity and infectiousness
    - Treatment of clinical cases can reduce transmission, but only if antivirals are given within a day of symptoms starting, because cases are at their most infectious soon after symptoms develop

Intervention

- Treatment
  - **George Miller, Responding to simulated pandemic influenza in San Antonio, Texas, 2008**
    - Healthcare Complex Model: simulates healthcare delivery to the patient throughout a network of medical facilities

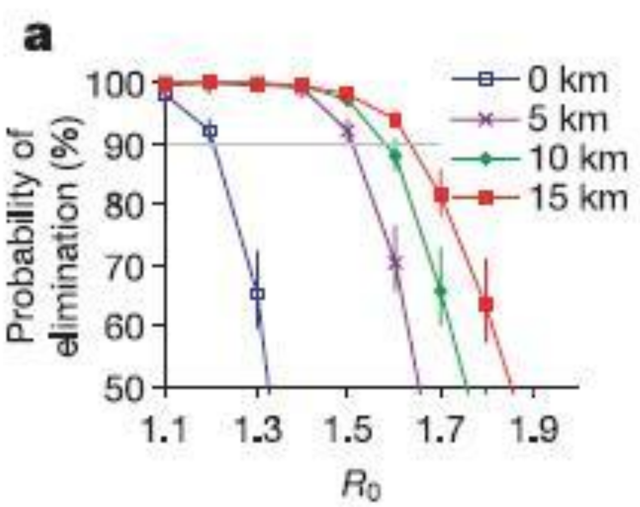


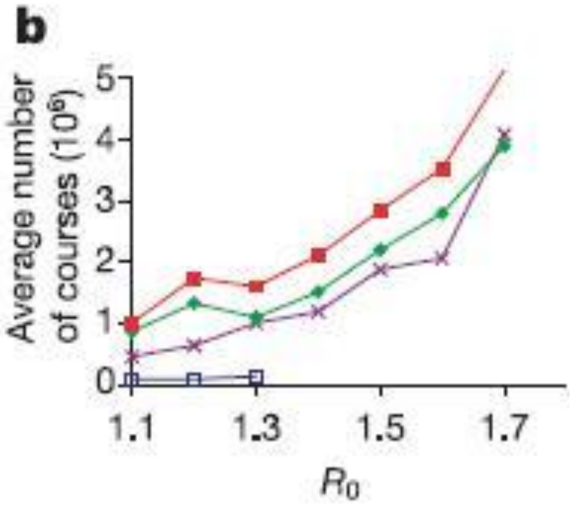
Intervention

- **Vaccination or antiviral prophylaxis**
  (Ferguson, 2005)
  - Two principle outcome measures
    - The probability of preventing a large outbreak
    - The number of courses of drug required to achieve containment
  - Targeted strategies
    - Minimize drug usage while maximizing effect
  - Social targeting: household, school, or workplace
  - Geographic targeting: whole population in the neighborhood

Intervention

- **Prophylaxis Strategies** (Ferguson, 2005)





Intervention

- **Vaccination or antiviral prophylaxis**
  - **Bruce Y. Lee, et.al., A computer simulation of employee vaccination to mitigate an influenza epidemic, 2010**
    - Consider various combinations of different employee vaccination scenarios under different sets of simulation runs:
      - Employee vaccination timing
      - Employee vaccination coverage and compliance
      - Vaccine administration speed
      - Employer sector
    - Timely vaccination of the large-company workforce can play an important role in epidemic mitigation

Intervention

- **Vaccination or antiviral prophylaxis**
  - **Nicole E.Basta, et.al., Strategies for pandemic and seasonal influenza vaccination of schoolchildren in the United States, 2009**
    - Vaccinating children can substantially reduce population-level illness attack rates over a wide range of scenarios
  - **Neil M. Ferguson, 2006**
    - Vaccine stockpiled in advance of a pandemic could significantly reduce attack rates even if of low efficacy
    - Widespread prophylaxis can significantly reduce attack rates, but would be more logistically challenging

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