Models for Understanding and Controlling Global Infectious Diseases HUMBIO 154D / HRP 204

Session 1

Jason Andrews

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2020

Agenda

1. Intros/backgrounds
2. Course overview/structure
3. Motivating Example: COVID-19
4. Introduction of Topics and Background for Infectious Disease Modeling

Course personnel

- Instructors:
  - Jason Andrews
  - Jeremy Goldhaber-Fiebert
- Teaching Assistant:
  - Tess Ryckman

Putting names with faces and challenges of being totally online

Course Focus and Time-Critical, COVID-19 Work

Local Government, Health Departments and Hospitals

State Governments and Entities

International Governments and Entities with a focus on Developing Countries

Course themes

- Infectious Diseases
- Populations
- Models
- Outcomes
- Uncertainty
- Interventions

Learning goals (1)

- Translate infectious disease epidemiology into a formal model
- Understand how biological, epidemiological, and clinical data and theory can produce inputs to formal models and how such models also help us to understand the data
- Interpret outputs from models in terms of impacts on incidence, prevalence, and severity and assess their robustness/uncertainty

Learning goals (2)

- Develop familiarity with the dynamics of transmission of infectious diseases, including the roles of susceptibility, immunity, herd immunity, and pathogen characteristics like reproductive numbers and serial intervals
- Explore how including realistic demography in infectious disease models has implications for epidemiologic outcomes and intervention effects

Learning goals (3)

- Understand the conditions under which infectious diseases may die out, remain endemic, become epidemic in a particular population and the link to designing effective control strategies and health interventions
- Evaluate critically how particular models represent common infectious disease treatment, control, and prevention policies and how these representations may influence findings of model-based analyses

Two courses in one

- Undergraduate and graduate students
  - Undergraduates = HUMBIO 154D
  - Graduate students = HRP 204

- Lectures and labs are for both groups
- Additional graduate section for students enrolled in HRP 204
  - Thursdays, 5:15-6:15 pm, starting Week 2 (April 16) and on Tuesday for the last week of the course in June

- Our experience is that courses that mix undergraduate and graduate students produce excellent discussions and learning

Large virtual course with auditors

- We are delighted to be able to have a large class this year – currently ~60 people registered plus many auditors

- Given the large size and the fact that the course is virtual and communications with students will be via email means that unfortunately
  - Taking questions during class time will need to be limited to enrolled students
  - Being unable to grade or provide feedback on labs or exams for auditors

Grades and Course Assignments

- Grades
  - This year, per the university's policy: ***All*** grading will be S/NS
- Assignments
  - 4 ungraded problem sets: 40% (for submission)
  - 1 midterm problem set: 20%
  - Final exam: 40%
  - HRP 204 Graduate Section: Requirements above count for 80% of the graduate grade in their proportions, and the remaining 20% come from presentation and weekly participation in the section

Attendance

- Given the current situation, attendance for the main class sessions is not mandatory and the lectures/laboratory sessions in class will be recorded

- For the graduate section, we strongly encourage attendance (understanding that the situation may present extenuating circumstances for some on some days). Each student will be responsible for presenting part of one paper on a given week, so on that week it is important to make every effort to attend and present. *Further details coming very soon*.

Remote Learning

- Lectures and R labs (both on Zoom) will be recorded and posted to Canvas
- Zoom etiquette
  - Please attend lectures (live) when possible
  - Video encouraged (not required), mute on please
  - We will use the chat feature for students to ask questions and pause periodically to answer them

Textbook/software

- Keeling MJ, Rohani P. Modeling Infectious Diseases in Humans and Animals.
  - Additional readings of journal articles that are all available through Stanford library and/or the course website
  - Graduate students in HRP 204: additional list of readings
  - NOTE: Readings may be modified during the quarter given the changing conditions and teaching by Zoom
- Labs are in the R programming language (suggest students download R Studio; we will be giving appropriate tutorials and support specifically adapted to the distance learning situation this year)

Review/Catch-up Materials

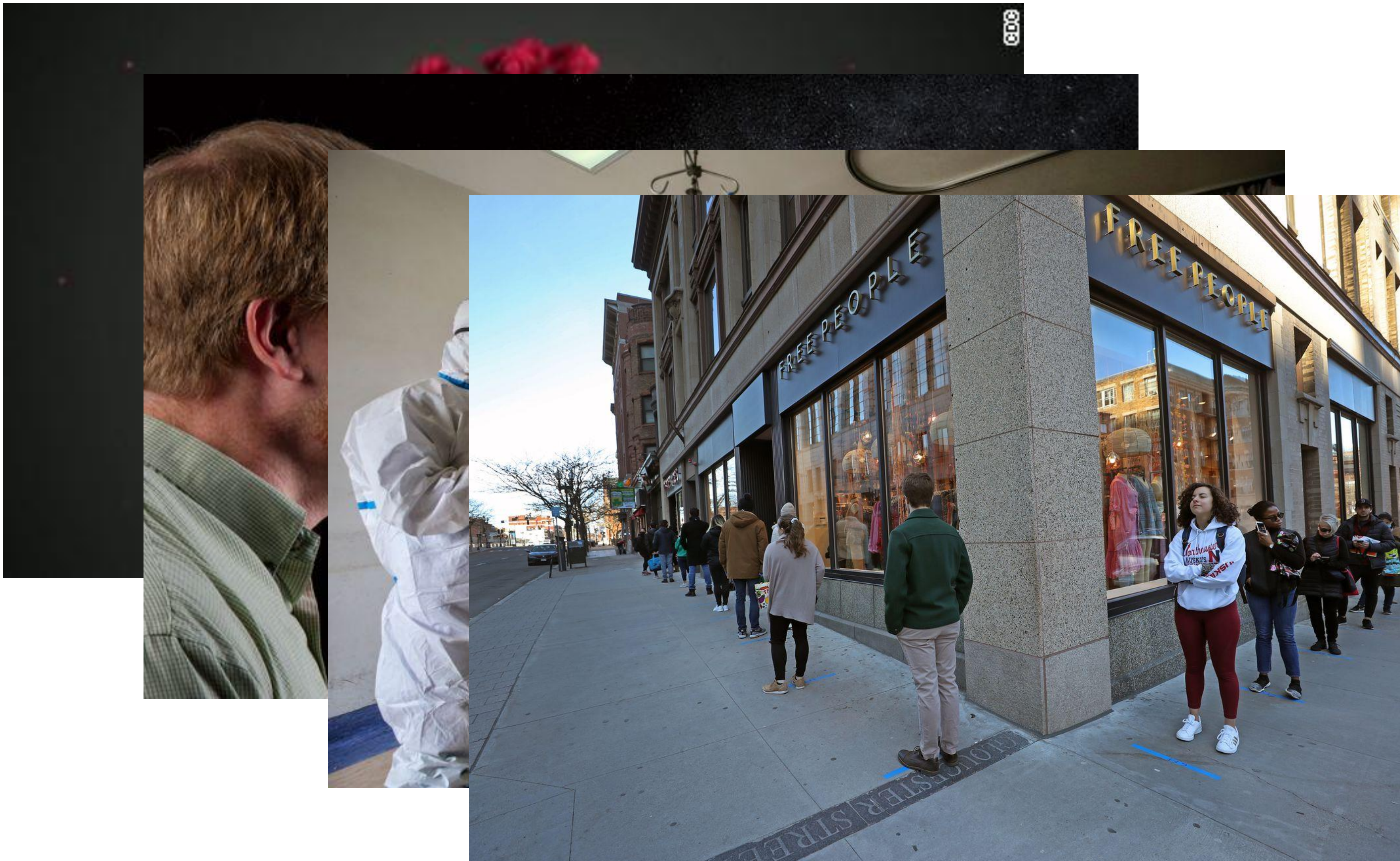
- Course will draw upon prior knowledge of mathematics, infectious diseases, epidemiology and statistics
- We have posted recommended readings and references in these four areas
- If you have not completed the course perquisites, or it has been some time, would recommend reviewing these materials in the first couple weeks
- May also be useful as reference during course

Policies

- Course conforms to all university policies
  - Students who may need an academic accommodation based on the impact of a disability must initiate the request with the Student Disability Resource Center (SDRC) within the Office of Accessible Education (OAE).
- See syllabus for further course policies details

MOTIVATING EXAMPLE

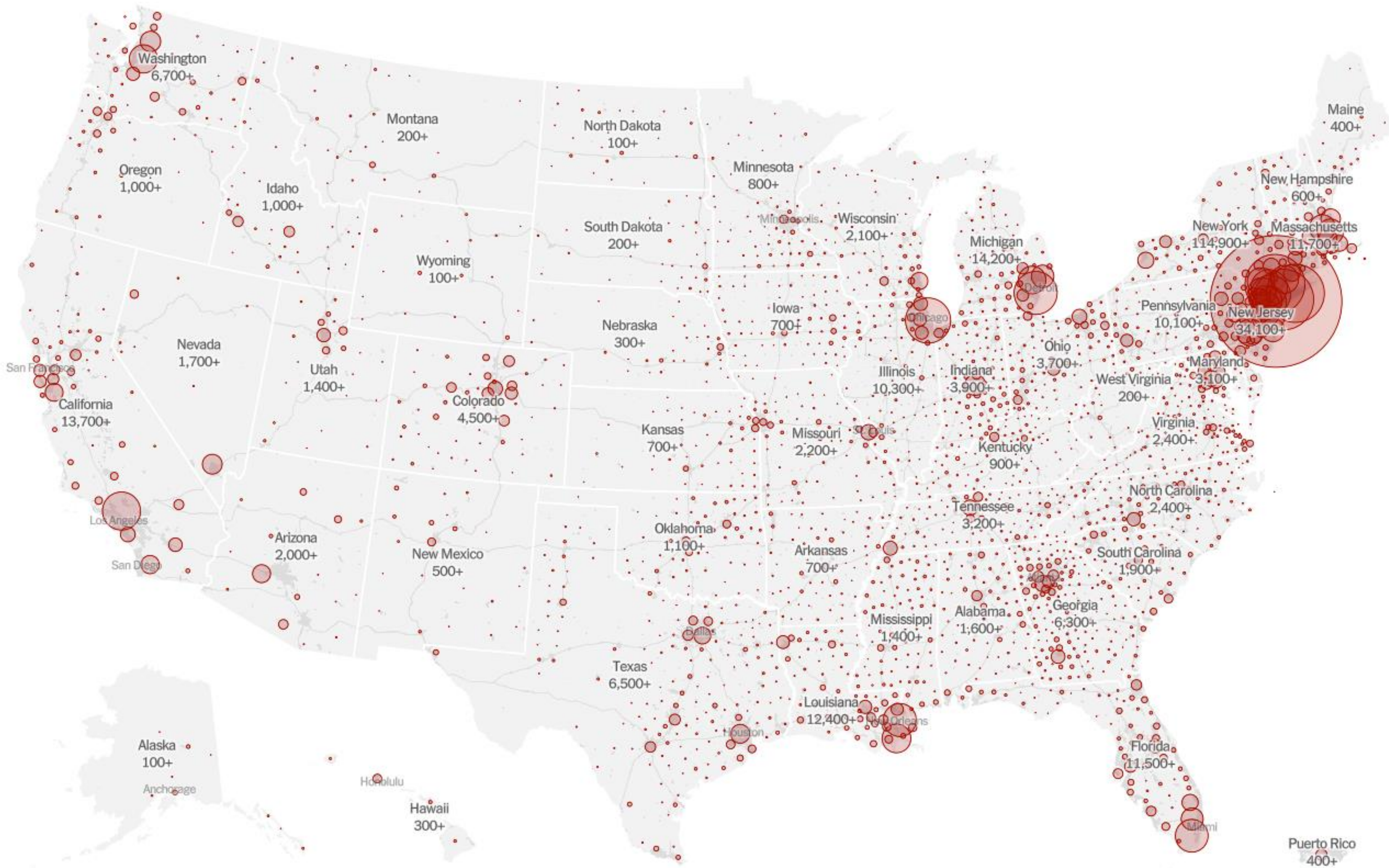
COVID-19: Perspectives



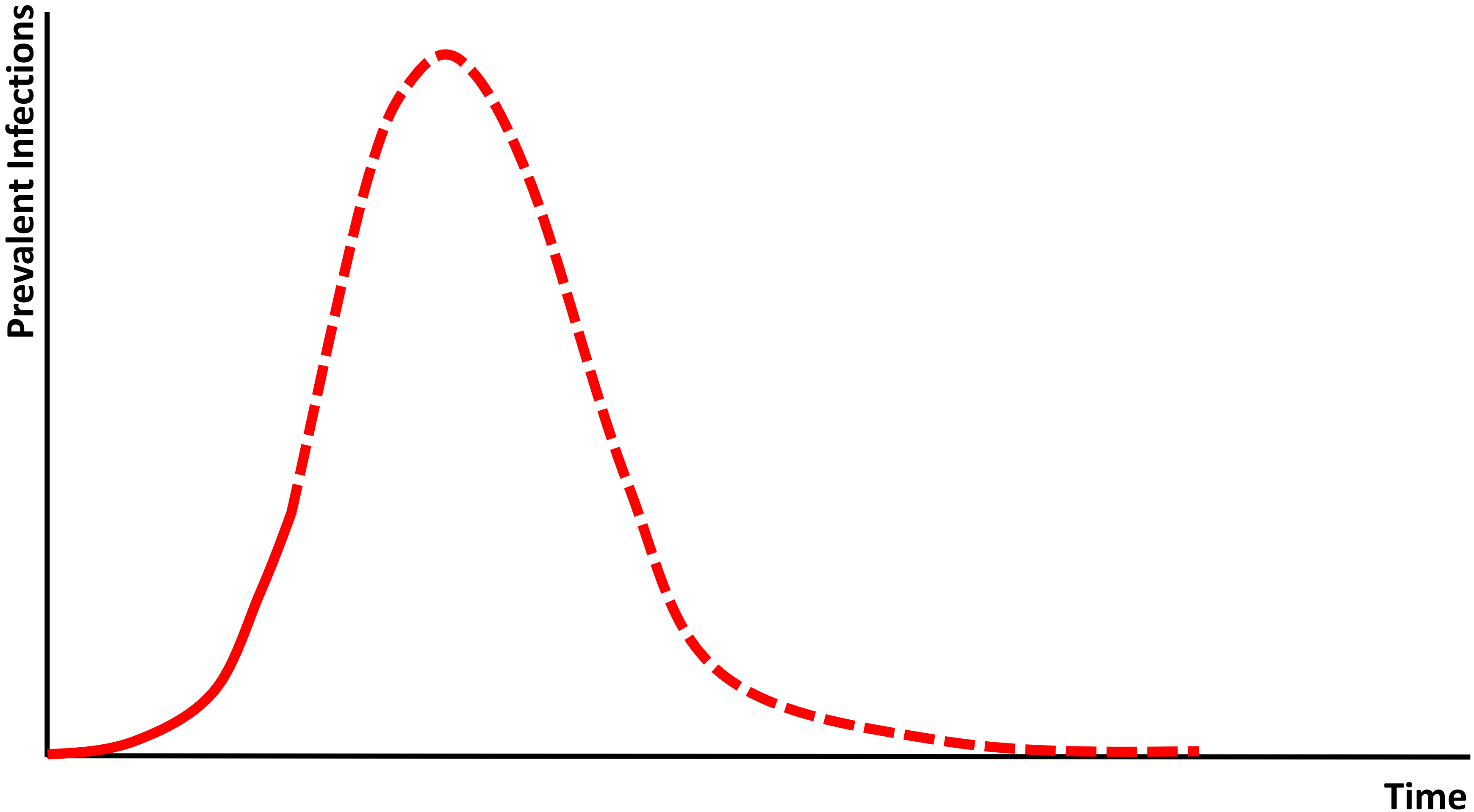
Coronavirus Epidemiology

- Highly transmissible
- ~80% of cases mild, some totally asymptomatic
- 15-20% severe, mortality uncertain but substantial
- Transmission occurs from both asymptomatic and symptomatic people
- Transmission occurs both by droplets (sneezing) and aerosol (tiny suspended droplets that can hang in the air)

The New York Times



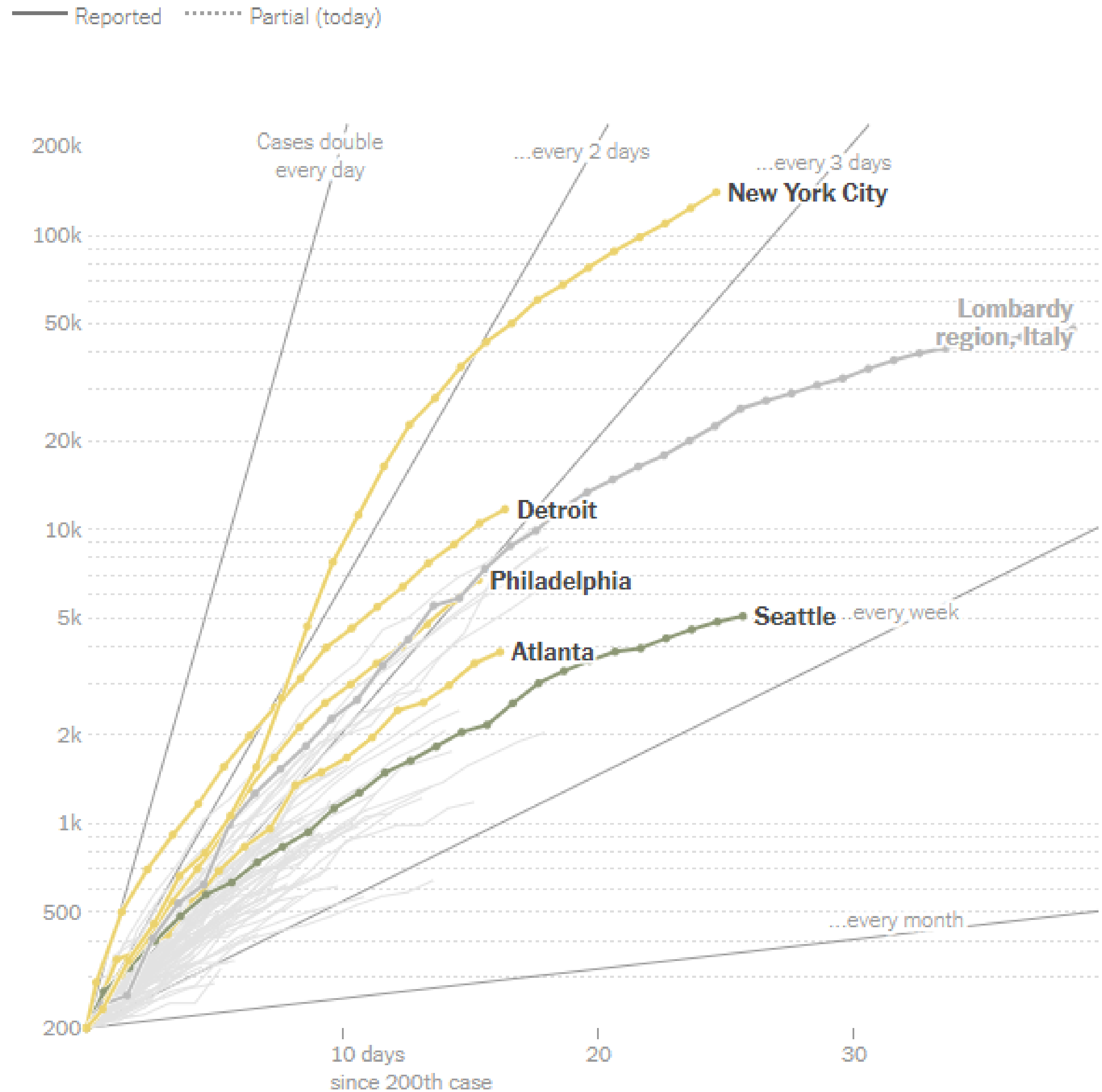
The Initial Path of an Epidemic



The New York Times

Confirmed cases by metro area

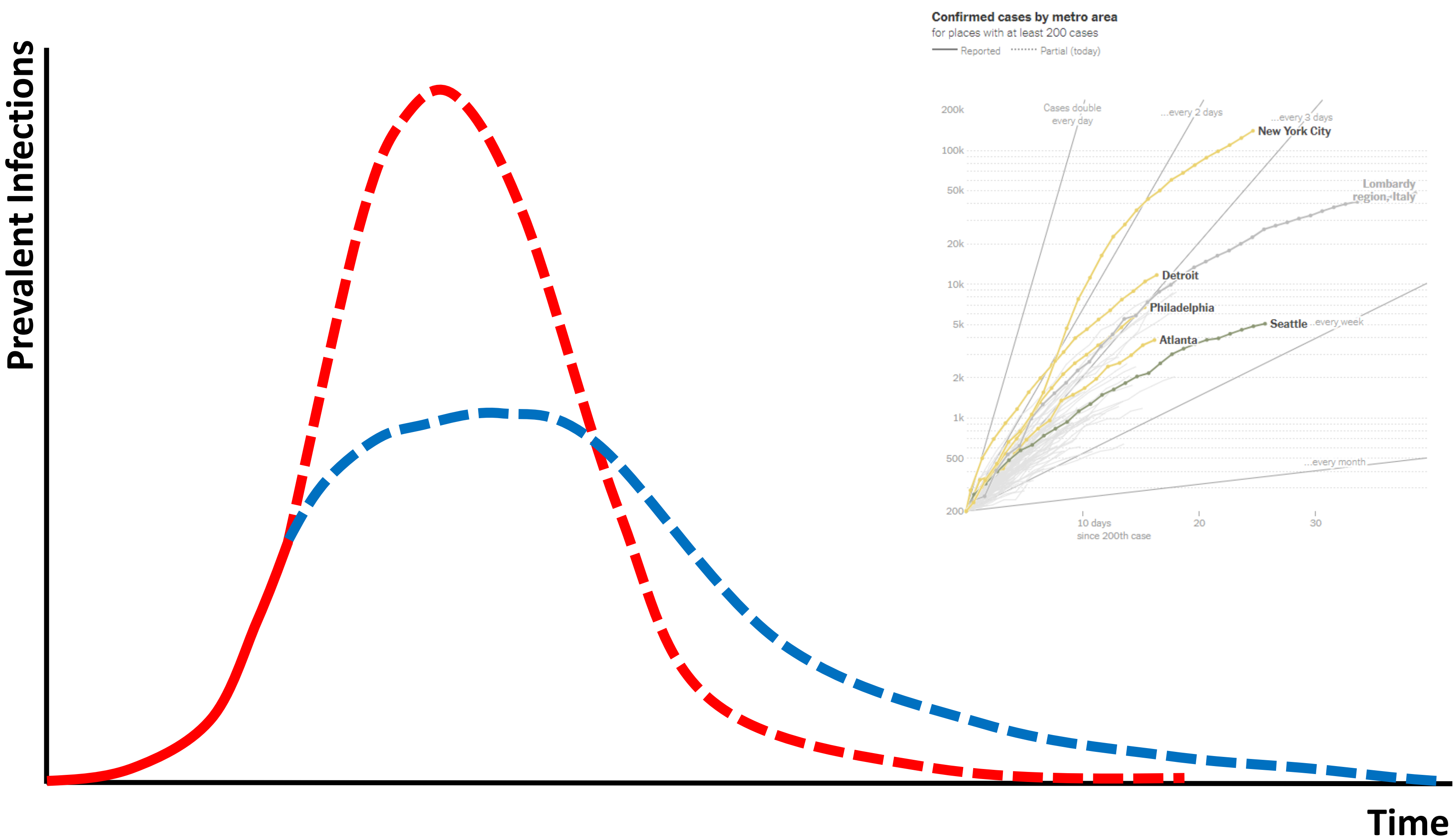
for places with at least 200 cases



Social (Physical) Distancing

- Tool to mitigate an infectious disease epidemic
- Two main goals
  - Reduce total number of infections
  - Slow spread of infection
- Slowing critical: enable people and systems to prepare
- Slowing critical: prevent the health care system from being overwhelmed
  - 1 infection/day for 14 days better than 14 infections in 1 day

The Initial Path of an Epidemic



Popular Latest **The Atlantic** Sign In

TECHNOLOGY

Don't Believe the COVID-19 Models

That's not what they're for.

ZEYNEP TUFEKCI **APRIL 2, 2020**

TOM BRENNER / REUTERS

"So if epidemiological models don't give us certainty—and asking them to do so would be a big mistake—what good are they? Epidemiology gives us something more important: agency to identify and calibrate our actions with the goal of shaping our future. We can do this by pruning catastrophic branches of a tree of possibilities that lies before us."

“All models are wrong; but some models are useful”

-- George Box and Norman Draper, 1987

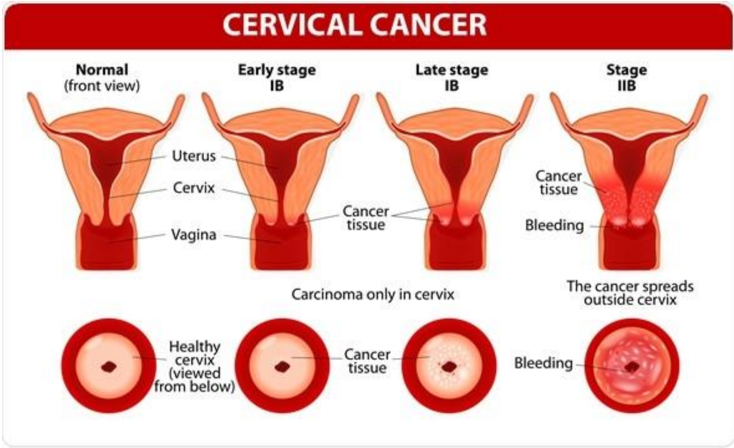
INTRODUCTORY TOPICS AND BACKGROUND

Infectious Disease

- A disease is infectious when it is caused by a pathogenic microorganism that can be spread (transmitted), directly or indirectly, from one person to another
  - Examples include tuberculosis, measles, COVID-19
- The primary risk factor for infectious disease is contact with an infectious source (e.g., an infected person or contaminated water source)

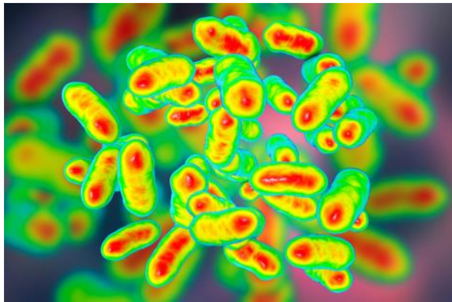
Infectious Disease

- While we have focused thus far on infection and transmission, we should remember that infections can cause disease – disruptions to the body's normal functioning
  - Human papillomavirus infections can cause cellular changes leading to cervical cancer



Types of Infectious Pathogens

- Micro: Bacteria, Virus, Protozoa, Prions, Fungi
- Macro: Helminths
- Fascinating biological differences, but for our course, we are interested in their particular:
  - Transmission characteristics
  - Duration and severity of infection and disease
  - Ability to provoke immune responses
  - Available interventions like vaccines
  - Ability to adapt/evolve due to selection



Susceptible, Infectious, Recovered (SIR)

- We turn our attention from pathogens to individual people residing in a population
- To represent many kinds of infectious diseases in a population, we can think of people as being in 1 of 3 states:
  - <u>Susceptible</u>: Not infected and not immune to infection
  - <u>Infectious</u>: Infected and able to transmit to others
  - <u>Recovered</u>: Not infected and immune to infection

Variants / Extensions to the SIR Classification

- How would you think about a disease like gonorrhea that does not produce long-term immunity? What states do you need?

- Throughout the course we will consider a variety of extensions to this basic framework which can capture many types of infections in many different types of populations

Pathogen Transmissibility (1)

- One can characterize how easily and quickly a pathogen is transmitted using a concept known as the basic reproductive number (R0)
- R0 defines the number of secondary infections an infectious individual will produce on average in an otherwise entirely susceptible population
  - Measles' R0 is estimated as 17 in mid-1900s UK

Pathogen Transmissibility (2)

- While R0 is sometimes conceived of as a characteristic of a pathogen it is actually the characteristic of a pathogen and a given population
  - For example, Keeling and Rohani report HIV's R0 for MSMs in the UK as 4 and for female CSWs in Kenya as 11. Why do you think that is?

Control Measures (1)

- Vaccination
  - Reduces the number of susceptible people to reduce rate of epidemic growth or ideally make it impossible for an epidemic to take hold
  - Important to remember that vaccination does not provoke sufficient immune response in all individuals – not all vaccinated individuals are immunized

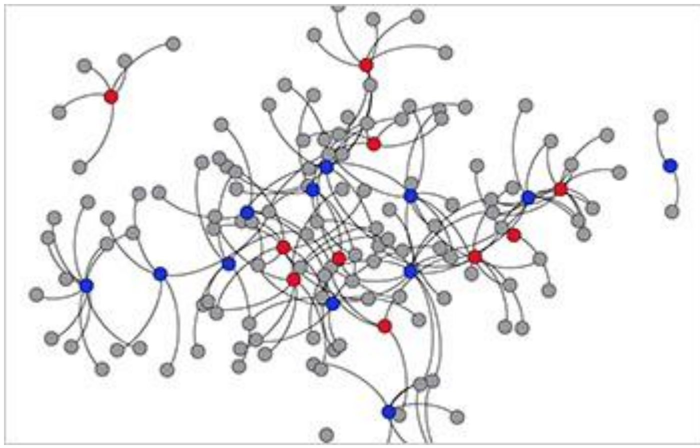
Control Measures (2)

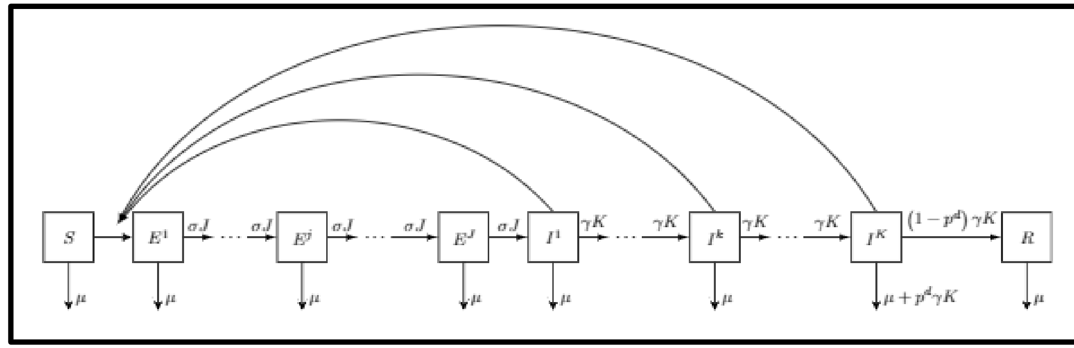
- Quarantine and isolation
  - Reduce the number of infectious people circulating in the population
  - Isolation: separation of infectious individuals often identified via symptoms
  - Quarantine: separation of people who may have been exposed to infection for sufficient duration to determine whether they are infected/infectious
  - Generally less effective if implementation delayed
  - Quarantine can have high social costs

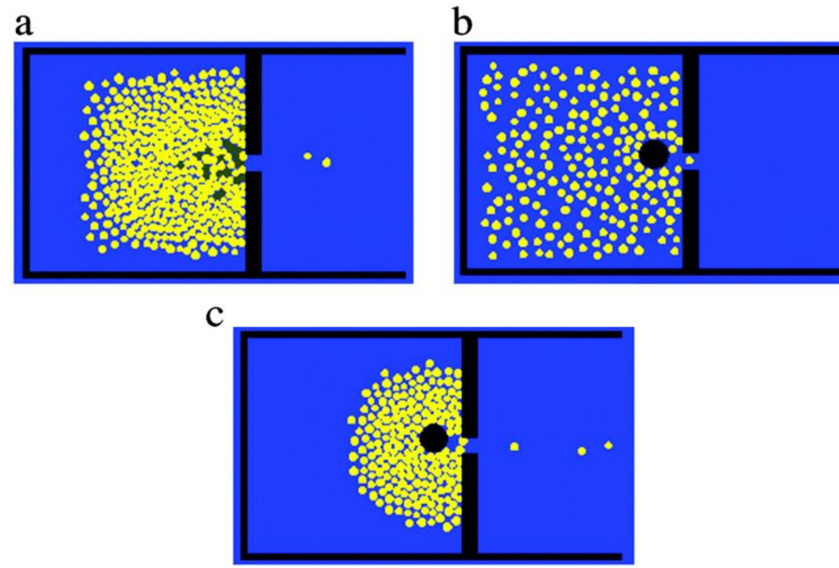
Control Measures (3)

- Other interventions
  - Pharmaceutical interventions which reduce infectiousness or limit duration of infectiousness
  - Vector control like mosquito spraying to limit infectious contacts

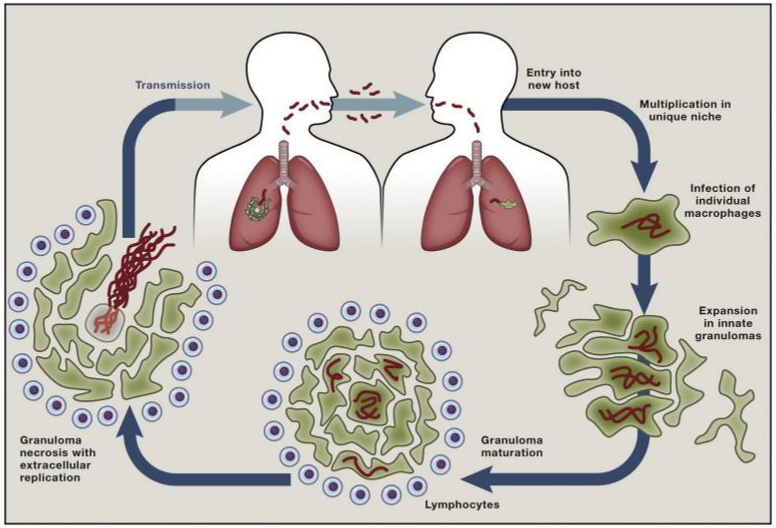
Types of Models (1)

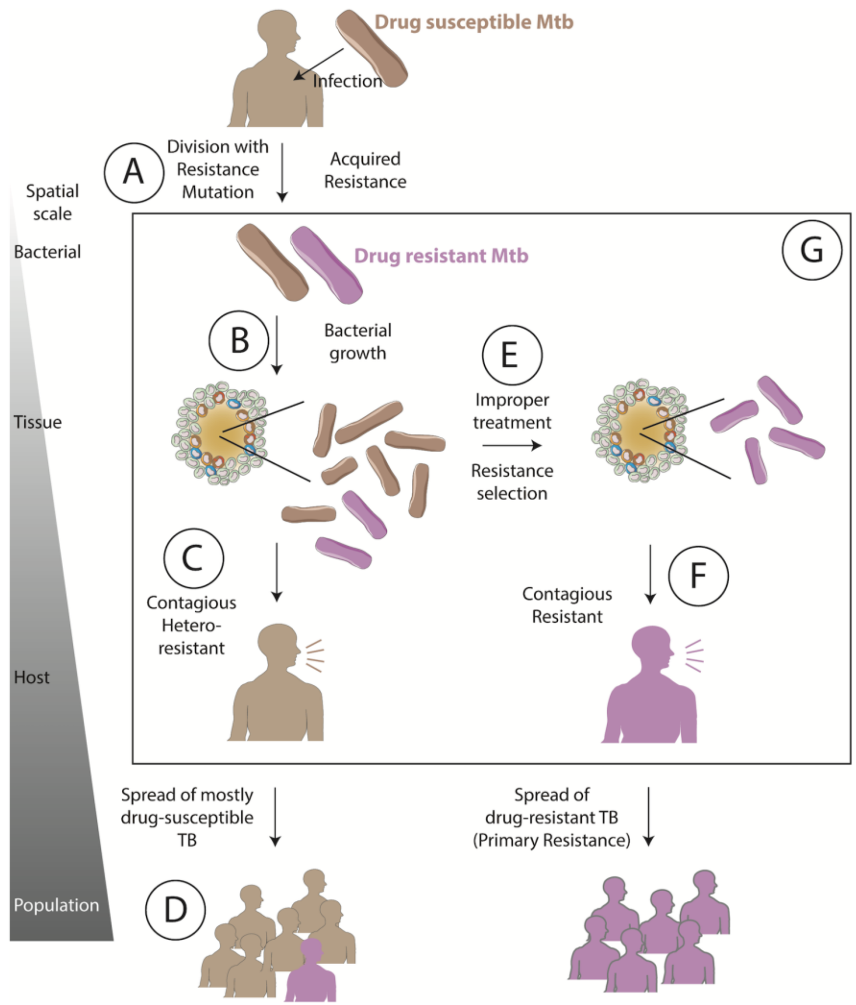






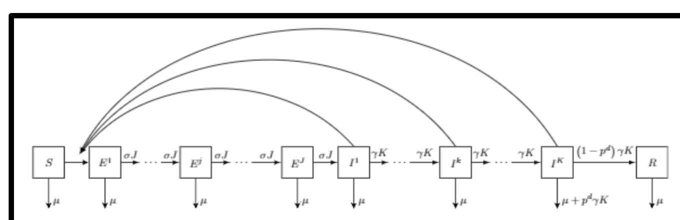
Types of Models (2)

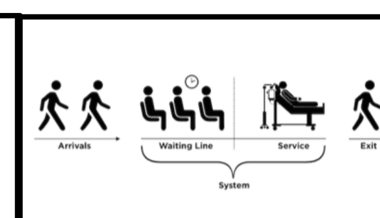




Mathematical Models (1)

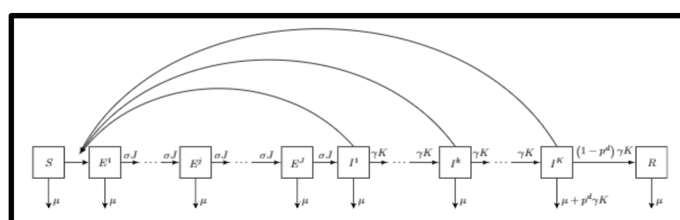
- Representation of how objects in a system interact and behave
- Predict the population-level dynamics of an infectious disease from individual-level knowledge of epidemiological factors, extrapolate long-term behavior from early dynamics, and project the effects of control measures

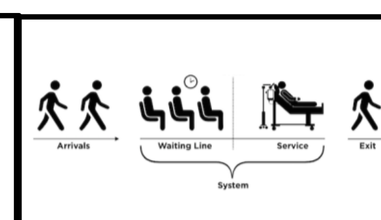




Mathematical Models (2)

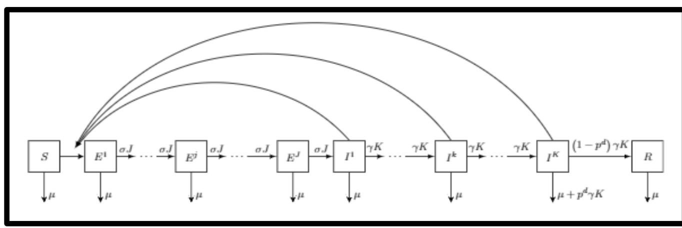
- Choosing the ***right*** type/complexity of model depends on being useful for the question posed
- Choosing involves balancing between advantages and disadvantages in terms of accuracy, transparency, and flexibility

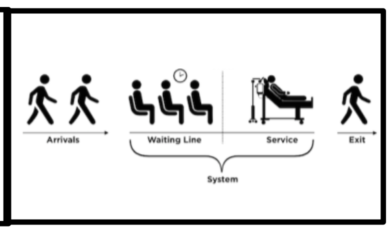




Mathematical Models (3)

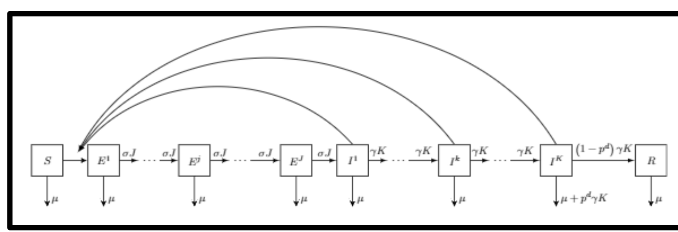
- <u>Accuracy</u>: Ability to faithfully represent real-world data and all its heterogeneities and particularities (push to complexity)
- <u>Transparency</u>: Ability to be understood and to understand why the model behaves as it does
- <u>Flexibility</u>: Mechanistic models vs. black box time-series prediction (machine learning/neural nets)

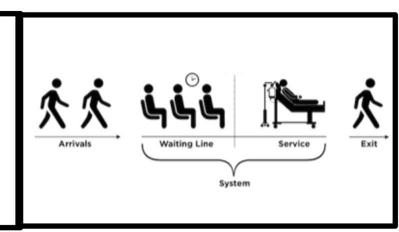




Uses of infectious disease models (1)

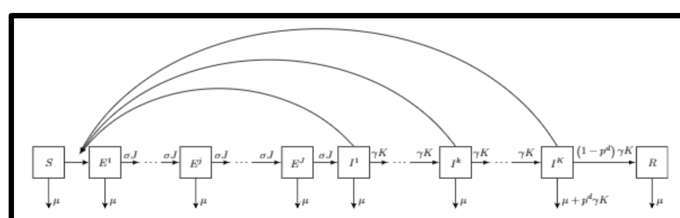
- Main uses of models include prediction and understanding

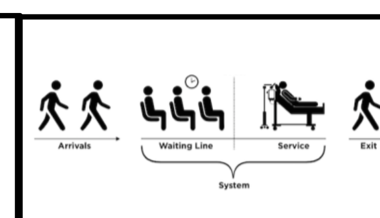




Uses of infectious disease models (2)

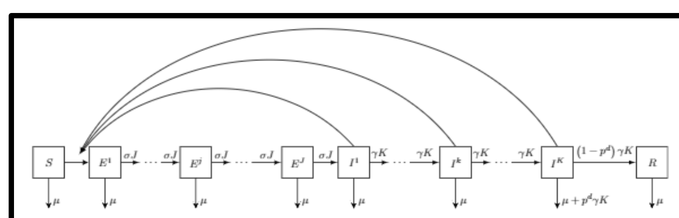
- To forecast the burden of a disease (cases, deaths, antimicrobial resistance)
  - Ex. Early Covid-19 models
- To project the impact of interventions against infectious diseases
  - Ex. What would be the impact of shelter-in-place against COVID-19? How would vaccines given to different age groups affect overall incidence?

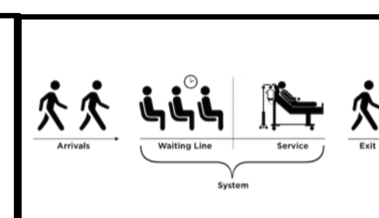




Uses of infectious disease models (3)

- Understand biological and epidemiological phenomena
  - Ex. How does HIV have such a long incubation period? (Lecture 12)
- Estimate important biological, medical or epidemiological parameters
  - Ex. What is the duration of immunity following cholera? What is the true infection fatality rate of COVID-19?





THE COURSE WILL DELVE DEEPLY INTO THESE AND OTHER TOPICS

Course Roadmap

1. First Models
2. SIR models with demography
3. Reproductive Number, Thresholds, Equilibria
4. Lab: Dynamic Models in R
5. Heterogeneous mixing and temporal modeling
6. Emerging infections: takeoff, growth, extinction
7. Lab: Emerging infections
8. Vectors, zoonoses, & environmental transmission
9. Stochastic dynamics
10. Spatial models, networks
11. Interventions and sensitivity analyses
12. Lab: Interventions and sensitivity analyses
13. Competition and evolutionary models
14. Within host evolution
15. Lab on Parameterization, calibration, and uncertainty
16. Health policy and economic evaluation models
17. Uses and abuses of models

Important Announcements

- Install and familiarize yourself with R and RStudio (see syllabus)
- Graduate section:
  - 5:15-6:15 pm on Thursdays (Zoom), starts Week 2 (April 16)
  - Week 1 reading (Blower et al, announced on Canvas) has been pushed to Week 2
  - See upcoming Canvas announcement from Tess with details on expectations and to sign up for a presentation slot
- TA Office Hours: 3:30-5:30 pm on Wednesdays (Zoom)
- For those less familiar with course background: supplementary readings on Canvas
- Please direct initial email questions to Tess