Learning Objectives
1. Define what models mean
2. Identify key concepts in ID mathematical modeling
3. Describe key differences in endemicity and transmission

A Brief History
- Daniel Bernoulli
  - First epidemic model
- William Farr
  - Dynamic shape of an epidemic
  - Assumption of the second ratio
- Arthur Ransome
  - Depletion of susceptible individuals in the population can cause an epidemic to recede

A Brief History (cont.)
- Pyotr Dimitrievich En'ko
  - Calculated the number of infectious cases expected to occur in a generation of an epidemic;
  - Based on the probability of members of the current susceptible population making contact with a member of the current infectious population
- Ronald Ross
  - Model of malaria transmission
A Brief History (cont.)

- Wade Hampton Frost and Lowell Reed
  - Formula to calculate the number of cases seen in a generation:
    \[ C_{t+1} = S_t (1 - q^C_t) \]
- Anderson Gray McKendrick
  - Model that represented transmission dynamics as a compartmental model expressed as continuous time ordinary differential equations

Why need to do modeling in ID?

- For understanding population dynamics of the transmission of infectious agents
- To assess the potential impact of ID control programs, especially those that are vaccine preventable

What is a mathematical model?

- It is an explicit mathematical description of the simplified dynamics of a system. Models approximate events.
- A model can be simple or complex
  - Simple model (e.g. Bernoulli model)
    \[ P(X=1) = p; \quad P(X=0) = 1 - p \]
  - Complex model (e.g. Logistic model)
    \[ P(D) = \frac{1}{1 + e^{-\beta y}}; \quad \hat{R}_0 = \left[1 + \exp(-\hat{R}_0)\right]^{-1} \]
Practical Example

What is a mathematical model? (…continued)

- Humans use models to approximate how things work. Two common formats:
  - Mental common sense (Mental model)—subjective explanation of the operations of a phenomenon. Often ambiguous and difficult for others or plain wrong.
  - Mathematical model—assumptions-based explanation of a complex phenomenon that could be tracked and repeated but understood by a few.

Why mathematical modeling?

- Think of staging immunization activity to control ID in community with 50k people.
- Limited role of specialized areas of ID to contemplate the feasibility of the activity
  - Microbiology—biochemical/genetics
  - Clinical—natural history and pathology
  - Epidemiology—rates, risk factors, transmis.
  - Vaccine—its efficacy against agent
- To extrapolate the effect of immunization activity in 50K people accounting for all factors, need mathematical modeling.
Uses and Functions of models

- Help in determining biological plausibility of epidemiological explanations
- Provide understanding by demonstrating unexpected interrelationships among empirical observations
- Predict the impact of changes on the dynamics of a system
- Allow integration of theoretical strategies in explaining trends

Models could be disasters!

The Minds Behind the Meltdown

How a swashbuckling breed of mathematicians and computer scientists nearly destroyed Wall Street

The story behind the marketing of “derivatives”

Why study modeling of IDs?

- Epidemiologists frame the questions
  - Describe the incidence
  - Describe the transmission methods and the risk characteristics
  - Describe the dynamics of the referent population
- Computational biologists design the computer model
  - Describe sequential and iterative approaches based on laid assumptions
Components of ID modeling

- ID modeling blends various fields like
  - Pop. biology
  - Ecology
  - Demography
  - Genetics
  - Mathematics
  - Statistics

- Time of transition from being infected to spreading the infection is a complex interplay of clinical microbiology, host immunity, and epidemiology (Figure 6.3)

Stages of Infection (SIR Model)

Simple illustration

- Let, $A_c$ = Agent characteristics
  - $R_t$ = Risk of transmission
  - $V_e$ = Vaccine efficacy
  - $I_{D+}$ = Incidence of diseases
  - $I_{D+} = f(A_c, R_t, V_e)$

- This can be modeled using complex computer calculations taking into account all the parameters of the model under different values.
Primary purpose of mathematical modeling in ID

- Mathematical models in ID deal with the transmission of infectious agents.

- Transmission ($T_m$)—Direct (person-to-person)
  - Indirect (when vector-borne)

  $T_m = \text{Transmission (} T_m = 1 \text{True or} T_m = 0 \text{False)}$

  $A_e = \text{Agent characteristics (} A_e^+ \text{ or} A_e^-)$

  $i_1, i_2, \ldots, i_n = \text{individuals at risk}$

  $\therefore T_m = 1\{|i_1 A_e^+ \leftrightarrow i_2 A_e^-\} \Rightarrow i_2 A_e^+$

Primary purpose of mathematical modeling in ID (…continued)

- Endemicity is when transmission ($T_m$) is maintained in a population

  Endemicity = 1\{|i_1 A_e^+ \leftrightarrow i_2 A_e^- \ldots, i_n A_e^-\} = N| I_s, I_e$

- Endemicity is eliminated when $T_m$ is interrupted in a population due to:
  1. Environmental and social condition may no longer support the agent
  2. Rx may eliminate the agent from host or population may get immunity
  3. Herd immunity may get high in the population

Primary purpose of mathematical modeling in ID (…continued)

- Mathematical models provide the theoretical framework how $T_m$ is maintained and can be interrupted

- Mathematical models best work when $T_m$ is direct and infection confers lifelong immunity (Example: Measles)
Terminology

- **Infection** — the stage of ailment that begins with entry of the agent in the susceptible host till recovery or death (sometimes subclinical level may linger for a long time)
- **Disease** — the stage in which the host exhibits clinical manifestations of the infection
- **Incubation Period** — time from infection to onset of symptoms or clinical manifestations
- **Latent Period** — time from infection to threshold of infectivity (i.e., the point at which the causative agent reaches effective level for transmission)

Stages of Infection (SIR Model)
Kermack-McKendrick Threshold Theorem

- Specifies that an epidemic can only be established in a population if the initial susceptible population size is large than some critical value, which depends on the parameters governing the spread of disease.
- \( X(t) \) = density of susceptible at time \( t \)
- \( Y(t) \) = density of infectious at time \( t \)
- \( Z(t) \) = density of removals at time \( t \)

Where density = \( n/\text{area} \)
SIR Model for Closed Population

\[
\begin{align*}
\frac{dX}{dt} &= -\beta XY \\
\frac{dY}{dt} &= \beta XY - \gamma Y \\
\frac{dZ}{dt} &= \gamma Y \\
&= X + Y + Z = N
\end{align*}
\]

- Susceptibles = \(X\)
- Infectives = \(Y\)
- Removals = \(Z\)
- Total in Closed pop = \(N\)

\(\beta XY\) = infection rate
\(\gamma Y\) = removal rate

Reproduction Ratio (\(R\))

- \(R\) is the number of secondary cases generated from a single infective case introduced into a susceptible pop.

\[R \equiv (\beta N)(1 / \gamma) = cq(1 / \gamma)\]

Where \(C\) = contact rate; \(q\) = probability of Tm/contact

- Eradication = \(R' < 1\)
- Endemicity = \(R' > 1\)

Other ID Epidemiologic Models

- When modes of Tm is indirect (Vector)
  - Number of mosquitoes becoming infective after biting infected person
  - Number of people becoming infective after bites of an infected mosquito
- Natural Histories—SIS model
  - Susceptible \(\rightarrow\) Infective \(\rightarrow\) Susceptible
- Host Genetic Factors—genotype driven
- Pathogen Genetic Factors
- Bioterrorism