Mathematical modelling of infectious disease transmission

Dennis Chao

Vaccine and Infectious Disease Division
Fred Hutchinson Cancer Research Center

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Role of models in epidemiology

Mathematical models can help epidemiologists:

- How fast will an epidemic spread?
- How severe will an epidemic be?
- How effective would an intervention strategy be?
- Testing hypotheses about disease transmission.

Kinds of models

Statistical
*Discover correlations and patterns* (e.g., regressions, time series analyses)


Mechanistic
*Simulate processes, dynamics* (e.g., differential equations, agent-based models)

Mechanistic (or “mathematical”) models can be used to test interventions.
How does vaccination reduce transmission?

- **Individual-level benefit:** Vaccination reduces the chance of infection. (VE)

- **Population-level benefit:** Vaccination reduces the number of people a person can infect.
Transmissibility and $R_0$

- $R_0$ is the number of people that a typical infected person infects in a fully susceptible population.
- $R_0$ must be greater than 1.0 for an outbreak to occur.
- Epidemics initially grow exponentially.

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How does vaccination reduce transmission?

- If infected people infect less than 1 other on average, outbreaks should not occur.
How many people do we need to vaccinate?

$R_0 = 2.0$

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How many people do we need to vaccinate?

50% for $R_0=2.0$

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Vaccinating 50% for $R_0=2.0$ results in an effective $R_0$ of 1.0 (assuming a perfect vaccine).
How many people do we need to vaccinate?

\[ R_0 = 3.0 \]

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(assuming a perfect vaccine)
How many people do we need to vaccinate?

67% for $R_0 = 3.0$

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(assuming a perfect vaccine)
How many people do we need to vaccinate?

$R_0 = 8.0$

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How many people do we need to vaccinate?

87.5% for $R_0=8.0$

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(assuming a perfect vaccine)
The critical vaccination fraction is the proportion of the population that needs to be vaccinated to prevent outbreaks.

Basically, vaccinate enough to drive $R_0$ below 1.

The critical vaccination fraction depends on $R_0$ and the vaccine efficacy, $VE$:

$$\frac{1 - 1/R_0}{VE}$$
Unanswered questions

- What if we don’t vaccinate enough people to prevent outbreaks?
- How many people will an epidemic infect?
- How fast will an epidemic spread?
- What if we vaccinate *during* an outbreak?

*Dynamic* modeling can help answer these questions.
Modeling infectious disease transmission

\[
\begin{align*}
\frac{dS}{dt} &= -\beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]
Math models consider a small number of essential disease states ("compartments").
Putting people in the compartments

How many people are in each disease state ("compartment")?
Transitioning between compartments

- **Susceptible** population is exposed to pathogen and become **Infected**.
- **Infected** people **Recover** and become immune to infection.
- Add rates of transition between compartments (disease states):
  - \( \beta I \): Force of infection is proportional to the number of Infected people.
  - \( \gamma \): Recovery rate is the inverse of the serial interval. For influenza, the serial interval is about 3.4 days, so \( \gamma = \frac{1}{3.4} \).
Ordinary differential equations (ODEs) are used to model the flow of people between compartments.
Modeling an influenza epidemic

- We can solve the SIR equations for how many Infected people there will be at any time.
- Starting with a population of 1000 people: 999 Susceptible and 1 Infected...

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\[ \frac{dS}{dt} = -\beta SI \]
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\[ \frac{dR}{dt} = \gamma I \]
Why does the epidemic peak then decline?

- \( \frac{dl}{dt} = \beta SI - \gamma I \)
- In the beginning, the population is fully susceptible and \( S \) is large.
- The epidemic grows exponentially.
What happens as the outbreak progresses?

\[ \frac{dl}{dt} = \beta SI - \gamma I \]

- As people are infected then recover, the pool of susceptible people shrinks.
- Growth slows as susceptibles are consumed.
- The epidemic declines when the infected population becomes smaller and smaller.

![Graph showing the progression of infected people over time.](image-url)
When does the epidemic stop?

- When a infected person can not infect more than one other, the epidemic will shrink.
- The epidemic stops before all Susceptibles are infected.
- The epidemic can not resume unless immunity wanes or more susceptibles are added (e.g., birth or immigration).

$R_0 = 2.0$, “effective” $R = 1.0$
Both mass vaccination and large epidemics deplete susceptible individuals

- **Vaccination** reduces the susceptible population.
If we know $R_0$ for a pathogen, we can set $\beta$ in an SIR model using:

$$\beta = \frac{R_0 \gamma}{N}$$

If part of the population is not susceptible, then we might use the term “R” instead of $R_0$.

The epidemic peak time is determined by both transmissibility ($\beta$) and the serial interval ($1/\gamma$).
“Indirect protection” or “Herd immunity”

- There is both **direct** and **indirect** protection from vaccination.
- **Vaccinated people** are less likely to become infected *and* less likely to infect others. Therefore, vaccines can protect vaccinated *and* unvaccinated people.
- If some people are vaccinated, epidemics may be smaller.
- If enough people are vaccinated, epidemics should not spread and there is “**herd immunity**”.
Evidence of indirect protection from mass cholera vaccination

Mathematical modeling was used to understand the relationship between coverage and incidence.

- If a vaccine is 65% effective, then one should avert at least 65% of cases.
- The observed reduction in a large-scale trial was greater.
- Indirect protection can be important for cost-effectiveness studies.
Other benefits from mass cholera vaccination

- Mass vaccination can *reduce* and *delay* the epidemic peak.
- The size of the peak may be important for hospital capacity planning.
- Delaying the peak might give officials time to implement other interventions.

Mathematical modeling can be used to predict how mass vaccination (or other interventions) could slow down an epidemic.

Some practical applications of SIR models

- Epidemic peak timing and height (e.g., for emerging diseases)
- Final attack rate
- Predicting effectiveness of mass vaccination
  - Understanding “indirect protection”, “herd immunity”, or “population” immunity
  - Computing the vaccination coverage needed to prevent outbreaks


Related models

SIRS model

Ross-Macdonald model

Waterborne

People

Mosquitoes

SIR model
SIRS model when immunity is not lifelong

- When Recovered people can become Susceptible again, the epidemic can persist.
Ross–Macdonald model for vectorborne disease

- An early (and still used) malaria model.
- Two populations: People and Mosquitoes.
- Infected Mosquitoes bite Susceptible humans.
- Infected humans are bitten by Susceptible Mosquitoes.
- Because both infection rates depend on the biting rate, transmissibility is a function of the biting rate squared.

Ronald Ross
1857–1932
Waterborne disease model

- People are infected by contaminated Water.
- Infected people contaminate Water.
- The pathogen in the Water declines over time.
- If the decay rate of pathogen in the Water is slow (i.e., the water remains contaminated for a long time), the epidemic can be prolonged.
More complex models (malaria)

- System of 7 difference equations.
- States: Negatives (no parasites), have liver parasites, have blood parasites
More complex models (typhoid)


- System of 10 difference equations.
- States: Susceptible, exposed (asymptomatic or symptomatic), infectious (latent, sick, or carrier), resistant, dead
- Each compartment needs an equation.
- Each relationship between compartments needs a parameter.
Summary and conclusions

• Mathematical modeling is a quantitative tool based on our understanding of disease transmission.
• Simple mathematical models can be useful and general, and more complex models can be developed when needed.
• Mathematical modeling can be used to predict the speed and size of an outbreak.
• Modeling can be used to test hypotheses about disease transmission.
• For vaccines, models have been used to:
  • Predict the effectiveness of mass vaccination.
  • Predict the effectiveness of vaccinating different subpopulations (e.g., children).
  • Quantify the benefits of “indirect protection”, “herd immunity”, or “population” immunity.
  • Establishing thresholds for vaccine coverage to eliminate a disease.
Thank you!

Boukan Kare, Haiti.
Photo by D. Chao

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May 11–15, 2015