Simple Epidemiological Models

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Infectious Diseases

Diseases caused by micro-organisms

- Viruses
- Bacteria
- Parasites
- Protozoa
- and/or their biological products (e.g., toxins).

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Why Are Infectious Diseases "Different"?

- **Communicability:** "a case is also a risk factor"
  - cases may be unrecognized.
- In models, communicability manifests as "**positive feedback**"
  - the more cases you have the more cases you get!
- Variety, capacity for change, and continuing emergence
- Interventions
  - Control depends on "**herd**", not just individuals.

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Classification of ID's

- Classification according:
  - ***Clinical syndrome***:
    - E.g., diarrheal, respiratory, central nervous system.
  - ***Microbiology***:
    - E.g., bacterial, viral, fungal, parasitic.
  - ***Mode of transmission***:
    - E.g., contact, foodborne, airborne, vector-borne, perinatal.
  - ***Reservoir:***
    - E.g., human, animal (zoonosis), soil, water.

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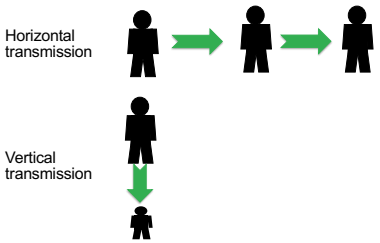
Vertical vs. Horizontal Communicability



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Characterization of Infectious Diseases (1)

- **Infectivity:** capacity of organism to infect individuals exposed to disease.
  - *Shigella* species have an ID_{50} of ~200 organisms while *Salmonella* sp. have an ID_{50}-200,000 organisms.
  - Infectivity of *Shigella* >> *Salmonella*.
- **Pathogenicity:** likelihood that **infected individuals** will become clinically ill.
  - Very likely to feel physically unwell if infected with common cold, or with SARS.
  - Both have high pathogenicity, but different **virulence**.

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Characterization of Infectious Diseases (2)

- **Virulence:** likelihood of **severe illness** among those infected.
  - SARS highly virulent, with case fatality rate ~ 17%. Avian flu (H5N1) even more virulent with CFR ~75% in 2004.
  - Norovirus infection: high infectivity, high pathogenicity ("no-walk virus") but CFR is low in otherwise healthy adults!

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Characterization of Infectious Diseases (3)

- **Immunogenicity:** infection results in long-lasting immunity, so host not infected again.
  - High immunogenicity: childhood exanthems like measles, chicken pox→only infected once.
  - Low immunogenicity: gonorrhea, chlamydia→infected repeatedly.
  - Intermediate immunogenicity: malaria. Can be reinfected, but subsequent infections less severe than first infection.

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Epidemiologic Parameters in Infectious Diseases

- **Attack rate:** quantitative analog of infectivity and pathogenicity: proportion of secondary cases of illness occurring among individuals exposed to an infectious individual or item (e.g., contaminated foodstuff).
  - **Clinical attack rate:** subset of infected/infectious individuals with recognizable symptoms.

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Epidemiologic Parameters in Infectious Diseases

- **Reproductive number (R):** number of secondary infections produced by each primary infectious individual.
  - **Special case:** R_0 or **"basic reproductive number"** = number of secondary infections when a single infectious case is introduced into a completely susceptible population.
  - When $R_0 > 1$ can have an **epidemic.**
  - When R = 1 disease stays **endemic.**

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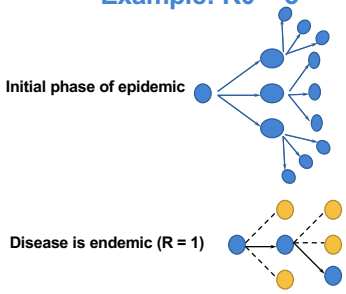
Example: R0 = 3



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Heterogeneity of COVID-19 Transmission

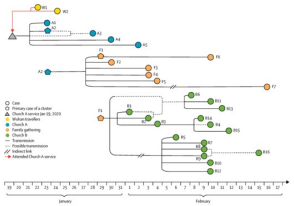

Figure 1 Transmission map of COVID-19

Yong et al. 2020

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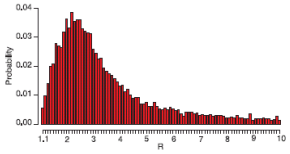
R_0 as a Distribution

- **Heterogeneity** among individual behaviors and infectiousness.
  - R_0 can be thought of as the mean of a **distribution**.



Lipsitch et al., 2003

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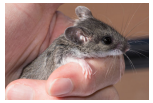
R_0 plays a critical role in disease dynamics

For perfectly immunizing (sterilizing) infections in a homogenously mixing population these include:

- The threshold for pathogen establishment
  - When R_0 is >1, a pathogen can invade.
  - When R_0 is <1, the chain of transmission will stutter and break resulting in pathogen fade-out.
  - For directly transmitted wildlife diseases there is often another measure called the critical host density for disease invasion.



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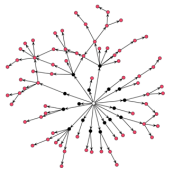
R_0 plays a critical role in disease dynamics

- As we saw last week, the final epidemic size is given by R_0
- In a stable population, the mean age of infection is ~ $A=L/(R_0-1)$. Where, L is the host life expectancy. (more about this later).
- The susceptible fraction at equilibrium is $S^* = 1/R_0$. A consequence of this is that for competing strains that elicit cross-protecting immunity, R_0 will determine competitive dominance and strain replacement.
- Contact tracing – can provide direct estimates of R0 (De et al. 2004).



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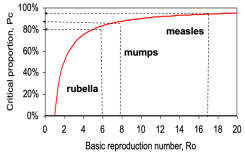
R_0 plays a critical role in disease dynamics

- The threshold for vaccine-induced herd immunity.
  - If a sufficient number of hosts are vaccinated, the effective reproductive number drops below 1 and the population will be resistant to pathogen invasion



$P_c = 1-1/R_o$

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Derivation of R_0

- Understanding disease dynamics forms the scientific basis for interventions
- Control measures operate by reducing transmission

$R_0 = cp \times D$

R_0 = number of secondary cases / primary case in a totally susceptible population

β

c = contact rate

p = probability of transmission given an infected contact

D = duration of infectiousness

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Part 2: Estimating R_0 from individual parameters

$R_0 = c*p*D$ where,

c = contact rate

p = probability of contact given a contact

D = duration of infectiousness

Why can't we just estimate it based on this relationship?

1.For many diseases we can't estimate the contact rate (how do we define a contact?) For STI's and vector borne diseases, where contacts are defined and countable it's a bit easier but highly heterogeneous.

2.Estimates based on R_0 expressions are highly model dependent.

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Important notes about rates and probabilities

- The book-keeping is important. Need to keep track of what is a rate and what is a probability and how to move between these 2 “currencies”.

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In modelling terms

- A **rate**, *x*/unit time (1/*x*) is the average time to an event (if the rate remains constant)
- A **probability** is defined on [0,1]. If we observe a probability *p* of something happening in a time interval we can back calculate the constant rate.
- We will discuss probabilities in much greater detail when we talk about stochastic models.

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Select Estimates of R_0

Pathogen	Estimated R_0	Reference
SARS	2-4	Lipsitch et al., 2003; Anderson et al., 2003.
Varicella zoster	10-12	Brisson and Edmunds, 2000.
Tuberculosis	~10	Blower, 2000.
Measles	10-20	Edmunds et al., 2000.
Smallpox	3-5	Gani and Leach, 2001.

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What Does R_0 Tell Us About a Disease?

- Index of **epidemic potential**.
- Relationship with **critical fraction to vaccinate** to eliminate a disease.
- Tells us about the **initial slope** of the epidemic curve (but doesn't tell us how to label the X-axis: dimensionless with respect to time!).
- Relation with "**final size**" of an epidemic.

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Epidemiologic Parameters for Infectious Diseases: Time

- **Incubation period:** time from infection until symptomatic. Forms basis of infection control measures such as quarantine.
  - Identify infectious individuals with onset of symptoms; they are already disconnected from susceptibles.
- **Latent period:** time from infection until actually infectious→ may have an infectious presymptomatic period (e.g., ½ day in flu?). May be difficult to institute control measures in the absence of symptoms.

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Epidemiologic Parameters for Infectious Diseases: Time (2)

- **Incubation period:**
  - May be **prolonged** (e.g., ~ 10 years in HIV).
  - Entire duration of infection may be asymptomatic (e.g., hepatitis C virus, 40% of flu cases).
- **Carriers:** Brief period of symptoms may be followed by prolonged asymptomatic period→ "**carrier state**" (e.g., *S. typhi* and Typhoid Mary!).

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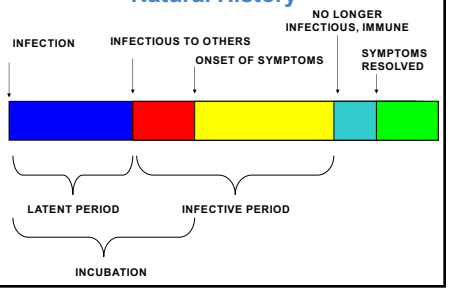
Infectious Diseases: A Taxonomy of Natural History



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Estimating R_0

- To estimate R_0 as an epidemic unfolds, need information on **both** case numbers (from epidemic curve) and estimate of time between "generations" of cases (a.k.a., **serial interval**).
  - A number of different methods exist for estimating R_0 when this information is available.

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Serial Intervals

- R_0 is *dimensionless* with respect to **time**.
- Rate of growth (per unit time) of an epidemic is a function of *both* R_0 and time interval between successive **generations** of cases→"**serial interval**".
  - Common heuristic = Latency + ½ Duration of Infectiousness (assumes transmission at midpoint).
- Example: Recall that both measles and TB have R_0 ~ 12.

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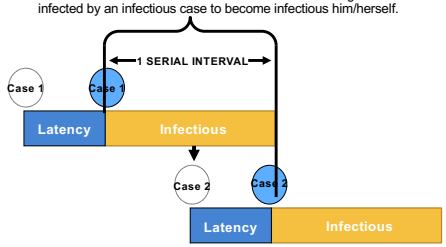
Serial Intervals

- Can think of serial interval as time it takes for an *average* case infected by an infectious case to become infectious him/herself.



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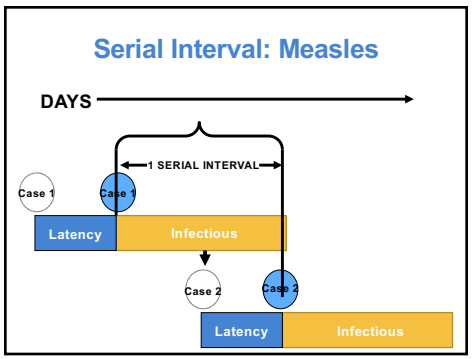
Serial Interval: Measles



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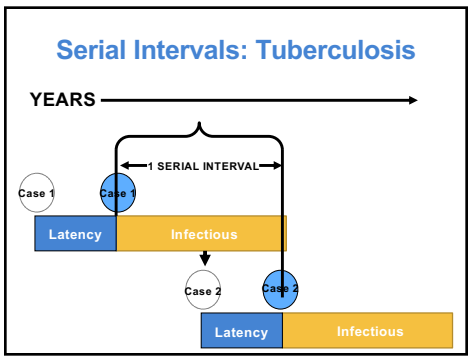
Serial Intervals: Tuberculosis



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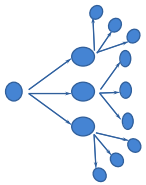
Serial Intervals

- For a given **generation** *(t)* and a given R_0 (say, 3) number *(n)* of **incident** infections in that generation is:



Generation	Cases (n_{t-1})	Cases (n_t)
0	---	1

$$n = R_0^t$$

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What Are Mathematical Models?

- Conceptual tools that explain how an object or system of objects will behave
- Models come in a variety of forms
  - Highly complex or simple (and anywhere in between)
  - Decision of which to use is determined by:
    - Precision / generality required
    - Available data
    - Time frame for getting results
  - Even the most complex models make simplifying assumptions
- Hope to capture the essential features

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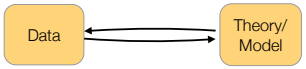
An important distinction

Statistical Models

- describe associations between variables
- used to derive parameter estimates from empirical data

Mathematical Models

- provide a framework that represents the proposed causal pathways
- Describe mechanisms that link exposures, interventions, infection and/or disease
- Used to make projections/ predictions



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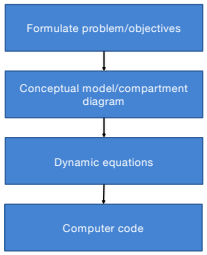
Steps in Developing a Model



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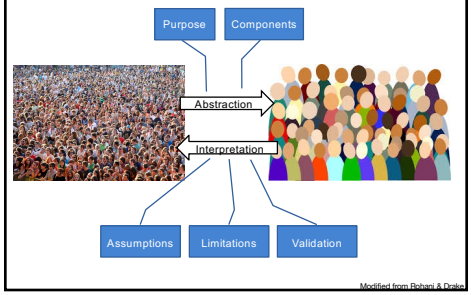
Abstraction



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Trade-offs Between Modeling Elements

- **Accuracy**
  - Reproduce observed data but do we need a qualitative fit or quantitative fit? Will depend on question
  - Improves with complexity but struggles with data
- **Transparency**
  - Understanding how the model components influence the dynamics
  - Usually in direct opposition with accuracy
- **Flexibility**
  - Ease of adapting to new situations

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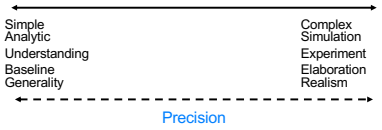
What Is A Good Model?

- **Suited to its purpose**
  - appropriate balance of accuracy, transparency and flexibility
- **"Parameterizable"** (where necessary) from data
- **Highly context dependent**



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What Models Can Not Do

- There is no fully accurate model (e.g. influenza transmission)
- We will never be able to predict the precise course of an epidemic or which people will be infected
- Models can provide confidence intervals on epidemic behaviour and determine the risk of infection for various groups of hosts

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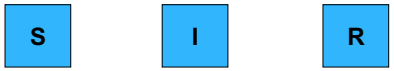
Translating a process into a model

1. Define host population of interest
2. Define the states of individuals that will be in the model (compartments)



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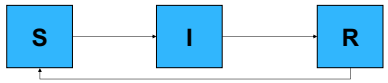
Translating a process into a model

3. What are the transitions in and out of the states?



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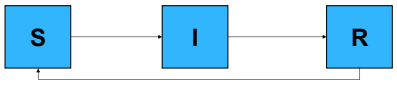
Translating a process into a model

4. Define how infection incidence depends on exposure to infectious people

c = Number of contacts / time
p = probability of infection given an exposure
λ = force of infection = β I / N (risk of new infection / time)
R0 = number of secondary infections caused by single infected individual in a wholly susceptible population



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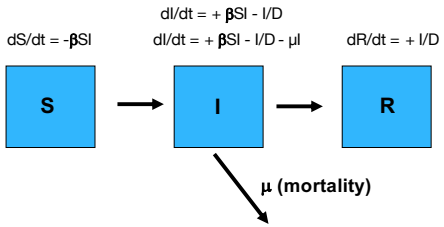
A Simple Schematic Model of an Infectious Disease



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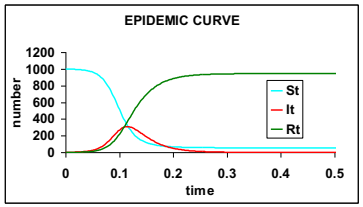
A Simple Schematic of an Infectious Disease (R_0=3)



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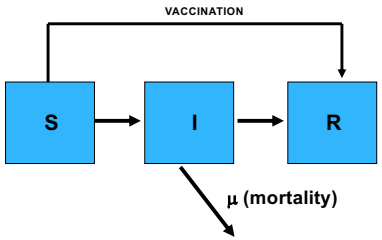
Schematic Model of Vaccination



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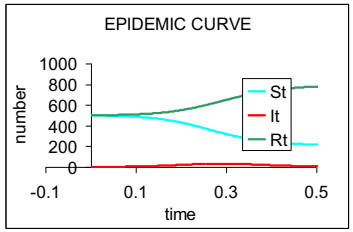
A Simple Schematic of an Infectious Disease (R_0=3), P_{vax} = 0.5



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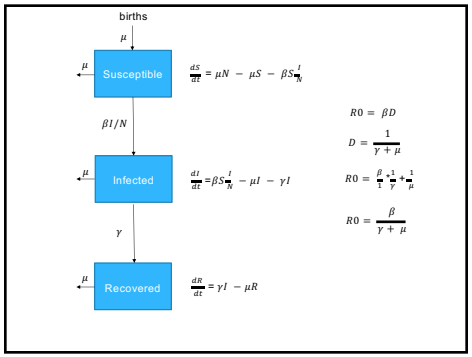

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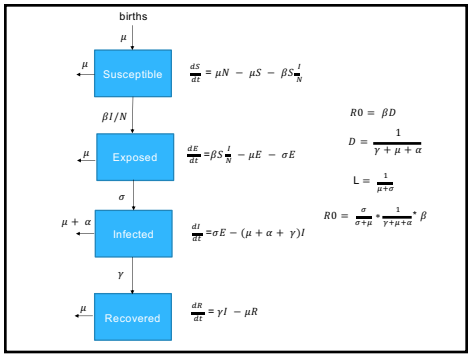

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Summary: Infectious Disease Epidemiology

- Infectious diseases differ from non-infectious diseases in **transmissibility**, and importance of immune "herd" for control.
- **Reproductive numbers**: tell us about epidemic potential, fractions to vaccinate, epidemic size in the absence of intervention.
- **Serial intervals**: tell us how fast (for a given R0) an epidemic grows.
  - If we know serial interval, can estimate R0.

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