Mathematical Modelling for Infectious Disease: Theory and Practice

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Outline

Motivation

- Mathematical analysis and modelling is an important part of infectious disease epidemiology.
- The link between the biology of an infectious disease, the process of transmission and the mathematics is critical in the modelling process
- The mathematical description of disease epidemics immediately leads to several useful results, including the expected size of an epidemic and the critical level that is needed for an intervention to achieve effective disease control.

Types of models

Deterministic

- Based on the premise that if complete information on the system is known at a specific time, then its future behaviour can be predicted exactly
  1. Treats averages from the beginning.
  2. Reliable if large population is involved
- A deterministic model is one in which the values for the dependent variables of the system are completely determined by the parameters of the model
- Deterministic models have the advantage of often being amenable to mathematical analysis, as in the case of using ordinary differential equations

Types of models

Stochastic

- Stochastic, or probabilistic, models introduce randomness in such a way that the outcomes of the model can be viewed as probability distributions
- It is impossible to determine with absolute certainty the nature of the system for future times.
- These models provide a framework to represent uncertainty in mathematical modelling
- It provides more information, eg, means, variances, covariances Caters for all times: short and long term

Types of models

Discrete Time Models

- State transitions occur only at given points in time
- Inbuilt assumption that the time intervals between consecutive measurements are all equal
- May not give correct predictions about the actual situation

Types of models

Continuous Time Models

- Where DT models assume equally spaced data, CT models are more flexible and therefore, more appropriate for unequally data.
- Times between successive transitions are exponentially distributed.
- Changes of state do not only occur at fixed times but may occur at each point of time

Types of models

Simulation models

Model normally translated into a computer program for subsequent simulation

1. Complex system with random effects
2. Individual-based, network.

Outline

Basic infectious disease concepts

- An infectious disease is any disease caused by the direct effect of a pathogen. A pathogen may be cellular (bacteria, parasites, and fungi) or acellular (viruses, viroids, and prions).
  - Some infectious diseases are also communicable, meaning they are capable of being spread from person to person through either direct or indirect mechanisms.
  - Some infectious communicable diseases are also considered contagious diseases, meaning they are easily spread from person to person.
- Noncommunicable infectious diseases, noninfectious diseases (those not caused by pathogens) are an important cause of morbidity and mortality worldwide.

Basic infectious disease concepts

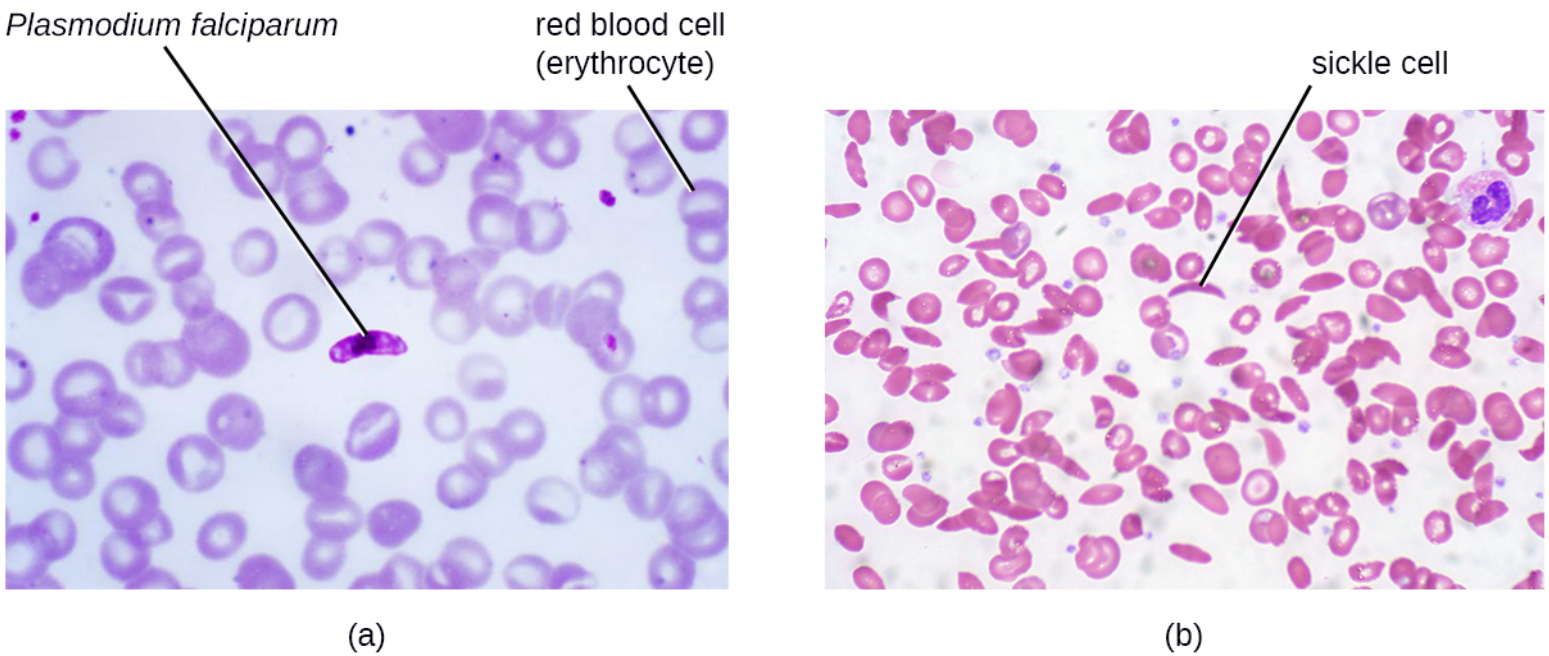
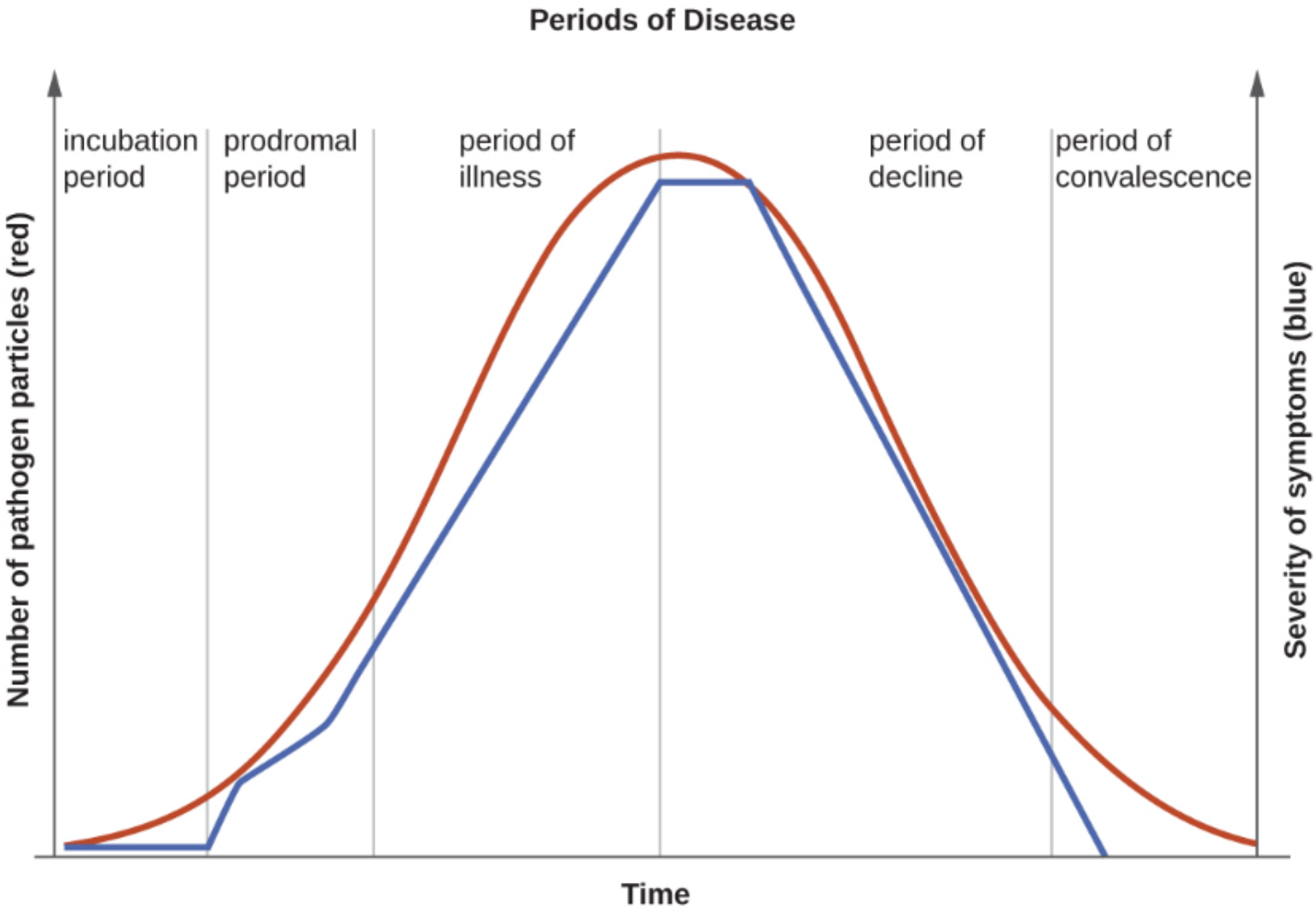


Figure: Blood smears showing two diseases of the blood. (a) Malaria is an infectious, zoonotic disease caused by the protozoan pathogen Plasmodium falciparum (b) Sickle cell disease is a noninfectious genetic disorder that results in abnormally shaped red blood cells.

Background information

- The incubation period occurs in an acute disease after the initial entry of the pathogen into the host (patient). It is during this time the pathogen begins multiplying in the host. However, there are insufficient numbers of pathogen particles (cells or viruses) present to cause signs and symptoms of disease. Incubation periods can vary from a day or two in acute disease to months or years in chronic disease, depending upon the pathogen.
- The prodromal period occurs after the incubation period. During this phase, the pathogen continues to multiply and the host begins to experience general signs and symptoms of illness, which typically result from activation of the immune system, such as fever, pain, soreness, swelling, or inflammation.
- Following the prodromal period is the period of illness during

Basic infectious disease concepts



Key Concepts

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- Diseases can either be noninfectious (due to genetics and environment) or infectious (due to pathogens).
- Some infectious diseases are communicable (transmissible between individuals) or contagious (easily transmissible between individuals); others are noncommunicable, but may be contracted via contact with environmental reservoirs or animals (zoonoses)

Type of infectious organisms

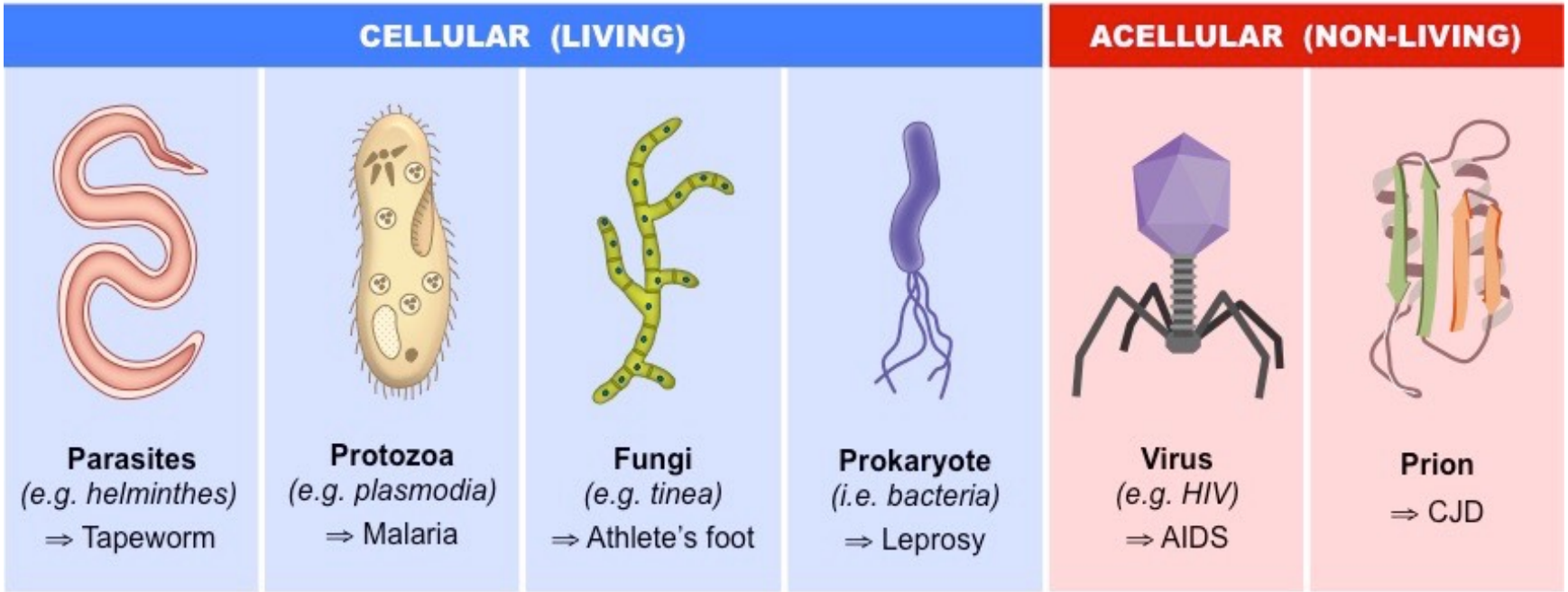

Figure: Some pathogens

Type of infectious organisms

- Virus: HIV, Measles, smallpox, SARS, influenza,
- Bacteria: Tuberculosis, typhoid fever,
- Protozoa: Malaria, African sleeping sickness
- Fungi: Fingernails or toenails infection, vaginal candidiasis

Type of infectious organisms

The outcomes of infection differ from one disease to another

1. Some disease are fatal, some diseases confer lifelong immunity,
2. some confer a temporary immunity,
3. others confer no immunity at all.

Outline

Compartmental Models for Disease Transmission Dynamics

- Define $S(t)$: susceptible; $I(t)$: infective and $N(t)$: total population at time t
- Let $\beta(N)$ be the effective contact rate per person per unit time
- $\beta(N)I/N$: average number of contacts with infectious individuals a susceptible individual makes per unit time
- Disease incidence (number of new cases): $g(S;I;N) = \beta(N)SI/N$
  - *(i)* Standard incidence if $\beta(N) = \beta$
    (based under the assumption that the contact rate is constant)
  - *(ii)* Mass action incidence if $\beta(N) = \beta N$
    (if the infection for a population changes then this is a better assumption)

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- It is further assumed that those who have recovered or died

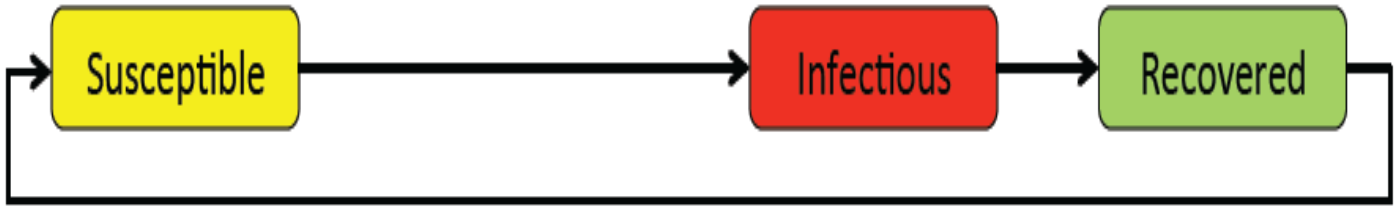
Basic Epidemiology Models

- SIR

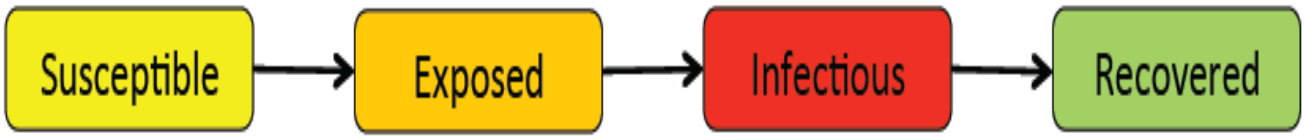
- SIS

No Immunities

- SIRS



- SEIR



SIR Model Assumptions

- Homogeneous mixing (each individual in the population has an equal chance of interacting with any other)
- Population is large enough so that all effects are demonstrated
- Closed population (no entry into or departure from the population, except possibly by disease-induced death)
- Time scale of the disease is assumed faster than the time scale of births and deaths (so that the impact of demographic effects on the population may be ignored)

SIR Model

- Kermack, W. O., & McKendrick, A. G. (1927). A contribution to the mathematical theory of epidemics. Proceedings of the royal society of london. Series A, 115(772), 700-721
- Consider a "cohort" of members who were all infected at one time, and let $u(s)$ denote the number of these who are still infective s time units after having been infected
- If a fraction (γ) of those leaving the infected class in unit time, then $\frac{du}{dt} = -\gamma u$
- Solution: $u(s) = u(0)\exp(-\gamma s)$
- Thus, the fraction of invectives remaining infective s time units after having become infected is $\exp(-\gamma s)$. Hence, the infective period is exponentially distributed with mean

SIR Model cont'd

- These assumptions lead us to a set of three ordinary differential equations for $S(t)$, $I(t)$, and $R(t)$:

$$\frac{dS}{dt} = -\beta S(t)I(t) \quad (1)$$

$$\frac{dI}{dt} = \beta S(t)I(t) - \gamma I(t) \quad (2)$$

$$\frac{dR}{dt} = \gamma I(t). \quad (3)$$

- Here $\gamma \geq 0$ is the recovery rate or $1/\gamma$ mean duration of infectivity.
- $\beta \geq 0$ measures the likelihood of transmitting the disease when an infected and a susceptible person come in contact or mean number of contacts an infective makes per unit time.

Basic Reproduction Number (R_0)

- Suppose at time $t = 0$ all individuals were susceptible (i.e., $S(0) = N$)
- Hence, at $t = 0$, one infected individual will infect $\beta S(0) = \beta N$ susceptible individuals per unit time
- Since an infected individual will remain infectious for an average period of $\frac{1}{\gamma}$, then$R_0 = \frac{\beta S(0)}{\gamma}$

Epidemiological implication

(i) Disease can be effectively controlled if $R_0 < 1$.

(ii) Disease persists in the community if $R_0 > 1$

Model: No Immunity (SIS)

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

$N = S + I$, Put $S = N - I$, model reduces to

$$\frac{dI}{dt} = \beta I(N-I) - \gamma I = [(\beta N - \gamma) - \beta I]I$$

$$= \left[\gamma\left(\frac{\beta N}{\gamma} - 1\right) - \beta I\right]I = [\gamma(R_0 - 1) - \beta I]I$$

$$= \gamma R_0 \left[1 - \frac{\beta I}{\gamma(R_0 - 1)}\right] I$$

Model: No Immunity (SIS) cont'd

- $R_0 = \frac{\beta N}{\gamma}$ is the reproduction number of the SIS model
- Equilibria:
  (a) $I^* = 0$ (corresponds to $S = N$);
  (b) $I^{**} = \frac{\gamma}{\beta N}(R_0 - 1)$.

Epidemiological implication

(i) If $R_0 < 1$, then all solutions of the model with non-negative initial conditions (except I^{**}) approach the limit 0 as $t \to \infty$.

(ii) Similarly, solutions (except $I^* = 0$) tend to I^{**} for $R_0 > 1$.

Model with Demographics)

$$\begin{aligned}
\frac{dS}{dt} &= \mu N - \beta SI + \mu S \\
\frac{dI}{dt} &= \beta SI - \gamma I - \mu I \\
\frac{dI}{dt} &= \gamma I - \mu R
\end{aligned}$$

(i) Recovery confers permanent protection against re-infection

(ii) Disease-free equilibrium (DFE): $(S^*; I^*; R^*) = (N; 0; 0)$ Under what conditions can the system settle at the DFE?

(iii) Answer determined by analysing the stability of the DFE.

Model with Demographics cont'd

Reproduction Number (denoted by R_0) is the average number of new cases a typical infected person will generate during his/her duration of infectiousness if introduced in a completely susceptible population.

R_0 is intuitively calculated using the first principle. That is,

$R_0 =$ (infection rate)$\times$(duration of infectiousness)

- For the SIR model with demographic,

$$\begin{aligned} R_0 &= \frac{\beta S^*}{\gamma + \mu} \\ &= \frac{\beta N}{\gamma + \mu} \end{aligned}$$

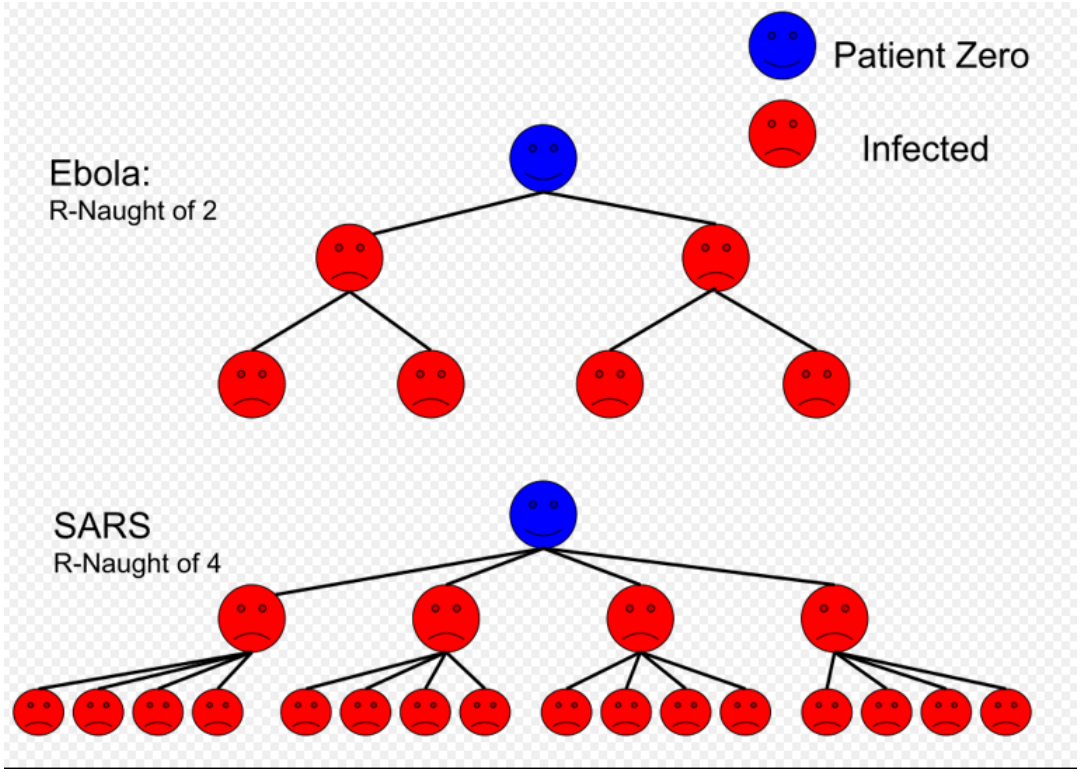
- Thus, disease would be effectively controlled if $R_0 < 1$.

Values of R_0 of well-known infectious diseases

Estimated R_0 and HIT (Wikipedia)

Disease	R_0	HIT
Measles	12–18	92–95%
Pertussis	12–17	92–94%
Diphtheria	6–7	83–86%
Rubella		
Smallpox	5–7	80–86%
Polio		
Mumps	4–7	75–86%
SARS	2–5	50–80%
Ebola (Ebola virus epidemic in West Africa)	1.5–2.5	33–60%
Influenza (influenza pandemics)	1.5–1.8	33–44%

R_0 - Visualization



Basic reproduction number

- When

$$R0 < 1$$

the infection will die out in the long run.

- But if

$$R0 > 1$$

the infection will be able to spread in a population.

Outline

The SIR model

- The SIR model divides the population to three compartments: Susceptible, Infected and Recovered.
  - *(i)* (S_t) = the number of susceptible individuals at time t
  - *(ii)* (I_t) = the number of infected individuals at time t
  - *(iii)* (R_t) = the number of recovered individuals at time t
- the flow of individuals is one direction from the susceptible group to infected group and then to the recovered group.
- Suppose on average every infected individual will contact (γ) person, and (κ) percent of these (γ) person will be infected.
- Then on average there are $(\beta = \gamma \times \kappa)$ person will be infected an infected individual.

The SIR model cont'd

- So with infected number (I_t) , they will infected (βI_t) individuals.
- Since not all people are susceptible, this number should multiple to the percentage of susceptible individuals.
- Therefore, (I_t) infected individuals will infect $(\beta \frac{S_t}{N} I_t)$ individuals.
- Another parameter (α) describes the percentage of infected individuals to recover in a time period. That is on average, it takes $(1/\alpha)$ periods for an infected person to recover