Epidemiological modeling

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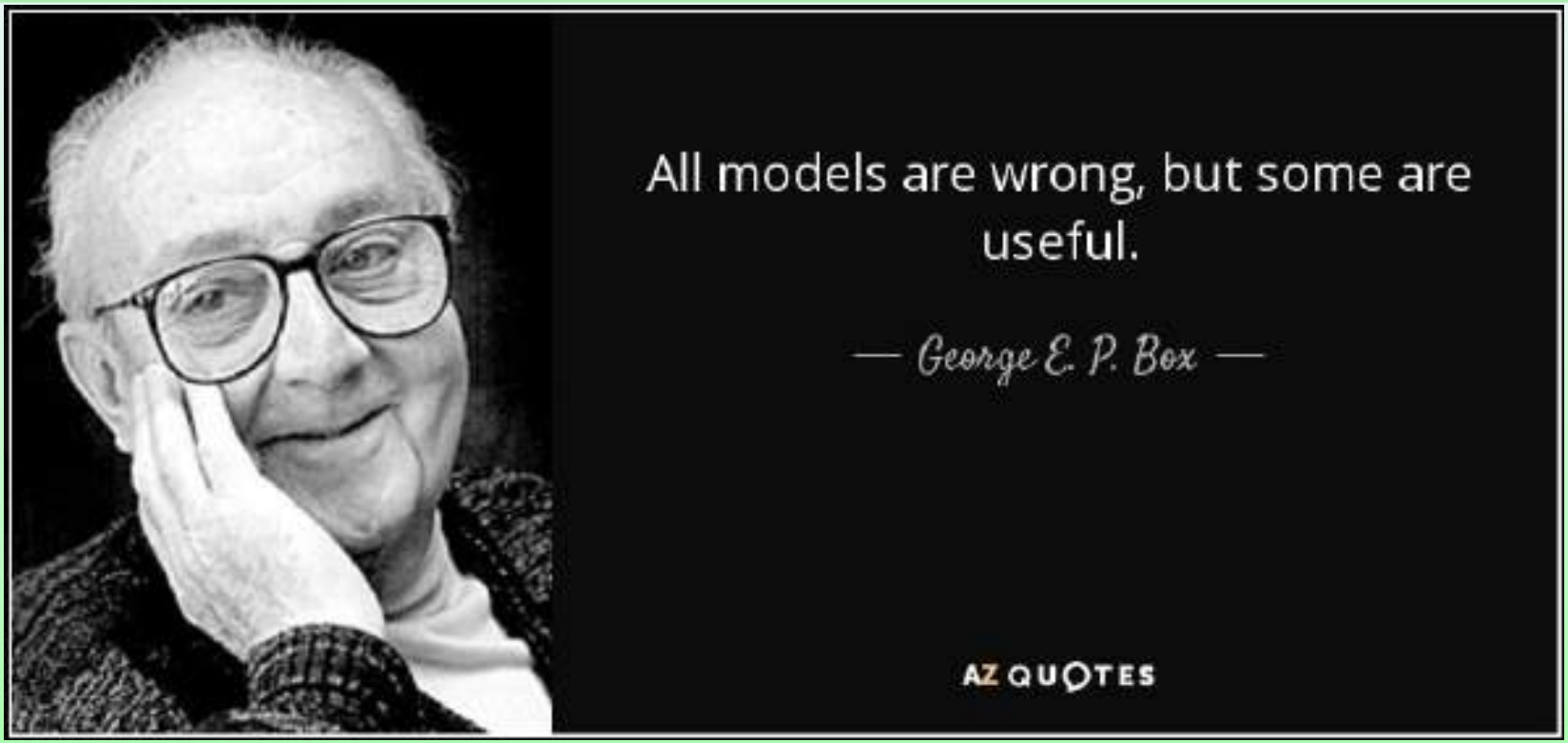
GOALS

- Introduce basic concepts of infectious diseases
- Derive the epidemic and endemic SIR models
- Explain approaches used to describe the transmission term
- Describe basic insights of infectious disease dynamics provided by the simple deterministic SIR models.
- Explain the difference between the basic and effective reproduction numbers and when each of them is useful
- Introduce realism and hence more complexity
- Compute of the basic reproduction number

Warning!



- **All models are wrong**
- **But some are useful**

George Box

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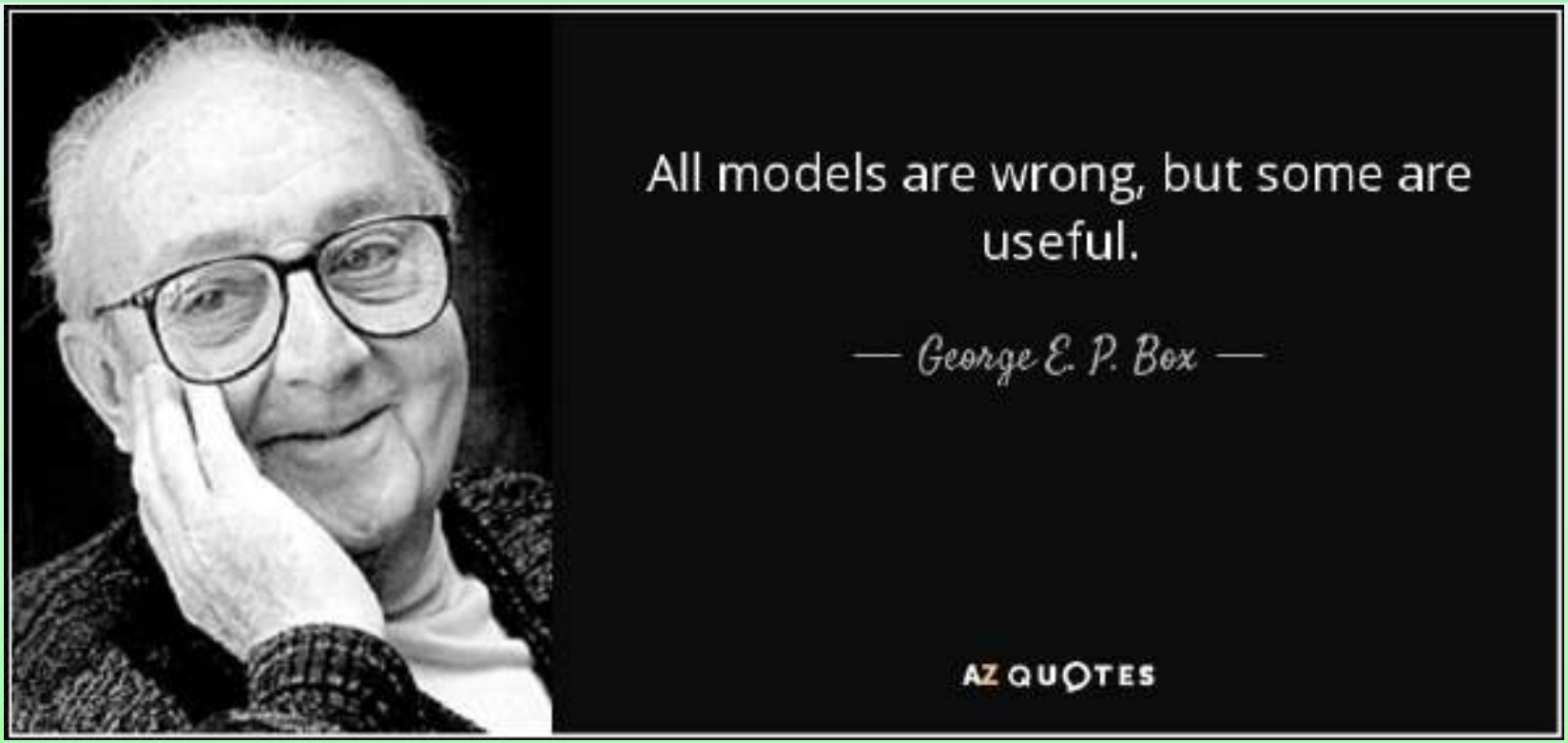

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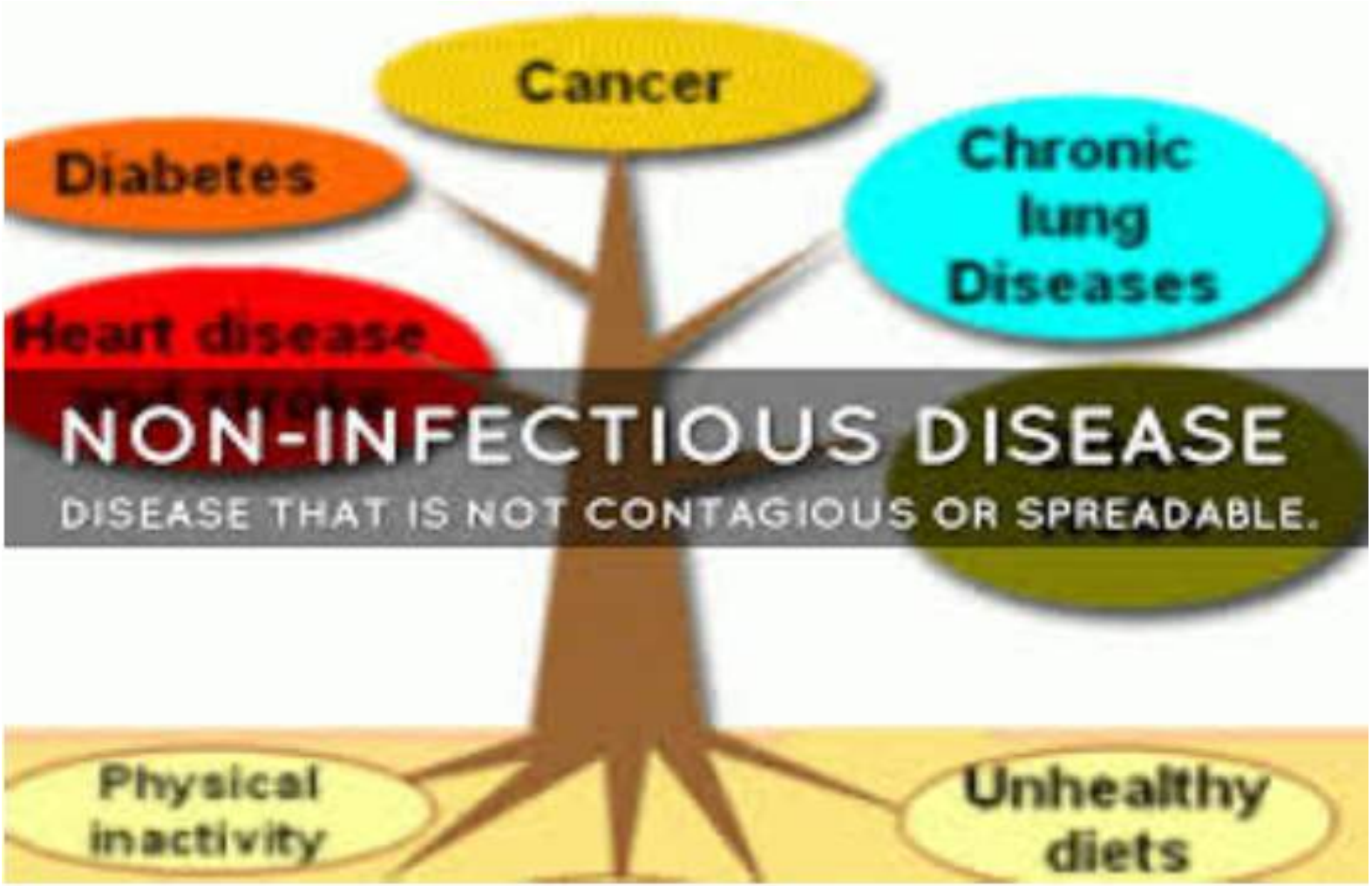
Non-infectious diseases



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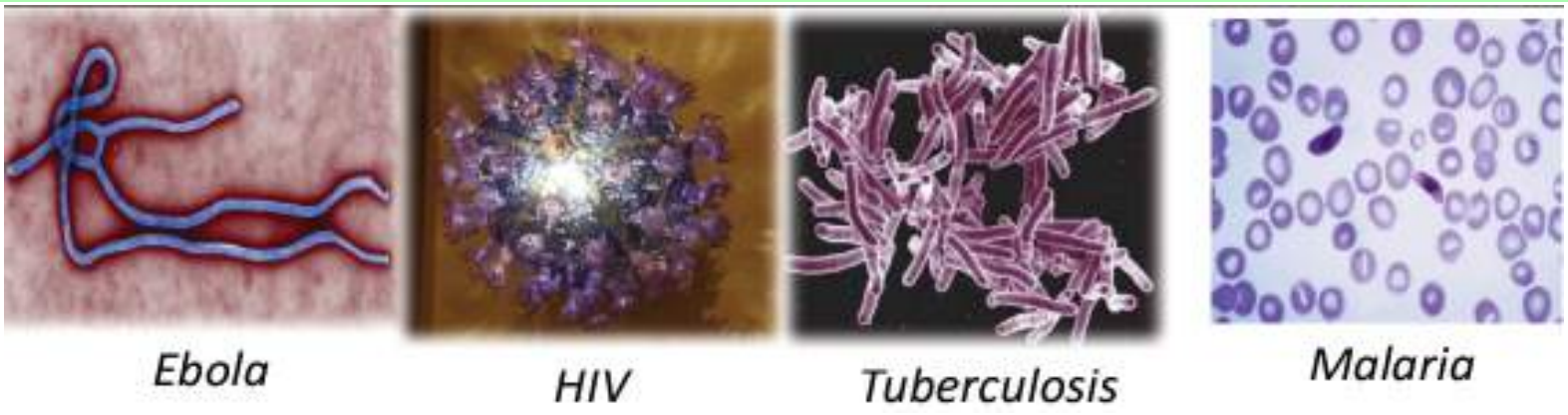
Infectious diseases: causative pathogen

- **Micro-organisms**
  - Small, often single cells organisms
  - Short generation time
  - Attain large populations within hosts
  - Dynamic unit is host infection/immune status



Infectious diseases: causative pathogen

Macro-organisms

- large
- multiicellar
- complex life cycles
- Dynamic unit of interest is the parasite burden
- e.g., nematodes, trematodes, ectoparasites and fungi.

Nematodes

hookworm

Trematodes

Schistosoma mansoni

Ectoparasites

western blacklegged tick

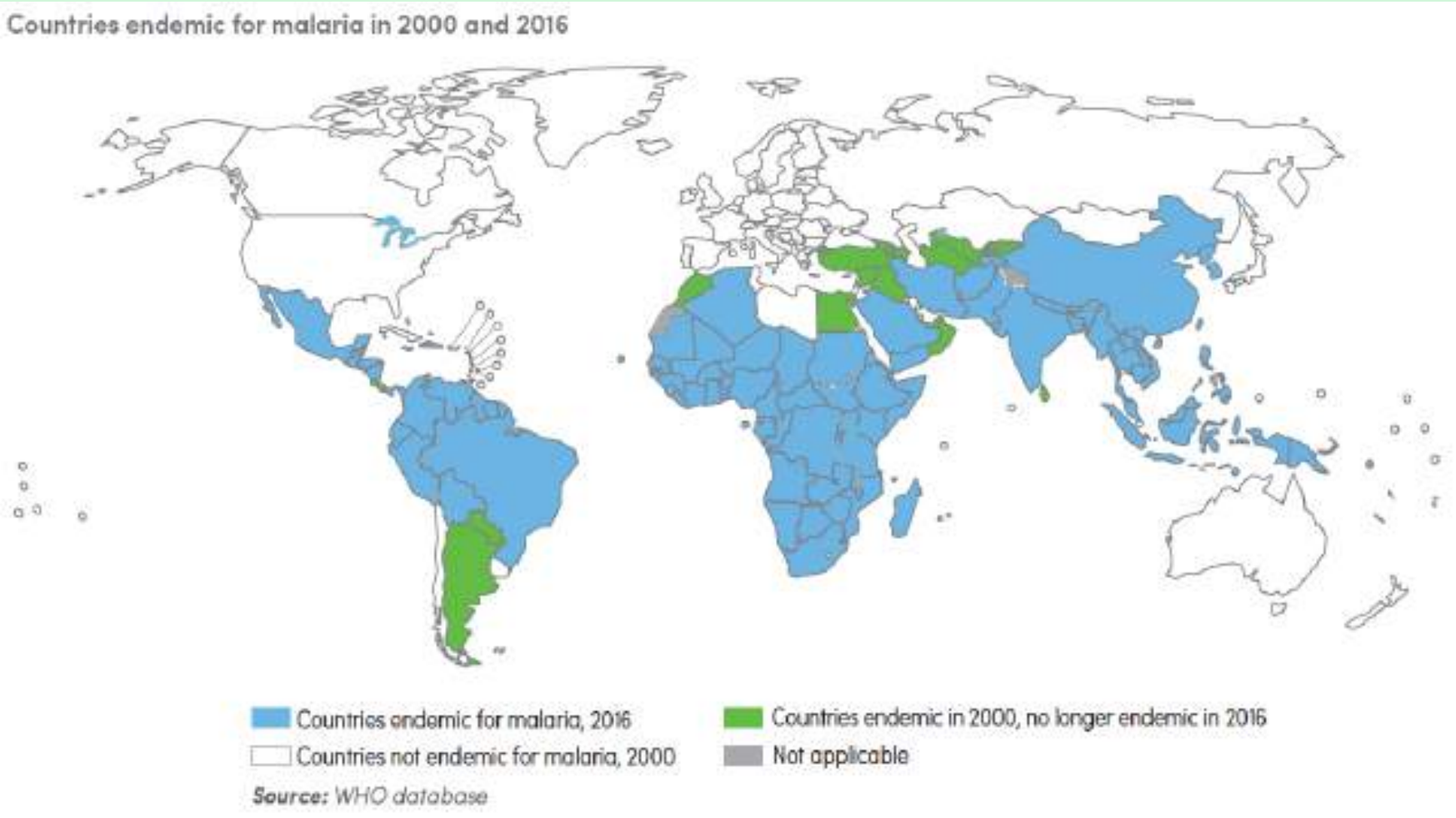
Infectious diseases: impact

- Have been natural enemies of humans for long
- Account for over 25% of mortalities worldwide
- Account for about 75% of mortalities among world poorest populations

Infectious diseases: impact

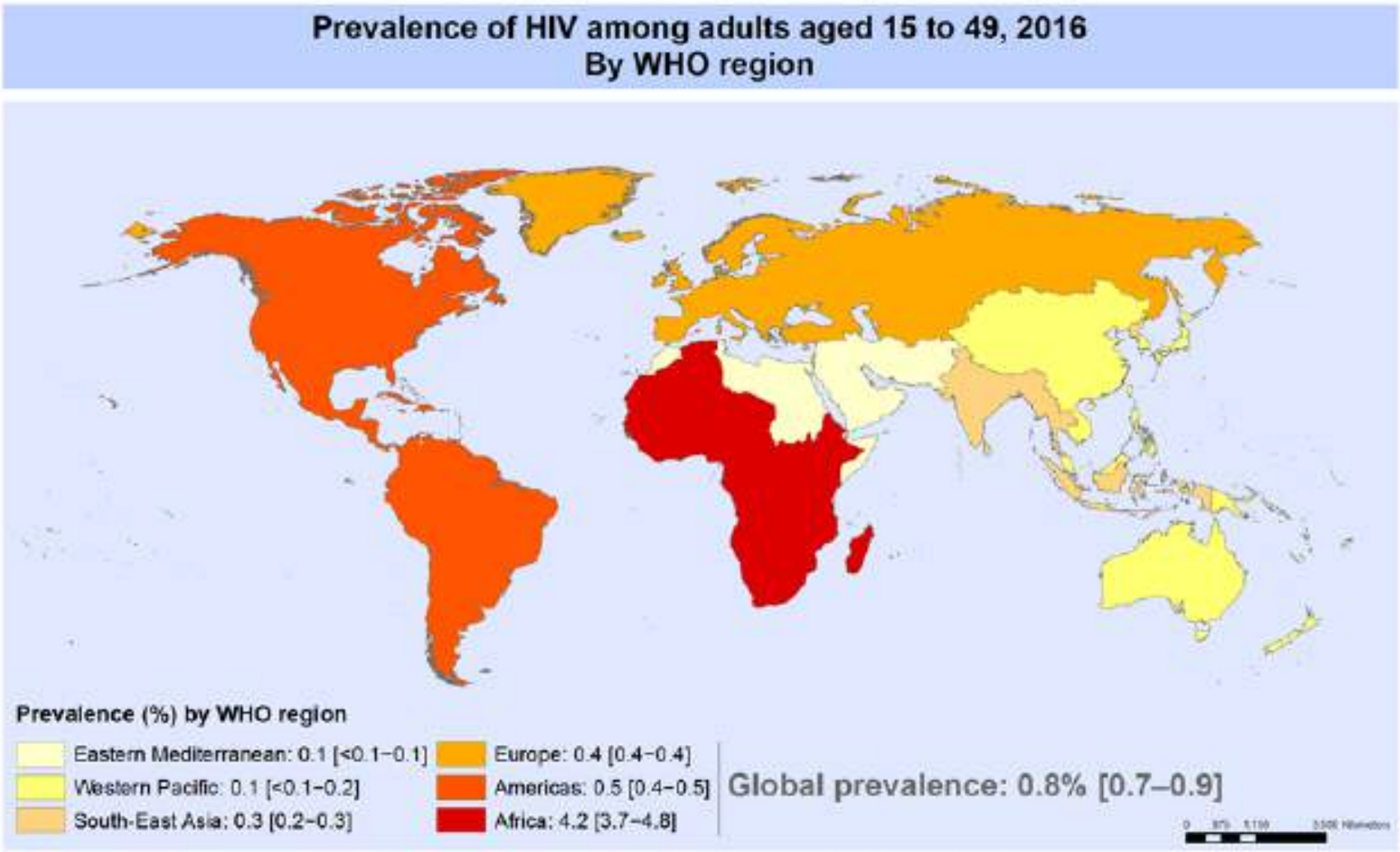
Example: Malaria

- 212 million cases and 438 thousand deaths in 2015
- 92% of mortalities in Africa
- 70% of mortalities among children under 5



Infectious diseases: impact

Example: HIV



Infectious diseases

- Hope to bury infectius disease burden by the 20th century impeded by:
  - Emergence of new diseases, e.g., HIV
  - Re-emergence of diseases, e.g., tuberculosis and malaria
  - Emergence of drug-resistance
  - Infectious disease emergence (often of zoonotic origin)
  - Climate change and environmental deterioration
  - Globalization

Epidemiological disease patterns

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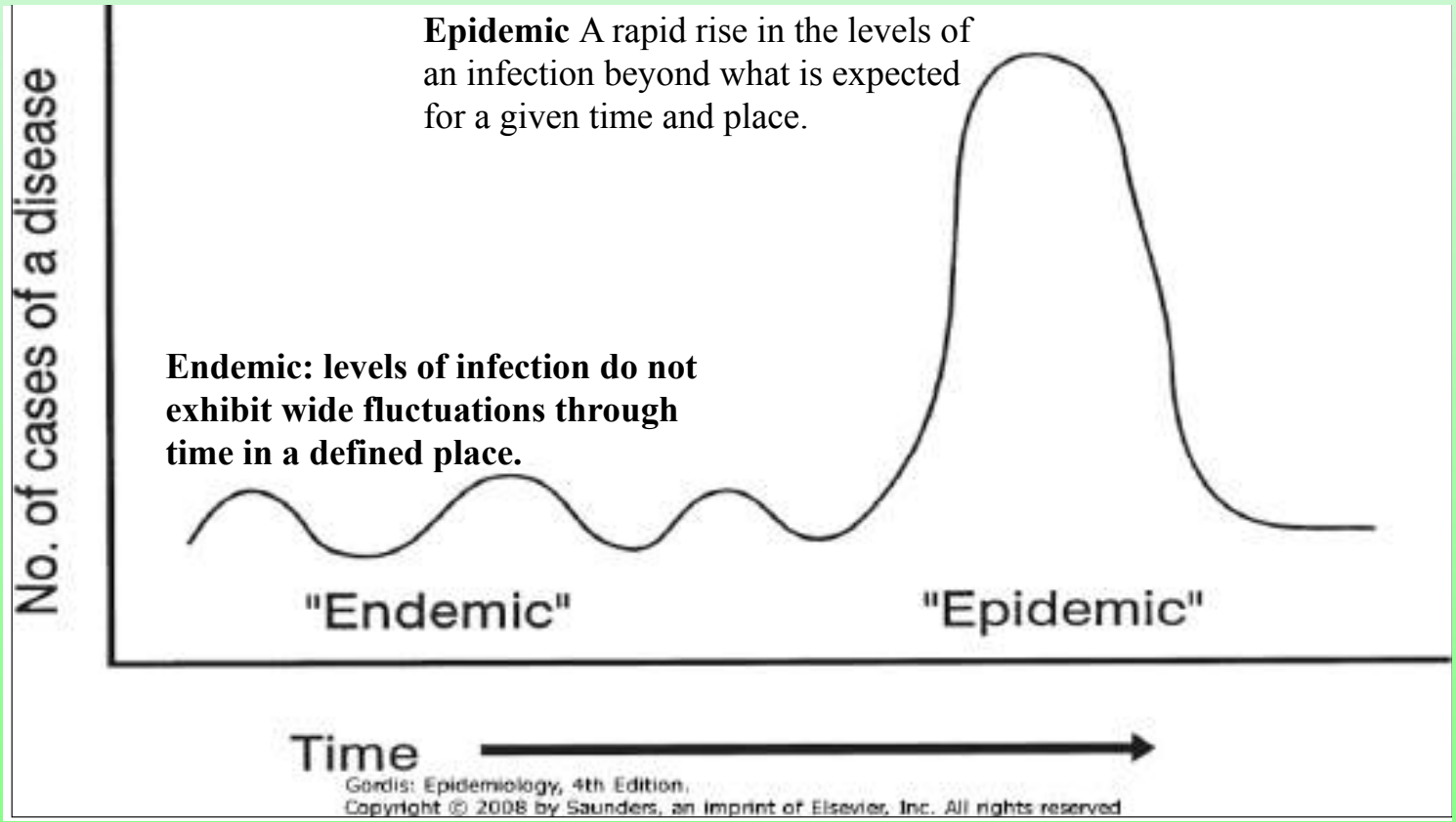

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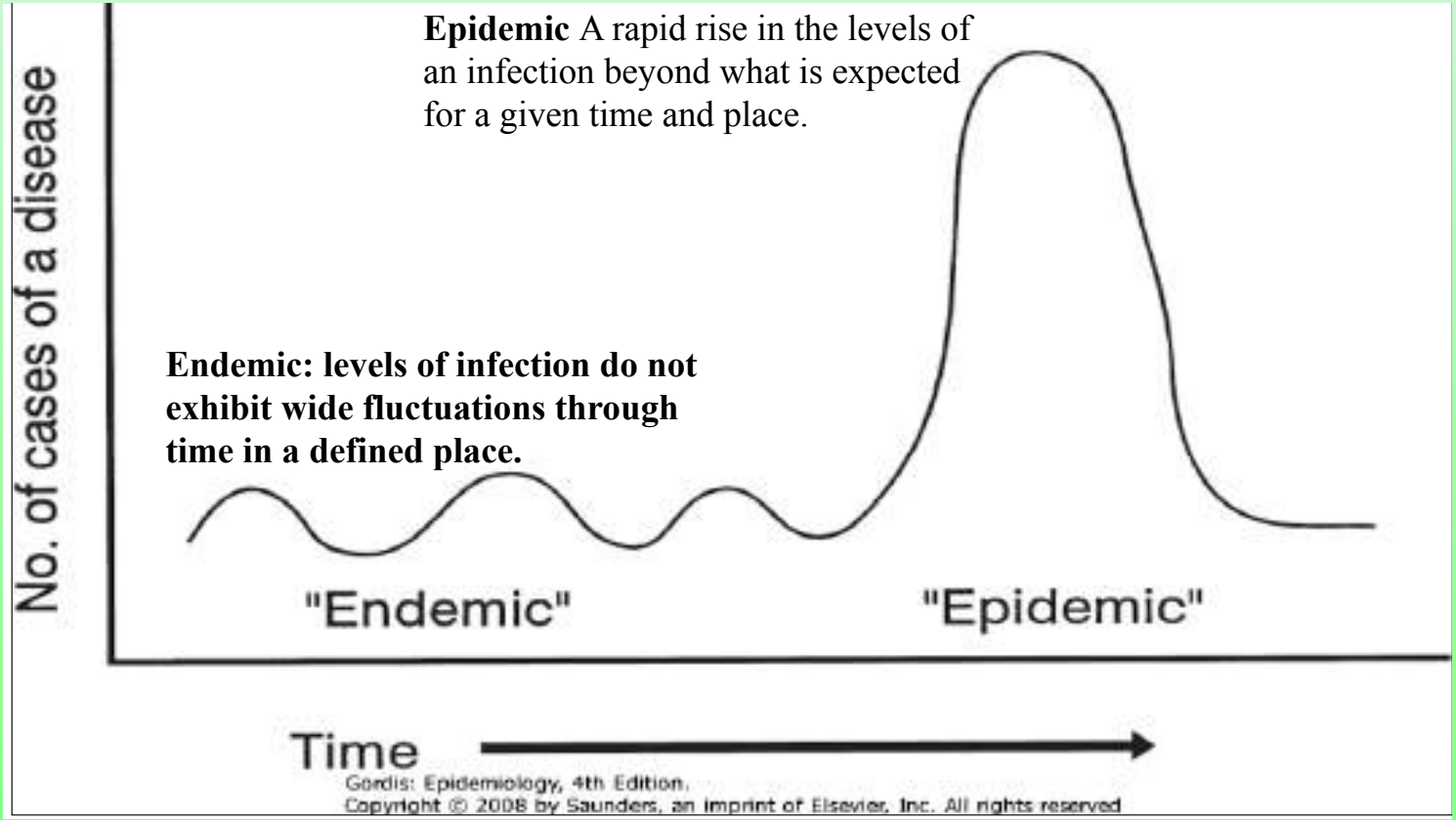

Incidence versus prevalence

- **Incidence**: Number of new cases at a given time (emergent rate)
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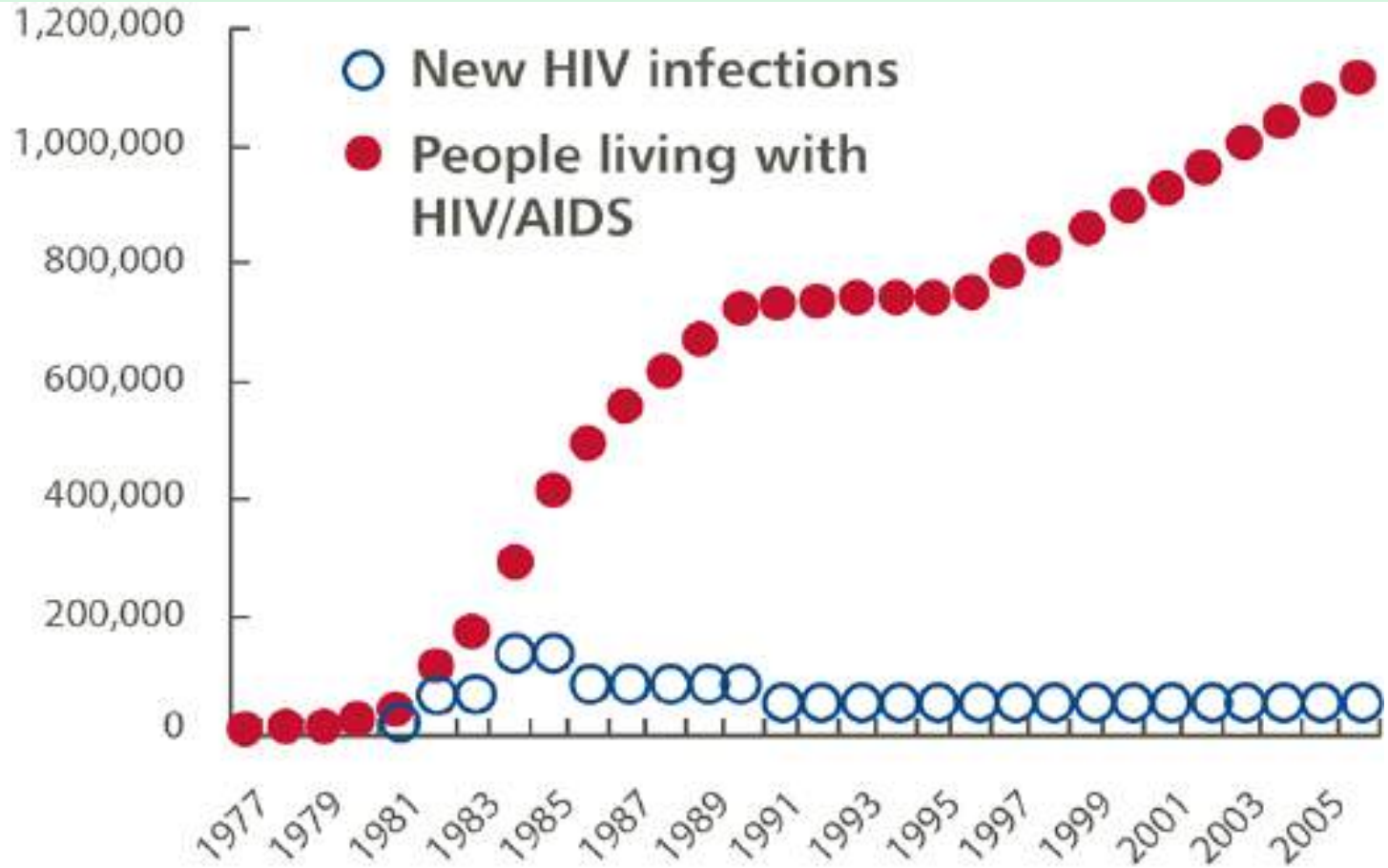

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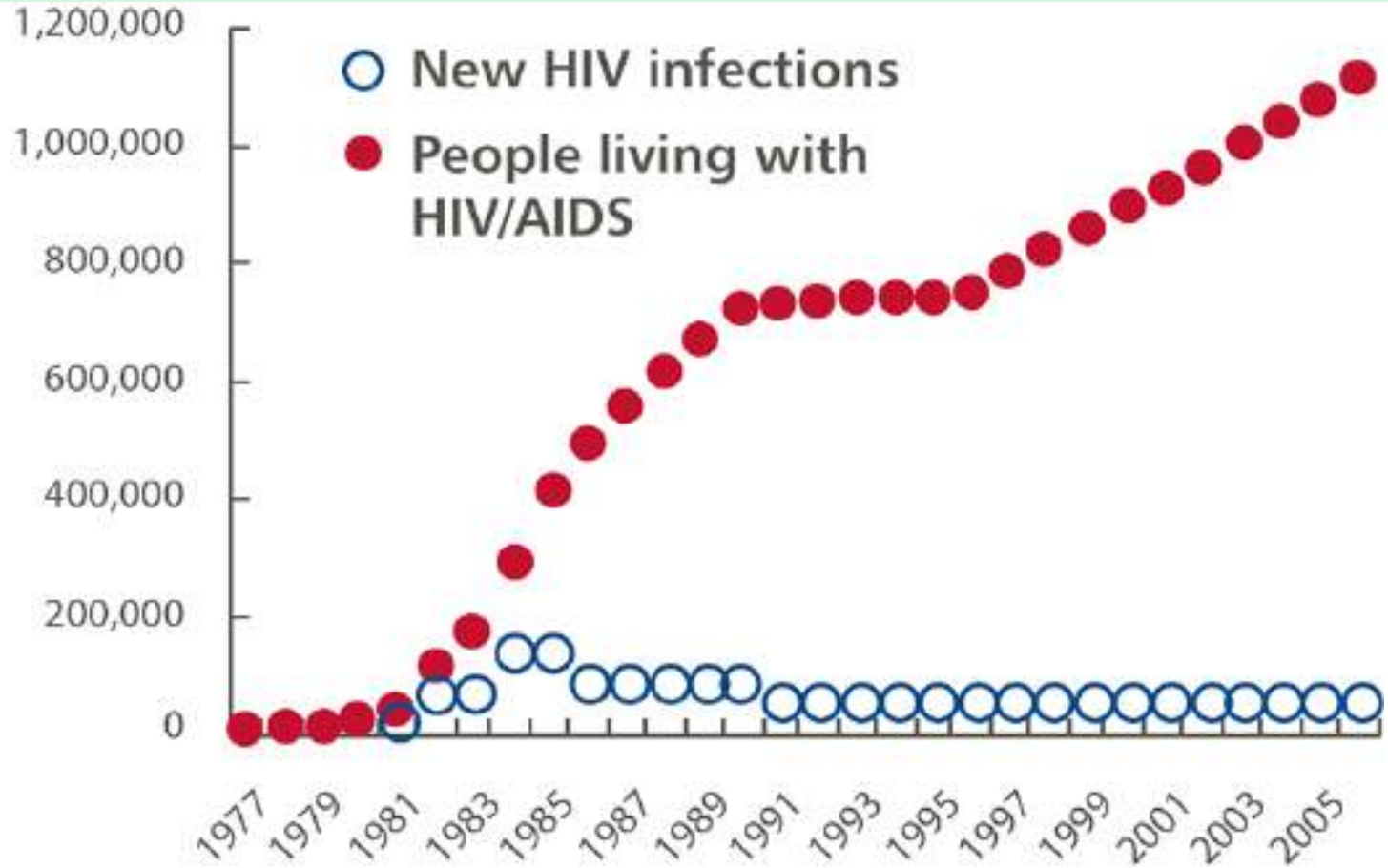

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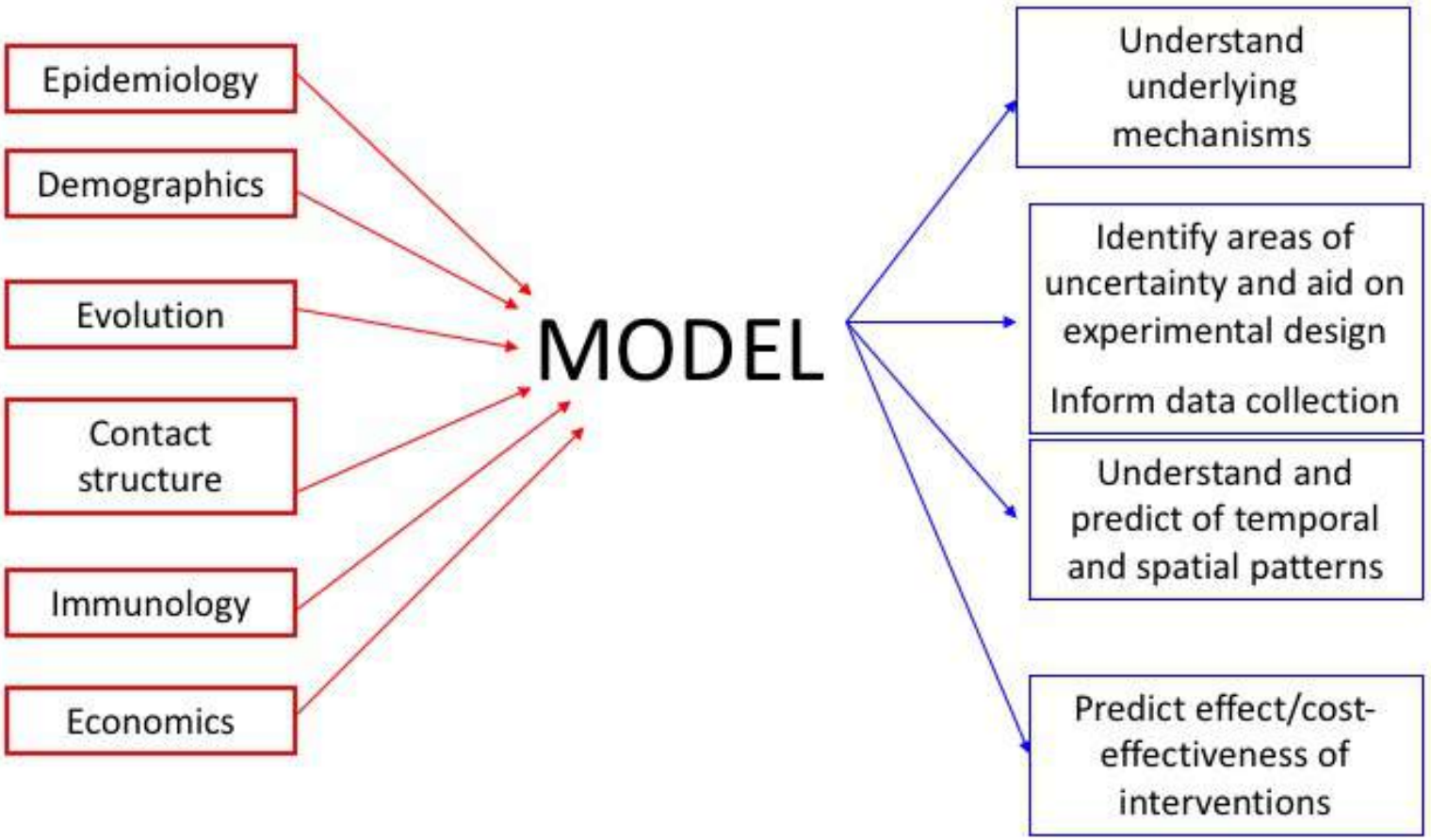
Infectious disease modeling

Represent systems or hypotheses in a mathematical/statistical language
Use mathematical/statistical techniques to study, test, and improve models

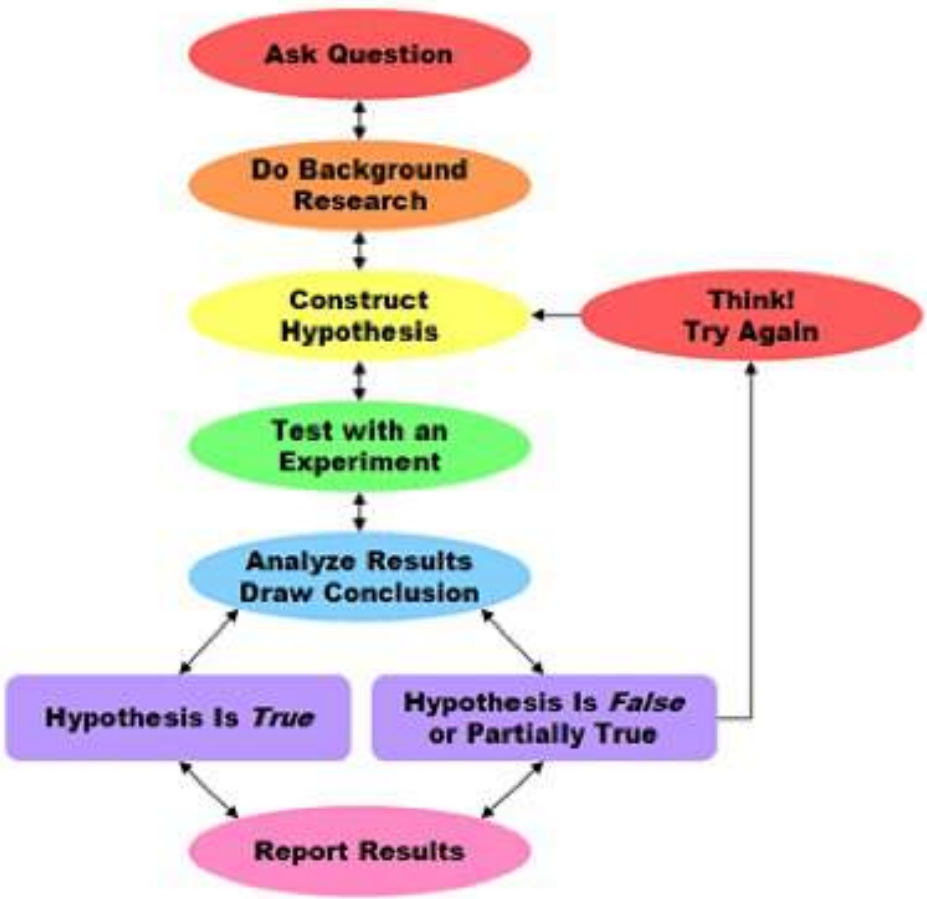


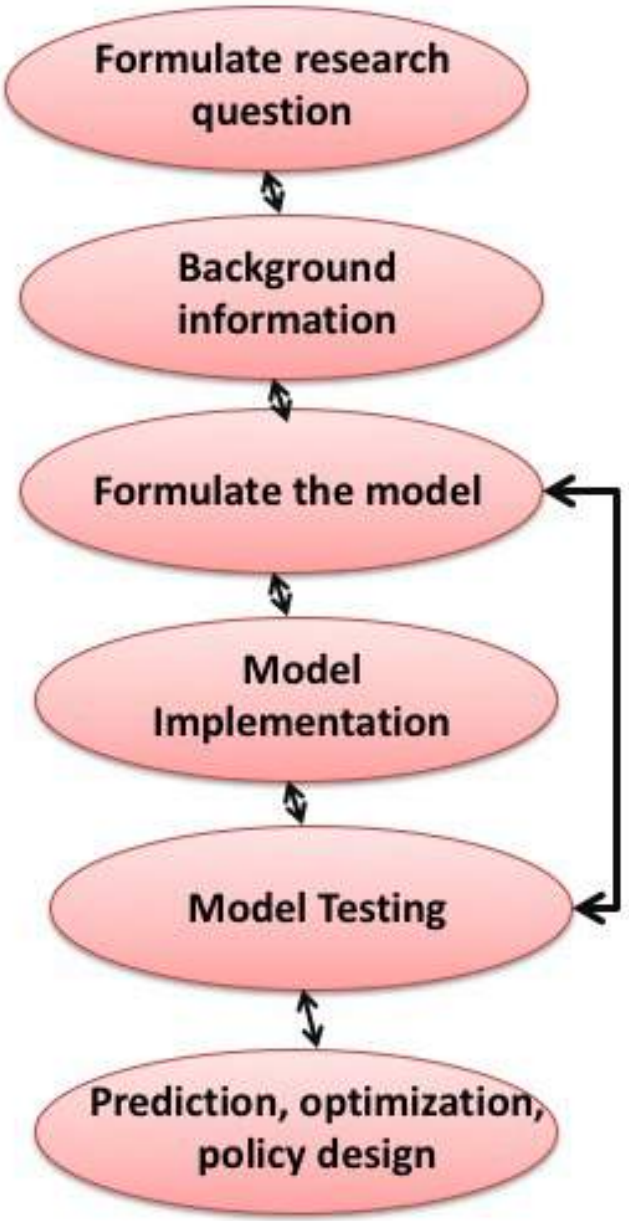
Why model infectious diseases?

Mathematical models provide quantitative and qualitative frameworks for linking different disease states of interest.

- Provide insights on the complex processes and interactions underlying disease-spread across time and space
- Plan for outbreaks (predict the time course and impact of an outbreak)
  - Speed of spread, e.g., timing of an outbreak
  - Severity, e.g., size of epidemic
- Identify areas of uncertainty where new knowledge is required
- Inform the collection of data
- Explore the efficacy of control interventions

Scientific approach versus modeling





Infection and disease timeline

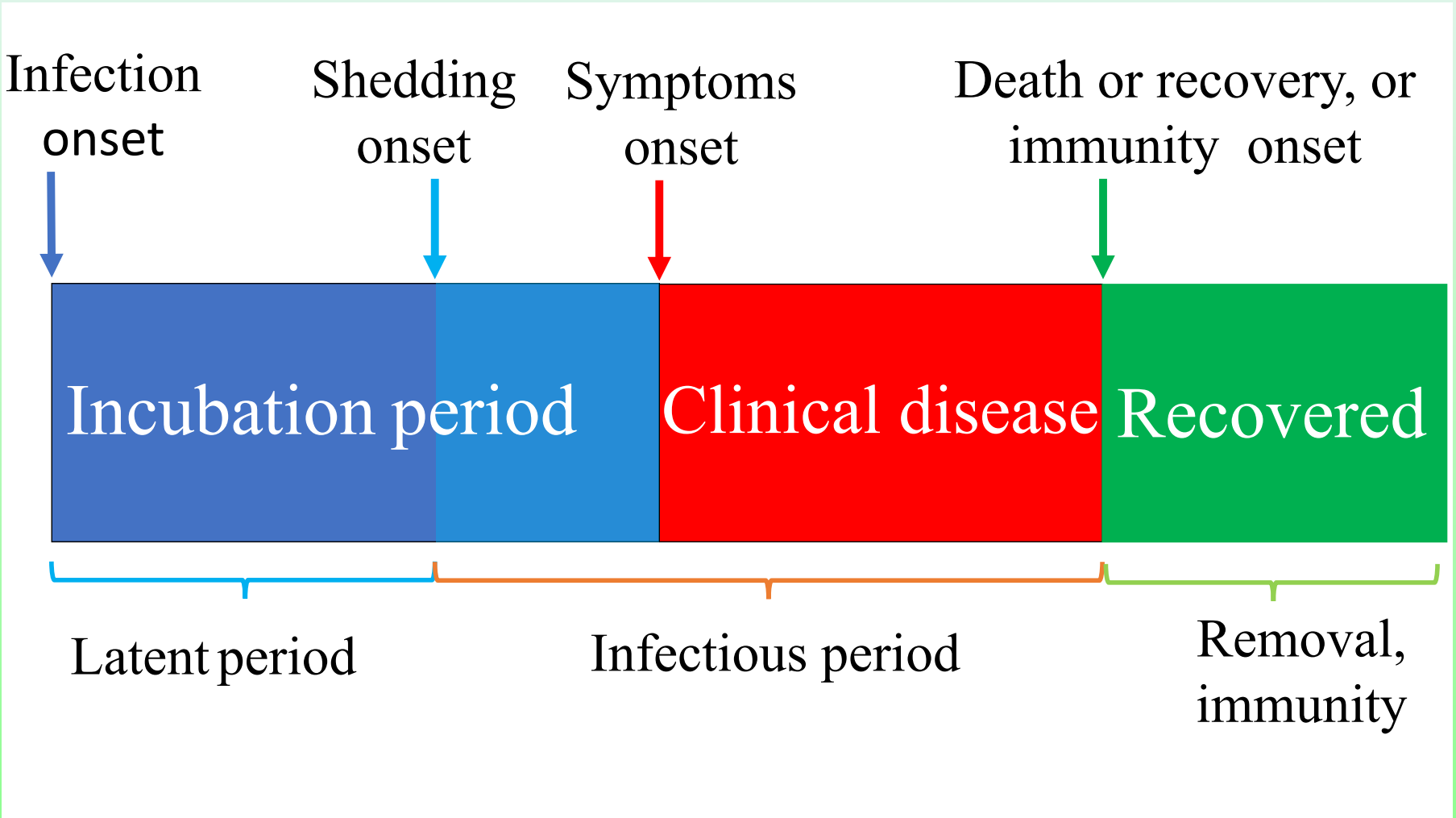


Table 3.1 Incubation, latent and infectious periods (in days) for a variety of viral and bacterial infections. Data from Fenner and White (1970), Christie (1974), and Benenson (1975)

Infectious disease	Incubation period	Latent period	Infectious period
Measles	8–13	6–9	6–7
Mumps	12–26	12–18	4–8
Whooping cough (pertussis)	6–10	21–23	7–10
Rubella	14–21	7–14	11–12
Diphtheria	2–5	14–21	2–5
Chicken pox	13–17	8–12	10–11
Hepatitis B	30–80	13–17	19–22
Poliomyelitis	7–12	1–3	14–20
Influenza	1–3	1–3	2–3
Smallpox	10–15	8–11	2–3
Scarlet fever	2–3	1–2	14–21

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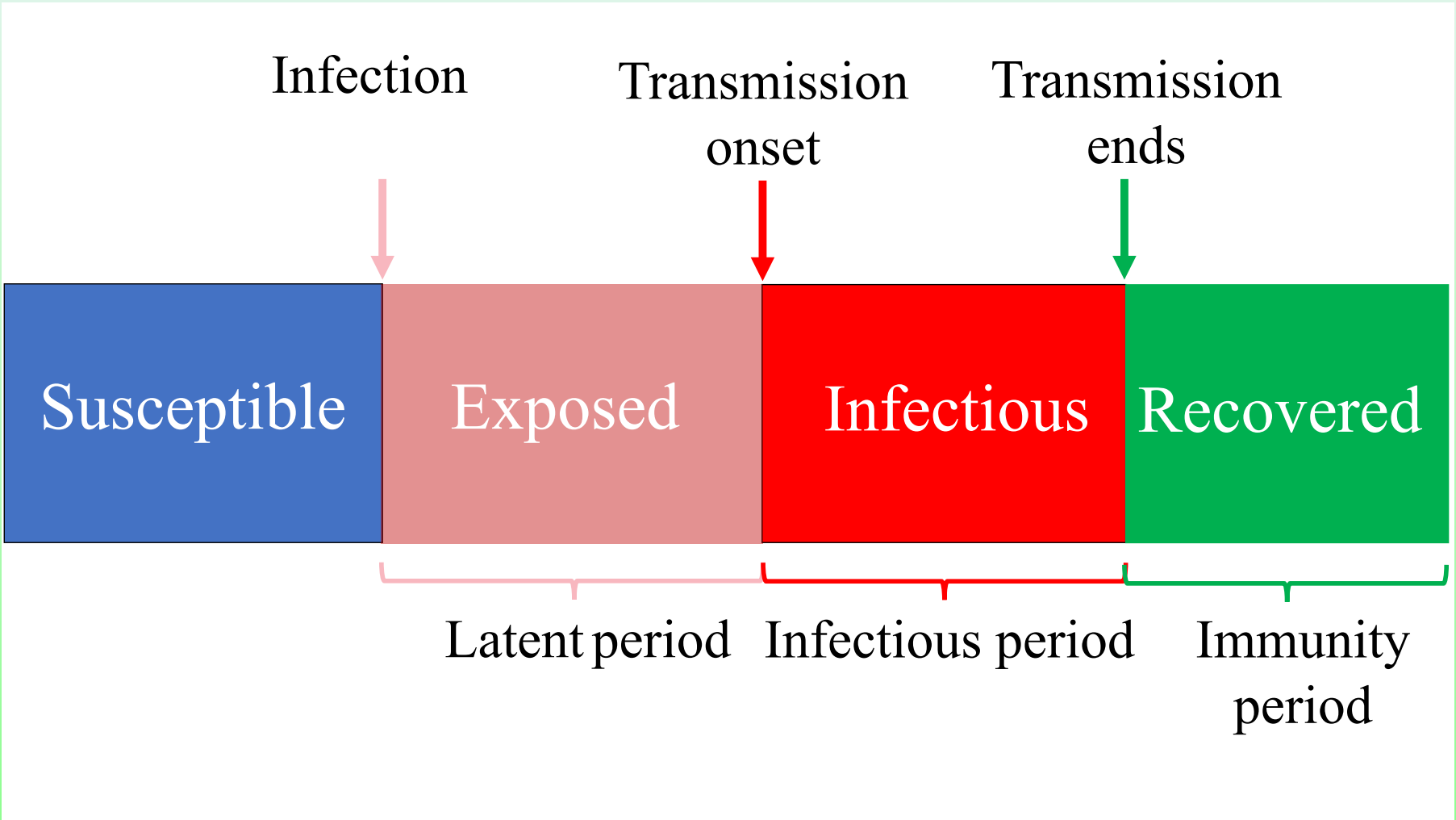
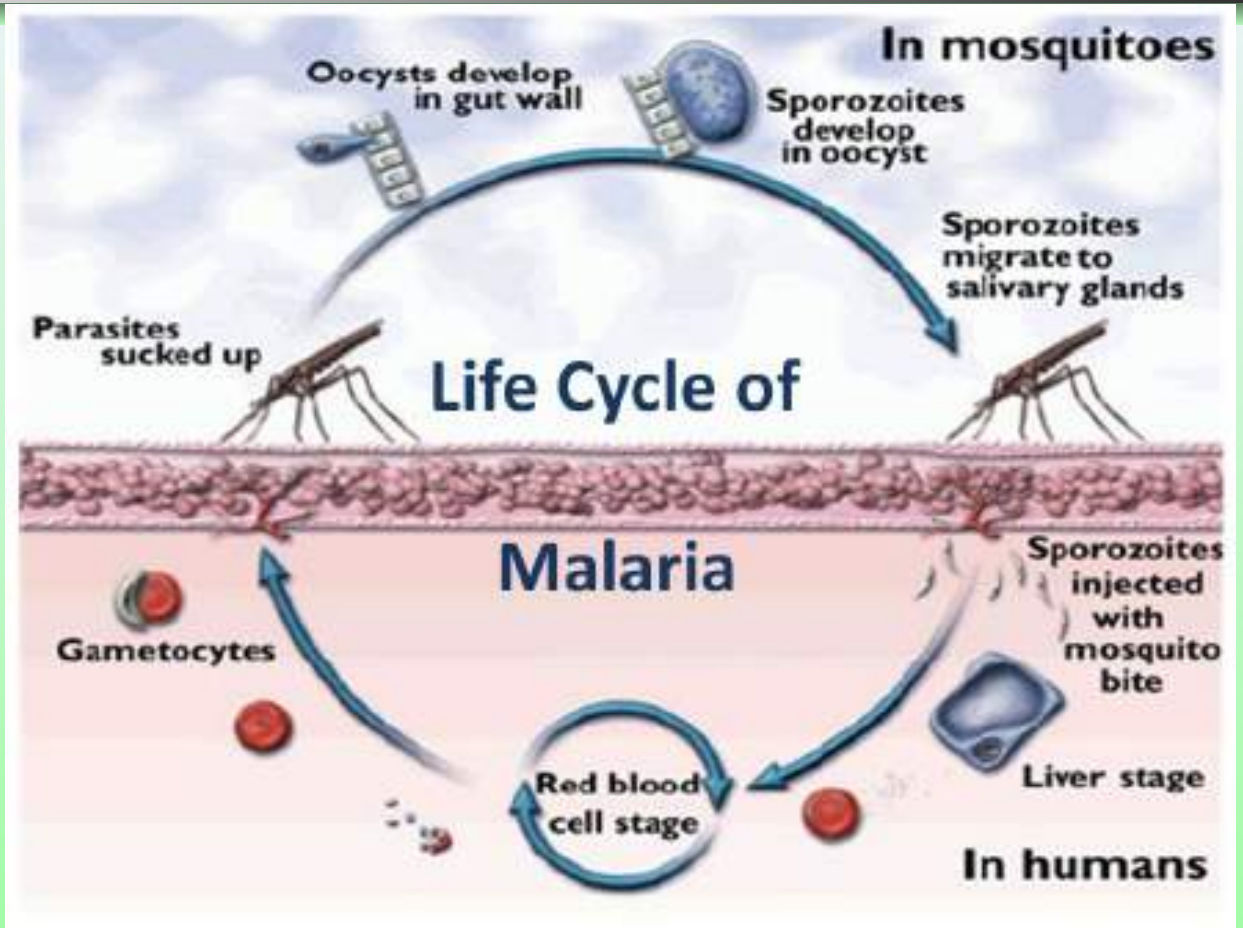


Classification of individuals: Infection status



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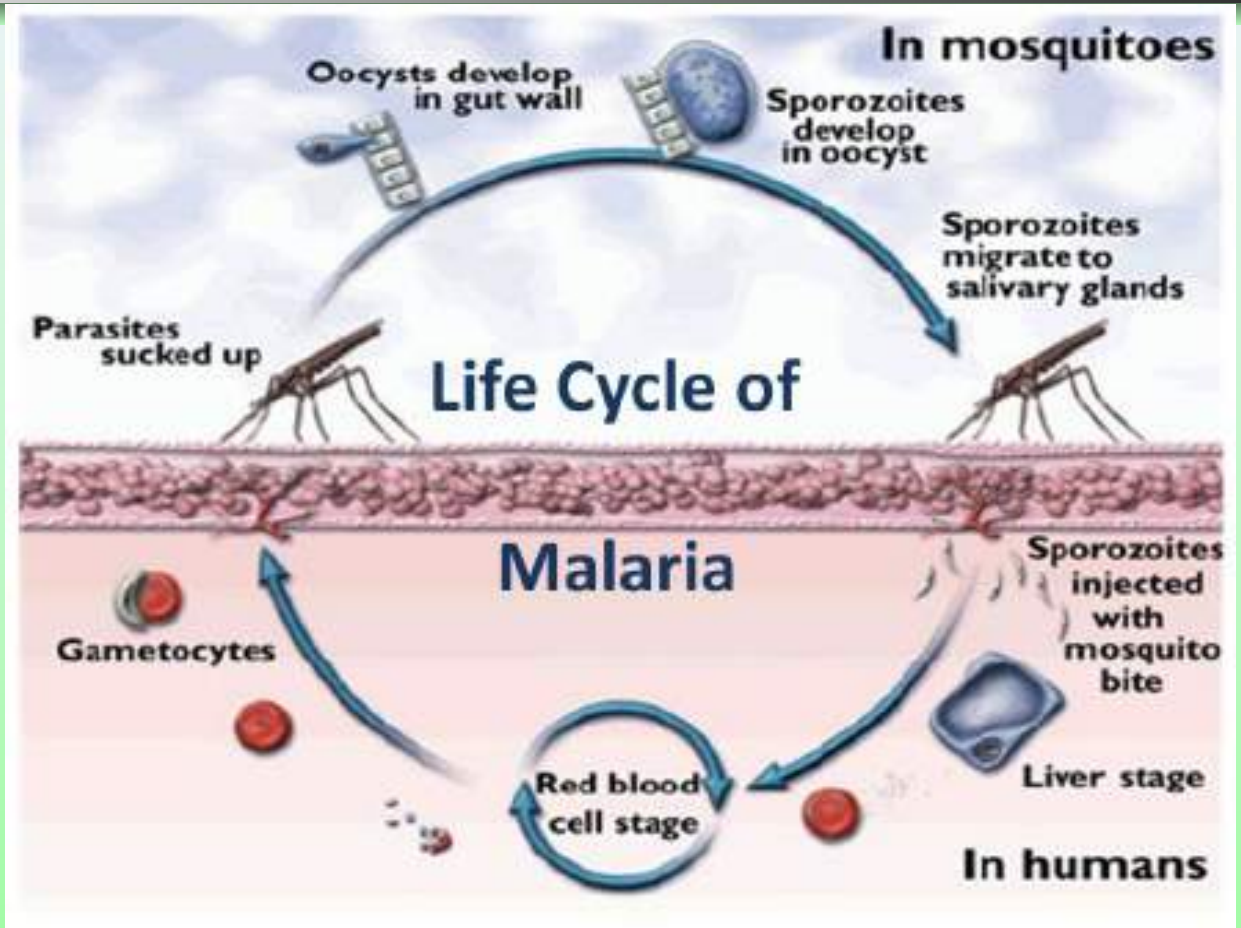

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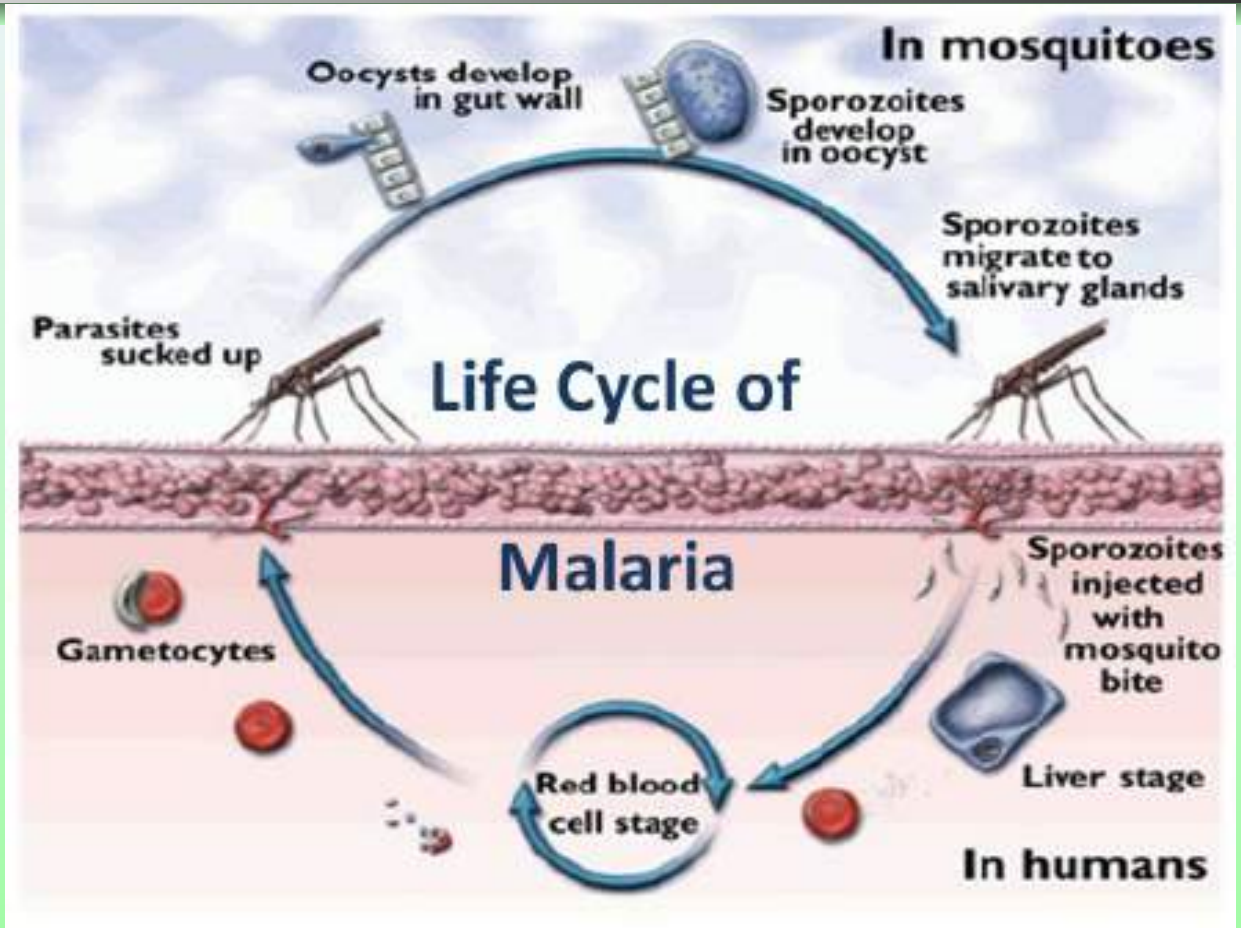

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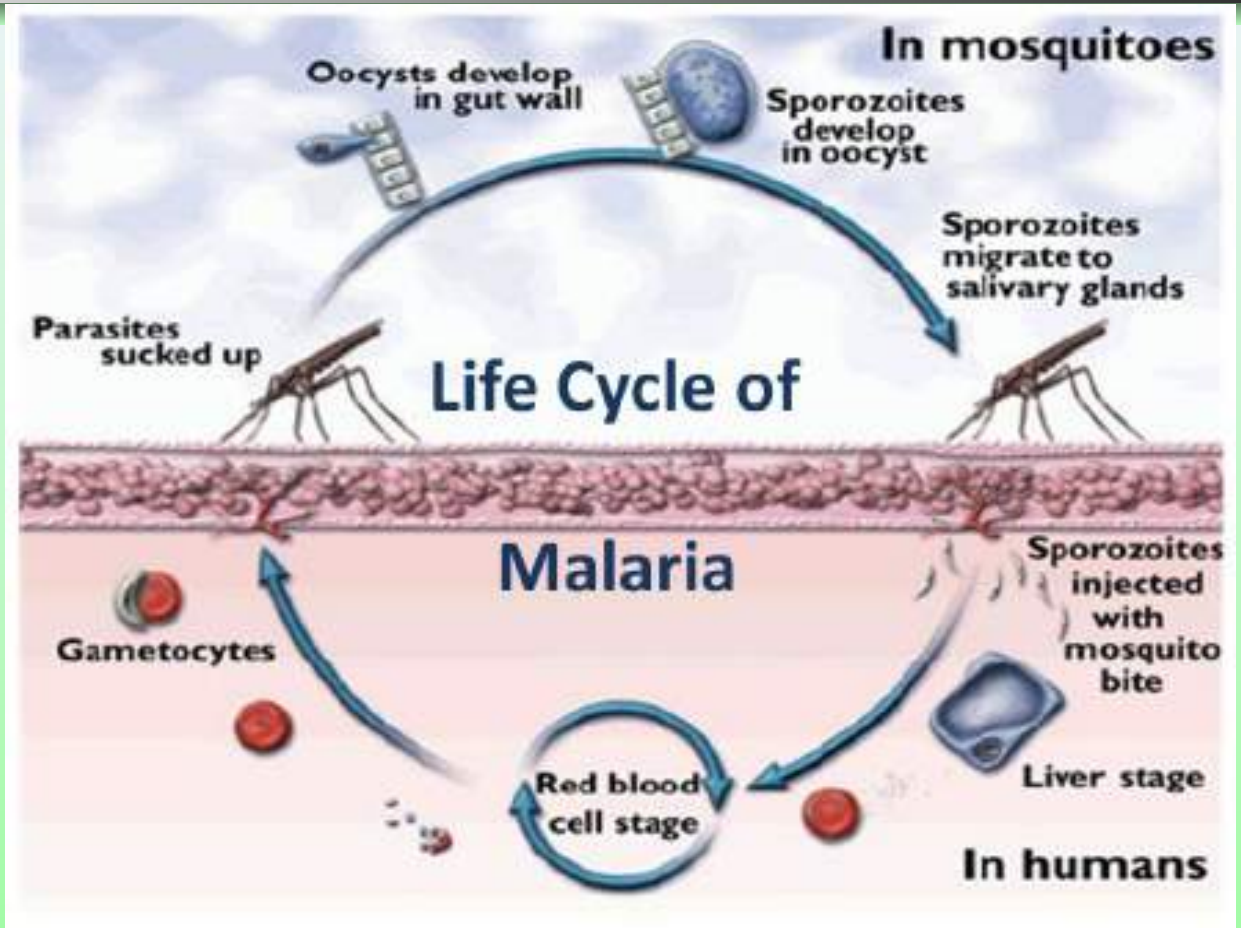

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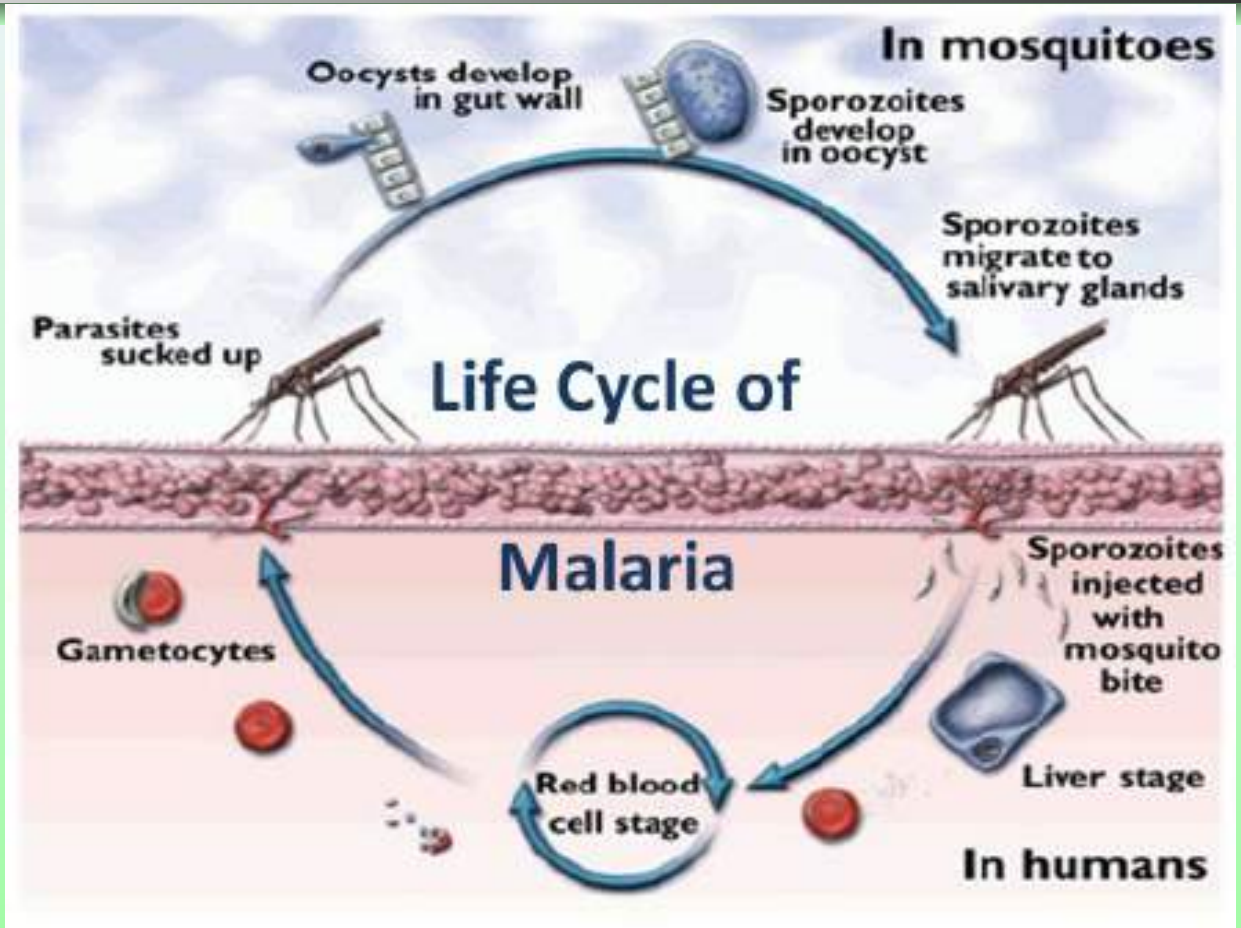

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What is required to contruct an infectious model

- **Infection and disease timeline data**
  - *Latent period*: time from infection to transmissibility
  - *Infectious period*: duration (and intensity) of shedding infectious stages
  - *Duration of the immunity*: how long and how effective? etc.
- **Population data**
  - Population size and structure
  - Birth and death rates, survival, immigration and emigration
  - Rates of contact within and between population groups
- **Transmission mode**
- **Epidemiological data**
  - Transmissibility
  - density dependence, seasonality

Types of models

- **Statistical models** (regressions, time series)
  - Explore correlations and patterns in data
  - Examples
    - Univariate linear models
    - Multivariate linear models
    - Generalized linear models
    - Generalized linear and mixed models, etc.
- **Dynamic models**: Explore processes that evolve with time
  - Deterministic: No randomness
  - Stochastic: Randomness is important, explore outcomes, obtain distributions of outcomes.
  - Network
  - Individual or agent based

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Further breakdown of dynamic models

Continuous versus discrete models

- **Continuous time, deterministic dynamics**: Ordinary and partial differential equations
- **Discrete time, deterministic dynamics**: Difference equations, e.g., Reed-Frost type models
- **Continuous time, stochastic dynamics**: Continuous time Markov chains, stochastic differential equation.
- **Discrete time, stochastic dynamics**: Discrete time Markov chains

Deterministic models

- Deterministic progression
  - Same outcome for same parameters and initial conditions
- Useful for a quick assessment of possible model outcomes and when there is limited data
- Relies on simplifying assumptions that must be tracked
  - Assumes large populations. Can be misleading for small populations
  - Assumes constant rates. Can fail to reproduce important (observed) dynamics for variable rates
  - Homogeneity within compartments

What kind of model do I need?

It depends on the question you want to answer

Epidemic theory simulation

VIDEO: The model

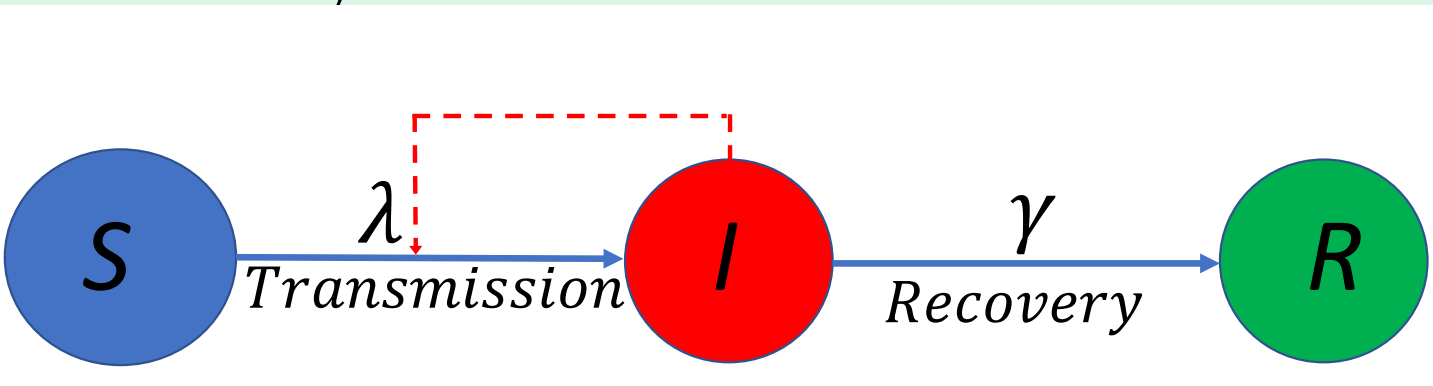
VIDEO: Proof

Model formulation

- **Compartmental models**: Individuals are subdivided into broad subgroups (compartments) and the model tracks changes overtime for these individuals collectively.
- **Variables**: Entities that change overtime)
  - Susceptible (S)
  - Infectious (I)
  - Recovered (R)
- **Parameters**: Contact and transition rates

The SIR compartmental model: epidemic model

- Describe outbreaks
- Considers only flows related to the infection



- λ: Force of infection (per capita transmission rate)
- γ: Per capita recovery rate
- $1/\gamma$: Average duration of infection

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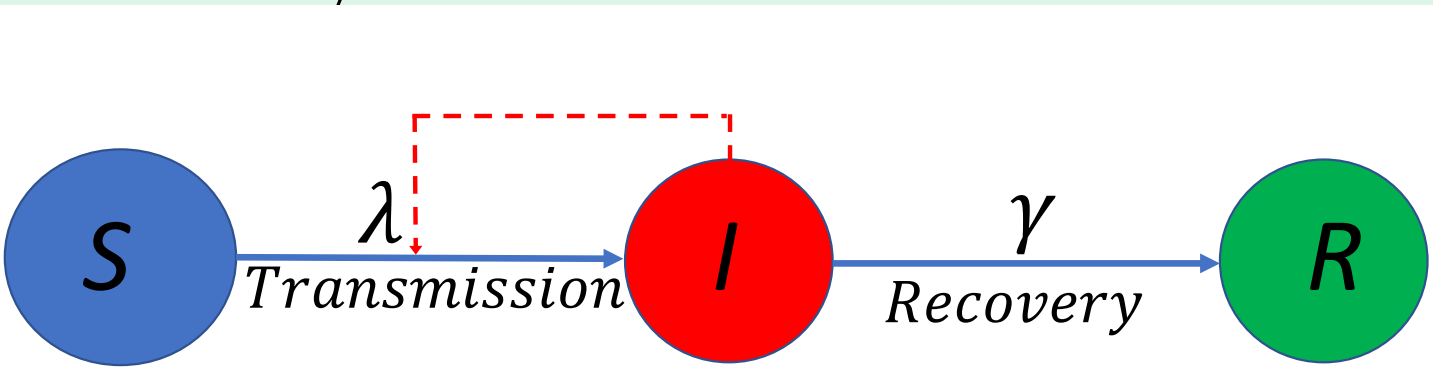

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Change in susceptibles : $\frac{dS}{dt} = -transmission$

Change in Infectious : $\frac{dI}{dt} = +transmission - Recovery$

Change in Removed : $\frac{dR}{dt} = +Recovery$

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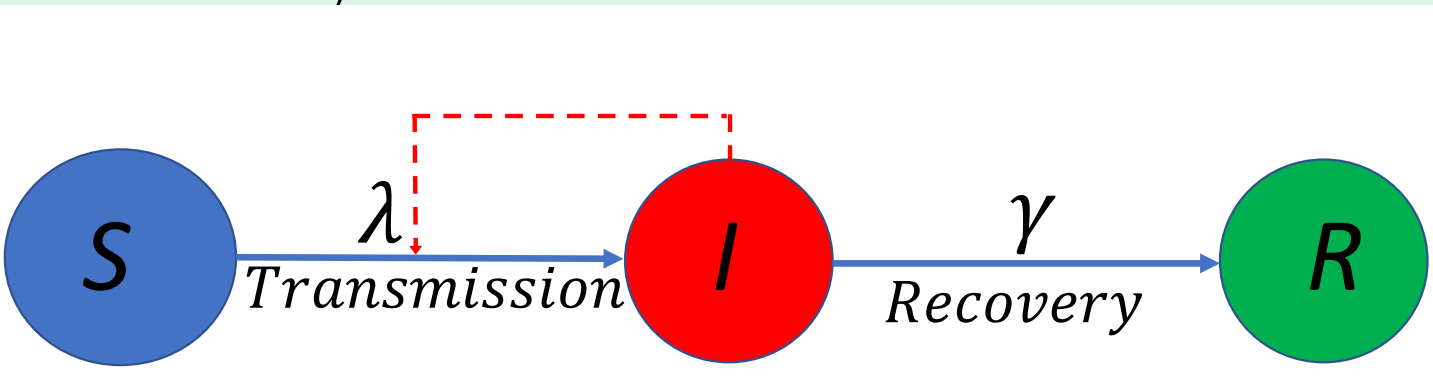

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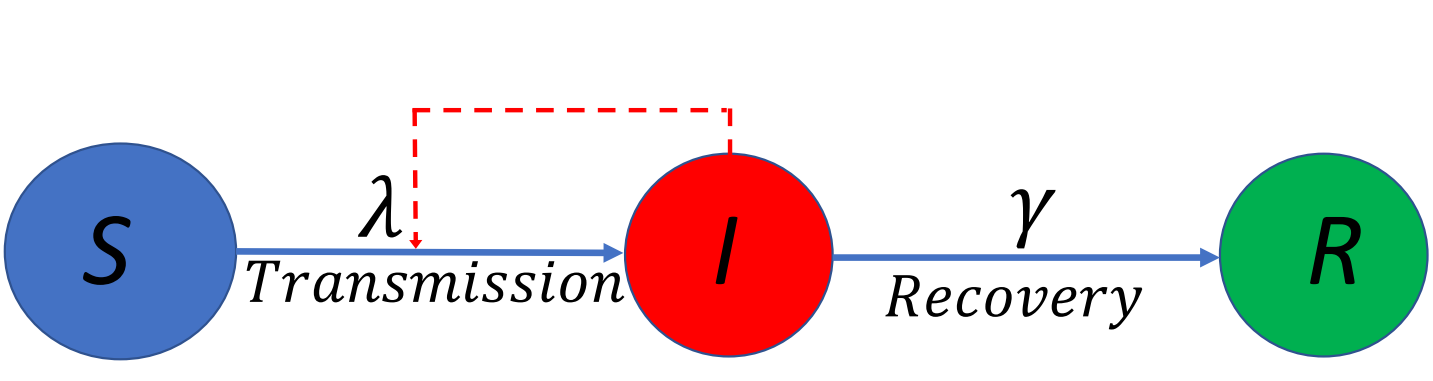

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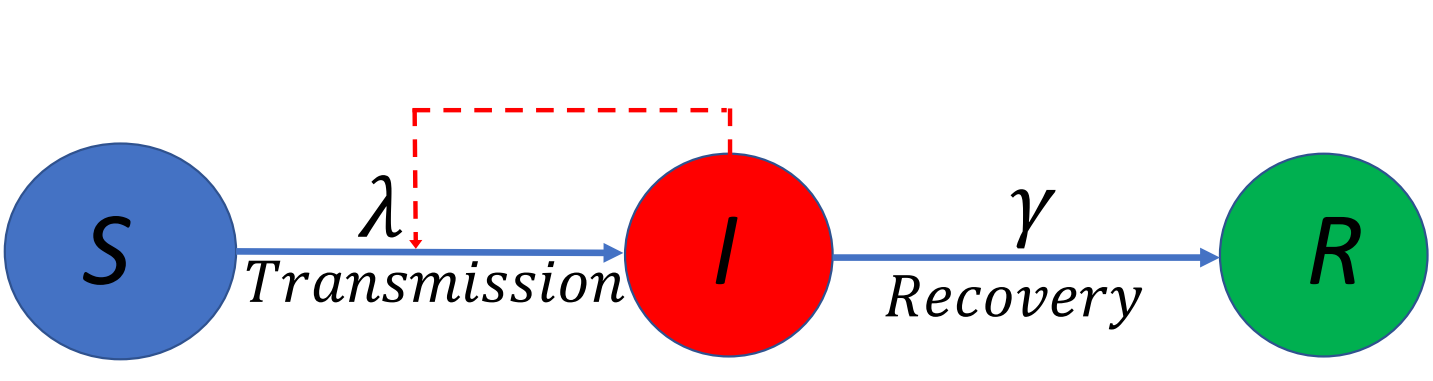

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- $\lambda = cpI = \beta I$

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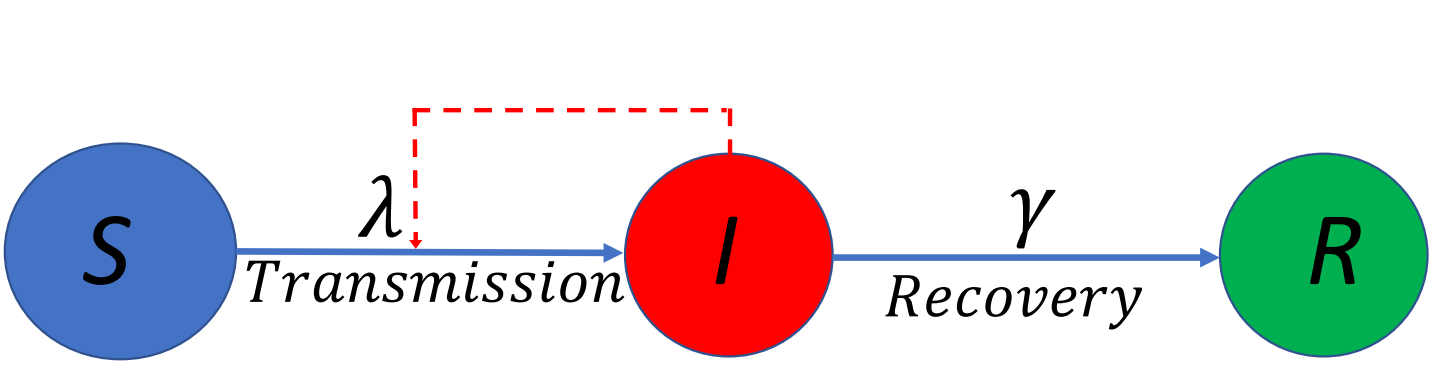

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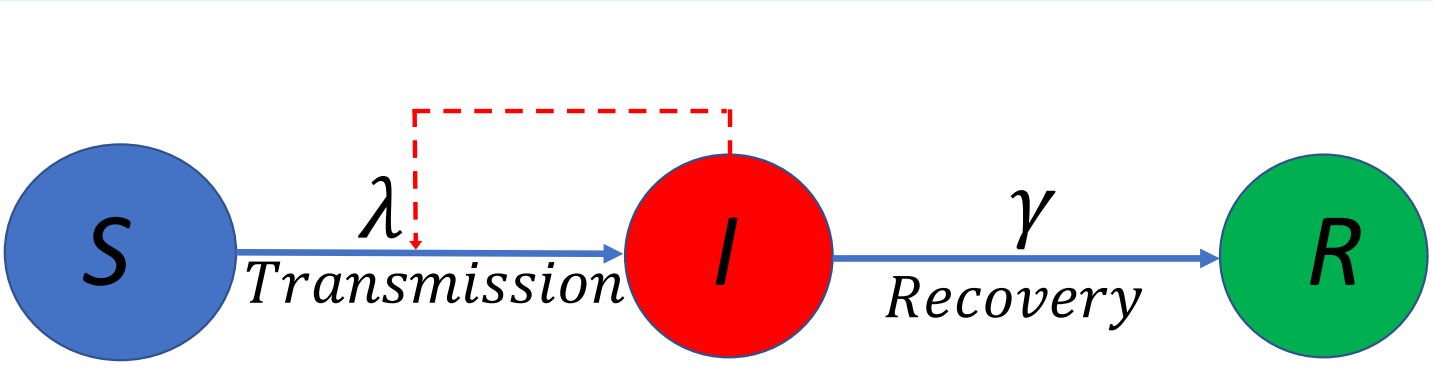

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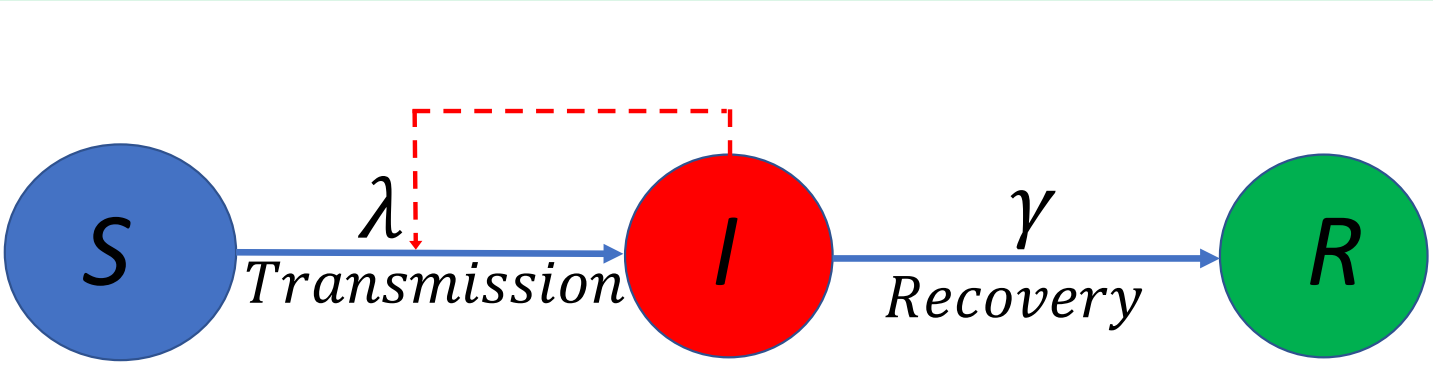

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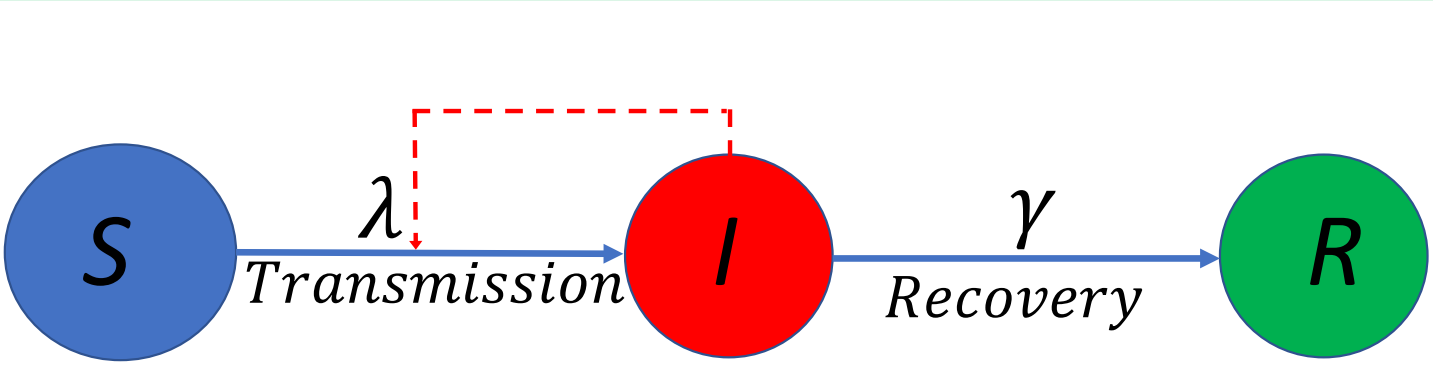

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  - Per capita force of infection rises with prevalence (frequency of infectives)
  - Assumes homogeneous mixing
- $\lambda = \beta \frac{I}{N}$

The SIR compartmental model

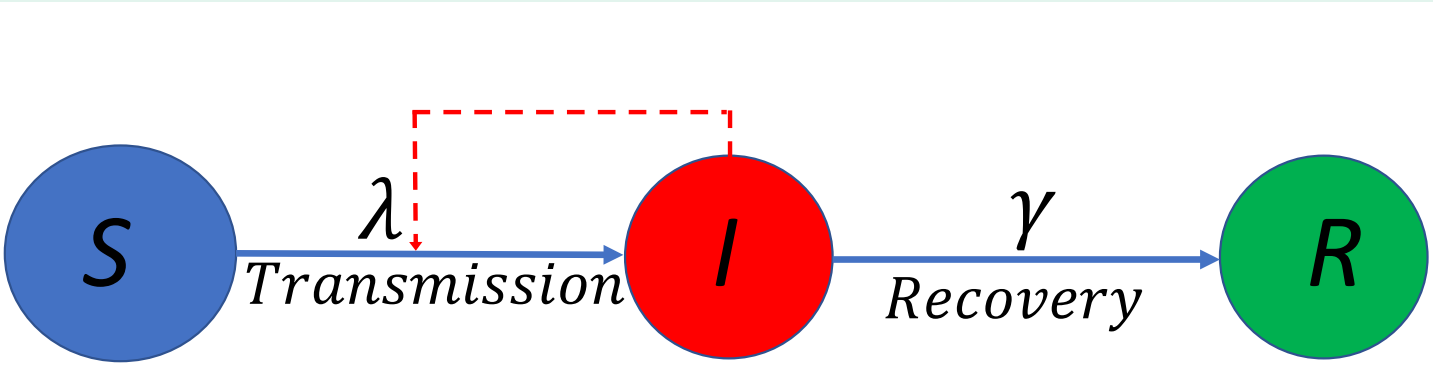
Table 1. Some proposed forms for the transmission function

Number	Function[a]	Comments	Ref
1	βSI	Mass action	4–7
2	$\beta SI/N$	Frequency-dependent transmission	13,
3	$\beta S^p I^q$	Power relationship; Constants: $0 < p < 1$, $0 < q < 1$. Phenomenological	23,
4	$\beta I (N - I/q)$; $I < qN$ 0; $I \geq qN$	Constant: $0 < q < 1$. Embodies a refuge effect (q = proportion of the population potentially susceptible, because of spatial or other heterogeneities)	16,
5	$kS \ln\left(1+\frac{\beta I}{k}\right)$	Negative binomial. Small k corresponds to highly aggregated infection. As $k \to \infty$, expression reduces to βSI (mass action)	23,
6	$\frac{N}{1-\varepsilon+\varepsilon N}\frac{F(S,I)}{N}$	Asymptotic contact function separated from the mixing term $F(S,I)$, which may be any of those above. If constant $\varepsilon = 0$, contacts are proportional to N. If $\varepsilon = 1$, contacts are independent of N	28,
7	$\frac{\beta SI}{c+S+I}$	Asymptotic transmission. c is a constant	4,3

[a] I is the density of infected hosts, S is the density of susceptible hosts, and N is the total host density. β is the transmission rate. Other parameters, where necessary, are identified under comments.

McCallum et al. *Trends Ecol Evol* 16: 295-300 (2001)

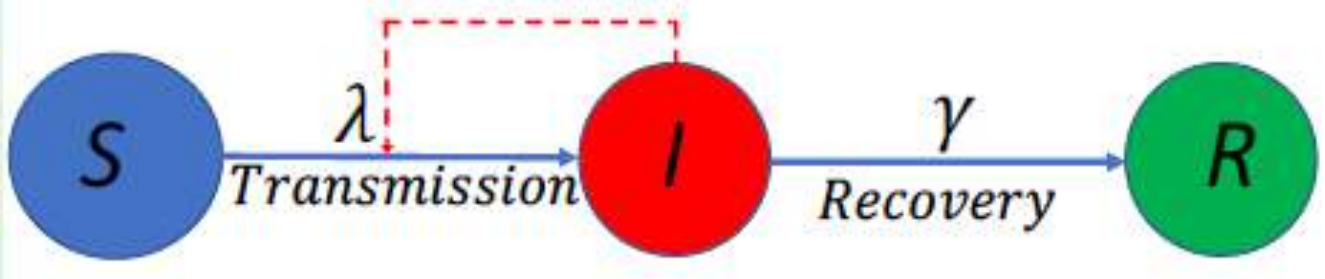
The SIR epidemic model



Basic assumptions

- Closed population (no demography). Realistic for a quick disease of short duration
- Homogeneous mixing
- Disease confers life-long immunity (realistic for certain diseases,e.g., acute diseases like measles)
- Infected individuals are also infectious
- Rates remain constant

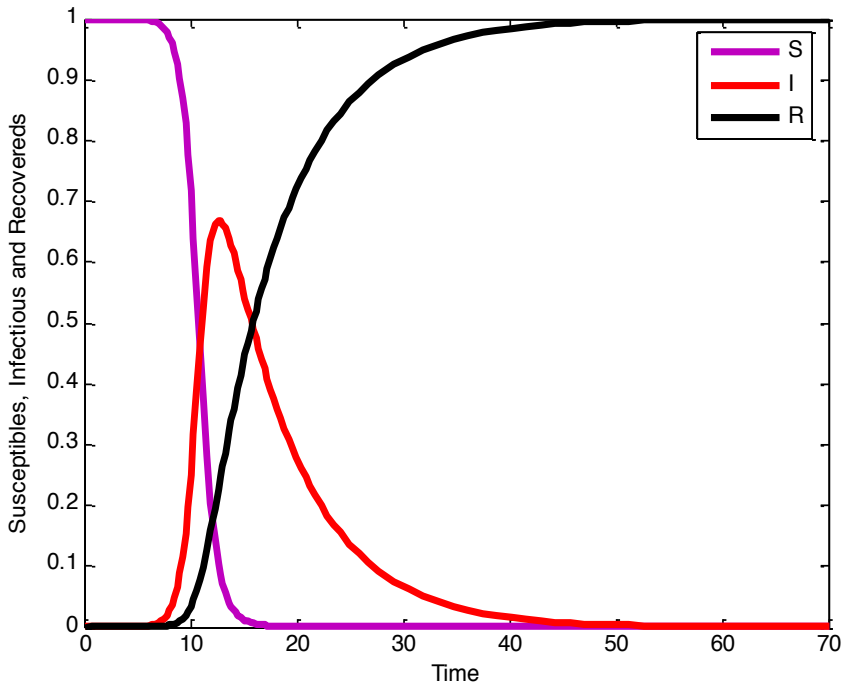
The SIR epidemic model



$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$



SIR epidemic model

- **Threshold phenomenon**
  - $I(0)$ infectious introduced into a population of $S(0)$ susceptible individuals
  - Equation for infectious: $\frac{dI}{dt} = \beta IS - \gamma I = \beta I(S - \frac{\gamma}{\beta})$
  - What happens if $S(0) > \gamma/\beta$?
  - What happens if $S(0) < \gamma/\beta$?
  - "Threshold phenomenon" (Kermack and McKendrick, 1927): Initial proportion of susceptibles must be greater than a critical threshold for the disease to spread.
  - γ/β: relative removal rate – should be small enough to allow for disease invasion

- I starts increasing if

$$\dot{I}(0) = \beta I(0)(S(0) - \gamma/\beta) > 0$$

or

$$\beta S(0)/\gamma > 1$$

- I starts decreasing if

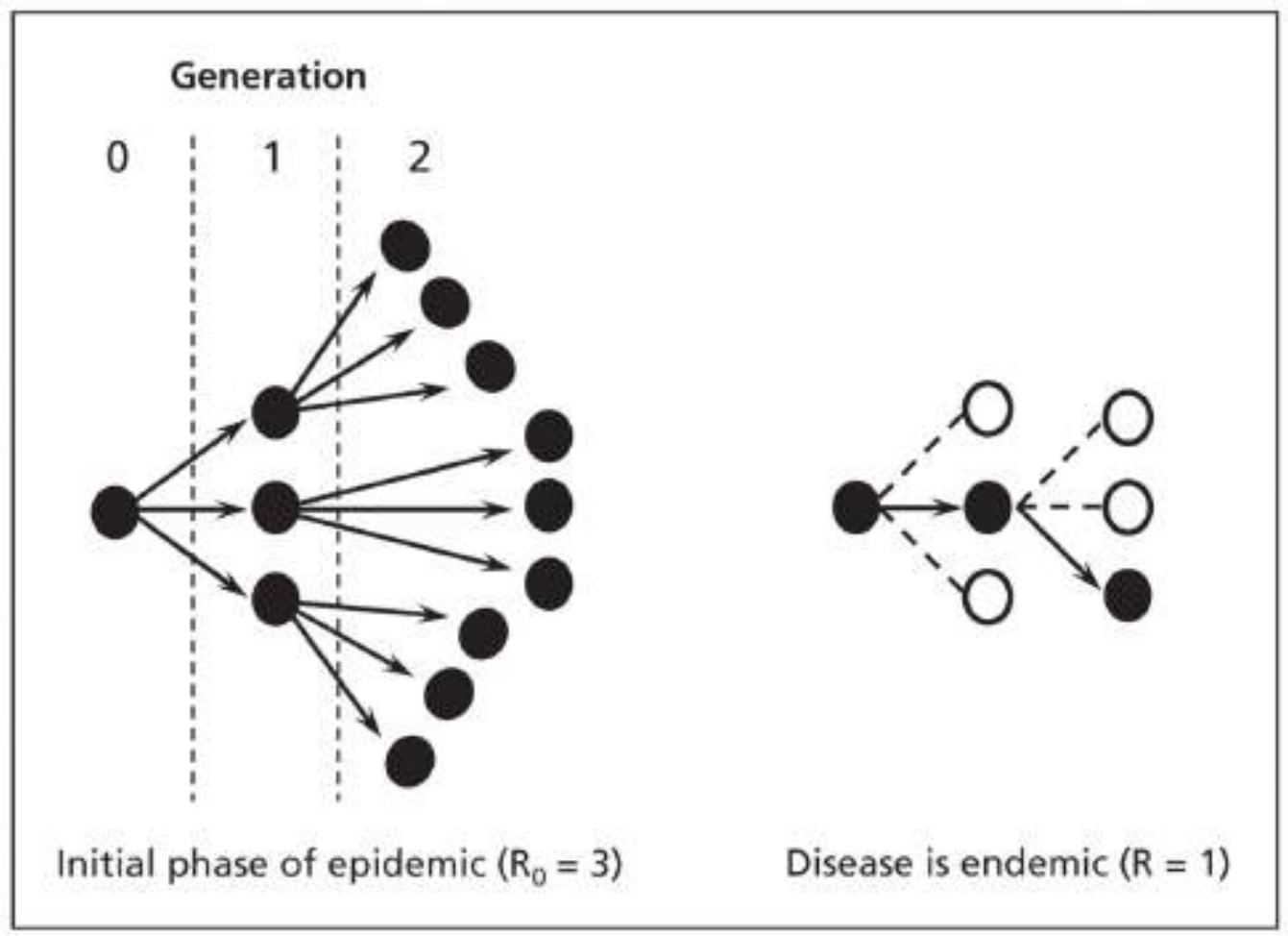
$$\dot{I}(0) = \beta I(0)(S(0) - \gamma/\beta) < 0$$

or

$$\beta S(0)/\gamma < 1$$

Basic Reproduction number, R_0

Average number of secondary cases generated by a single infectious individual through out the period within which the individual is infectious.



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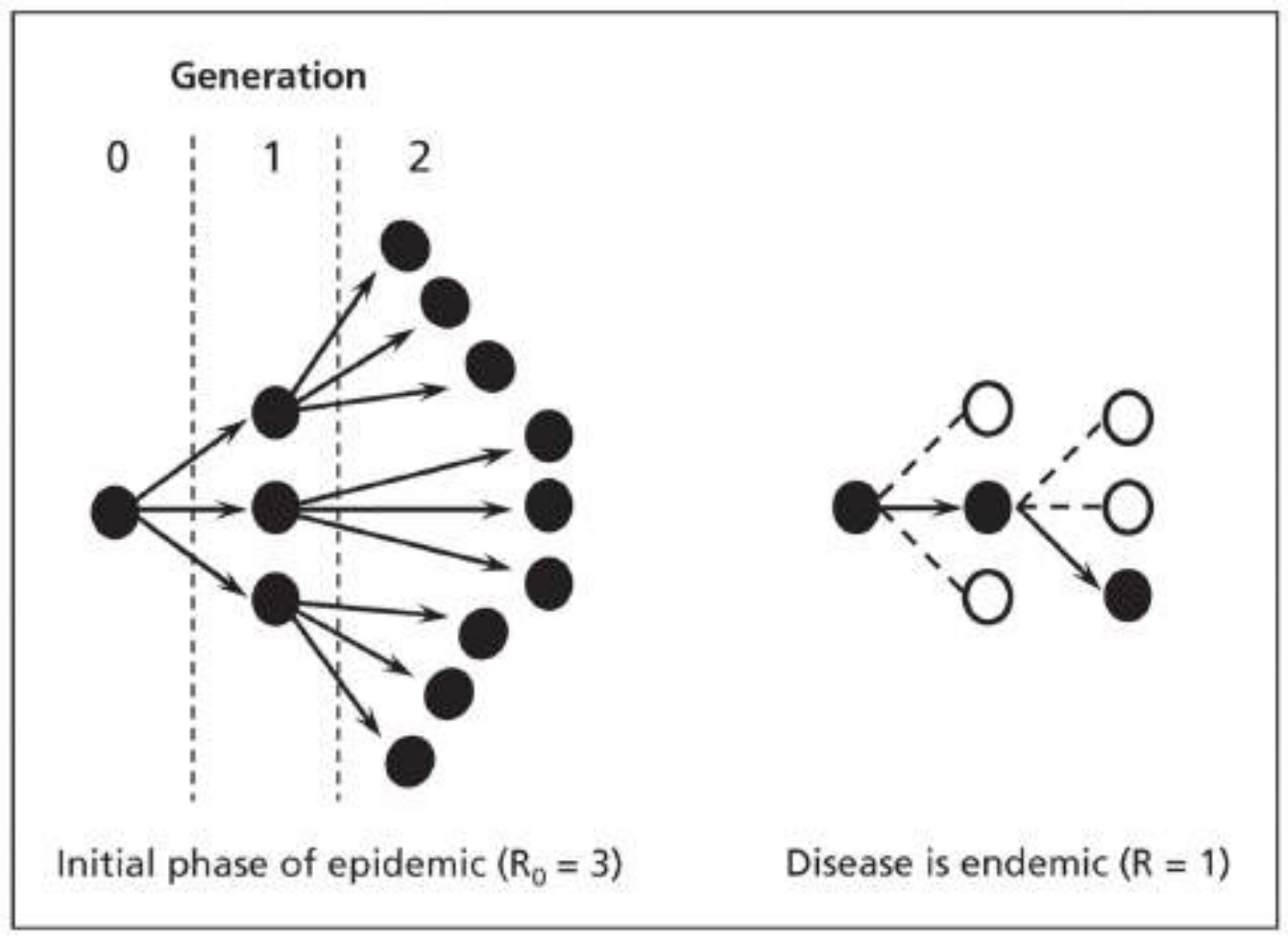
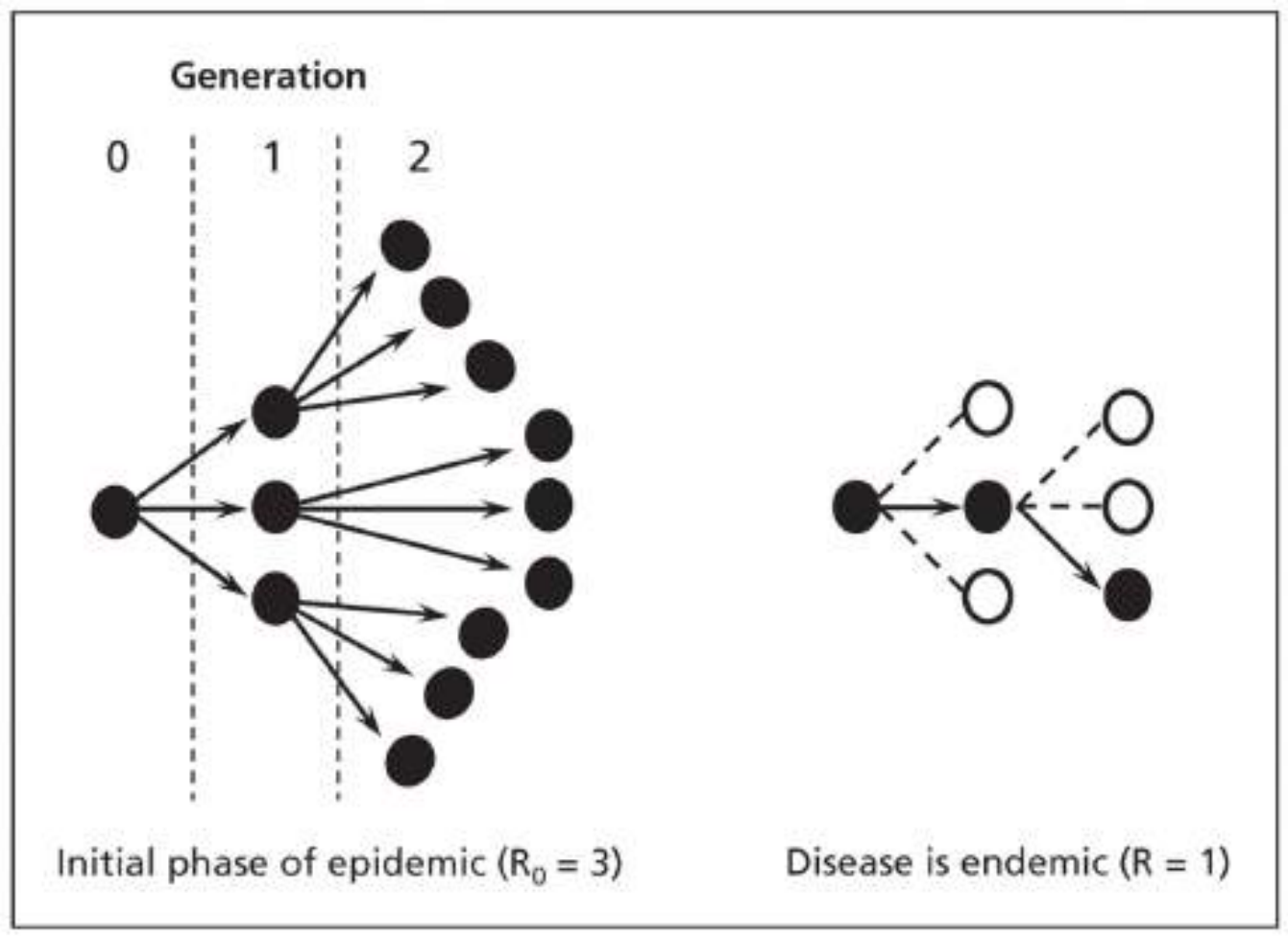


- Disease spreads when $R_0 > 1$
- Disease dies out when $R_0 \leq 1$

Basic Reproduction number, R_0

Average number of secondary cases generated by a single infectious individual through out the period within which the individual is infectious.



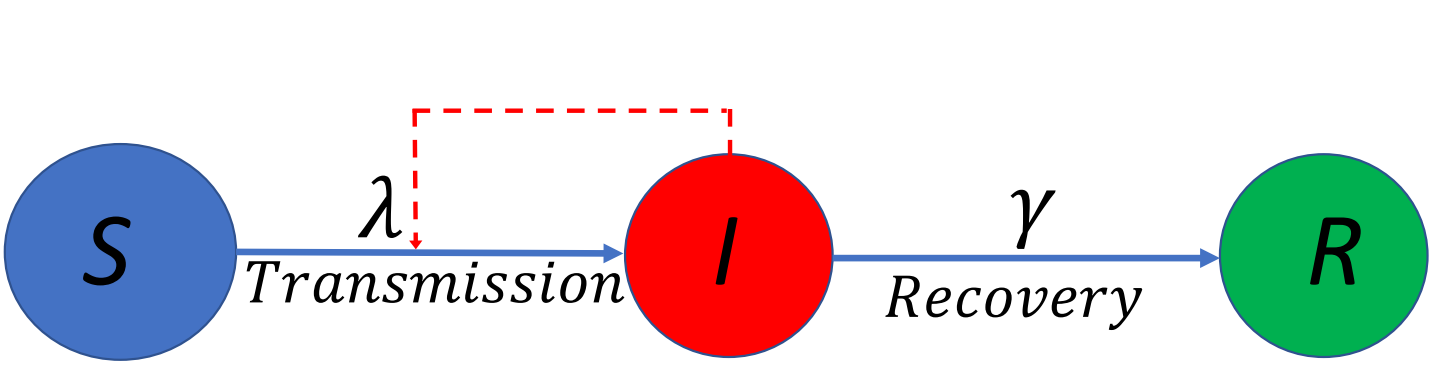
- Disease spreads when $R_0 > 1$
- Disease dies out when $R_0 \leq 1$

Basic reproduction numbers for some diseases

Disease	Transmission	R_0
Measles	Airborne	12–18
Diphtheria	Saliva	6–7
Smallpox	Airborne droplet	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4–7
HIV/AIDS	Sexual contact	2–5
Pertussis	Airborne droplet	5.5
SARS	Airborne droplet	2–5
Influenza (1918 pandemic strain)	Airborne droplet	2–3
Ebola (2014 Ebola outbreak)	Bodily fluids	1.5-2.5

Kretzschmar M et al. (2010), Wallinga J, Teunis P (2004), Mills CE et al. (2004), Althaus CL (2014), CDC, WHO

The SIR epidemic model



R_0 = Production rate of new infections by infectious individuals in a **completely susceptible population**

$\times$

fraction of new infected individuals who become infectious

$\times$

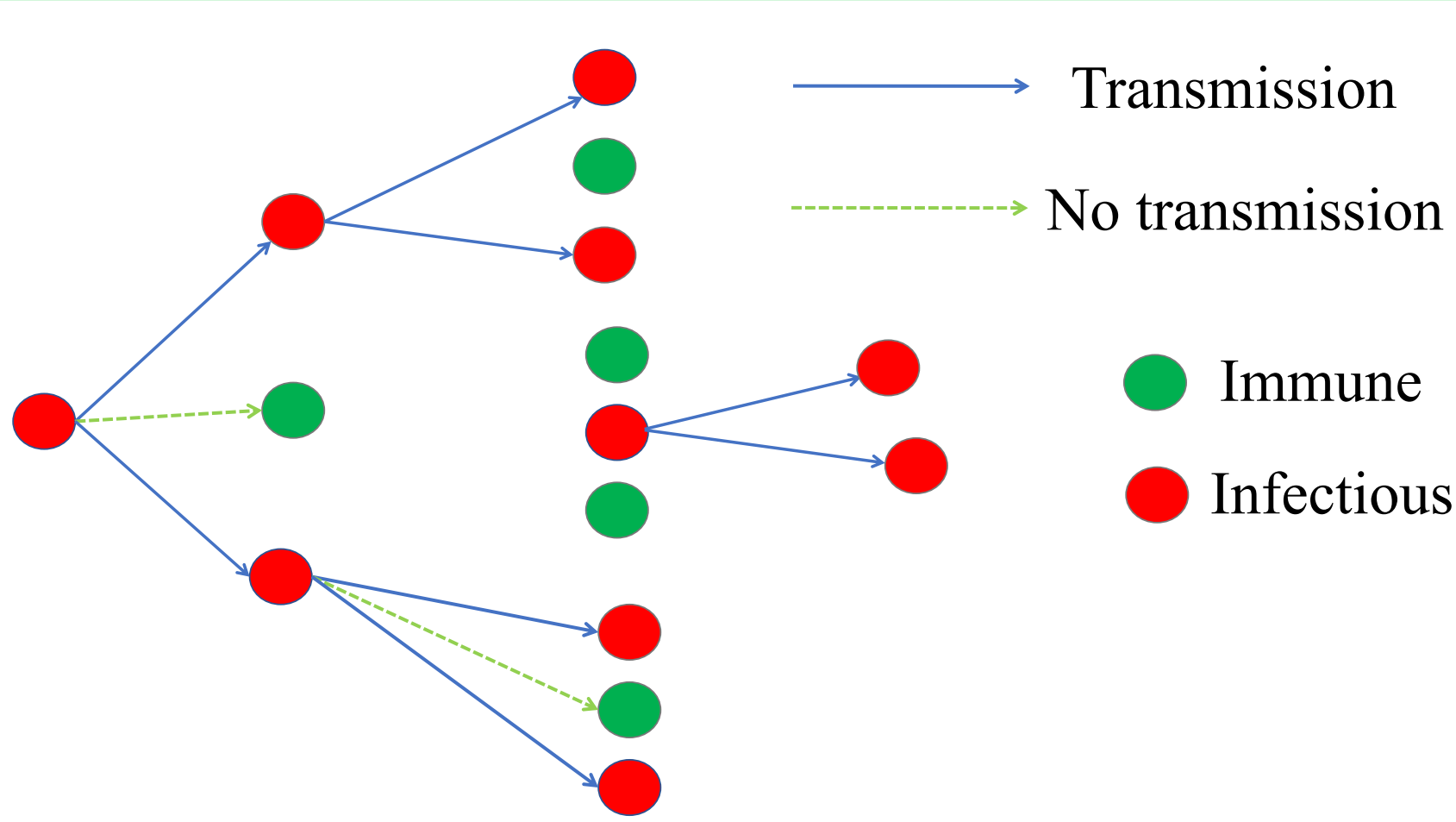
average duration of the infectious period

$= \beta \times 1 \times \frac{1}{\gamma}$

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

Effective reproduction number

- Average number of secondary infections in a population in which not everybody is susceptible (i.e., a population with some immunes) per infectious individual throughout the period within which the individual can transmit the disease.



Effective reproduction number

$\mathcal{R}$ = Production rate of new infections by infectious individuals in a population in which **not everybody is susceptible**

$\times$

fraction of new infected individuals who become infectious

$\times$

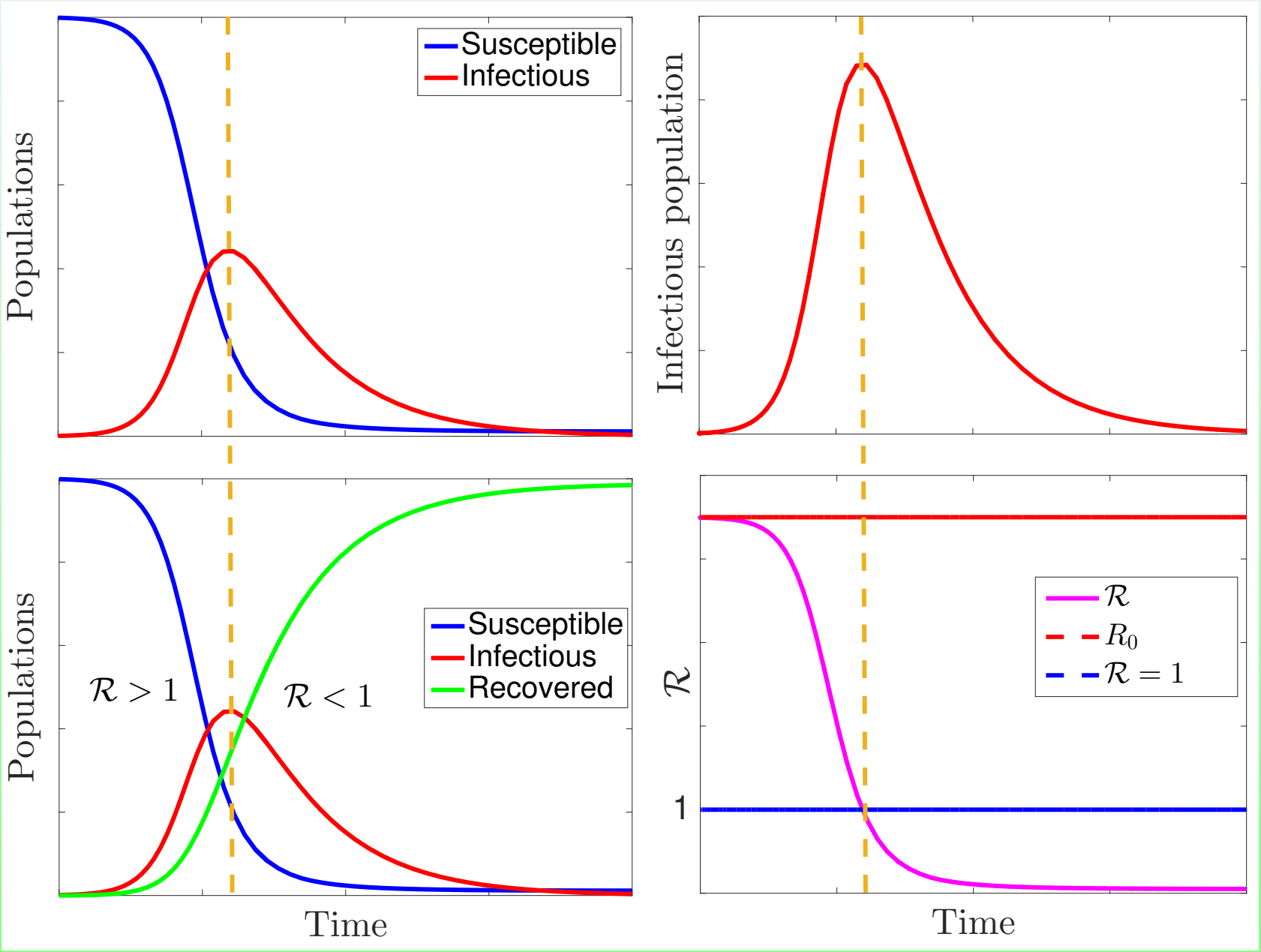
average duration of the infectious period

$$= \frac{\beta S}{N} \times 1 \times \frac{1}{\gamma}$$

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

- $\mathcal{R} = \frac{S}{N} R_0$

Effective reproduction number



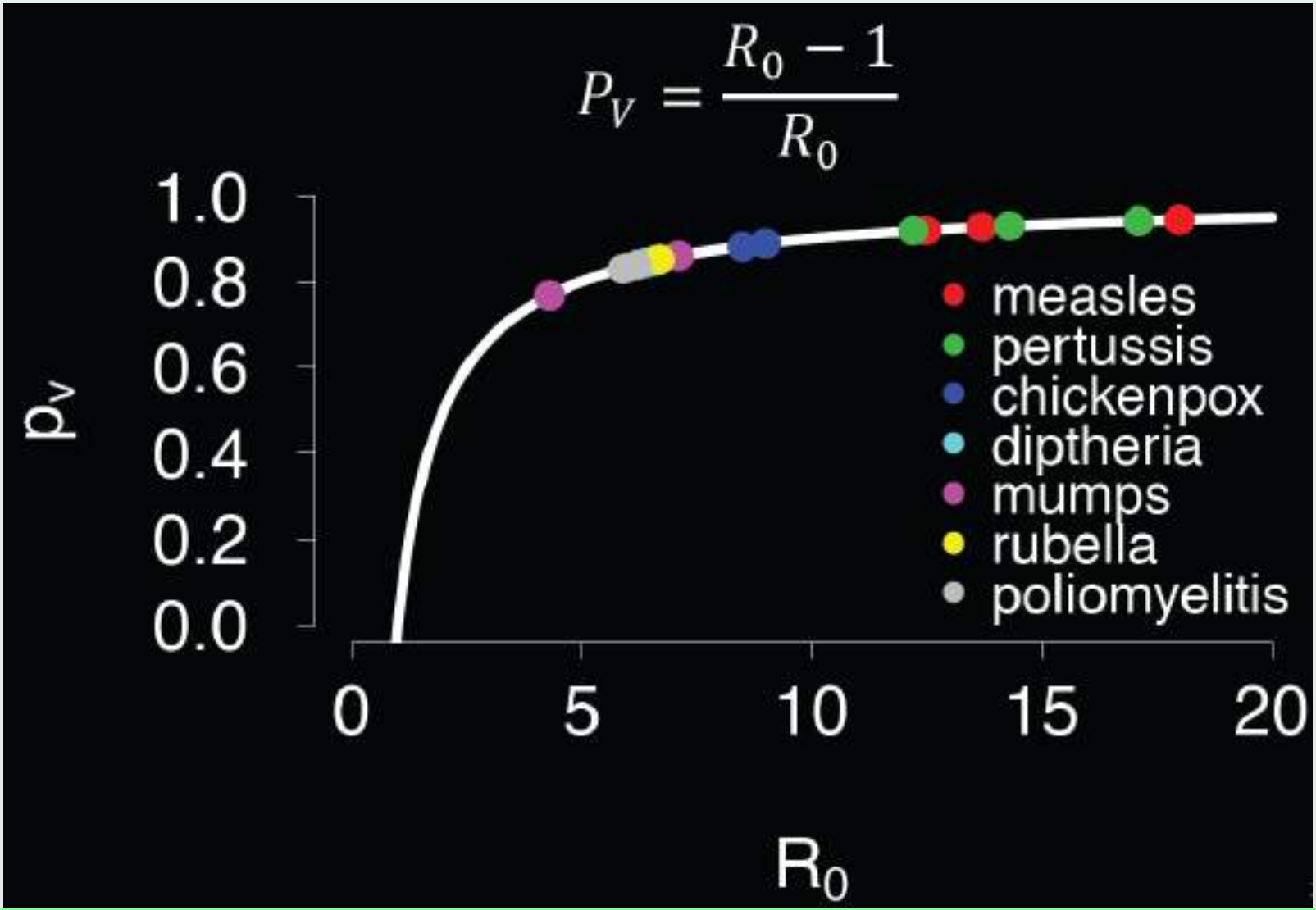
Proportion to vaccinate

- To get rid of disease, $\mathcal{R} \leq 1$
- That is, $\frac{S}{N} \leq \frac{1}{R_0}$
- What proportion must be vaccinated?
  - If P_v is the immune proportion, then

$$\begin{aligned} P_v &= 1 - \frac{S}{N} \\ &\geq 1 - \frac{1}{R_0} \end{aligned}$$

- $P_v \geq \frac{R_0 - 1}{R_0}$
- Not everybody must be vaccinated to stop transmission

Disease elimination threshold (through vaccination)

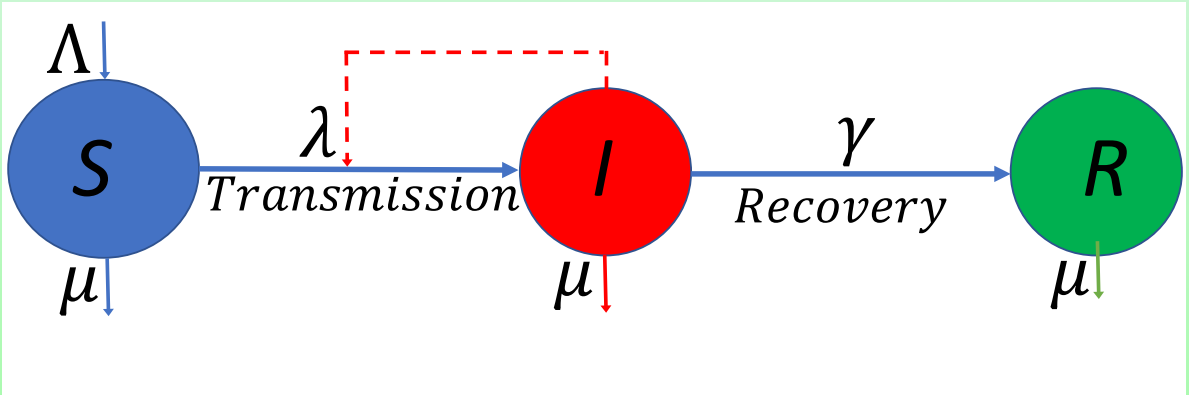


Importance of R_0 and $\mathcal{R}$

- **Disease invasion in a closed population**: Disease only invades if $S > \frac{1}{R_0}$.
- **Vaccination policy**:Eradication might be possible if $S < \frac{1}{R_0}$.
- **Outbreak peaks**: $\mathcal{R} = 1$
- **Proportion of population to vaccinate**: $P_v \geq \frac{R_0 - 1}{R_0}$

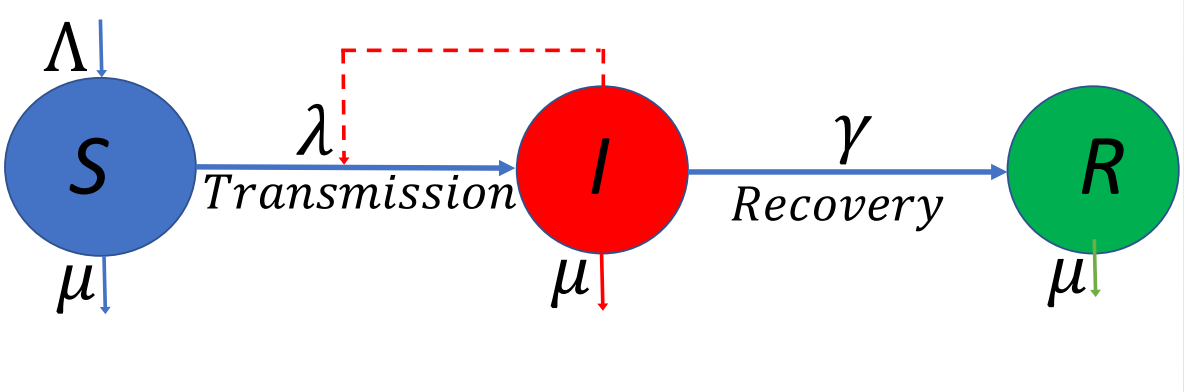
The endemic model

- Describe infection over long periods
- Considers flows related to the infection
- Considers flows related to demographic changes



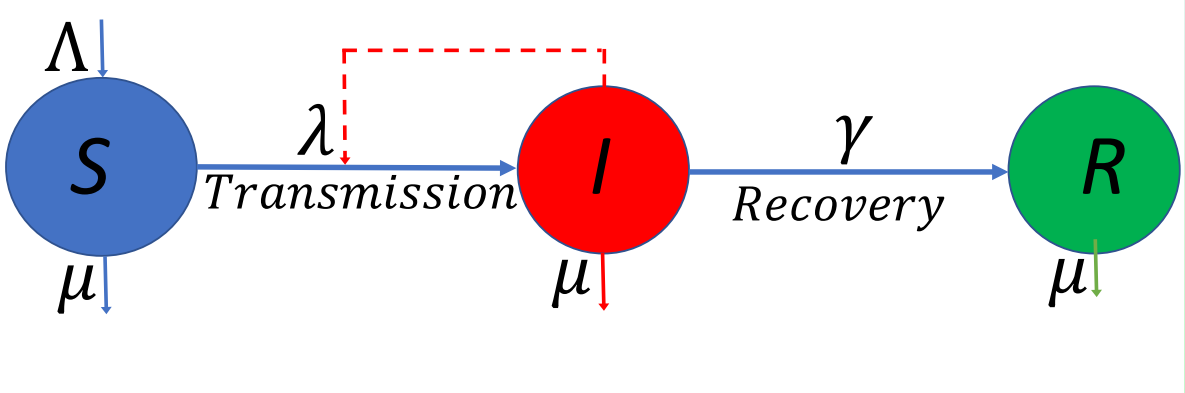
- $\Lambda = \mu(S + I + R)$ if the population size is constant
- Assumes no vertical transmission
- Assumes no disease-related deaths
- Assumes that disease confers permanent immunity

The endemic SIR model



- Λ: Recruitment rate
- μ: Per capita mortality rate

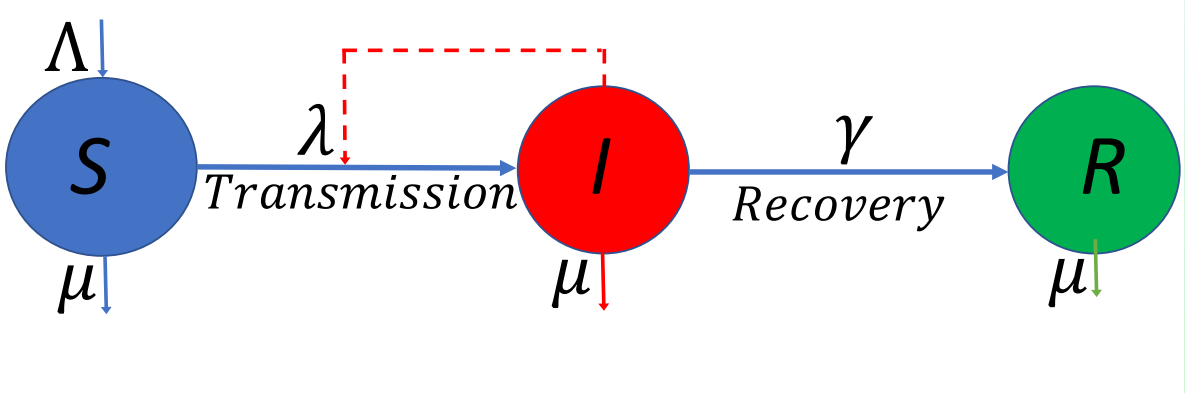
The endemic SIR model



- Λ: Recruitment rate
- μ: Per capita mortality rate

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta IS - \mu S, \\
\frac{dI}{dt} &= \beta IS - (\gamma + \mu)I, \\
\frac{dR}{dt} &= \gamma I - \mu R,
\end{aligned}$$

The endemic SIR model



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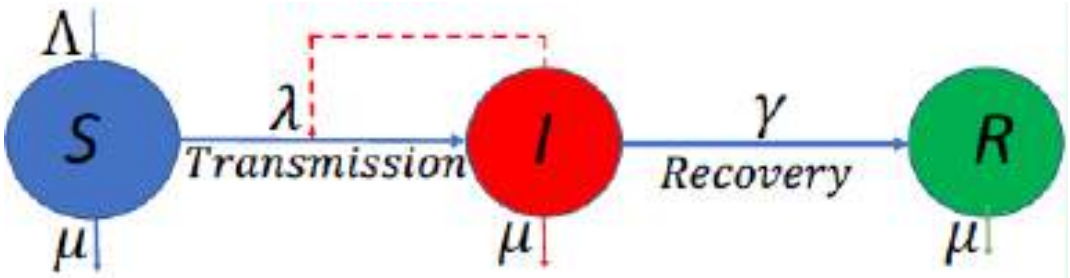

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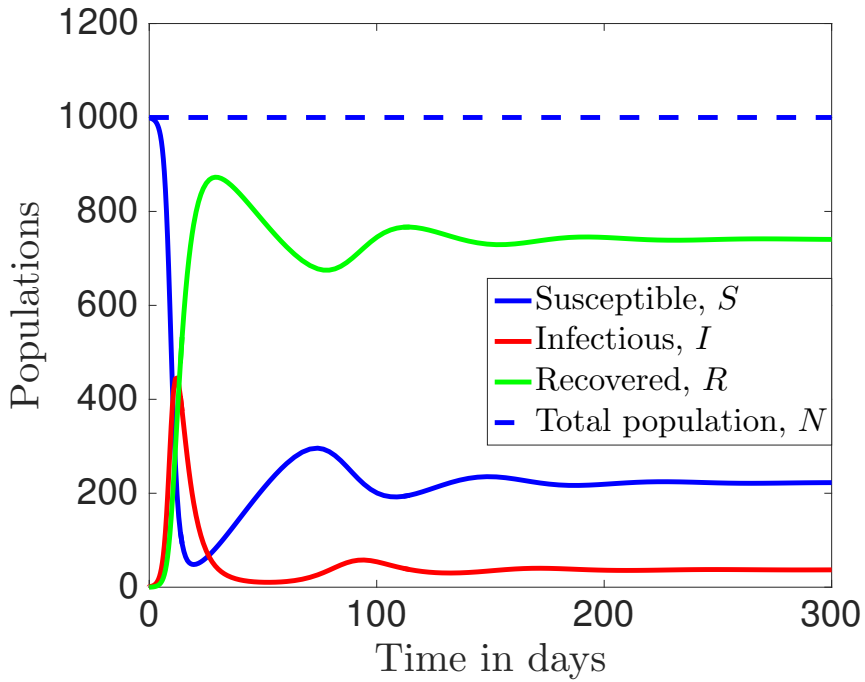

The endemic SIR model: analysis

- Equilibrium points

$$\frac{dS}{dt} = 0, \quad \frac{dI}{dt} = 0, \quad \frac{dR}{dt} = 0.$$

The endemic SIR model: analysis

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- Disease-free equilibrium

$$E_0 = (S_0^*, I_0^*, R_0^*) = \left(\frac{\Lambda}{\mu}, 0, 0\right)$$

The endemic SIR model: analysis

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- Endemic equilibrium

$$E_e = (S_e^*, I_e^*, R_e^*) = \left(\frac{\gamma+\mu}{\beta}, \frac{\mu}{\beta}\left(\frac{\beta}{\gamma+\mu}\frac{\Lambda}{\mu} - 1\right), \frac{\gamma}{\beta}\left(\frac{\beta}{\gamma+\mu}\frac{\Lambda}{\mu} - 1\right)\right)$$

$$= \left(\frac{\gamma+\mu}{\beta}, \frac{\mu}{\beta}(R_0 - 1), \frac{\gamma}{\beta}(R_0 - 1)\right)$$

The endemic SIR model: analysis

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$$= \left(\frac{\gamma+\mu}{\beta}, \frac{\mu}{\beta}(R_0 - 1), \frac{\gamma}{\beta}(R_0 - 1)\right)$$

The endemic SIR model: analysis

Local stability

- Perturb system from equlibrium, $E^* = (S^*, I^*, R^*)$ by setting $S = S^* + s, I = I^* + i, R = R^* + r$, where s, i, r are small.
- Substitute in right hand sides of equations
- Expand in a Taylor series and retain only linear terms to obtain

$$\begin{pmatrix} \frac{ds}{dt} \\ \frac{di}{dt} \\ \frac{dr}{dt} \end{pmatrix} = \begin{pmatrix} -(\beta I^* + \mu) & -\beta S^* & 0 \\ \beta I^* & \beta S^* - (\gamma + \mu) & 0 \\ 0 & \gamma & -\mu \end{pmatrix} \begin{pmatrix} s \\ i \\ r \end{pmatrix}$$

- Seek solutions of the form $\mathbf{x}(t) = \mathbf{v}e^{\alpha t}, \mathbf{x}(t) = (s(t), i(t), r(t))^T$.
  - α is an eigenvalue of the 3×3 matrix
  - What are the values of α for E_0?
  - What are the values of α for E_e?

The endemic SIR model: analysis

Local stability (short method)

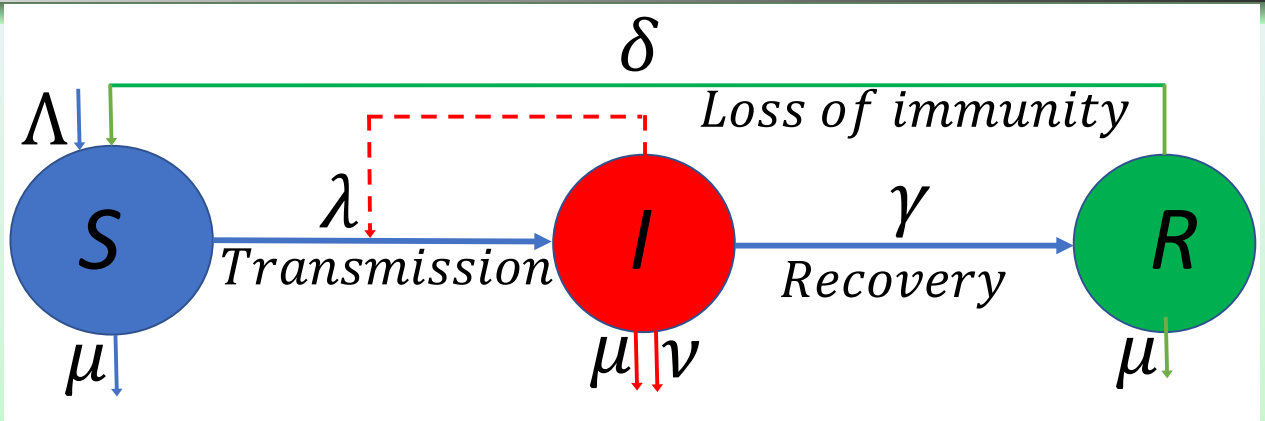
- Find Jacobian of system at equilibrium point, $E^* = (S^*, I^*, R^*)$. This is the same as the 3×3 matrix
- Find eigenvalues of Jacobian
- Equilibrium is locally asymptotically stable if all eigenvalues are negative
- Equilibrium is unstable if at least one eigenvalue is positive

The endemic SIR model: analysis

Next generation matrix approach for computing R_0

- Equation(s) for disease classe(s): $\frac{dI}{dt} = \beta IS - (\gamma + \mu)I$
- Vector of new cases: $F = (\beta IS)$
- Vector for transitions: $V = ((\gamma + \mu)I)$
- Matrix of new infections: $\mathcal{F} = \left(\frac{\partial F}{\partial I}(S_0^*, I_0^*, R_0^*)\right) = (\beta \frac{\Lambda}{\mu})$
- Matrix of transitions: $\mathcal{V} = \left(\frac{\partial F}{\partial I}(S_0^*, I_0^*, R_0^*)\right) = (\gamma + \mu)$
- Inverse of matrix of transitions: $\mathcal{V}^{-1} = \frac{1}{\gamma+\mu}$
- Next generation matrix: $\mathcal{F}\mathcal{V}^{-1} = \frac{\beta\Lambda}{\mu(\gamma+\mu)}$
- Spectrum of the next generation matrix: $\left\{\frac{\beta\Lambda}{\mu(\gamma+\mu)}\right\}$
- Spectral radius of the next generation matrix: $R_0 = \frac{\beta\Lambda}{\mu(\gamma+\mu)}$

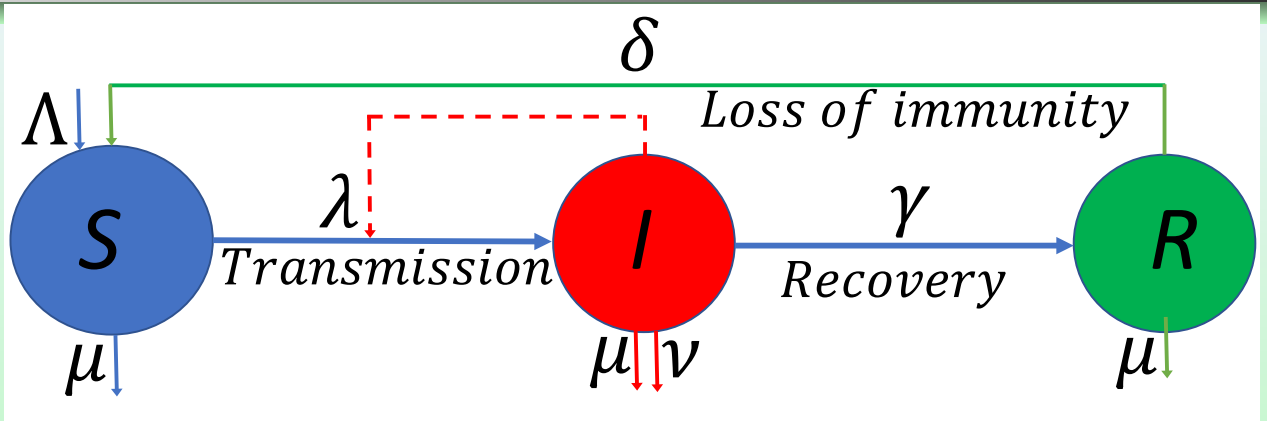
Relaxing assumptions: SIRS with disease-deaths



- Disease-related mortalies are not negligible (rate: ν)
- No permanent immunity, e.g., some STDs (immunity lost at rate δ)
- $1/\delta$: average duration of immunity

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \delta R - \beta IS - \mu S, \\
\frac{dI}{dt} &= \beta IS - (\gamma + \mu + \nu)I, \\
\frac{dR}{dt} &= \gamma I - (\delta + \mu)R,
\end{aligned}$$

Relaxing assumptions: SIRS with disease-deaths



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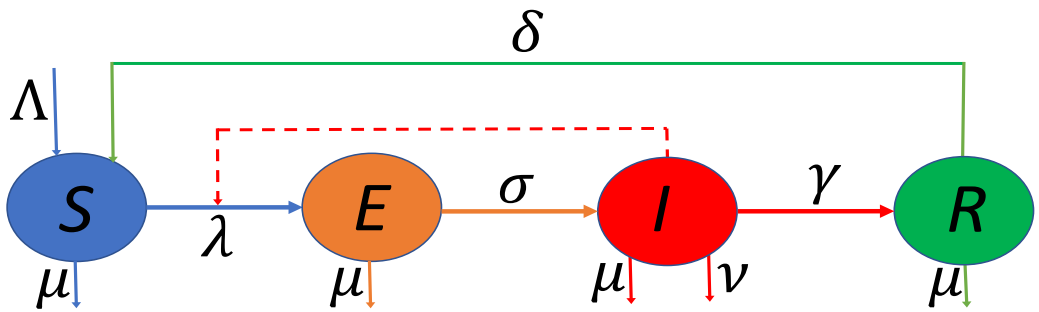
\end{aligned}$$

- What is the basic reproduction number?
- What are the equlibria of the system?

Relaxing assumptions: The SEIRS model



$$
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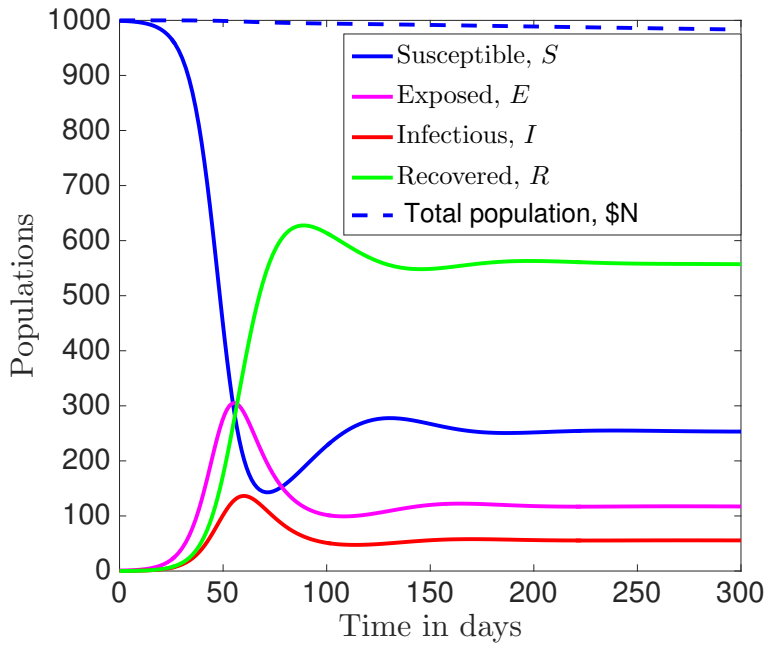
$$



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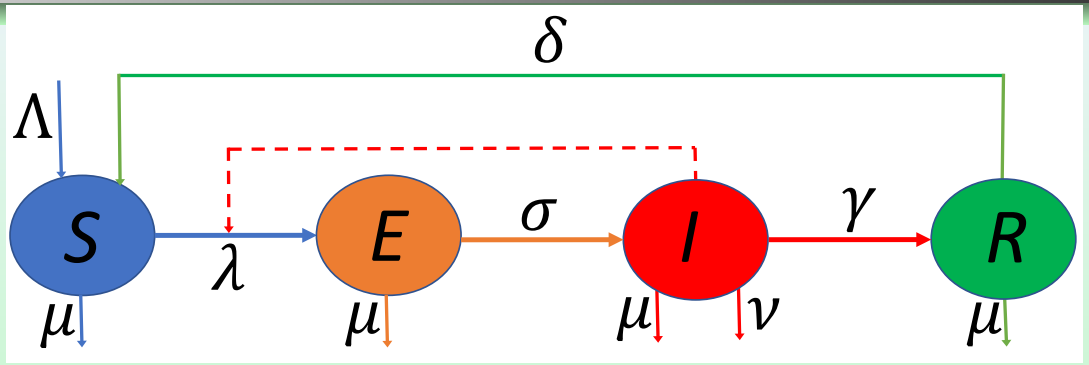

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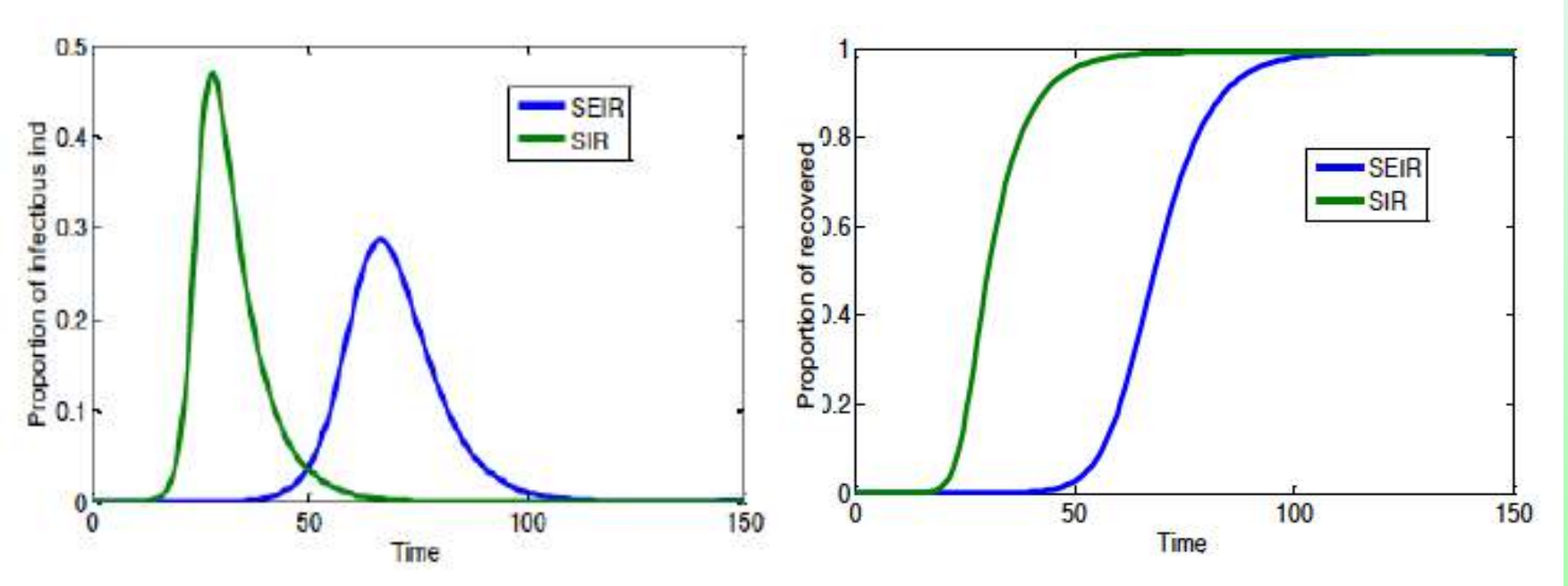
\frac{dE}{dt} &= \beta IS - (\mu + \sigma)E, \\
\frac{dI}{dt} &= \sigma E - (\gamma + \mu + \nu)I, \\
\frac{dR}{dt} &= \gamma I - (\delta + \mu)R.
\end{aligned}$$

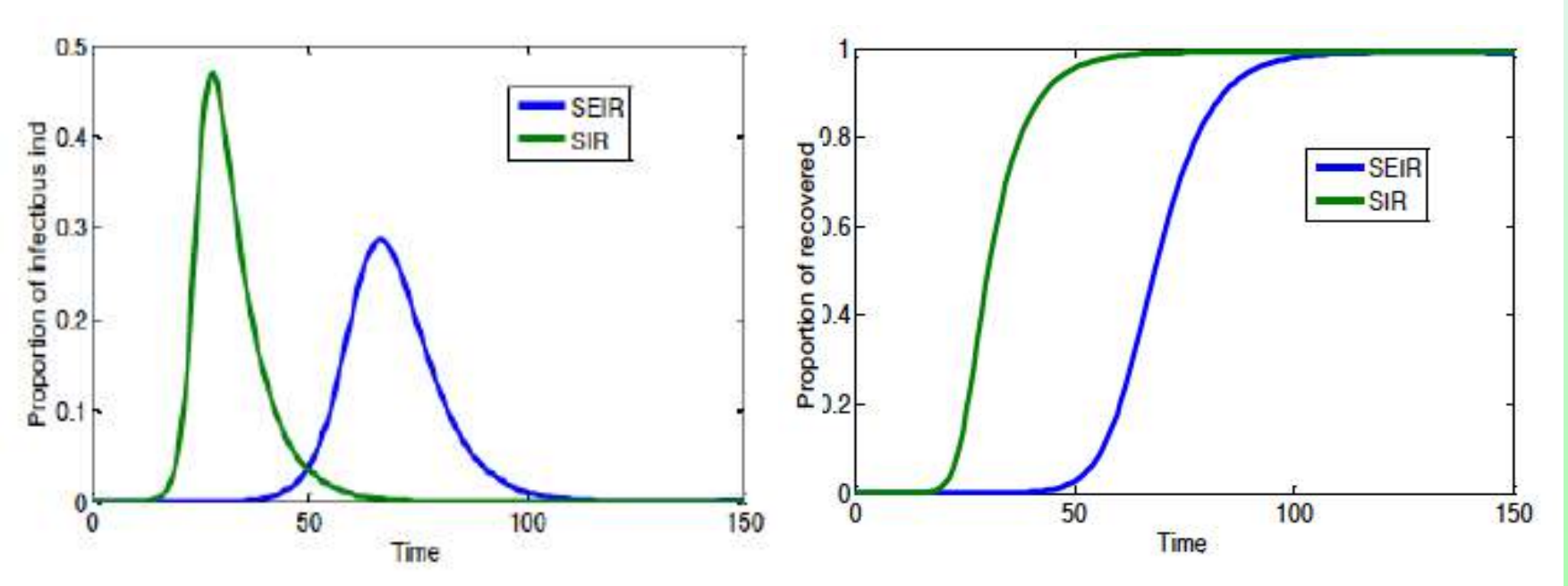
- What is the basic reproduction number?
- What are the equlibria of the system?
- Determine the stability of the equilibria

The Epidemic SIR versus SEIR model



- The E class causes a time-delay as individuals must pass through this class before contributing in disease transmission.
- Both the epidemic SIR and SEIR models have the same basic reproduction number and final epidemic size.

The Epidemic SIR versus SEIR model



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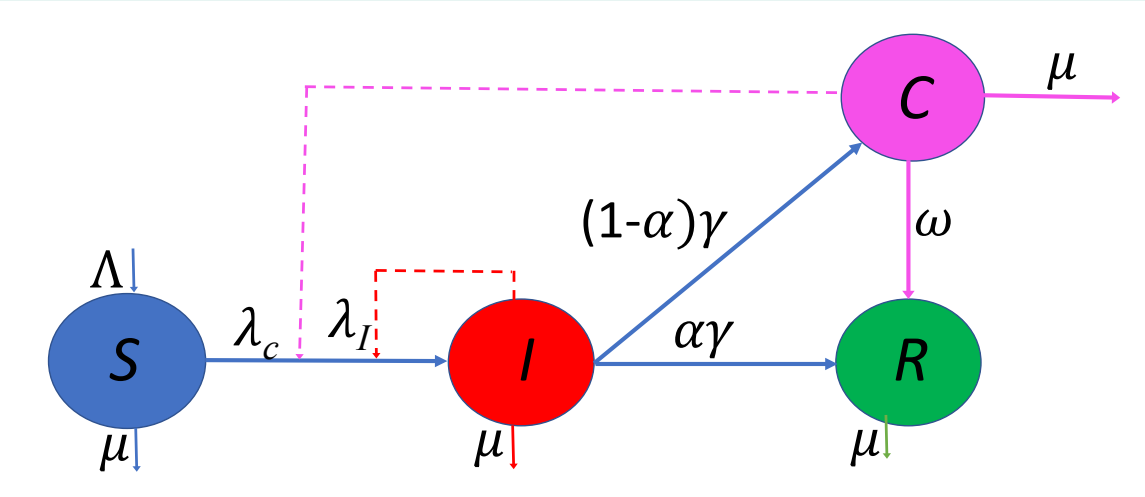
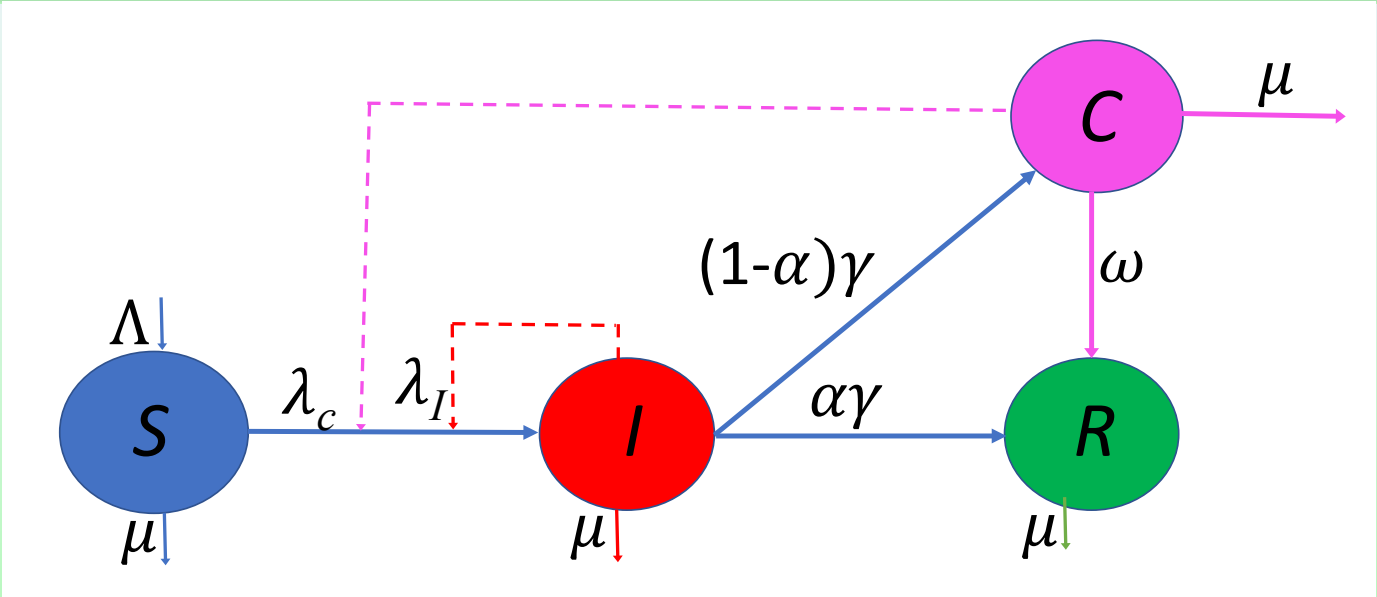
Adding complexity: Models with a carrier state



- The biology and history of some diseases are complex
- Some diseases have chronic carriers (C)
- Examples: hepatitis B, herpes, Salmonella
  - Can transmit disease at low rates for many years, e.g., hepatitis B
  - Might not transmit disease for a while, but might become infectious again

Adding complexity: Models with a carrier state



$$\dot{S} = \Lambda - (\beta I + \epsilon\beta C)S - \mu S,$$

$$\dot{I} = (\beta I + \epsilon\beta C)S - (\mu + \gamma)I,$$

$$\dot{C} = \alpha\gamma I - (\omega + \mu)C,$$

$$\dot{R} = (1 - \alpha)\gamma I + \omega C - \mu R.$$

Epidemic cycles

- Some infections exhibit seasonal behavior
- Example: Measles
- Incorporation of some seasonal forcing (sine or cosine wave)

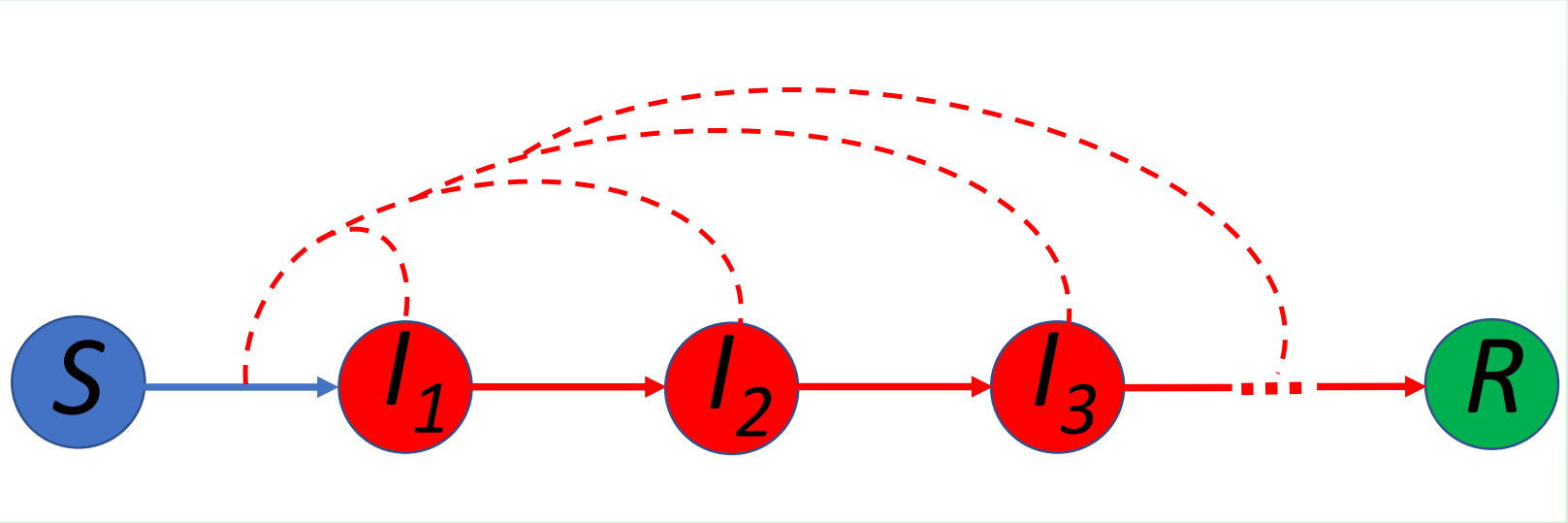
$$\begin{aligned} \dot{S} &= \mu(S+I) - \beta(t)\frac{I}{N}S, \\ \dot{I} &= \beta(t)\frac{I}{N}S - \gamma I. \end{aligned}$$

- $\beta = \beta(t) = \beta_0(1 + \beta_1 \cos \omega t)$
  - β_0: Background or average transmission rate
  - $0 \leq \beta_1 \leq 1$: amplitude of seasonality
  - ω: Period of forcing

Multi-compartments and time since infection

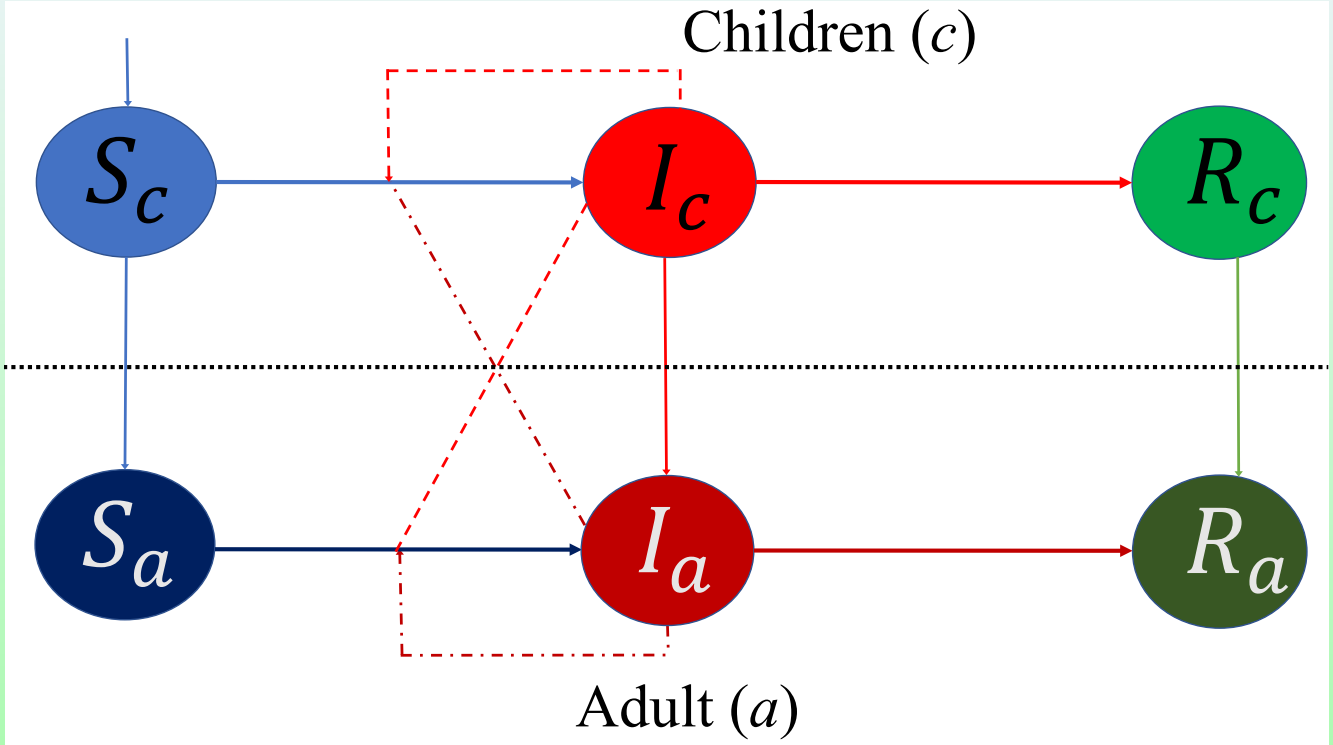
- Multiple compartments may be useful under certain scenario
  - Introducing multiple infectious compartments and hence infectious periods might be important when we are interested in having control over the distribution of the infectious period as opposed to the assumption of exponential case when there is a single infectious class
  - Different susceptible classes might be necessary for infections with much variation among different population groups.
  - Multiple vaccinated or immune classes may be necessary when we try to track immunity boosted by different vaccine doses
- More subdivisions of the infectious class results in fast growth rate and shorter epidemics.

Multi-compartments



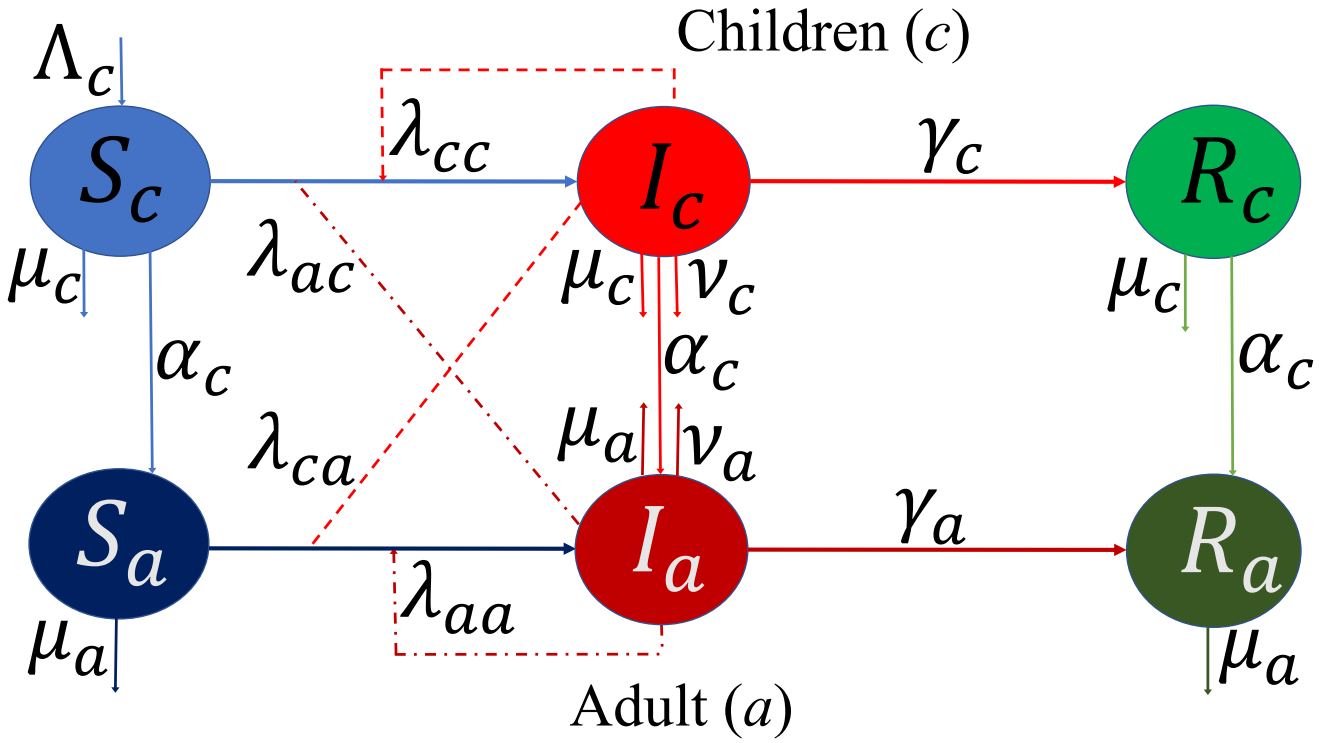
$$
\begin{aligned}
\dot{S} &= \Lambda - \beta \left(\sum_{i=1}^{n} I_i \right) S - \mu S, \\
\dot{I}_1 &= \beta \left(\sum_{i=1}^{n} I_i \right) S - (n\gamma + \mu + \nu) I_1, \\
\dot{I}_i &= n\gamma I_{i-1} - (n\gamma + \mu + \nu) I_i, \quad i = 2, 3, 4, \ldots, n, \\
\dot{R} &= n\gamma I_n - \mu R.
\end{aligned}
$$

Age-structured models



- Two age-groups: children and adults
- Childhood diseases, e.g., measles, whooping cough, mumps, smallpox
- β becomes a matrix and no longer a number
- Implications of non-random mixing and Who Acquires Infection From Whom (WAIFW) matrix

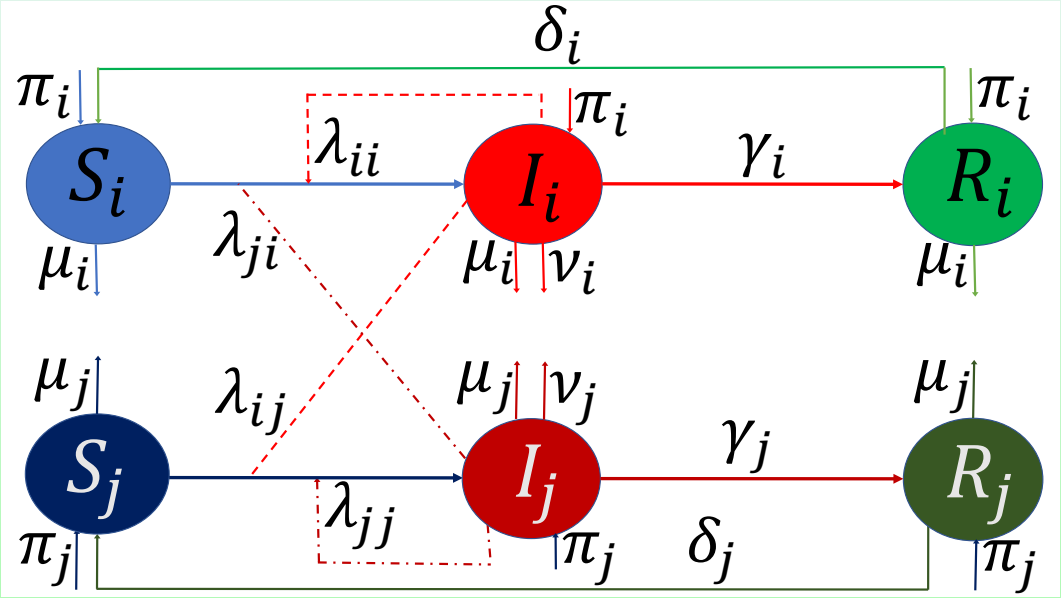
Age-structured models



$$
\begin{aligned}
\dot{S}_c &= \Lambda_c - (\beta_{cc} I_c + \beta_{ac} I_a) S_c - (\alpha_c + \mu_c) S_c, \\
\dot{I}_c &= (\beta_{cc} I_c + \beta_{ac} I_a) S_c - (\alpha_c + \mu_c + \gamma_c + \nu_c) I_c, \\
\dot{S}_a &= \alpha_c S_c - (\beta_{ca} I_c + \beta_{aa} I_a) S_a - \mu_a S_a, \\
\dot{I}_c &= \alpha_c I_c + (\lambda_{ca} I_c + \lambda_{aa} I_a) S_a - (\mu_a + \gamma_a + \nu_a) I_a.
\end{aligned}
$$

$$
\lambda = \beta_{..} I_{.}, \qquad \beta = \begin{pmatrix} \beta_{cc} & \beta_{ca} \\ \beta_{ac} & \beta_{aa} \end{pmatrix}
$$

Multigroup models



Multigroup models can be used to model:

- risk structure
- STDs
- etc.

Multigroup models, risk-structure, and STDs

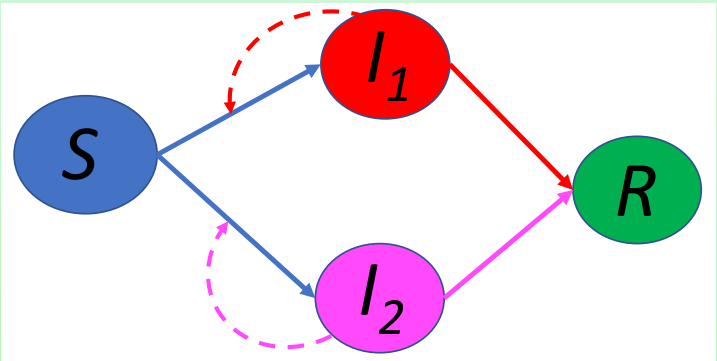
- Risk structure is essential for some diseases, e.g., STDs
- STDs are different from other diseases in a number of ways:
  - Restricted to the sexually active
  - Carrier often asymptomatic during later stages of the infection
  - Recovery upon treatment with the exception of HIV/AIDS
  - Little or no acquired immunity
  - Possibility of vertical/horizontal transmission for some STDs
  - Appearance of new strains might be common
  - Short incubation periods for many veneral diseases (with the exception of AIDS), e.g., 3-7 days for gonorrhea compared to the infectious period

Multi-strain models

- Hosts can be infected by different diseases and/or different strains of the same disease
- Examples
  - **Malaria**: *Plasmodium falciparum, vivax, ovale, malariae*
  - **Dengue**: 4 strains (DENV 1-4)
  - **HIV**: HIV-1 and HIV-2
  - **Influenza**
  - **Salmonella**, etc.
- Strains differ on drug resistance, antigens and immune response, virulence factors

Multi-strain models

- Strains of the same disease can interact with each other
- Immunity to one strain might result in immunity to another strain
- Two strains with complete cross-immunity



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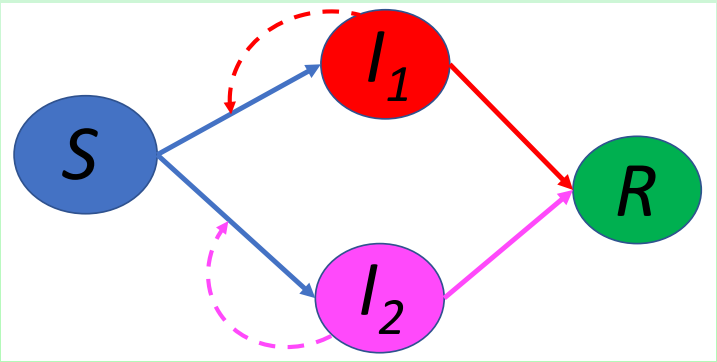

$$
\begin{aligned}
\dot{S} &= \Lambda - (\beta_1 I_1 + \beta_2 I_2)S - \mu S, \\
\dot{I}_1 &= \beta_1 I_1 S - (\mu + \gamma_1 + \nu_1) I_1, \\
\dot{I}_2 &= \beta_2 I_2 S - (\mu + \gamma_2 + \nu_2) I_2, \\
\dot{R} &= \gamma_1 I_1 + \gamma_2 I_2 - \mu R.
\end{aligned}
$$

Multi-strain models

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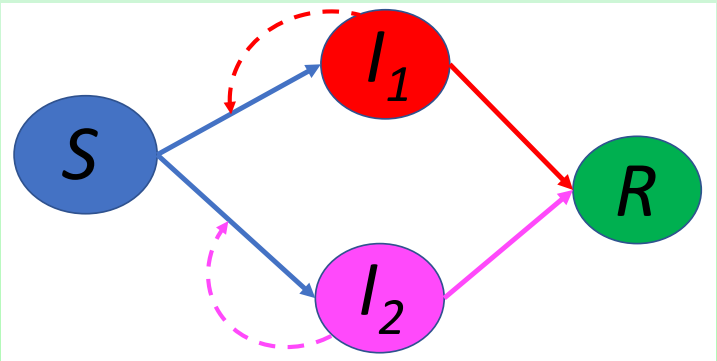
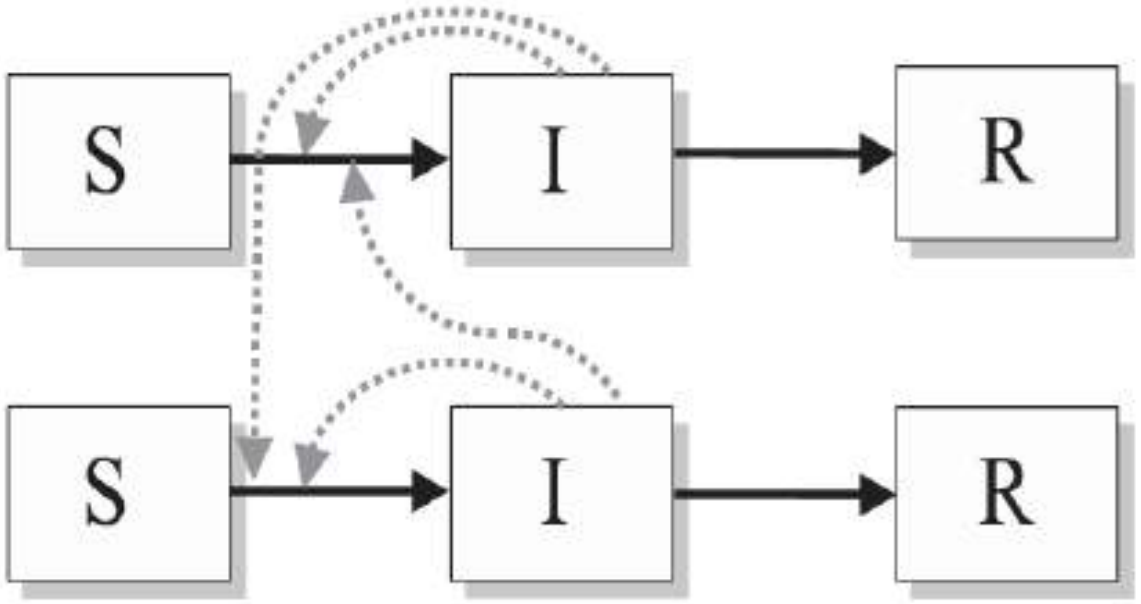


$$
\begin{aligned}
\dot{S} &= \Lambda - (\beta_1 I_1 + \beta_2 I_2) S - \mu S, \\
\dot{I}_1 &= \beta_1 I_1 S - (\mu + \gamma_1 + \nu_1) I_1, \\
\dot{I}_2 &= \beta_2 I_2 S - (\mu + \gamma_2 + \nu_2) I_2, \\
\dot{R} &= \gamma_1 I_1 + \gamma_2 I_2 - \mu R.
\end{aligned}
$$

Multi-host models

- Some diseases can infect multiple hosts
- **Examples**
  - Vector-borne diseases, e.g., malaria (parasite conveyed from one-human to the other by mosquitoes)
  - Zonotic diseases. Animal diseases that can also be spread to humans, e.g., Ebola, West Nile Virus
- Transmission matrix might no longer be symmetric

Multiple host models



Keeling and Rohani 2008

$$
\begin{aligned}
\dot{S}_1 &= \Lambda_1 - (\beta_{11} I_1 + \beta_{12} I_2) S_1 - \mu_2 S_1, \\
\dot{I}_1 &= (\beta_{11} I_1 + \beta_{12} I_2) S_1 - (\mu_1 + \gamma_1 + \nu_1) I_1, \\
\dot{R}_1 &= \gamma_1 I_1 - \mu_1 R_1, \\
\dot{S}_2 &= \Lambda_2 - (\beta_{22} I_2 + \beta_{21} I_1) S_2 - \mu_2 S_2, \\
\dot{I}_2 &= (\beta_{22} I_2 + \beta_{21} I_1) S_2 - (\mu_2 + \gamma_2 + \nu_2) I_2, \\
\dot{R}_2 &= \gamma_2 I_2 - \mu_2 R_2.
\end{aligned}
$$

Multiple host models: Vector-borne diseases

Focus: Mosquito-borne infections

- Mosquitoes do not recover from infection
- Three parties involved
  - The human (host)
  - the mosquito (vector)
  - the pathogen (disease agent)
- Transmission matrix has zero diagonal entries
- Transmission defined through mosquito biting rates and transmission probabilities
- Ratio of mosquitoes to humans important understanding disease dynamics and in computing R_0

Multiple host models: Mosquito-borne infections

- Mosquitoes are vectors for many important human infections
- Malaria
  - Host: the human
  - Vector: the female *Anopheles* mosquito
  - Pathogen *Plasmodium* parasites (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*)
- Zika
  - Host: the human
  - Vector: *Aedes aegypti* and *Aedes albopictus*
  - Pathogen: *Zika virus*
- Dengue
  - Host: the human
  - Vector: *Aedes aegypti*
  - Pathogen: 4 Dengue virus serotypes

Multiple host models: Mosquito-borne infections

Vector-borne disease life cycle

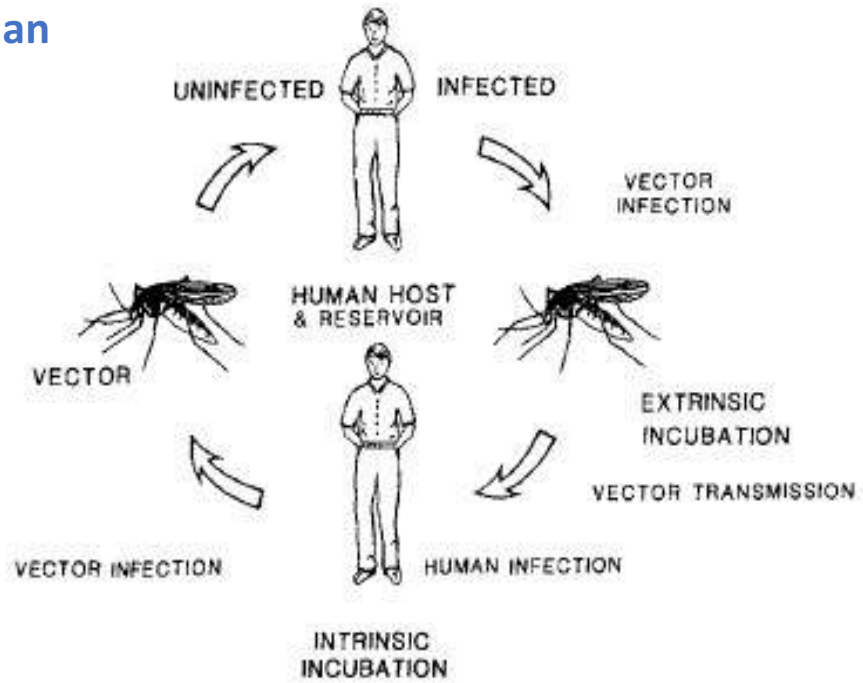
Adult female mosquitoes require blood for egg production

1. Adult female mosquito bites an infectious human

2. Incubation of parasite or virus within the mosquito extrinsic incubation period is ~ 7-14 days (temperature dependent)

3. Infectious mosquito bites a susceptible human

4. Parasite or virus incubates within human average intrinsic incubation period is ~ 4-5 days average human infectious period is ~ 4-5 days



Cycle repeats

Lifecycle involves the mosquito biting twice at appropriate times

Multiple host models: Malaria

Ross model

$$\begin{aligned} \dot{I}_h &= abI_v m\,(1 - I_h) - \gamma_h I_h, \\ \dot{I}_v &= acI_h(1 - I_v) - \mu_v I_v. \end{aligned}$$

- m: Ratio of mosquitoes to humans
- a: biting rate of mosquitoes
- b: transmission from mosquitoes to humans
- c: transmission from humans to mosquitos
- $1/\gamma_h$: Average duration of infection in humans
- $1/\mu_v$: Average mosquito life span

- Developed for malaria but used as generic model for many vector-borne diseases

Metapopulations

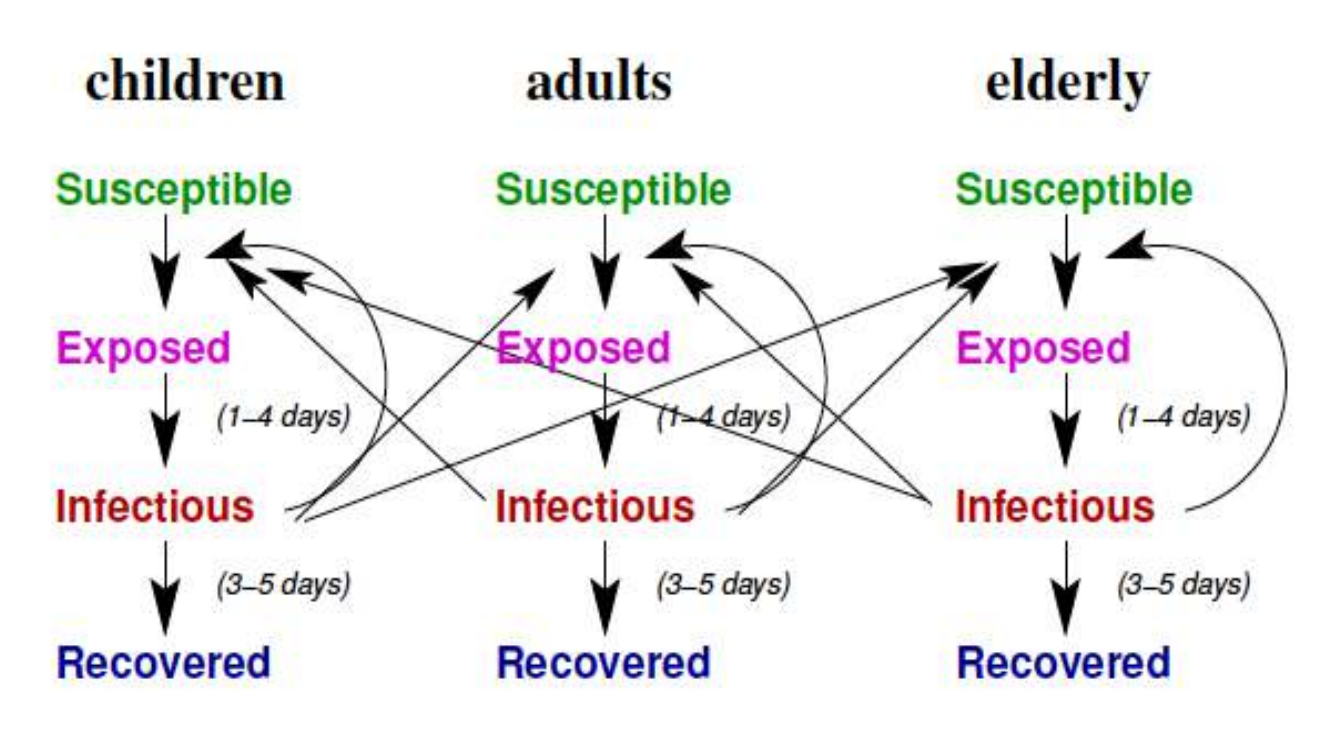
- **Metapopulation**: Set of subpopulations grouped into various patches connected by movement of individuals.
- Useful tool for modeling diseases in which host are naturally grouped into spatial subunits.
- Spread of human infection best accounted for by movements of individuals to and from home
- Example: Simplified epidemic SI patch disease model

$$\begin{aligned}
\dot{S}_1 &= -\beta I_1 S_1 + m_{21} S_2 - m_{12} S_1, \\
\dot{I}_1 &= \beta I_1 S_1 + m_{21} I_2 - m_{12} I_1, \\
\dot{S}_2 &= -\beta I_2 S_2 + m_{12} S_1 - m_{21} S_2, \\
\dot{I}_2 &= \beta I_2 S_2 + m_{12} I_1 - m_{21} I_2.
\end{aligned}$$

Network models

- Networks: Considers nature of individual disease transmission
- Individuals are linked if infections can pass between them.

Agent-based models

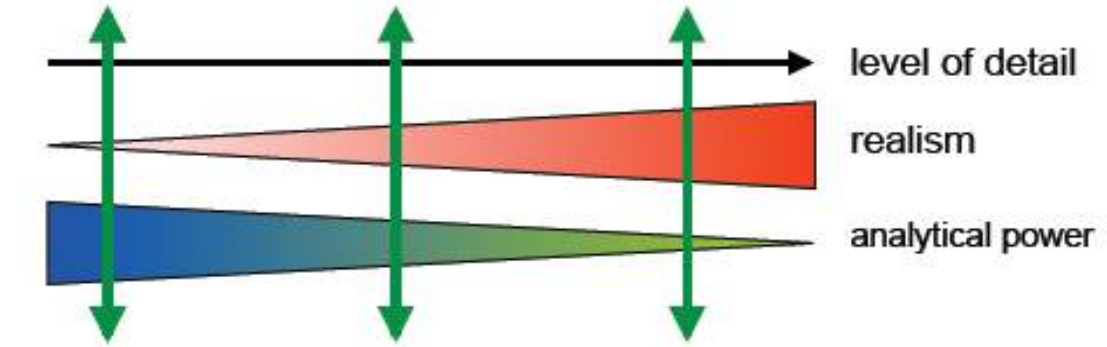


- Compartmental models: one compartment for one state
- Each important class of hosts requires a compartment.

Agent-based models

- Hosts are the agents
- Each agent has a set of attributes, e.g., age, gender, disease status, vaccination status.
- Set of rules for how agents interact.
- How disease spreads from infectious agents to susceptible agents.
- Conceptual diagrams from compartmental models can be used to represent agent states.
- Individual-based models: account for properties of individual hosts and (spatial) interactions between individual hosts.

Trade-off between complexity and tractibility



Simple models

no structure
well-mixed
deterministic

Intermediate complexity

age structure
spatial structure
stochasticity
...

Detailed, biology-rich model of Aedes aegypti : Skeeter Buster

✓ Easy to analyze and simulate
gain general insights and understanding

✓ Few parameters
don't need detailed information on the system

✗ Highly simplistic
unlikely to be realistic

✗ Difficult to analyze and simulate
unlikely to yield general insights or understanding

✗ Many parameters: need to have very detailed information on the system

✓/✗ Very specific to a given situation

✓ Has the *potential* to be more realistic provided that we have enough information to parameterize

✗ **Easy to be seduced by its apparent realism**