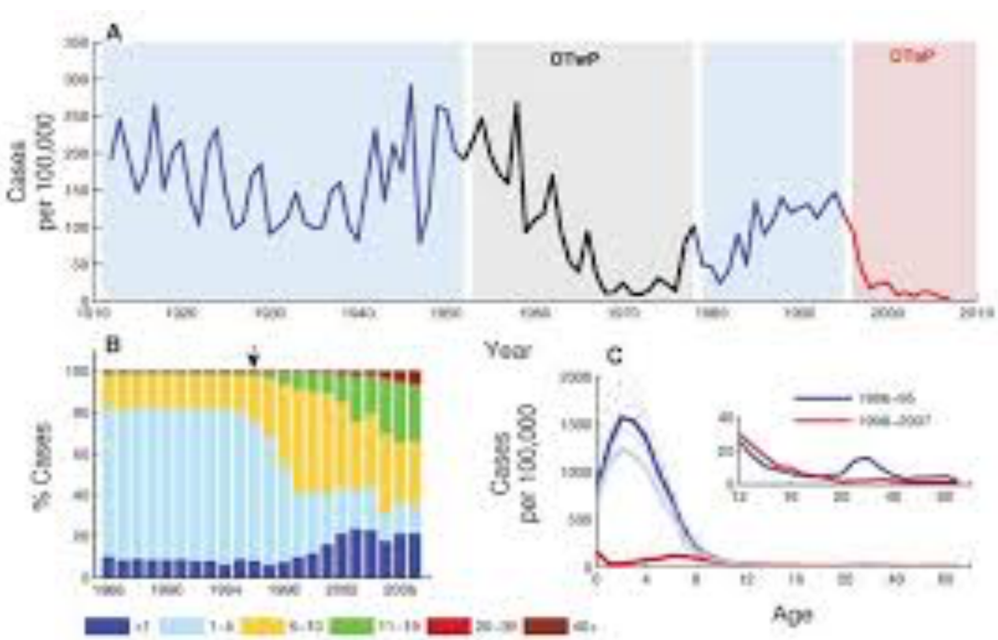
Mathematical Modelling for Infectious Diseases

What is a mathematical model?

Mathematical models are tools that create synthetic populations *in silico* that have features similar to real populations where options for disease control and elimination interventions are being considered.



What is an Infectious Disease?

- Infectious diseases
  - caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi;
  - diseases can be spread, directly or indirectly, from one person to another.
  - Zoonotic diseases are infectious diseases of animals that can cause disease when transmitted to humans.

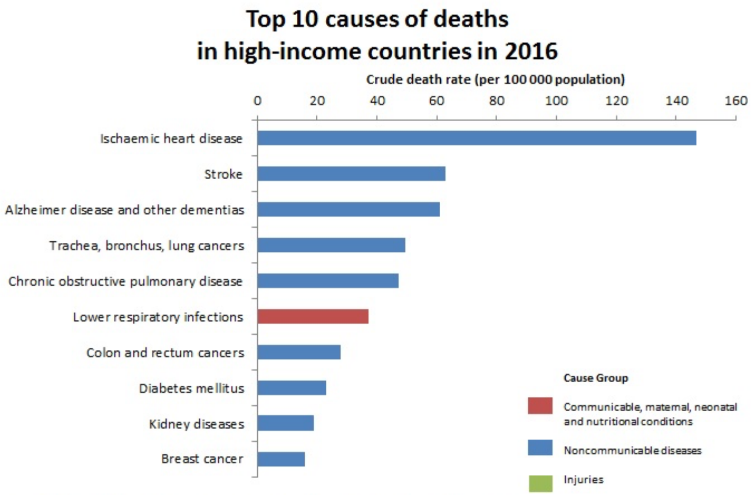
- World Health Organisation

Why Infectious Diseases?

"By the end of the Second World War, it was possible to say that almost all of the major practical problems of dealing with infectious disease had been solved."

- Sir McFarland Burnett, 1962

Why Infectious Diseases?



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.
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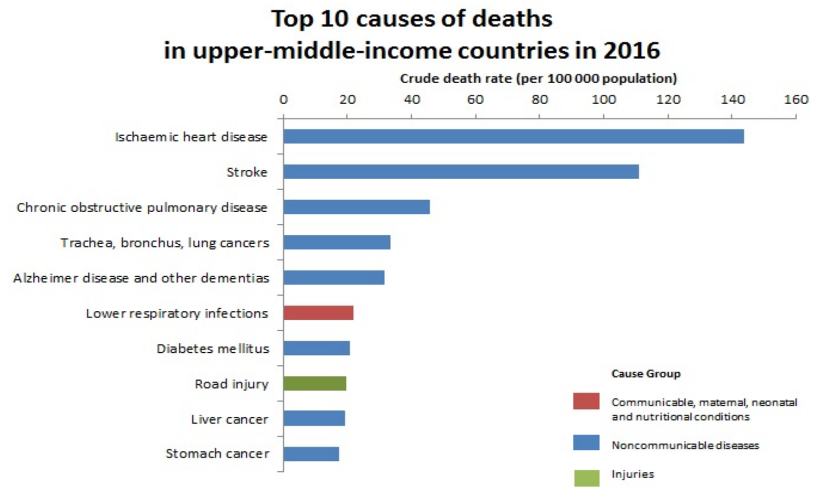

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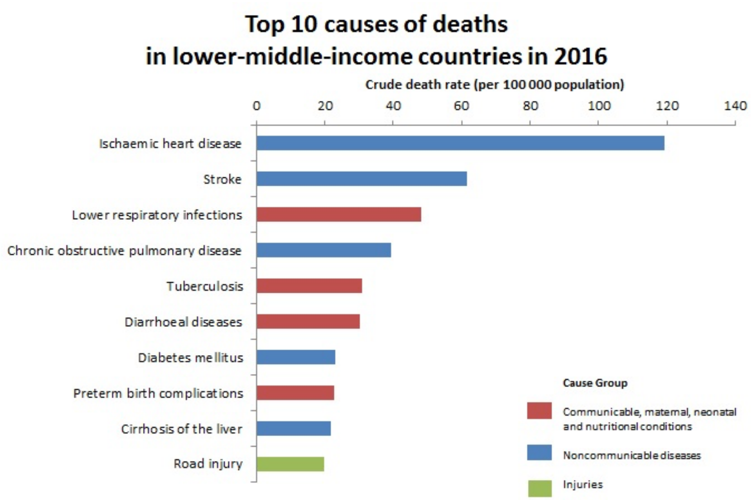

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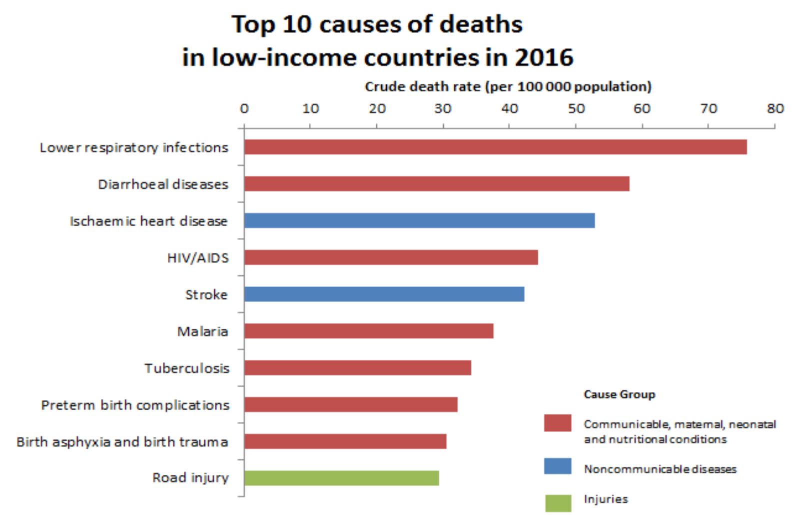

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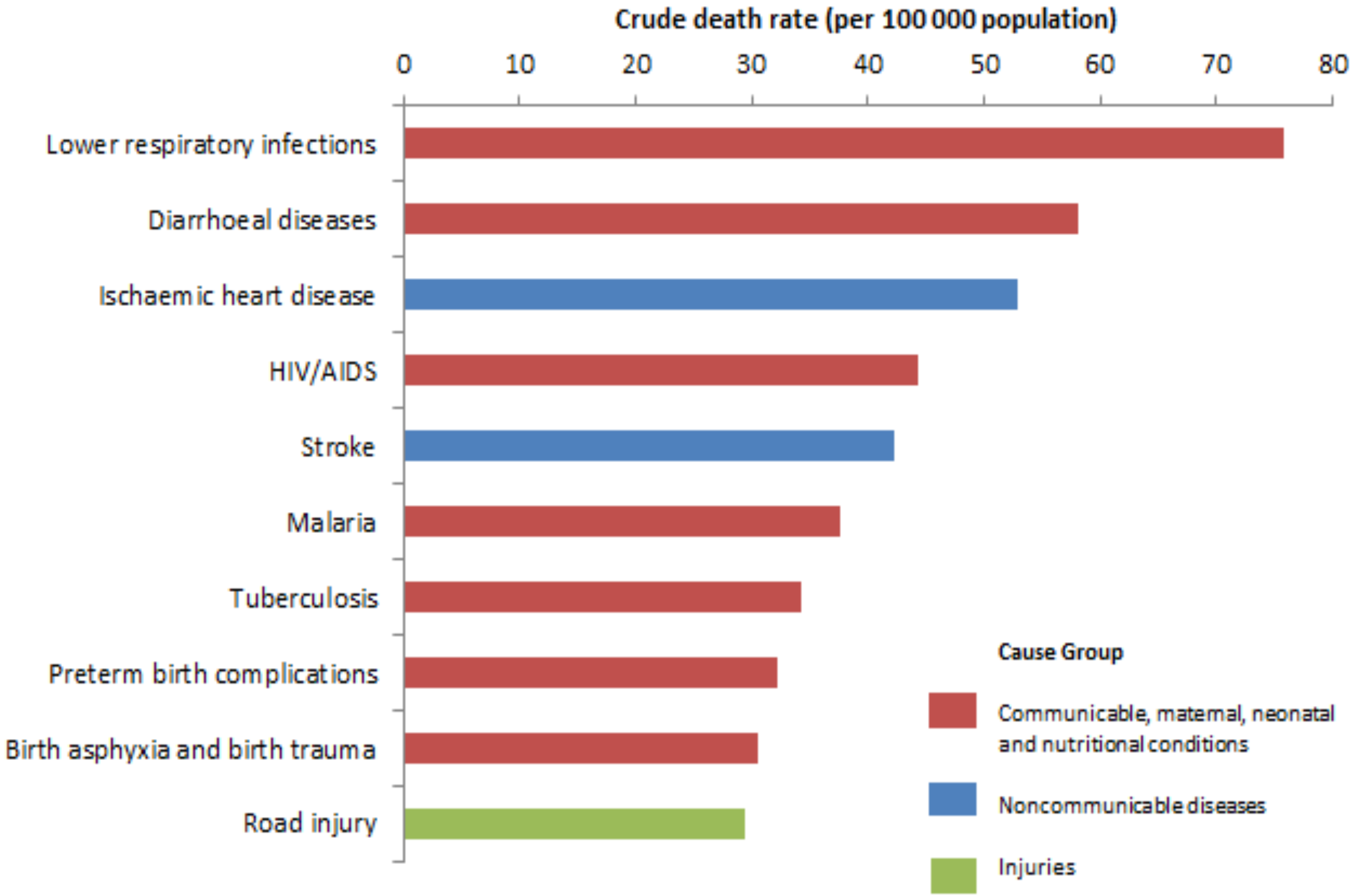
Top 10 causes of deaths in low-income countries in 2016



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Why now?

- Factors to explain re/emergent diseases
  - Human demographics and behaviour
  - Technology and industry
  - Economic development and land use
  - International travel and commerce
  - Microbial adaptation and change
  - Breakdown of public health measures

How can modelling help?

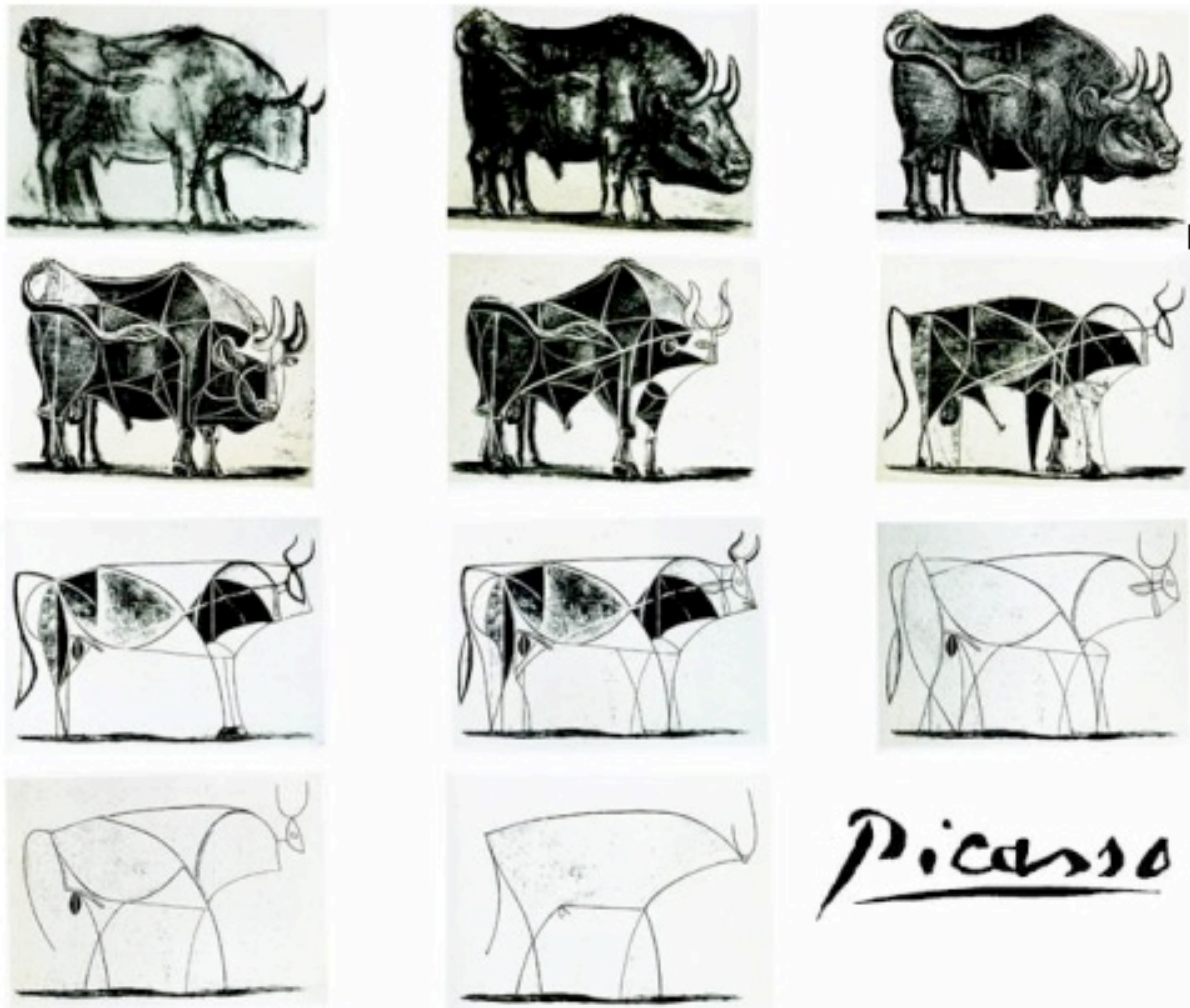
- Modelling has become an important ally
  - Project future occurrence of infectious disease
  - Distribution of resources for control/prevention
  - Help determine the plausibility of epidemiological explanations
  - Predict unexpected interrelationships among empirical observations (improve understanding)
  - Help predict the impact of changes in the system

What is a mathematical model?

- an explicit mathematical description of the simplified dynamics of a system.

- ALWAYS wrong

- BUT may be a useful approximation ($\cong$ rather than =), permitting conceptual experiments which would otherwise be difficult or impossible to do.



Pablo Picasso, Bull (plates I - XI) 1945

Types of mathematical models

- Static model
- Transmission dynamic model
- Compartment models
- Deterministic models
- Stochastic models
- Network models
- Metapopulation models
- Individual/Agent based models
- More!!

Types of mathematical models

- Static model
  - A model that assumes the incidence of infection is independent of the prevalence of infection and, therefore, time.
- E.g. Markov (decision tree) models used in medical decision- making and health economics

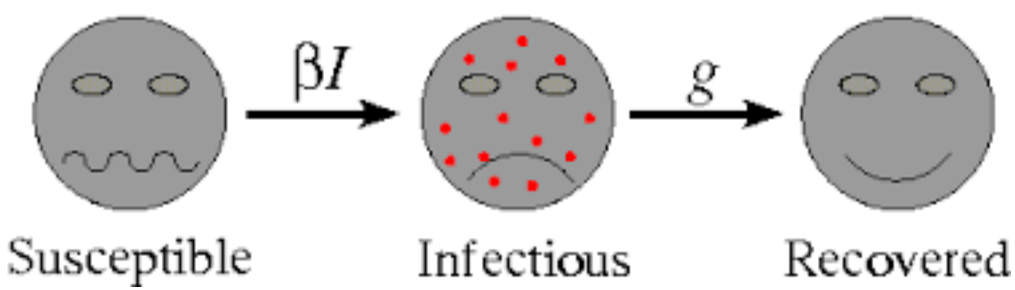
Types of mathematical models

- Transmission dynamic model
  - A model that describes the force of infection as a function of the prevalence of infection and therefore time.
  - Force of infection? – instantaneous probability of infection of a susceptible host
- Dynamic populations <u>fluctuate</u> as a result of
  - birth, death and migration
  - How incidence changes with time E.g. prevalence, immunity, or differential mortality of high-risk individuals.

Types of mathematical models

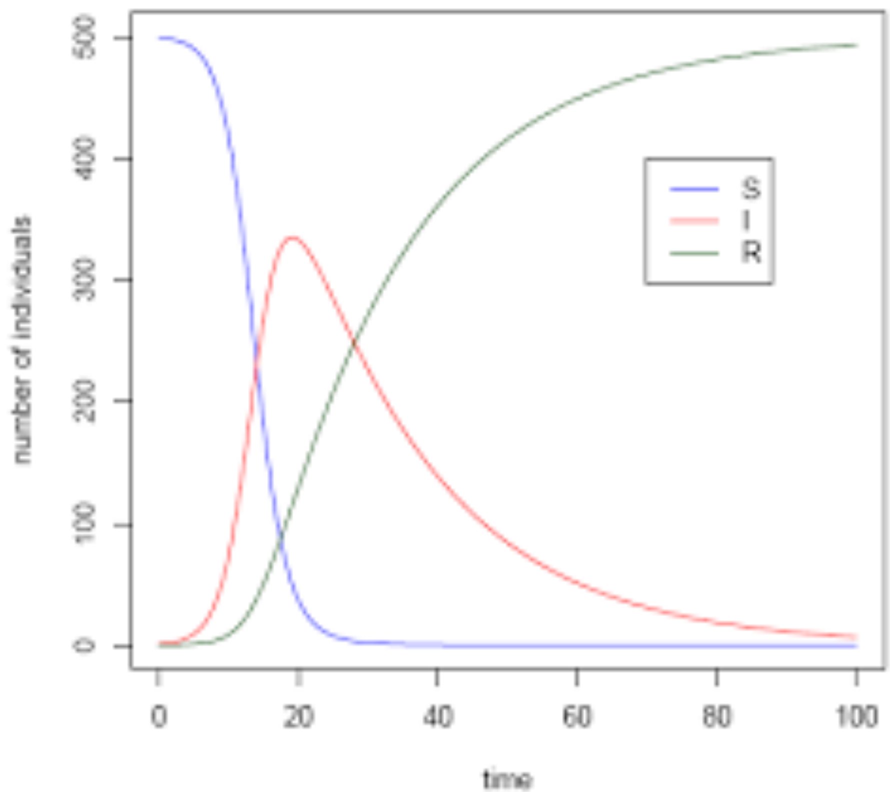
- Compartment Models
  - categorises hosts into key stages (ie, compartments or states) of infection (E.g. susceptible, infected
  - movements between these states

    occur through flows.
- Assume that a population is homogenous (all people are the same) and the only distinction is in their disease state.



Types of mathematical models

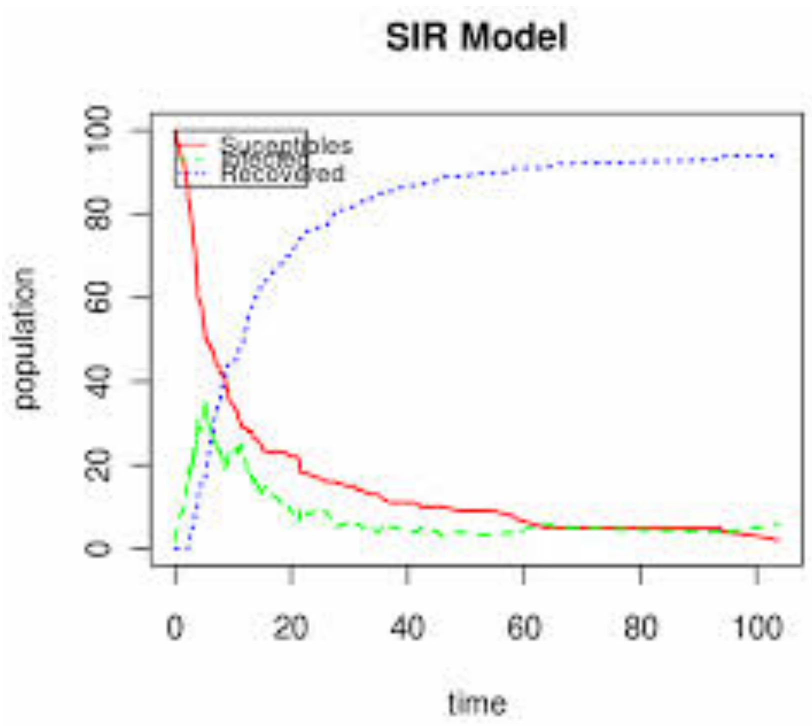
- Deterministic Models
  - compartmental models: every host follows the same average clinical life course
  - course of infection is <u>always</u> the same for all simulations under the predefined model
- reflect the 'average' behaviour of the system.

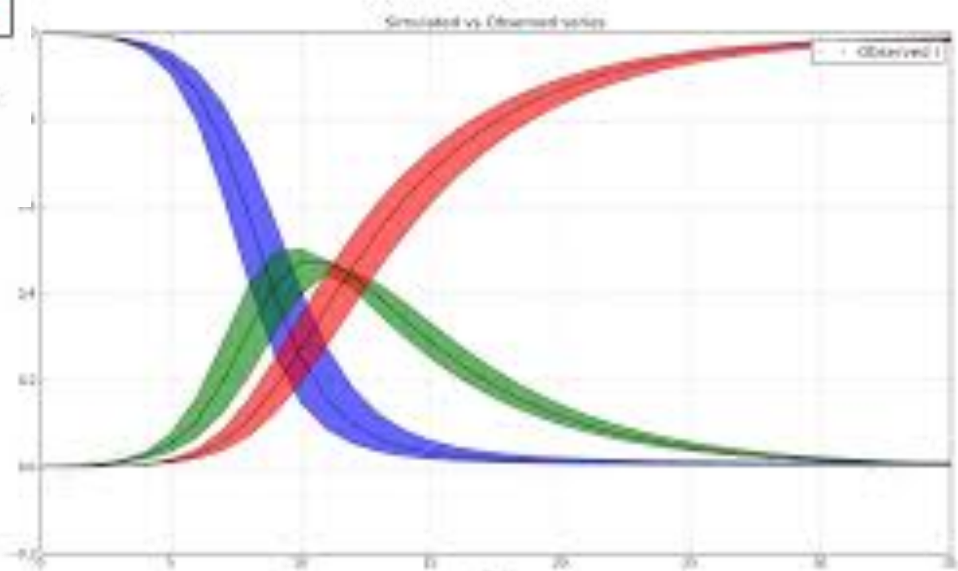


Types of mathematical models

- Stochastic Models
  - probabilistic models that represent stochastic (random) processes
  - Each transition denotes an event that can occur to each individual in a time interval according to a probability that is proportional to the corresponding rate in the deterministic framework.
  - Used where random fluctuations are likely to be important: localised outbreaks, small population sizes, rare diseases

Types of mathematical models



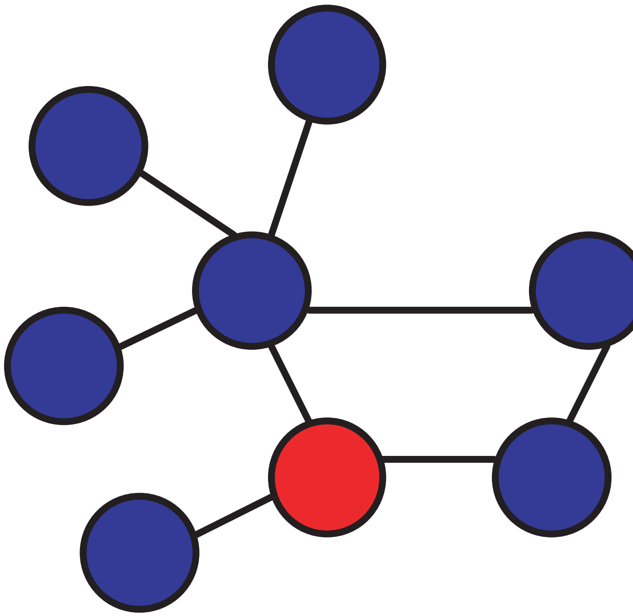


Types of mathematical models

- Network Models
  - full contact structure of individuals over a given period of time is explicitly represented and studied
- Solved analytically using

  network theory
- Advancement is limited

  due to complexity

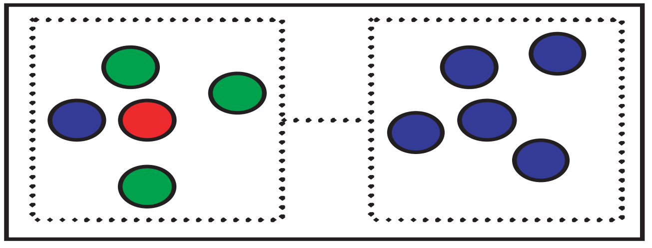


Network structure

Types of mathematical models

- Metapopulation Models
  - incorporate the within and between interplay of subpopulations (disaggregated in space or social networks)
  - movements between these states

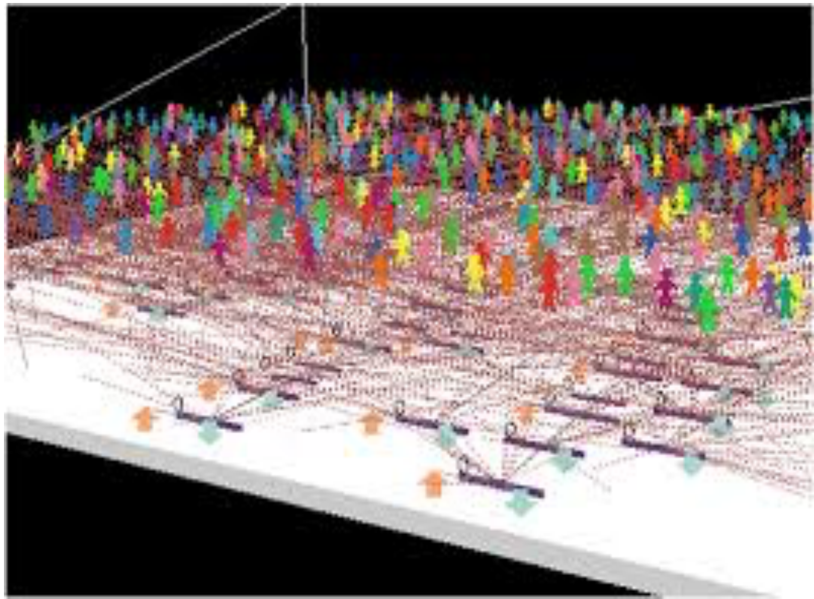
    occur through flows.
- By separating yet linking these two different groups of hosts, we may obtain better realisations of the transmission dynamics of infection over space and time



Patch structure

Types of mathematical models

- Individual based models
  - each individual host is represented uniquely
  - necessarily stochastic and are solved using simulation techniques.
  - different sources of heterogeneity
  - (eg, biological, behavioural, contact patterns, mobility)



SIR model

Kermack and McKendrick (1927)

SIR Model

- S is the susceptible population
- I is the infectious population
- R is the recovered population
- β is the number of contacts per unit time
- γ is the rate of recovery

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

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

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

SIR Models: Characteristics

- Fixed population N (S+I+R)
- Members of the population mix homogeneously
- No entry into or departure (Assume that dynamics of the disease are faster than the time scale of birth and death
- Any inherent age, demographic and spatial structure is ignored
- No initial immunity ('members' of the susceptible population are equally likely to get infected)
- The model infers permanent immunity
- The incubation period of the infectious agent is instantaneous
- Duration of infectivity is the same as the duration of the disease
- Discrete individuals do not exist in the model
- Individuals in the compartments are identical and variation among individuals is unimportant – well mixed

R_0: The basic reproductive No.

- Single most important measure

- **Expected number of secondary cases produced by a single (typical) infection in a completely susceptible population**

- Dimensionless (not a rate)

R_0: The basic reproductive No.

$$\mathcal{R}_0 \propto \left(\frac{\text{infection}}{\text{contact}}\right) \cdot \left(\frac{\text{contact}}{\text{time}}\right) \cdot \left(\frac{\text{time}}{\text{infection}}\right)$$

- Specifically, $\mathcal{R}_0 = \tau \cdot \bar{c} \cdot d$
- τ is the transmissibility (i.e., probability of infection given contact between a susceptible and infected individual)
- c-bar is the average rate of contact between susceptible and infected individuals
- d is the duration of infectiousness

R_0: The basic reproductive No.

- How to compute R_0?
  - Determine the individual terms conceptually
  - Use the threshold analysis approach (determine conditions congruent to increases in infection)
  - Next generation method:
    - Let F(i) be the rate of appearance of new infections in compartment i.
    - Let V(i) be the transfer of individuals out of compartment i by all other means.
    - x0 be the disease free equilibrium
    - Then R_0 is the largest eigenvalue of

Matrix of partial derivatives

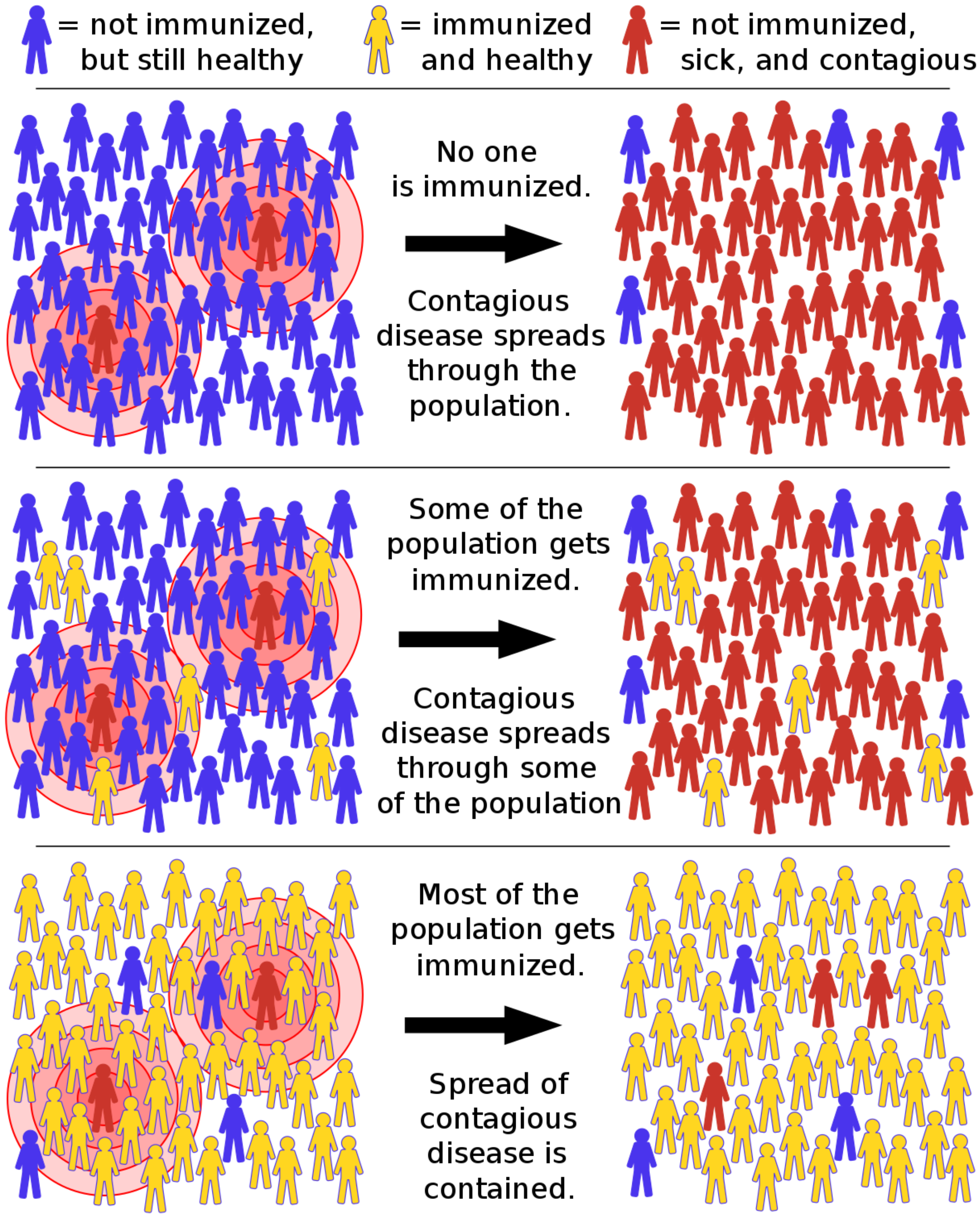
$$\left[\frac{\partial F_i(x_0)}{\partial x_j}\right] \cdot \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]^{-1}$$

Matrix of partial derivatives.

- Note that R0 has a different formula for every different compartmental model structure. Therefore be careful when comparing R0.

Herd Immunity

- A.k.a. herd effect, community immunity, population immunity, or social immunity
- form of indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who are not immune


= not immunized, but still healthy
= immunized and healthy
= not immunized, sick, and contagious
No one is immunized.
Contagious disease spreads through the population.
Some of the population gets immunized.
Contagious disease spreads through some of the population
Most of the population gets immunized.
Spread of contagious disease is contained.

Herd Immunity

- The greater the proportion of individuals in a community who are immune, the smaller the probability that those who are not immune will come into contact with an infectious individual
- p* - Prop immune in population

$$R_v = R_0(1 - p^*) = 1 \implies p^* = 1 - \frac{1}{R_0}$$

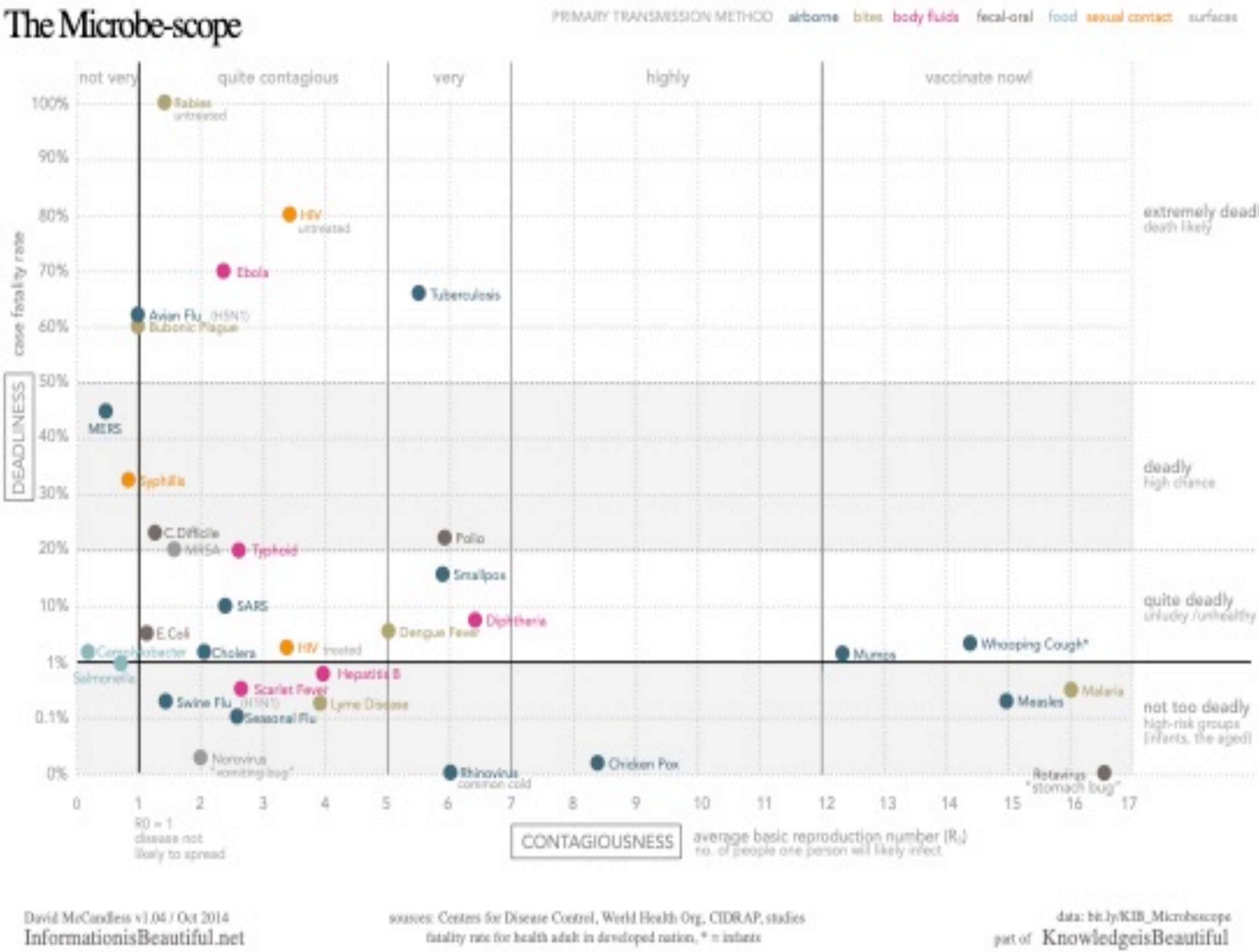
$$p > p^* \implies R_v < 1 \quad \text{No epidemic!}$$

Herd Immunity

Estimated R_0 and HITs of well-known infectious diseases[51]

Disease	Transmission	R_0	HIT
Measles	Airborne	12–18	92–95%
Pertussis	Airborne droplet	12–17[52]	92–94%
Diphtheria	Saliva	6–7	83–86%
Rubella	Airborne droplet		
Smallpox		5–7	80–86%
Polio	Fecal-oral route		
Mumps	Airborne droplet	4–7	75–86%
SARS		2–5[53]	50–80%
Ebola (Ebola virus epidemic in West Africa)	Bodily fluids	1.5–2.5[54]	33–60%
Influenza (influenza pandemics)	Airborne droplet	1.5–1.8[52]	33–44%

Unless noted, R_0 values are from: History and Epidemiology of Global Smallpox Eradication From the training course titled "Smallpox: Disease, Prevention, and Intervention". The Centers for Disease Control and Prevention and the World Health Organization. Slide 17. Retrieved 13 March 2015.



The Microbe-scope
PRIMARY TRANSMISSION METHOD airborne bites body fluids fecal-oral food sexual contact surfaces
not very
quite contagious
very
highly
vaccinate now!
DEADLINESS
case fatality rate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
1%
0.1%
0%
extremely deadly
death likely
deadly
high chance
quite deadly
unlucky /unhealthy
not too deadly
high-risk groups
(infants, the aged)
Rabies
untreated
HIV
untreated
Ebola
Tuberculosis
Avian Flu (H5N1)
Bubonic Plague
MERS
Syphilis
C.Difficile
MRSA
Typhoid
Polio
Smallpox
SARS
Diphtheria
E.Coli
Dengue Fever
Campylobacter
Cholera
HIV treated
Mumps
Whooping Cough*
Salmonella
Hepatitis B
Scarlet Fever
Swine Flu (H1N1)
Lyme Disease
Seasonal Flu
Measles
Malaria
Norovirus
"vomiting bug"
Chicken Pox
Rhinovirus
common cold
Rotavirus
"stomach bug"
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
R0 = 1
disease not
likely to spread
CONTAGIOUSNESS
average basic reproduction number (R0)
no. of people one person will likely infect
David McCandless v1.04 / Oct 2014
InformationisBeautiful.net
sources: Centers for Disease Control, World Health Org, CIDRAP, studies
fatality rate for health adult in developed nation, * = infants
data: bit.ly/KIB_Microbescope
part of KnowledgeisBeautiful