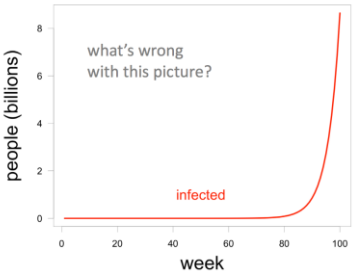
How do we model Disease Dynamics?
(Infectious Disease Dynamics)
We're going to build a simple transmission cycle for influenza.
We have:

- An infected person
- An uninfected person (the one that's susceptible)
- Transmission (sneezing)

Simple transmission cycle:

- Each **infected person** transmits (by sneezing) influenza to **two other people.**
- For each infected person, they will sneeze on two people
- $N_{t+1} = N_t \times (1+2)$
  -Malthusian growth level
  -number of people infected (in red)
  -multiplied by factor of 1 because they stay infected
  -plus two extra people

How to Model Disease Dynamics:



What is wrong with the diagram?

- Exponential growth
- Within 100 weeks, there's more people infected than more people in the earth
- The population should be **finite,** so add this to the model
- **Move people from the susceptible population to the infected population**
- If we run that model of susceptible to infected, we get this:
- The exponential growth hits a maximum number and stops
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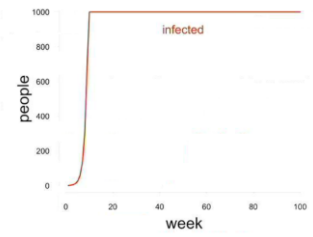
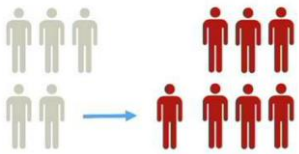
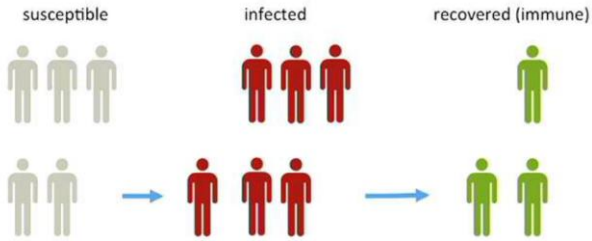


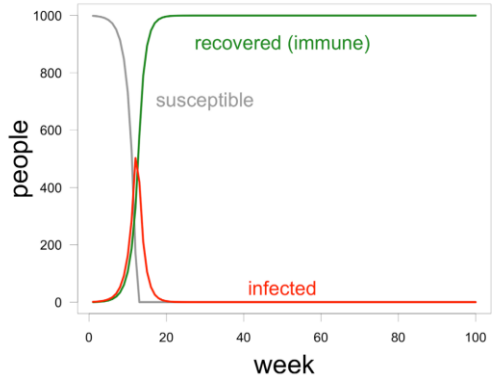


- The problem with this is that it **assumes people are forever infectious and keep infecting people.**
- So it is much more realistic to add another population in this: **the recovered (immune)**

- For many diseases, people **recover** and become immune to infection, so this should be included in the model

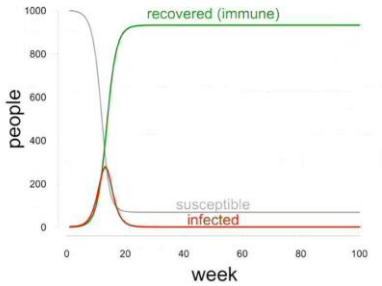


-
- you can get sick again and again but it will always be a different virus
- once you experience a virus, you can't get it again because you've developed a strain
- infected people move into the immune state
- So if we add this into our model:



- looks more like expected in a fixed population
- something iffy about this → by around 15 weeks, there aren't many susceptible left
  -fewer susceptible
  -more immune
- half the population are immune
- very few susceptible
- transmission looks soooooo fast
- fewer susceptible = less likely that infected people sneeze of susceptible = slower transmission
- Our model assumes each infected can always find 2 susceptibles → like they're out seeking people to infect
- Instead, we need to form a **density dependence:** transmission rates should drop as more people become immune → because **infectious-susceptible contacts becoming rarer.**
- SO instead of infected people sneezing on exactly two people, we say **each infected meets and sneezes on some number of randomly selected people**
- Only **some fraction** of these are **susceptible**

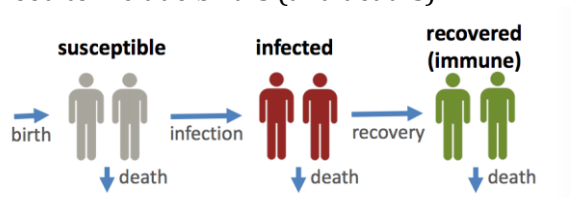
- so if that happens, we have a slightly smoother relationship:

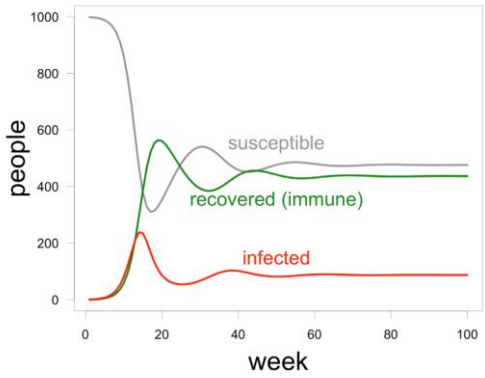


- more realistic
- as the number of recovered people increase, the number of infected people decrease
- so rare that the disease disappears
- less susceptible people
- people recover and become immune, pathogen runs out of people to infect

So why do pathogens keep coming?

- If new susceptibles keep being added to the population, it can keep infecting people and persist
- Need to include births (and deaths)

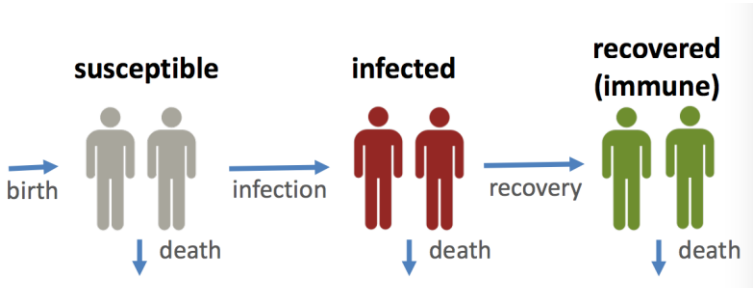




(assuming as many deaths as births, to keep N=1000)

- eg. Measles has a high capacity to spread
- weird behaviour in graph
- infected people increases, more people recovered and stay immune and starts building up, then susceptible drops, new susceptible people come in, and then infection rate decreases and tehn increase again
- nothing being added, so ends up settling
- the no of people infected stays at an average number → **assistance of pathogen when more people are added to the population**
- this is how diseases become **endemic**
- if there aren't enough susceptibles being added to the population (to keep up with the rate of recovery), the disease will die out
- eg. Measles can only persist in cities with at least 300,000 inhabitants, so that **enough susceptible children** are born to sustain transmission
- if enough of these children are vaccinated, endemic measles is easily prevented

Our transmission model:

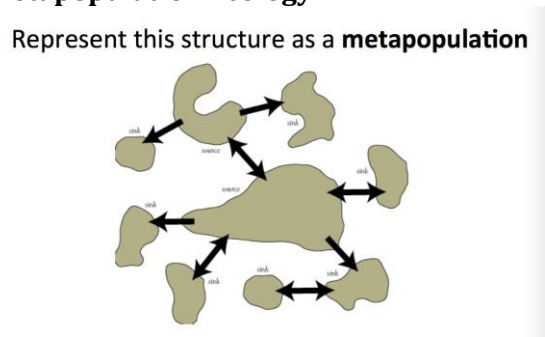


- **Infection:** 1.26 sneezings per infected per week
- **Recovery:** 50% per week
- **Death:** 10% per week (regardless of infection)
- **Birth:** 300 per week (same as number of deaths)
- **This is the classical SIR model (SUSCEPTIBLE, INFECTED, RECOVERED)**

Population mixing

- **Perfect mixing is unrealistic** → you don't have an equal chance of meeting anyone in Melbourne
- You meet some people much more than others due to: **space** (campus), d**emography** (most hang out with their own age group) and **social networks** (we hang out with our mates)

POPULATION ECOLOGY APPROACH
How the number of individuals in a population change over time
Metapopulation Ecology



- Subpopulations connected as a network, with movement (dispersal) between them
- Bigger patches = bigger population
- Network of patches

Metapopulation Epidemiology
Amount of mixing (movement) **within a population** is crucial for determining the **size of an outbreak**

- Movement **between populations** (in different places) determines **whether it goes pandemic**
- The **same processes at different scales**
- Different ideas mixing on a broader scale
- Eg. Human mobility – **airline travel**
- More people fly now from London- Sydney for less money and less time
- Depends massively on transmission parameters
- May help for diseases with short incubation period, but not so much for long incubation such as ebola
- **Overland international travel:**
- HIV pandemic spread rapidly in South Africa along highways due to a very mobile high-risk population: eg. Truck drivers and sex workers at truck stops

How can we estimate dispersal?

- Human mobility – **cell phone data**
- It shows where the person was at the time
- Eg. Making a phone call you can see
- Use that information to record dispersal
- Cell phone data predicted cholera spread in Haiti

WEEK 4
Tuberculosis (TB)

- An infectious disease caused by the bacteria **Mycobacterium tuberculosis**
- The bacteria grows very slowly (division every 15-20 hours), preferring tissue that has high oxygen content, such as the lungs
- It is a disease of poverty: 22 low- and middle- income countries account for more than 80% of the active cases globally
- Aerosol transmission by infected human, risk highest within 2 years of infection

	Effect
HIV, Diabetes	Greatly increased susceptibility to infection
Under-nutrition and vitamin deficiencies	Increased risk with under-nutrition, low body-mass index, and vitamin D deficiency
Smoking, silicosis, indoor air pollution, alcohol	2-3 times increased risk with each contributing factor
Overcrowded living conditions	Increased risk of transmission
Gender	men : women is about 2 : 1
Genetics	A growing list of genes associated with risk of tuberculosis, including for natural resistance

- death from TB was largely inevitable until the beginning of antibiotics
- can be cured by chemotherapy over 6-9 months
- some forms of T are ‘resistant’ to this treatment
- the rate of increase in multi-drug resistant TB varies across countries
- is spread through throat coughs, sneezes, speaking → sending germs into the other person to breathe in

How is this relevant to evolutionary theory?
Victorian Government:

- Some bacteria have developed resistance to antibiotics that were once commonly used to treat them

Not-for-profit organisation:

- Some bacteria have developed resistance to antibiotics that were once commonly used to treat them.
- They are then no longer sensitive to that antibiotic.
- When this happens, antibiotics that previously would have killed the bacteria, or stopped them from multiplying.

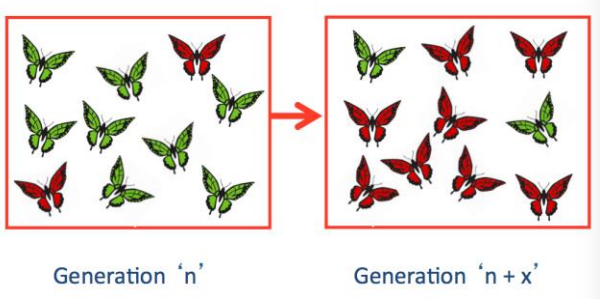
Department of Health, Australian Commonwealth Government

- Antimicrobial resistance (AMR) is the ability of a microorganism (such as bacteria, virus) to stop an antimicrobial (such as antibiotics) from working against it

EVOLUTIONARY ISSUE
Language:

- Antibiotic (or antimicrobial) may develop in an individual bacterium
- The increase in abundance of antibiotic strains is an evolutionary process
- Antibiotic resistance would not occur in the absence of using antibiotics
- While AMR is a natural phenomenon, certain human actions accelerate this process including the underuse, overuse and misuse of antibiotics in both human and animal health and in agriculture

-Darwin's theory of Evolution
Evolution: a change in trait frequency over generations



Red: proportional increase as a result of lower mortality or high fecundity
Green: Proportional decrease as a result of higher mortality or lower fecundity
The colour trait (adaptation) determines the difference in mortality or fecundity
Fecundity: actual reproductive rate of an organism or population (fertility)
Mortality: death
Evolution of Adaption by Natural Selection
Observation 1: potential increase in population size
Observation 2: Typically, population size remains stable

Deduction 1: struggle for existence among individuals
Observation 3: heritable variation in organisms

Deduction 2: differential survive (i.e natural selection)

Premises

- There is variation in the trait within a population
- The trait is heritable
- More individuals are born than can possibly survive

Evolution

- Change in trait frequency over generations

Natural Selection

- The mechanism of evolution
- Differential mortality and/or fecundity between individuals with different traits
- **N_{t+1} = n_t x (birth rate) x (mortality)**
- t= number at the time
- Selection acts on traits associated with mortality
- Selection also acts on traits associated with fecundity

Unit of Selection

Species:

- Competition occurs between individuals only
- Differential species mortality and or survivorship unlikely

Groups:

- Groups comprise 'selfish' individuals
- Differential group mortality and/or survivorship unlikely
- Empirical studies of individual behaviour

Individuals:

- Phenotype and genotype destroyed at meiosis

How is natural selection relevant to antibiotic resistance?

- Think antibiotics as a selection pressure, like predation, parasitism, or food shortage
- Think of the capacity to prevent antibiotics as an adaptation

EG. HEAD LICE

Head louse: obligate ectoparasite of humans (one of 3 groups of human lice)
-can't fly or jump, spends entire life in scalp

mutant strains of lice have resistance

-head lice shampoos contain insectides, either malathion or permethrin
-these insectides paralyse the lice by interfering with the nervous system
-in permethrin-resistant lice, a mutation prevents the action of permethrin, ensuring lice survives

Why has permethrin-resistance evolved?

- Variation in capacity of lice to survive permethrin assault, and this capacity is inheritable
- Not all lice are killed, especially of only 'mild' assault (eg. Single application)
- Surviving lice reproduce, and their offspring have that 'adaptation'
- Childs head now has numerous 'resistant' lice that, as adults, are transferred to others

How do we reduce spread of resistance?

- Ensure entire population of childs head of lice is killed
- Use other methods of removing lice that don't exert a selection pressure

CAUSES OF EVOLUTION OF ANTIBIOTIC RESISTANCE

- **Correlation** between resistance to E. coli and the use of ciprofloxacin (CIP) and co-amoxicillin-cavulanic acid (AMCL) across medical specialties within hospitals
- **Medical specialties:** urology, geriatrics, pulmonary diseases, orthopaedic surgery, internal medicine, surgery, cardiology, paediatrics, gynaecology, neurology