An introduction to modelling

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Objectives

By the end of this session you should:

- know the key uses of mathematical modelling of infectious diseases
- be able to set up a simple model using "difference equations"

What is a model?

1. Any simplification of a complex phenomenon (ECCD manual)

2. Any representation of a designed or actual object (Oxford English dictionary)

3. A stylized representation or a generalized description used in analysing or explaining something (Mangel and Hilbourne)

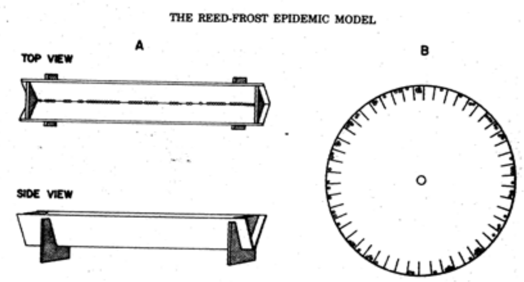
Types of epidemiological models

1. Animal models 

2. Physical or mechanical models, eg Reed-Frost teaching model

3. Mathematical models consisting of equations such as

$$\frac{dS}{dt} = -\beta S(t)I(t)$$
$$\frac{dI}{dt} = \beta S(t)I(t) - rI(t)$$
$$\frac{dR}{dt} = rI(t)$$



When might we need models?

Answer:
When we need to address questions which are difficult to answer using traditional epidemiological studies…

Example: Pandemic influenza

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Bird flu 'could kill 150m people'

A flu pandemic could happen at any time and kill between 5-150 million people, a UN health official has warned.

David Nabarro, who is charged with co-ordinating responses to bird flu, said a mutation of the virus affecting Asia could trigger new outbreaks.

Experts fear birds will carry the virus across borders

"It's like a combination of global warming and HIV/Aids 10 times faster than it's running at the moment," Dr Nabarro told the BBC.

But the World Health Organisation has distanced itself from the figure.

The WHO spokesman on influenza, Dick Thompson, told a news conference in Geneva that the WHO's official estimate of the number of people who could die was between two million and 7.4 million.

BBC NEWS:VIDEO AND AUDIO

Watch Dr Nabarro's statement on bird flu

VIDEO

BIRD FLU

KEY STORIES

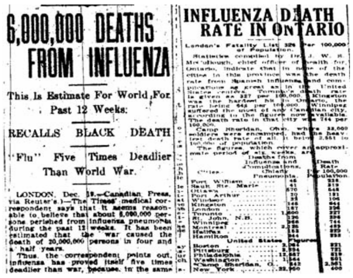
- French swans have deadly bird flu
- Man dies of bird flu in Vietnam
- WHO chief issues bird flu warning
- Clues to pandemic bird flu found

ANALYSIS AND BACKGROUND

Bird flu journey
Watch how the lethal virus has spread

- Bird flu: Still a threat?
- Q&A: Bird flu
- Your concerns answered
- Guide to countries' preparations
- Map: Global impact
- Quick Guide: Bird flu

Newspaper clippings from 1918…



Images from 1918…

Policemen in Seattle, December 1918

Streetcar in Seattle

www.archives.gov/exhibits.influenza-epidemic/records-list.html and
Seattle Museum of History and Medicine

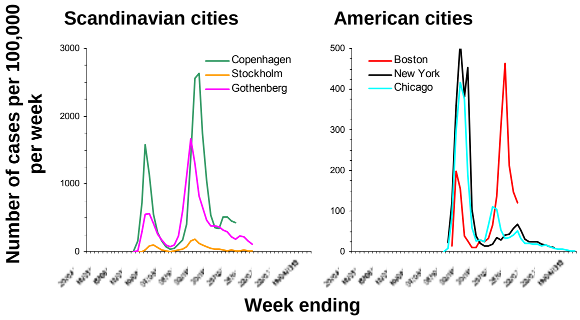
Images from 1918…

National Museum of Health and Medicine, AFIP
Emergency hospital during 1918 influenza epidemic, Camp Funston, Kansas

Considerations for planning interventions during a future pandemic

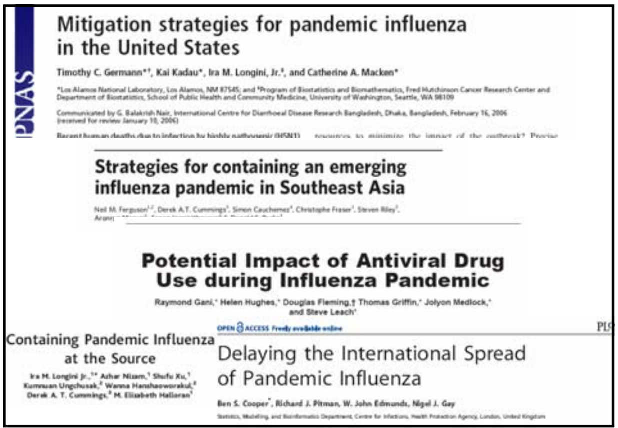
- Several months may elapse between the emergence of a virus which is transmissible to humans and the development of a vaccine
- Influenza pandemics sometimes occur in several waves and the quality of the vaccine available for the first wave may be poor
- There are limited supplies of antivirals e.g. for <25% of the population
- The age group most likely to be affected is unknown
- Treatment must be taken as soon as possible after onset, for maximum effectiveness

Data on the notification rates of influenza in Scandinavia and the US during the period 1918-1919



Control strategies against pandemic influenza – key questions

- If a vaccine becomes available, how should it be distributed e.g. Should children get it first?
- Should individuals be vaccinated with the poor quality vaccine before the first wave or wait until a high quality vaccine is available for the second wave
- Would travel restrictions have any impact on the spread of influenza?
- Will shutting schools have an impact?
- What will happen if antivirals run out?


Mitigation strategies for pandemic influenza in the United States

Timothy C. Germann, Kai Kadau, Ira M. Longini, Jr., and Catherine A. Macken

Strategies for containing an emerging influenza pandemic in Southeast Asia

Potential Impact of Antiviral Drug Use during Influenza Pandemic

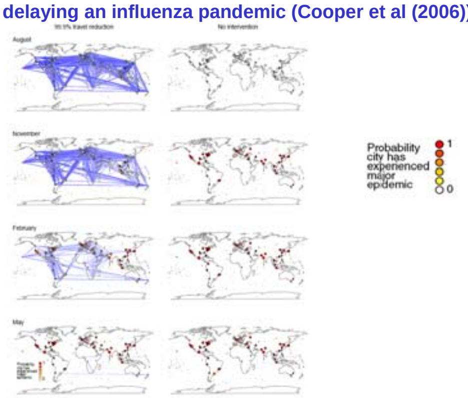
Raymond Gani, Helen Hughes, Douglas Fleming, Thomas Griffin, Jolyon Medlock, and Steve Leach

Containing Pandemic Influenza at the Source

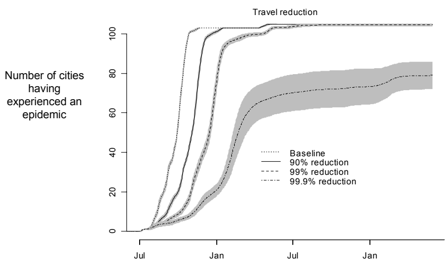
Delaying the International Spread of Pandemic Influenza

Ben S. Cooper, Richard J. Pitman, W. John Edmunds, Nigel J. Gay

Model predictions of the effect of travel restrictions on delaying an influenza pandemic (Cooper et al (2006))



Model predictions of the effect of travel restrictions on delaying an influenza pandemic (Cooper et al (2006))



Travel restrictions are made after: 1000 cases in city of origin (Hong Kong) ; 1 case in each other city.

How are models used?

1. Determining the impact of control strategies
2. Predicting the future numbers of cases
3. Elucidating the natural history or epidemiology of the infection

Added benefit – models can help to identify areas which require further study

1. Use of modelling to determine the impact of control strategies

- Centres around the theme of **thresholds**: to control transmission, we just need to reduce the numbers of cases to a sufficiently low ("threshold") level.
- First applied by **Ross (1908)**: to control malaria, it was sufficient to reduce the density of mosquitoes in a population to a sufficiently low level
- Developed further by
  - Kermack and McKendrick (1927)
  - Macdonald (1950/2) - defined the "basic reproduction rate" (→ "number" or "ratio") or "Z_0" > 1 for malaria to persist → Garki project → herd immunity thresholds

Revision of basic and net reproduction numbers etc

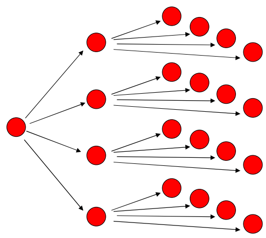
Basic reproduction number (R_0): the average number of secondary infectious cases resulting from each infectious case following his/her introduction into a totally susceptible population.

Net reproduction number (R_n): the average number of secondary infectious cases resulting from each infectious case in a given population (ie in which some individuals may already be immune).

Herd immunity threshold: the proportion of the population that needs to be immune to control transmission.

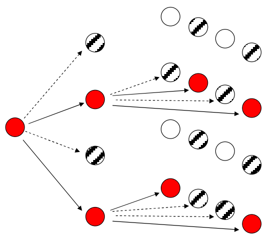
Herd Immunity: the proportion of the population that is immune to infection and/or the indirect protection resulting from the presence of immune individuals in the population.

What is the R_0 in this population?



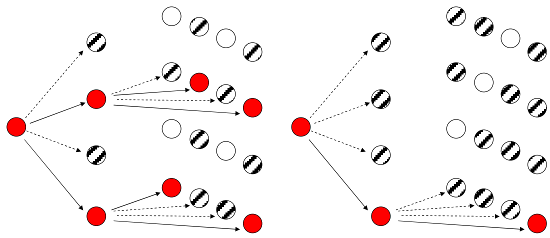
What proportion of the population would need to be immune to control transmission?

What is the net reproduction number in this population?



$$R_n = R_0 \times \textit{proportion susceptible}$$

What will be the trend in disease incidence in these populations?



The relationship between R_n and trends in disease incidence (revision)

The size of the R_n usually correlates with the trend in the disease incidence

Each case leads to **>1** infectious case => disease incidence ↑

Each case leads to **<1** infectious case => disease incidence ↓

Each case leads to **1** infectious case => disease incidence remains stable

Herd immunity threshold = % of the population that needs to be immune for the disease incidence to remain stable (i.e. R_n=1)

The relationship between R_n and the herd immunity threshold (revision)

Assuming random mixing,

$R_n = R_0 \times$ proportion susceptible (s)

At the herd immunity threshold, R_n =1,

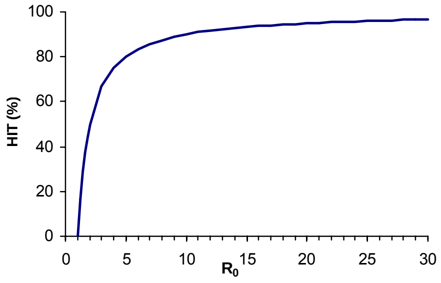
and so $R_n = R_0 \times s = 1$

so proportion susceptible (s) at the herd immunity threshold is $1/R_0$

Proportion immune (1-s) when R_n =1 i.e. at the herd immunity threshold is therefore given by

$1 - 1/R_0$

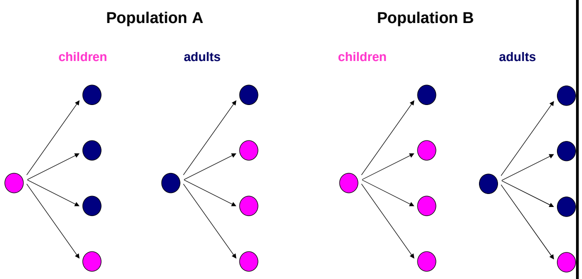
The relationship between R_0 and the herd immunity threshold (revision)



Summary of the herd immunity threshold for different diseases

Infectious disease	Herd immunity threshold (%)
Malaria	99
Measles	90-95
Whooping cough	90-95
Chickenpox	85-90
Mumps	85-90
Rubella	82-87
Poliomyelitis	82-87
Diphtheria	82-87
Scarlet fever	82-87
Smallpox	70-80

In which population is it easier to reduce transmission in the overall population by vaccinating children?



Other vaccine policy related questions

- For how long do you need to vaccinate in order to control transmission?
- Is mass vaccination at periodic intervals more effective at reducing transmission than vaccinating a fixed proportion of individuals each year?
- If no cases have been observed eg for 1 year, what is the probability that control has been achieved?
- What might be the impact of catch-up campaigns e.g. among teenagers?

These questions have been explored in relation to rubella, measles, polio, meningococcal disease etc...

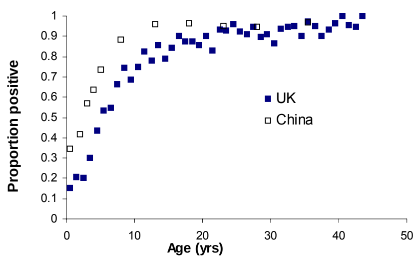
Designing optimal vaccination (or other control) programmes - use of modelling

Example: rubella and CRS (Congenital Rubella Syndrome)

Infection with rubella during pregnancy may result in the child being born with Congenital Rubella Syndrome (CRS)

In settings with a high rubella infection incidence, the burden of CRS is very low: few women are first infected when pregnant since they were infected and became immune in childhood.

Comparison between the proportion seropositive to rubella antibodies in China and the UK (Wannian (1985), Farrington (1990))



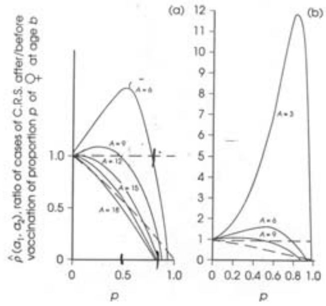
Question: In which population should you be more cautious about introducing infant MMR or rubella vaccination?

Considerations:

The introduction of vaccination

- => ↓ prevalence of infectious individuals
- => ↓risk of infection
- => ↑ proportion who are still susceptible by child-bearing age
- => ↑ burden of CRS.

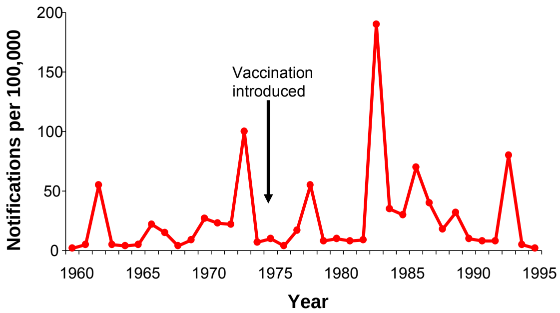
Answer - possibly China, but we need a model to investigate the possibilities!



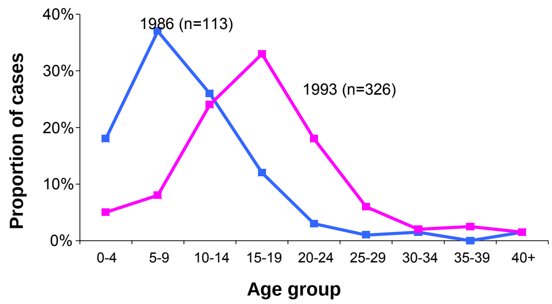
Vaccination coverage

Anderson and May (1991)

Notifications of Rubella in Greece

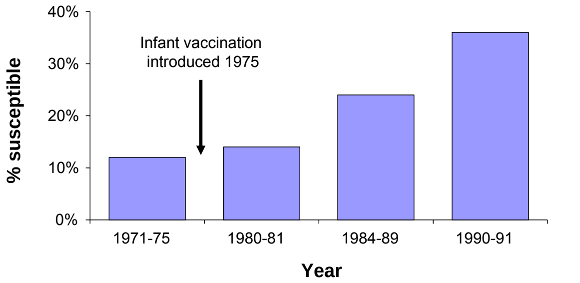


Age distribution of outpatient rubella cases, Athens



from Panagiotopoulos et al, BMJ, 1999

Proportion of pregnant women susceptible to rubella Athens, 1975-91



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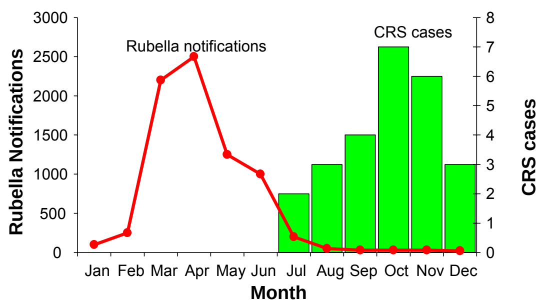
Rubella and CRS in Greece, 1993



Types of models

Stochastic

- incorporate chance variation
- provide the probability of a given outcome or range in which the outcome is likely to occur eg
  - probability that transmission ceases
  - 95% certain that 10-15 cases will be seen

Deterministic models

- describe what will happen on average in a population
- individuals are subdivided into categories ("compartments")
- describe transitions between compartments

Susceptible S_t → ($\beta S_t I_t$) → InfEcted E_t → Infectious I_t → Immune ("Recovered") R_t

Number susceptible at time t+1 =

Number susceptible at time t

- Number newly infected between t and t+1

Probability that 2 specific individuals come into effective contact between t and t+1 ("β") ×

Number susceptible at time t × Number infectious at time t

So $S_{t+1} = S_t - \beta S_t I_t$

Susceptible S_t → ($\beta S_t I_t$) → InfEcted E_t → ($f E_t$) → Infectious I_t → Immune ("Recovered") R_t

Number infected at time t+1 =

Number infected at time t

+ Number newly infected between t and t+1 ($\beta S_t I_t$)

- Number who become infectious between t and t+1

rate at which individuals develop infectious disease ("f") ×

Number infected at time t

So $E_{t+1} = E_t + \beta S_t I_t - f E_t$

Susceptible S_t → InfEcted E_t → ($f E_t$) → Infectious I_t → ($r I_t$) → Immune ("Recovered") R_t

Number infectious at time t+1 =

Number infectious at time t

+ Number who become infectious between t and t+1 ($f E_t$)

- Number who recover from infectious disease between t and t+1

rate at which individuals recover from infectious disease ("r") × Number infectious at time t

So $I_{t+1} = I_t + f E_t - r I_t$

Susceptible S_t → InfEcted E_t → Infectious I_t → ($r I_t$) → Immune ("Recovered") R_t

Number immune at time t+1 =

Number immune at time t

+ Number who recover from infectious disease between t and t+1 ($r I_t$)

So $R_{t+1} = R_t + r I_t$

Susceptible S_t → ($\beta S_t I_t$) → InfEcted E_t → ($f E_t$) → Infectious I_t → ($r I_t$) → Immune ("Recovered") R_t

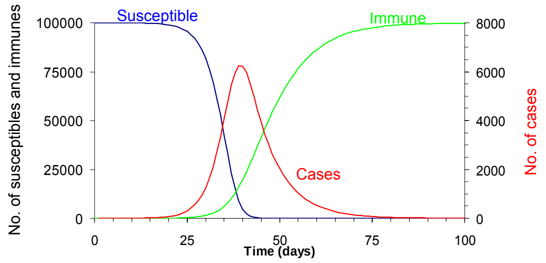
$S_{t+1} = S_t - \beta S_t I_t$

$E_{t+1} = E_t + \beta S_t I_t - f E_t$

$I_{t+1} = I_t + f E_t - r I_t$

$R_{t+1} = R_t + r I_t$

Predictions of the numbers of susceptible, infectious and immune individuals derived using the simple model for measles



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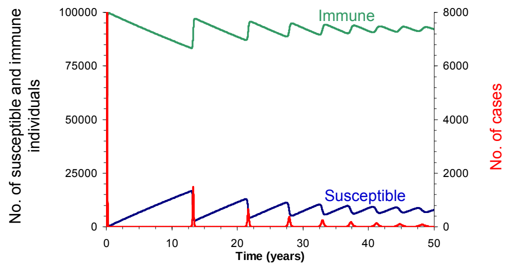
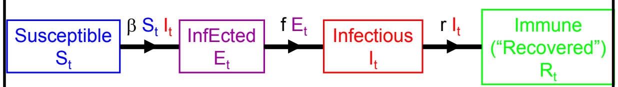


In conclusion

Modelling may:

- provide helpful insights into questions whose answers are not immediately obvious
- help define optimal control strategies for infections
- identify factors for which more information is required
- help elucidate patterns in the occurrence of infection and disease



$S_{t+1} = S_t - \beta\ S_t\ I_t$

$E_{t+1} = E_t + \beta\ S_t\ I_t - f\ E_t$

$I_{t+1} = I_t + f\ E_t\ - r\ I_t$

$R_{t+1} = R_t + r\ I_t$

To be continued in the computer practical…