Modelling the Spread of Infectious Diseases

Transcript

Date: Tuesday, 18 March 2014 - 1:00PM

Location: Museum of London
Welcome to the last of my lectures this academic year and thank you for coming along.

This year I have taken as my theme some examples of fundamental concepts of mathematics and how they have evolved.

In this lecture I will be talking about an application of mathematics which helps to explain and quantify the spread of infectious diseases and how to assess the impact of vaccination strategies.

Examples of the diseases I will be talking about are measles, mumps, rubella, smallpox and chickenpox. One characteristic I will assume for these diseases is that if you survive the infection or are vaccinated against it you will have lifelong immunity.

Vaccination is one of the major medical advances of all time and has saved thousands of lives in the UK alone as well as millions of lives worldwide. Although vaccination began with the work of Edward Jenner in the late eighteenth century it was only in the last century that safe and cheap vaccines could be produced in large quantities. The aim of vaccination is to prevent infection happening in the first place and so avoid the need to treat the symptoms of infection.

In simple terms vaccines work by stimulating the immune system to produce antibodies but without infecting us with the disease. Antibodies are substances produced by the body to fight the disease.

Mathematics is of use in modelling the spread of infectious diseases and then in assessing the impact of various vaccination strategies.

Let me give you an overview of what I will be talking about.

**Slide: Overview of the lecture**

*Compartment models*

As we will be considering diseases which if you survive them you then have lifelong immunity it is natural to divide the population into three compartments – those susceptible to the disease, those infected with the disease and those recovered and therefore immune from the disease.

People can move between categories, for example a susceptible person can become infected and an infected person could recover and become immune. Also people can join the susceptible compartment usually by being born. And of course death causes you to leave the population!

*Reproductive rates*

To make any further progress we need to quantify the transfer rate between the various compartments and the birth and death rates for the population. Crucial to this progress is the idea of the *basic reproductive rate*.

The basic reproductive rate is the number of secondary cases produced by one infected person when all the population is susceptible.

Different infections have different basic reproductive rates. This is because different infections vary in, for example, the ease with which they are transmitted and for the length of time for which a person remains infectious. The basic reproductive rate also can vary between populations because of different social behaviours, for example the frequency and nature of contacts between individuals.

*Average age of infection*

The basic reproductive rate is hard to observe and evaluate. We can use our simple compartment model to show how the basic reproductive rate is related to the average age at which people get the infection. Essentially we will show the intuitively obvious result that the larger the basic reproductive rate the lower the average age at which the infection is acquired. Indeed we will see that the average age of infection is inversely proportional to the basic reproductive rate so doubling the basic reproductive rate halves the average age at which infection is acquired.
Later I will introduce more complicated models and it can be shown that the same relationship still holds between basic reproductive rate and average of infection.

Waves of infection

I will set up a simple model for this movement between the susceptible, infected and recovered compartments and, using a spreadsheet, see how the model explains epidemics or regular cycles or waves of disease. We will also see that even though the model is very simple it mimics observed patterns.

Jenner, vaccination and eradication

In this section on vaccination I will give you a little background about Edward Jenner. Jenner was an English doctor, the pioneer of smallpox vaccination and often called the father of immunology. Vaccination has been very important not only in saving lives but in improving the quality of life.

I will find the critical proportion of the population that it is necessary to vaccinate to eradicate an infection. It is a simple expression involving the basic reproductive rate of the disease. If we cannot achieve this critical proportion then vaccinating a lower proportion does reduce the number infected but also raises the average age at which infection is acquired compared to the average age before the start of the vaccination campaign. This increase in average age can be significant for a disease like rubella or German measles which if caught later in life when a woman is pregnant can cause serious disorders to the baby if it is acquired during the first 20 weeks of pregnancy.

Beyond the simple models

My last section will indicate some improvements that could be made to the basic model I have used and consider what to do whenever a vaccine does not provide lifelong immunity and consider how vaccination might be used in a future outbreak of foot and mouth disease in livestock.

Slide: compartment models

Here the population is divided into three compartments:

S is the collection of susceptible people and we will also use it, S, to denote the number of susceptible people.

I is the collection of infected people and we will also use it, I, to denote the number of infected people.

R is the collection of recovered people and we will also use it, R, to denote the number of recovered people. This is frequently known as the SIR model.

A person will move from the susceptible compartment to the infected compartment if they acquire the disease and on recovery will leave the infected compartment and enter the compartment of those who have recovered and we will assume subsequently have lifelong immunity.

So we need to think of the quantities S, I and R as varying with time.

The model also has other inputs and outputs. The most important ones are births and deaths.

Slide: Compartment Model – add births

An obvious way of adding births to the model is to use the birth rate, b, for the population. For the United Kingdom, for example, the birth rate is about 12 births per thousand adults per year.

So the birth rate per person in the United Kingdom is 0.012 per year.

Then if b is the birth rate, N is the total population, which is S + I + R, the number of births is bN and we make the assumption that all of these enter the susceptible compartment. In the UK, if we take the population as about 60 million then the number of births is 60 million times 0.012 which is 720,000 births per year.

Slide: Compartment Model – add deaths

But there are also deaths as well as births and in this slide I distinguish two death rates which I call the natural death rate, affecting all compartments and the disease induced death rate which only affects compartment I.

An example giving a disease induced death rate is measles.

As the World Health organisation states in a factsheet issued last month:
Measles is still common in many developing countries – particularly in parts of Africa and Asia. More than 20 million people are affected by measles each year. The overwhelming majority (more than 95%) of measles deaths occur in countries with low per capita incomes and weak health infrastructures. As high as 10% of measles cases result in death among populations with high levels of malnutrition and a lack of adequate health care.

http://www.who.int/mediacentre/factsheets/fs286/en/

If there is little disease induced death we can work with the overall average death rate. In the United Kingdom this was about 12 per thousand per year in 1961 and has dropped to just over 9 per thousand per year in 2013.

Of course it is possible to modify the compartment model in very many ways.

**Slide: Modifications of compartment model**

Some are:
- Add a latent compartment of people who are infected but not yet infectious. Tuberculosis might be an example.
- For some diseases maternal antibodies may protect for the first three to nine months so infants are born into a new protected compartment and lose immunity in the first year.
- Immunity may be lost, not lifelong, for example vaccination against influenza.
- You can build in the age structure of the population so that you would know how many people there were at each age in each compartment. This can be important for modelling sexually transmitted diseases.
- We could then also divide the compartments into male, female to consider diseases such as mumps and rubella which have different effects on males and females at different ages.

But we will stay with our relatively simple model shown again here.

**Slide: Compartment Model – add deaths**

I want to discuss the transmission dynamics between categories, particularly from the susceptible to the infected. To do this I am going to introduce one of the most important ideas and concepts in epidemiology of infectious diseases which is that of reproductive rates.

**Slide: Basic reproductive rate**

The basic reproductive rate, R₀, is the number of secondary cases produced on average by one infected person when everyone in the population is susceptible. So R₀ gives the average number of new cases if one infectious person is introduced into a completely susceptible population.

R₀ combines the biology of the infection with social and behavioural factors influencing contact rates.

**Slide: Basic reproductive rate with table**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Basic Reproductive rate, R₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>12 – 18</td>
</tr>
<tr>
<td>Pertussis</td>
<td>12 – 17</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>6 – 7</td>
</tr>
<tr>
<td>Rubella</td>
<td>6 – 7</td>
</tr>
<tr>
<td>Polio</td>
<td>5 – 7</td>
</tr>
<tr>
<td>Smallpox</td>
<td>5 – 7</td>
</tr>
<tr>
<td>Mumps</td>
<td>4 – 7</td>
</tr>
</tbody>
</table>

This table gives the basic reproductive of some common infectious diseases in decreasing size of basic reproductive number. Measles and pertussis (commonly known as whooping cough) are very infective with a range between 12 and 17 or 18. There is such a variation in the range of R₀ because of measuring it in different places and societies with consequent variation in contact rates. Diphtheria and Rubella (also known as German measles) are about the same while polio, smallpox and mumps are slightly lower.

The basic reproductive rate is, as I have said, is the average number of new cases of the infection when an infective is placed in a completely susceptible population. But in practice this is not what happens. Not all the population will be susceptible some will be immune, others will be already infected, and this leads us to the definition of the effective reproductive rate.

**Slide: Effective reproductive rate**

The effective reproductive rate, R, is the number of secondary cases produced on average by one infected person when S people out of the population of N people are susceptible i.e. when not all the population is
susceptible.

There is a very important relationship between these two reproductive rates. It is that

\[ R = R_0 \]

cessive intervals of length equal to the length of time an individual is infectious which is roughly one week for measles. So we are dividing the timescale into weeks denoted by \( n = 1, 2, 3 \) and so on and each case only lasts a week the child recovers and immunity is conferred.

\[ S(n) = \text{the number susceptible at the start of week } n \]

\[ I(n) = \text{the number infected at the start of week } n \]

From the compartment model

\[ S(n + 1) = S(n) + bN - R_0 SS \]

of herd immunity and increase in the spread of infection - and we know that some of these diseases can have severe consequences.

I want to look now at the effect vaccination can have on the average age at which the infection is acquired. Vaccination essentially has the effect of lowering the effective reproduction number by decreasing the number susceptible in the population and we can show that this has the effect of increasing the average age of infection.

**Slide: Vaccinating below the subcritical level increases the average age at which infection is acquired**

Using the model I’ve described we can show that if we vaccinate a proportion \( p \) of the population which is a proportion below that required to eliminate the infection then in the steady state

**Average age of infection after vaccination**

\[ = \text{barrier or ring around infected individuals or farms needs to be of such a size that the number of secondary cases produced on average falls to less than one. Mathematical models and computer simulations help in deciding on the critical size of the ring surrounding infectious cases. It is important to build logistical factors into these mathematical models. For example is it possible to vaccinate all cases in the ring on the day that an infectious animal is discovered? Or if there are many initial cases in different geographical areas is it possible to vaccinate all animals in the required ring around each case?} \]

In spite of these logistical difficulties ring vaccination around infected cases does have the potential to reduce the impact of future outbreaks of foot and mouth disease.

In conclusion I hope that I have shown you that the use of mathematics can inform and influence the development and implementation of vaccination strategies.

Thank you for coming today and in the words of Nick Ross of the television programme Crimewatch:

*Don’t have nightmares, do sleep well*

Finally a note for your diary: September 16, 2014 when I start next year’s lectures, the details of which will appear in the Gresham College prospectus.

© Professor Raymond Flood, 2014