Episouth Training Module, Madrid (June 2008)

Use of models in decision making – modelling the impact of infant MMR vaccination on rubella transmission

Computer Practical

Emilia Vynnycky (HPA)

Overview and Objectives

This practical is based on practical that we run as part of our modelling shortcourse "An Introduction to Infectious Disease Modelling and its Applications", which is organized jointly between the London School of Hygiene & Tropical Medicine and the Health Protection Agency Centre for Infections.

By the end of this practical you should understand:

1. The effect of vaccination on the age-specific prevalence of infection and the incidence of infection
2. The differences between the impact of a universal as compared with a selective vaccination strategy on the transmission dynamics of rubella.

Introduction

The following figure contrasts the age-specific proportion of individuals who were found to have antibodies to rubella in China and the UK during the 1980s.

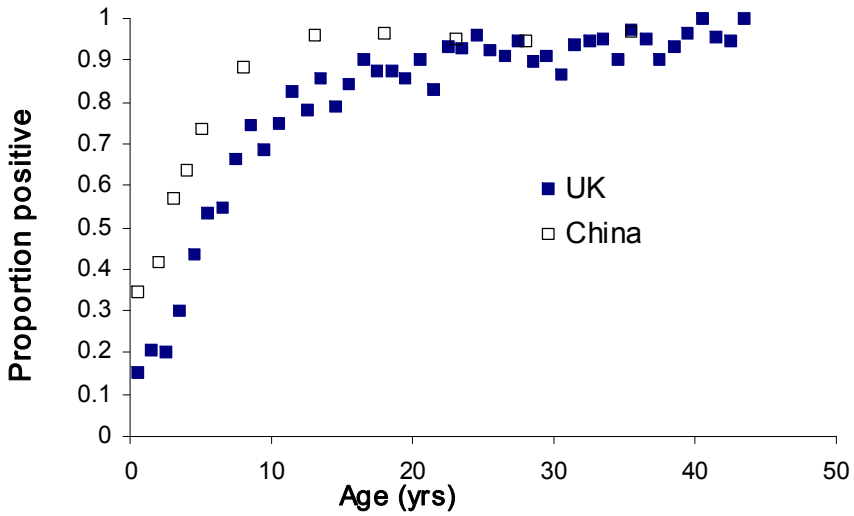


Figure 1: Age-specific proportion of individuals who had antibodies to rubella during the 1980s in the UK and China. Data source: Wannian (1985) and Farrington (1990)

According to these data, the force of infection (rate at which susceptible individuals are infected) was about 12% for the UK and 20% for China. As shown in the table below, these estimates imply that the basic reproduction number (R_0) in China and the UK was about 7

and 12 respectively. To successfully control rubella transmission, we would need to successfully vaccinate 86% and 92% of the population.

In this practical, we will contrast how different levels of coverage affect the age distribution of susceptible individuals in the population and the average age at infection. For simplicity, we will assume that individuals mix randomly in the population.

Table 1: Summary of the key parameters describing the transmission dynamics of rubella for China and the UK

Population	Force of infection (λ) (% pa)	Average age at infection (yrs) (1/λ)	R_0 (=1+L/A)	Herd immunity threshold (=1-1/R_0)
UK	12	9	7	86%
China	20	5	12	92%

Part I: Modelling the impact of infant MMR vaccination in China and the UK

Description of the model

In this practical we will use a model of the transmission dynamics of rubella with the general structure shown on the next page. It is very closely related to the models of the transmission dynamics of measles which you worked with in the last session, except that it is age-structured. Individuals are stratified into annual age strata, and move to the subsequent age stratum at the end of each year. The age of individuals is denoted by the number in the square brackets. The equations for the number of individuals in each compartment depend on whether or not they relate to the end of the year and are discussed in more detail in the Appendix.

The model has been set up in Berkeley Madonna.

1. Start up Berkeley Madonna and open the file rubvacbth.mmd.

You will see three windows: one contains the model equations, the second contains the actual parameters in the model and the third contains the model output, which is currently empty. We will refer to this window as the “Figures” window. You may want to look at the equations window once you’ve finished the practical.

You will also see a slider for R_0 and for the proportion of the population that is vaccinated (currently set to 12 and 0.0 respectively).

The model is currently set up to describe the transmission dynamics of rubella for China, as determined by the size of the R_0.

The population has a rectangular age distribution with 1000 individuals in each age group (and hence 60,000 individuals in the whole population). To see this, run the model by

clicking on the "Run" Run button on any of the windows. The number of individuals in single year age groups is plotted in Page 1 of the Figures window.

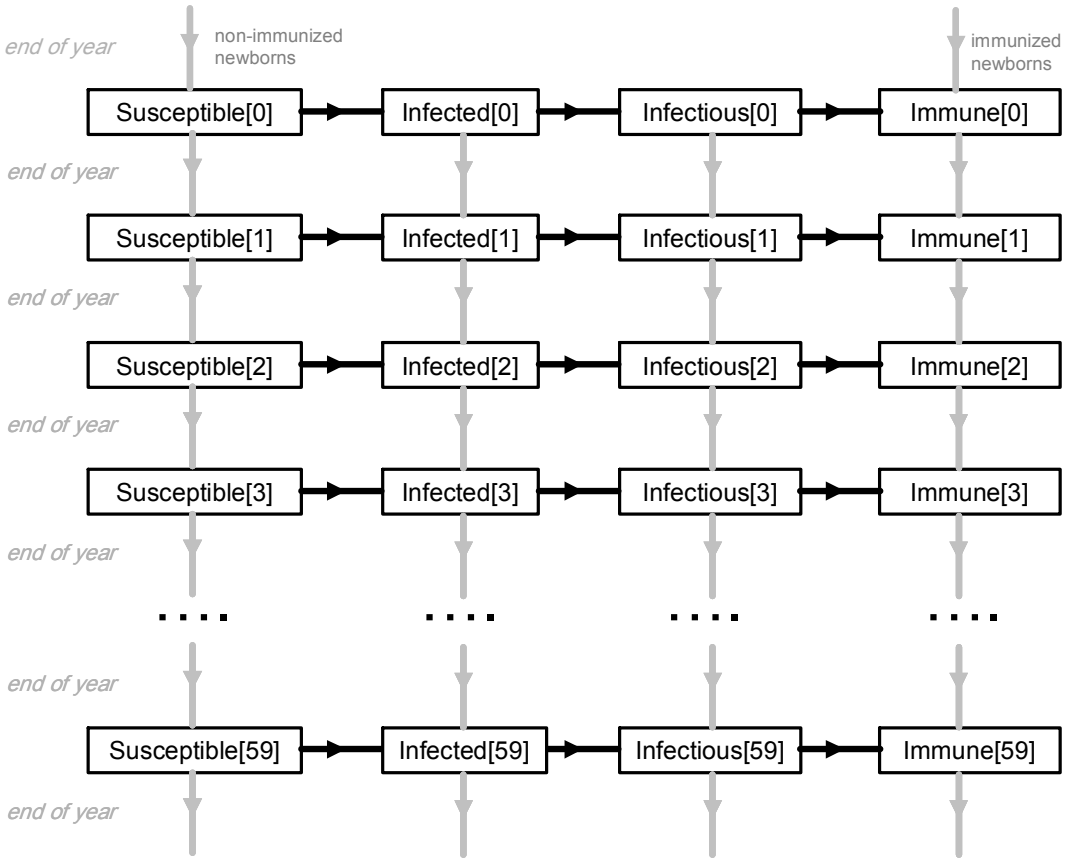


Figure 1: General structure of the model

The model makes daily predictions of the different variables in the model (force of infection, proportion of the population that is susceptible, the infection incidence in different age groups etc) in a similar way to that shown in the first computer session.

2. Click on page 2 of the figures window

Here you will see how the daily force of infection of infection changes over time.

Q1.1 What is the long-term average daily force of infection in the model? Is it consistent with the overall (annual) force of infection that is provided in Table 1? (Note that you can convert a daily force of infection into an annual force of infection by multiplying it by 365; you can see the value for the force of infection at a given time, by clicking on the line for the force of infection at that time point; the value will be displayed to the right of the buttons of the figures window.)

The corresponding proportion of individuals in selected age groups who are susceptible is provided in page 3 of the figures window. To see the number of individuals who are susceptible or immune in all age groups in the model at the end of the simulations, click on page 4 of the figures window. The values for the numbers or proportion of individuals who

are susceptible in both of these here pages should be approximately consistent with the values which are provided in Figure 1 of this handout.

We will now explore how different levels of MMR vaccination coverage in China affect the force of infection, age-specific prevalence of infection and the age-specific incidence of infection.

Simulating the impact of different levels of MMR vaccination coverage on the transmission dynamics of rubella

Vaccination of newborn individuals is introduced 100 years after the start of the simulations.

1. Change the vaccination coverage to be 40% by clicking and dragging the slider for prop_vacc to the right.

Q1.2 How does the introduction of infant MMR vaccination affect the long-term average force of infection? According to the formula A=1/λ, what is the long-term average age at infection following the introduction of infant MMR vaccination?

2. Click on page 4 of the figures window containing the proportion of 5, 20, 30 and 40 year olds who are susceptible to infection in the population.

Q1.3 Why does the average proportion of 5, 20, 30 and 40 year olds who are susceptible to infection increase in the short-term? How soon after the introduction of MMR vaccination does the proportion of 5, 20, 30 and 40 year olds who are susceptible peak? Is this what you would expect and why?

Q1.4 How does infant MMR vaccination affect the long-term average proportion of 5, 20, 30 and 40 year olds who are susceptible to infection? Why does this occur?

3. Click on the button labelled “prop_sus_all”. This will add predictions of the overall proportion of the population which is susceptible to the figure.

Q1.5 How does the introduction of infant MMR vaccination affect the overall average proportion of individuals who are susceptible to infection? Is this what you would expect? Why?

4. Click on page 5 of the figures window, where you will see a figure showing the daily infection incidence per 100,000 population among 5, 20, 30 and 40 year olds.

Q1.6 How does the introduction of infant MMR vaccination affect the infection incidence among 5 year olds? How does it affect the infection incidence among 20, 30 and 40 year olds? Why might this occur?

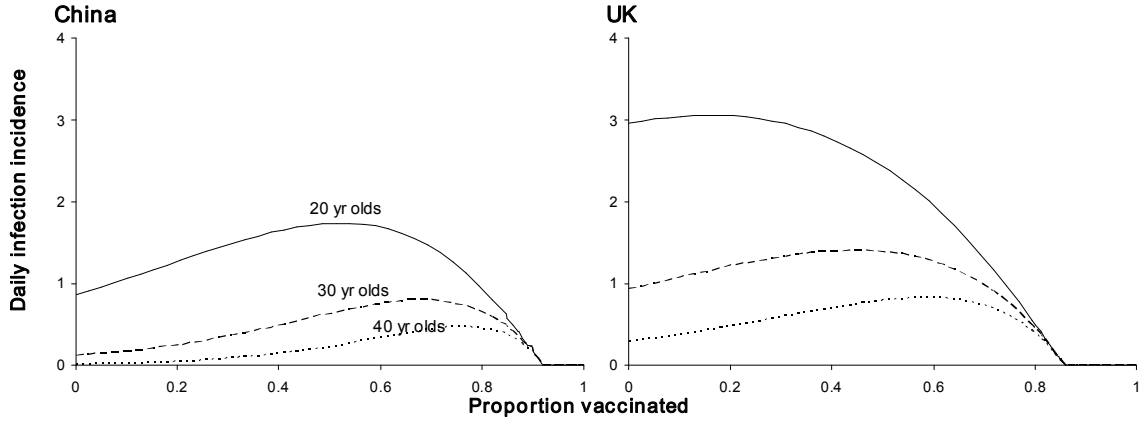
Q 1.7 How do these age patterns in the daily incidence of infection change if you increase the level of vaccination coverage to 50%, 60%, 70%, 80%?

Further insight into the likely impact of the introduction of infant MMR vaccination can obtained by plotting the long-term infection incidence among adults against the vaccination coverage, using Berkeley Madonna's parameter plot facility as follows.

5. Select the "Parameter plot" option from the "Parameters" option in the main menu. Specify that you would like to run the model 6 times, with prop_vacc as the parameter that you'd like to vary, ranging between 0 and 1.00. Specify that for each model run, you'd like to plot the final values of "new_infns_20", "new_infns_30", "new_infns_40" on the y-axis. Click on the run button to see the plot.

Q1.8 What do you conclude about the likely impact of the introduction of infant MMR vaccination on the rubella incidence among adults in China?

The following contrasts model predictions of the long-term average age-specific infection incidence predicted for different levels of vaccination coverage among newborns between China and the UK. In your spare time, you can re-run the parameter plot using the R_0 for the UK to check that you get similar results.



Q1.9 Should you be most cautious about introducing infant MMR vaccination in China or in the UK? Why? How might you amend your vaccination strategy to limit the number of adverse effects?

If you have time, try the questions in part II of this practical, which explore the effect of selective vaccination strategies against rubella.

Part II – Identifying the impact of infant MMR vaccination on rubella infection trends in specific age groups (optional)

1. Open up the Berkeley Madonna file "rubvaccb.mmd".

The model is similar to the one which you were using in the first part of the practical, except that it allows you to explore the effect of vaccinating individuals in different age groups. The basic reproduction number for rubella in this population is taken to be that for the UK.

2. Set the vaccination coverage among 13 year olds to be 50% by changing the value for prop_vacc_13 accordingly (add slider). Look at the figures of the force of infection, the age-

specific proportion of individuals who are susceptible and the age-specific infection incidence which are on pages 2, 4 and 5 of the figures window.

Q2.1 How does vaccination among 13 year olds affect
a) the force of infection in the population?
b) the age-specific proportion of individuals who are susceptible?
c) the age-specific incidence of infection?
Why does this occur?

Q2.2 How does your answer to the last question change if the level of coverage is 75%? 100%?

Q2.3 What are the relative benefits of a partial vaccination strategy as compared with the strategy of vaccinating all individuals in their first year of life?

References:

Farrington CP. Modelling forces of infection for measles, mumps and rubella. Stat Med 1990 Aug;9(8):953-67.
Wannian S. Rubella in the People's Republic of China. Rev Infect Dis 1985;7:S72-S73.

APPENDIX

Equations in the model

Considering individuals aged 20 years *at any time t apart from the end of year*, the difference equations are analogous to those which you saw in the first session, namely:

$$S[20]_{t+1} = S[20]_t - \lambda_t S[20]_t$$

$$E[20]_{t+1} = E[20]_t + \lambda_t S[20]_t - fE[20]_t$$

$$I[20]_{t+1} = I[20]_t + fE[20]_t - r\, I[20]_t$$

$$R[20]_{t+1} = R[20]_t + r\, I[20]_t$$

where

$S[20]_t$ is the number of susceptible individuals of age 20 years at time t
$E[20]_t$ is the number of individuals of age 20 years in the infEcted category at time t
$I[20]_t$ is the number of infectious individuals of age 20 years at time t
$R[20]_t$ is the number of immune individuals of age 20 years at time t
λ_t is the force of infection between t and t+1
f is the rate of infectious disease onset,
r is the rate at which infectious individuals recover and become immune.

The equations considering susceptible and infected individuals aged 20 years *at a time t at the end of year*, are as follows:

$$S[20]_{t+1} = S[19]_t - \lambda_t\, S[19]_t$$

$$E[20]_{t+1} = E[19]_t + \lambda_t\, S[19]_t - fE[19]_t$$

$$I[20]_{t+1} = I[19]_t + fE[19]_t - r\, I[19]_t$$

$$R[20]_{t+1} = R[19]_t + r\, I[19]_t$$

The equations considering any other age category (including those for individuals in their first year of life) are analogous to these equations.