Episouth Training Module, Madrid (June 2008)

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

Practical Solutions

PART I: Simulating the effect of infant MMR vaccination in China

Q1.1 The average force of infection can be obtained by positioning your mouse halfway between the highest and lowest points of the line for the force of infection and reading off the value at that point. This is about 0.000529/day, which corresponds to an average annual force of infection of approximately 19.31%.

Q1.2 The average daily force of infection is about 3.26×10^{-4}.

Using the formula of $A=1/\lambda$, this value for the force of infection translates into an average age at infection of about 8.2 years. i.e. the introduction of MMR vaccination among infants leads to an increase in the average age at infection.

Q1.3 The proportion of 5, 20, 30 and 40 year olds which is susceptible to infection increases initially after the introduction of vaccination among newborns. This initial increase is attributable to the fact that the introduction of vaccination leads to a reduction in the prevalence of infectious cases in the population and hence a reduction in the force of infection. In the short-term, this leads to an increase in the proportion of individuals of age e.g. 5 years who are still susceptible.

The proportion of 5, 20, 30 and 40 year olds who are susceptible decreases 5, 20, 30 and 40 years after the introduction of vaccination i.e. once the first cohorts of individuals who have been vaccinated reach these ages.

Q1.4 In the long-term, the proportion of 5 year olds who are susceptible is lower than that seen without vaccination, whereas the proportion of adults who are susceptible is greater than that seen without vaccination.

These effects are attributable to the facts that the long-term proportion of individuals who are susceptible in a given age group depends on

1. the direct effect of vaccination, whereby the proportion of individuals who are susceptible in a given age group is directly reduced because of vaccination
2. the indirect effect of vaccination, whereby vaccination leads to a reduction in the force of infection and hence to an increase in the proportion of individuals who are still susceptible by the time they reach the given age.

In the long-term, the proportion of 5 year olds who are vaccinated is the same as that for adults, and so the direct effect of vaccination is the same for both children and adults.

However, for 5 year olds, the indirect effect of vaccination is small, as compared with that for adults, since 5 year olds will have had few years of exposure to the reduced force of infection occurring as a result of the introduction of vaccination. As a result, the proportion of adults who are susceptible in the long-term is higher than that seen before the introduction of vaccination, whereas the proportion of 5 year olds who are susceptible is lower in the long term after vaccination than that seen before vaccination has been intrduced.

Q1.5 You should notice that for any level of coverage below the herd immunity threshold, the overall average proportion susceptible in the population remains unchanged. This follows from the fact that the net reproduction number is given by the expression:

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

If the infection is still endemic, then the net reproduction number is 1, and thus the overall proportion susceptible is given by:

$$1/R_0$$

Therefore, if the vaccination coverage is below the herd immunity threshold of 92%, the overall proportion susceptible should remain at about 8%.

This also highlights the fact that the introduction of vaccination at below the herd immunity threshold leads to a redistribution of susceptible individuals in the population, rather than to an overall reduction.

Q1.6 In the long-term, the introduction of MMR vaccination among newborns leads to a decrease in the infection incidence among 5 year olds and to an increase in the infection incidence among adults.

These age patterns can be explained by the facts that:

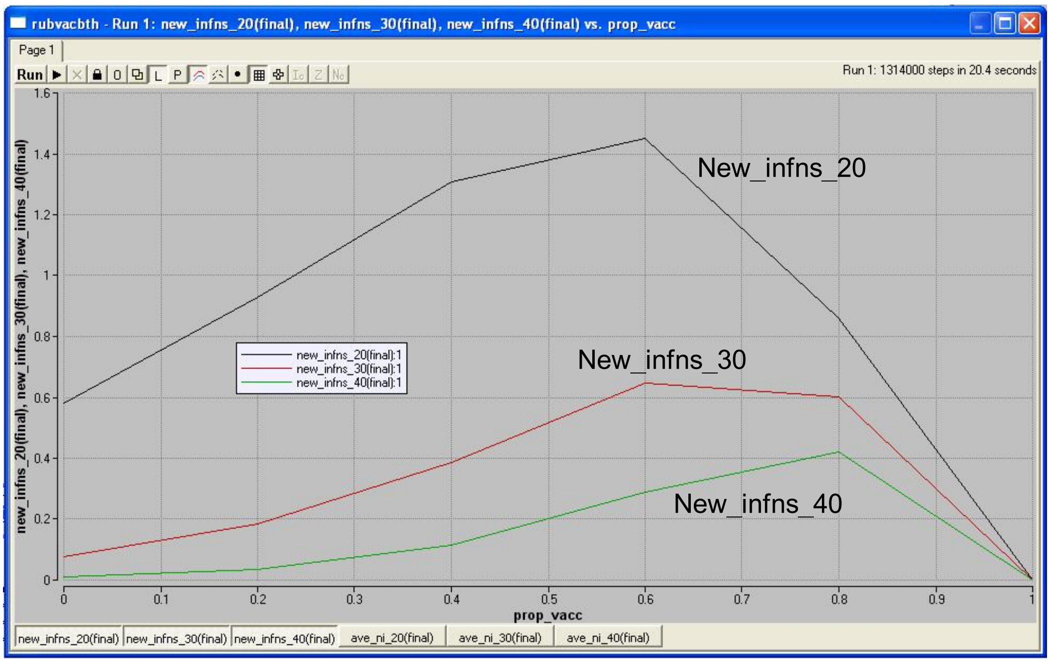
a) the infection incidence at any given age a at time t is given by $\lambda(t)s(a,t)$, where $\lambda(t)$ is the force of infection at time t and s(a,t) is the proportion of individuals of age a who are susceptible at a given time.
b) the introduction of vaccination among newborns leads to a reduction in the force of infection $\lambda(t)$.

Considering 5 year olds, the introduction of vaccination among newborns leads to a reduction in the proportion of 5 year olds who are susceptible in the long-term. The combined effect of this decrease and the decrease in the force of infection is that the infection incidence among 5 year olds is lower than that seen without vaccination.

Considering adults, the introduction of vaccination among newborns leads to an increase in the proportion of individuals of adults who are susceptible. For levels of effective vaccination coverage of 40% among newborns, this increase in the proportion of adults who are susceptible outweighs the decrease in the force of infection which is seen in the overall population. The net effect is that the infection incidence among adults is greater than that seen without vaccination.

Q1.7 Increasing the vaccination coverage to 50%, 60%, 70% and 80% among newborns leads to similar age patterns in the infection incidence to that predicted assuming a 40% vaccination coverage i.e. vaccination of newborns leads to an increase in the infection incidence among adults and to a decrease in the infection incidence among 5 year olds.

Step 5, page 5. Your parameter plot should have resembled the following:



Q1.8 Based on your parameter plot, you would conclude that the introduction of infant MMR vaccination in China is likely to lead to an increase in the rubella infection incidence among adults.

Q1.9 The graphs illustrate that for adult age groups and for a given level of vaccination coverage among infants, the infection incidence in the UK is higher than that in China, and therefore the incidence of Congenital Rubella Syndrome is likely to be higher in the UK than in China. However, the introduction of infant vaccination leads to a greater *relative* increase in the infection incidence in China than in the UK for all individuals of child-bearing age. For example, the infection incidence among 20 year olds in China is two-fold higher with 40% vaccination coverage, as compared with that in the absence of vaccination; in the UK, the infection incidence in the same age group with the same level of vaccination coverage is less than 1.25 times than that seen without vaccination. You might therefore be more cautious about introducing infant vaccination in China than in the UK.

To limit the incidence of CRS in both populations, you might consider implementing a mixed vaccination strategy e.g. include vaccination of all women of child-bearing age against rubella in addition to vaccination of infants.

Part II - Simulating the effect of selective vaccination campaigns

Q2.1

a) If 50% of 13 year olds are vaccinated, then the force of infection goes down only slightly e.g. from 0.00032/day to 0.00027/day.

b) The long-term proportion of 5 and 10 year olds who are susceptible increases slightly as a result of the introduction of vaccination among 13 year olds e.g. from about 53% to 58% for 5 year olds and from 30% to about 35% for 10 year olds. These increases are to be expected, since vaccination leads to a reduction in the prevalence of infectious cases in the population. This means that the opportunity for becoming infected decreases and therefore the proportion of young individuals who escape infection until later in life (i.e. the % susceptible) increases.

   You should notice decreases in the proportion of individuals aged over 13 years who are susceptible, occurring as a result of the introduction of vaccination among 13 year olds. Any decreases are largely attributable to these individuals having been vaccinated.

c) The infection incidence remains almost unchanged for 5 and 10 year olds as a result of the introduction of vaccination among 13 year olds, and decreases slightly for individuals aged over 15 years. Individuals aged over 13 years contribute little to the transmission dynamics in the population (since about 70% of them would already be immune); the introduction of vaccination among these individuals therefore hardly affects the overall amount of transmission in the other age groups.

Q2.2 You should notice that vaccinating 13 year olds leads to a reduction in the infection incidence for individuals aged over 15 years (which is attributable to the fact that they have been vaccinated), but that it has a relatively small effect on the infection incidence among children, even if the vaccination coverage is 100%. The latter is attributable to the fact that vaccinating 13 year olds has a small effect on the overall force of infectiion.

Q2.3 The strategy of vaccinating all individuals at birth aims to interrupt transmission for all individuals (in the long-term); the strategy of vaccinating 13 year olds aims to protect individuals who are the most “vulnerable” rather than the entire population and doesn’t substantially affect transmission in the youngest age groups in the population. (However, notice that in order to vaccinate only those most vulnerable, we should stratify the population by sex – and vaccinate only the women.)