Determining the long term cost of vaccination schedules

A case study of measles in the United Kingdom

Max Goulding

Thursday 26th April, 2012

Measles

Measles

- Highly infectious viral illness
- Extremely unpleasant
- Cold like symptoms / red eyes / light sensitivity / fever / spots in the mouth and throat
- Complications such as pneumonia. In rare cases death
- Complications when pregnant women are infected. Low birth weight. Premature birth. Miscarriage

Vaccination

- Before vaccination 200,000-700,000 notified infections and 30-300 deaths annually
- Vaccine introduced in 1968. Replaced by MMR in 1988
- Between 1998-2008, 2000-5000 notified cases and 0-3 deaths annually
- 89% of infants vaccinated in 2010/2011
- Current HPA recommendation first dose at 13 months and follow up 3-5 years

Maternal Antibodies

- Mother transfers antibodies to infant in the womb
- Mothers with high antibody titre generally have infants with high antibody titre and vice versa
- Maternal antibodies protect infants from infection and from successful vaccination
- Maternal antibodies decay over time
- Vaccination is often successful when an infant is no longer protected by maternal antibodies
- Window of susceptibility

Impact of vaccination of maternal antibodies

- Since the introduction of vaccination there has been a decline in antibody titre within population
- Vaccinated individuals have lower antibody titre than those who gain immunity through infection
- Lack of natural boosting
- Infants have lower maternal antibody levels
- Infants lose immunity sooner than prior vaccination
- Increased window of susceptibility

Project task

Should vaccination schedules be altered to account for the increased window of susceptibility in infants?

Project task

Should vaccination schedules be altered to account for the increased window of susceptibility in infants?

- Model different vaccination schedules for measles
- Determine which offers optimum results

Optimum?

What different ways are there to determine optimum results?

- Minimise number of infections
- Minimise number of infections to particular age groups, as certain groups may have greater risks if infected
- Speed to eradication
- Minimise overall cost of measles

How to model

There are two main possibilities to model diseases where the initial conditions are known.

- Stochastic
- Differential

General Methods

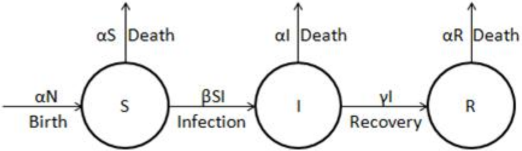
I use some common methods throughout :

- Model using ODEs
- All ODEs are solved using a fourth order Runge-Kutta method, with time step $h = \frac{1}{365}$
- Stable population of 60,000,000
- Initial values of $S = 6,400,000$, $I = 600,000$ and $R = 53,000,000$

SIR
Assumptions

- The population is divided up into three group :
  - Susceptible
  - Infectious
  - Recovered
- Transitions from groups are exponential decays
- Homogeneous mixing
- Individuals born susceptible
- Recovered immunity lifelong
- Death applies equally to each group

SIR
Model



$$N = S + I + R$$
$$\frac{dS}{dt} = \alpha N - \beta SI - \alpha S$$
$$\frac{dI}{dt} = \beta SI - \gamma I - \alpha I$$
$$\frac{dR}{dt} = \gamma I - \alpha R$$

SIR

Results

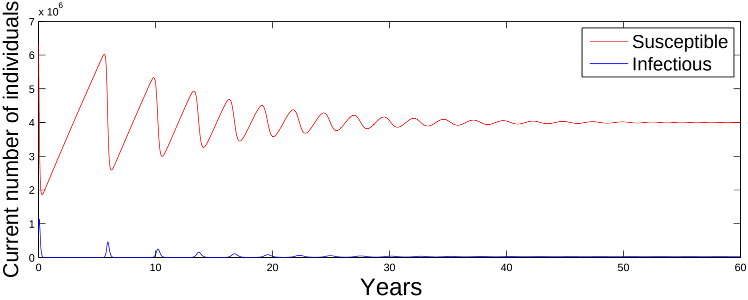


Figure: The current number of infectious and susceptible individuals at each time step. Initial values of $S = 6,400,000$, $I = 600,000$ and $R = 53,000,000$.

SIR

Challenges

Does NOT account for vaccination!!!

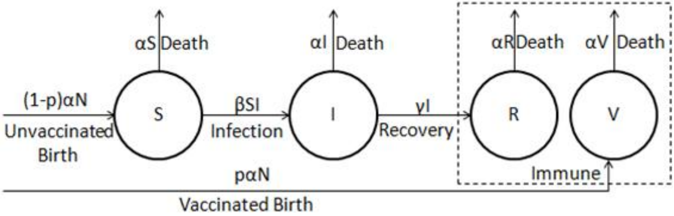
SVIR

Assumptions

- Inclusion of a Vaccinated group, V
- Vaccination occurs at birth
- Vaccination is always successful
- p proportion of the population are vaccinated
- Vaccinated immunity is lifelong

SVIR

Model



$$N = S + V + I + R$$

$$\frac{dS}{dt} = (1-p)\alpha N - \beta SI - \alpha S$$

$$\frac{dV}{dt} = p\alpha N - \alpha V$$

$$\frac{dI}{dt} = \beta SI - \gamma I - \alpha I$$

$$\frac{dR}{dt} = \gamma I - \alpha R$$

SVIR

Results

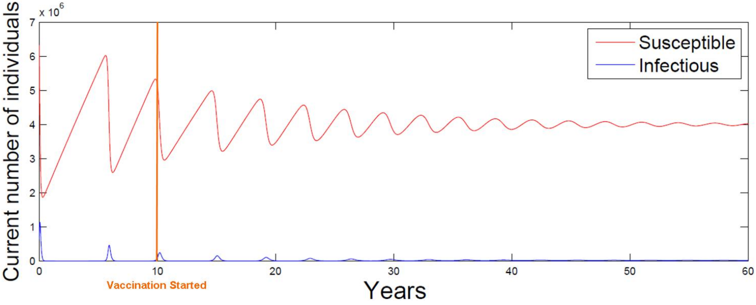


Figure: The current number of infectious and susceptible individuals at each time step. 30% vaccination introduced in 10th year. Initial values of $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

SVIR

Results

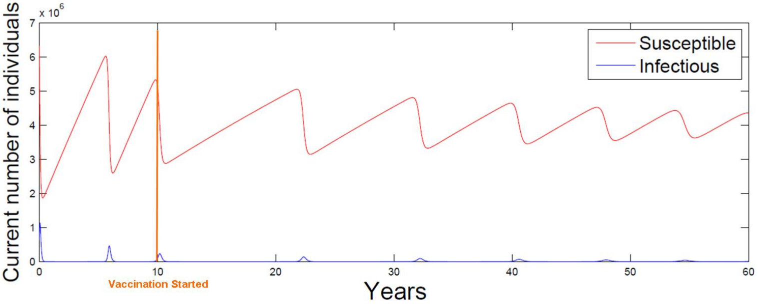


Figure: The current number of infectious and susceptible individuals at each time step. 70% vaccination introduced in 10th year. Initial values of $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

SVIR

Results

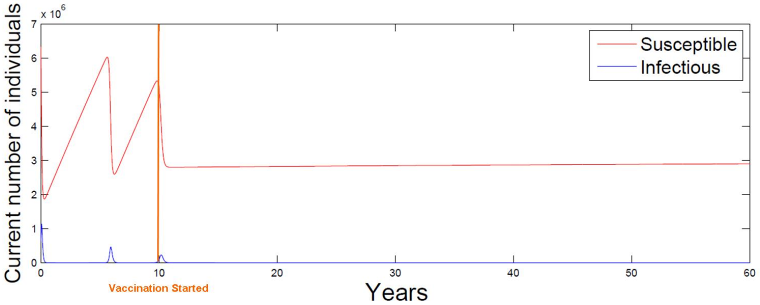


Figure: The current number of infectious and susceptible individuals at each time step. 95% vaccination introduced in 10th year. Initial values of $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

SVIR

Overall cost results

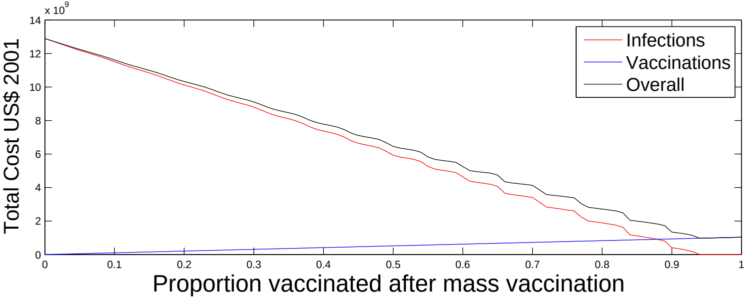


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US $307 (2001 levels) per measles case, US $22.1 (2001 levels) per vaccination and US $2.08 (2001 levels) per associated cost of vaccination.

SVIR

Overall cost results

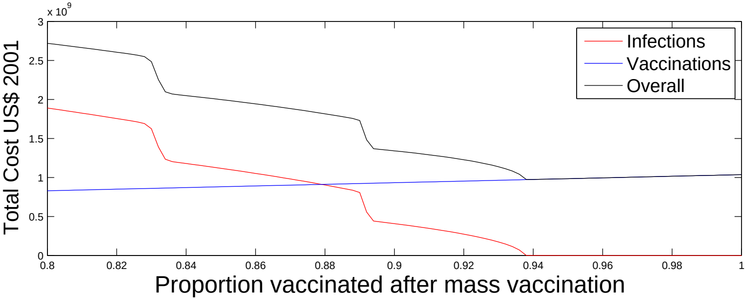


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US $307 (2001 levels) per measles case, US $22.1 (2001 levels) per vaccination and US $2.08 (2001 levels) per associated cost of vaccination.

SVIR

Challenges

Does NOT take account of protective maternal immunity!!!

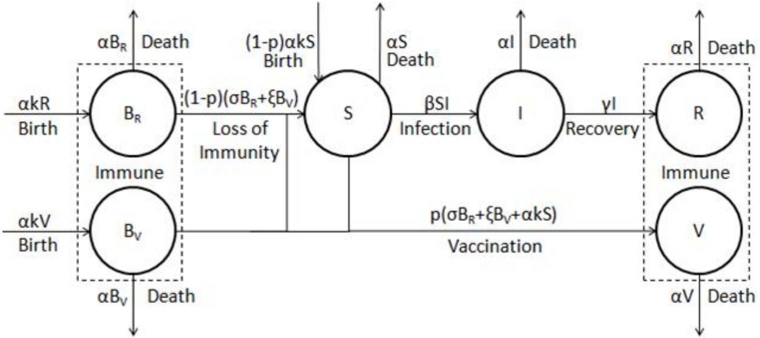
Ideal BSVIR

Assumptions

- Inclusion of birth immunity groups, B_R and B_V for infants of recovered and vaccinated mothers respectively
- Only individuals from S, R and V groups give birth with infants entering S, B_R and B_V groups respectively
- Births weighted to maintain stable population
- Birth recovered and vaccinated immunity exponentially decays at rate σ and ξ respectively
- Vaccination occurs when individuals become susceptible

Ideal BSVIR

Model



Ideal BSVIR
Model

$$
\begin{aligned}
N &= B_R + B_V + S + V + I + R \\
\frac{dB_R}{dt} &= \frac{\alpha NR}{(S+V+R)} - \sigma B_R - \alpha B_R \\
\frac{dB_V}{dt} &= \frac{\alpha NV}{(S+V+R)} - \xi B_V - \alpha B_V \\
\frac{dS}{dt} &= (1-p)\left(\frac{\alpha NS}{(S+V+R)} + \sigma B_R + \xi B_V\right) - \beta SI - \alpha S \\
\frac{dV}{dt} &= p\left(\frac{\alpha NS}{(S+V+R)} + \sigma B_R + \xi B_V\right) - \alpha V \\
\frac{dI}{dt} &= \beta SI - \gamma I - \alpha I \\
\frac{dR}{dt} &= \gamma I - \alpha R
\end{aligned}
$$

Ideal BSVIR

Results

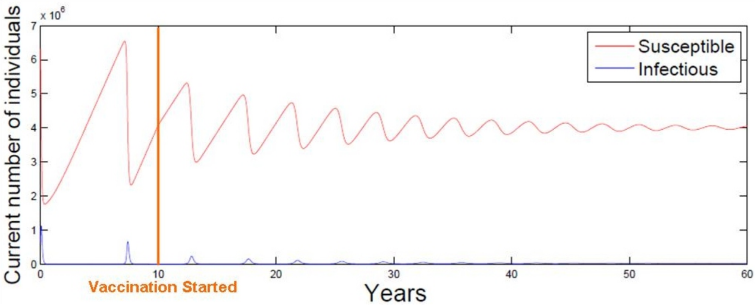


Figure: The current number of infectious and susceptible individuals at each time step. 30% vaccination introduced in 10th year. Initial values of $B_R = 0$, $B_V = 0$, $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

Ideal BSVIR

Results

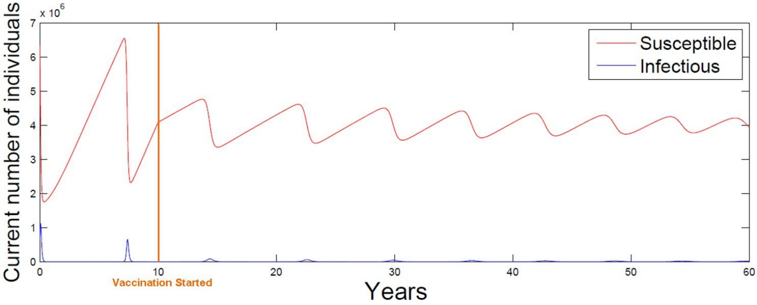


Figure: The current number of infectious and susceptible individuals at each time step. 70% vaccination introduced in 10th year. Initial values of $B_R = 0$, $B_V = 0$, $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

Ideal BSVIR

Results

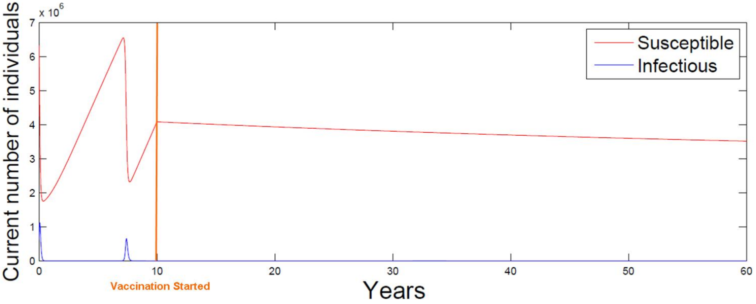


Figure: The current number of infectious and susceptible individuals at each time step. 95% vaccination introduced in 10th year. Initial values of $B_R = 0$, $B_V = 0$, $S = 6,400,000$, $V = 0$, $I = 600,000$ and $R = 53,000,000$.

Ideal BSVIR

Overall cost results

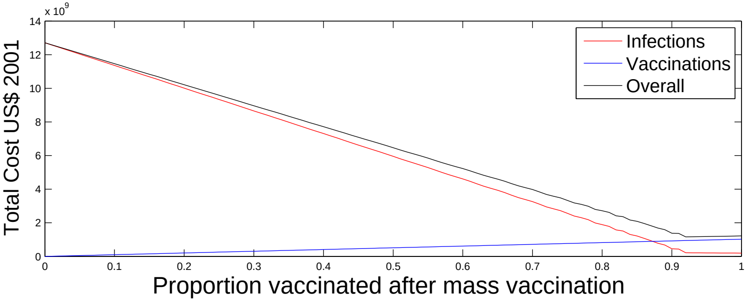


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US \$307 (2001 levels) per measles case, US \$22.1 (2001 levels) per vaccination and US \$2.08 (2001 levels) per associated cost of vaccination.

Ideal BSVIR

Overall cost results

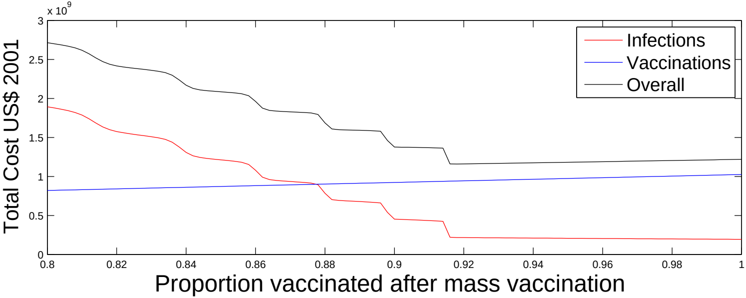


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US \$307 (2001 levels) per measles case, US \$22.1 (2001 levels) per vaccination and US \$2.08 (2001 levels) per associated cost of vaccination.

Ideal BSVIR

Challenges

Vaccination schedules are NOT realistic.
Loss of maternal immunity NOT realistic.

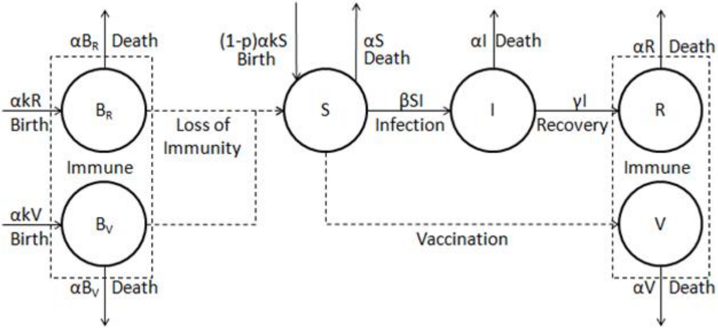
Realistic BSVIR

Assumptions

- Have an age-stratified model
- Store population as a matrix, with rows as immunity statuses and columns as age groups
- Age groups the same size as the time step
- Discretely apply vaccination to the appropriate age group(s). Only those susceptible have successful vaccination
- Only those in certain age groups give birth
- For double vaccination schedules, assume second vaccination is independent
- For computational reasons use a 'partially' age-stratified model, with those > 4 years in s single group

Realistic BSVIR

Model



Realistic BSVIR

Results

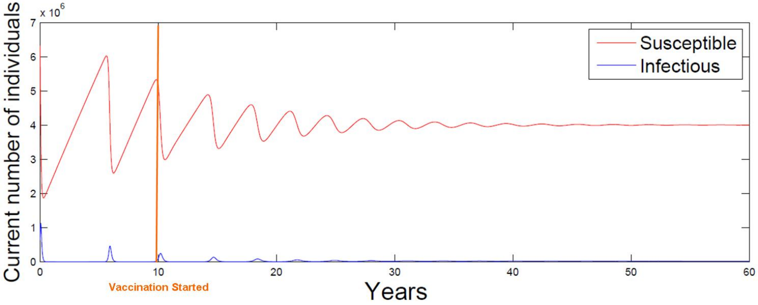


Figure: The current number of infectious and susceptible individuals at each time step. 30% vaccination introduced in 10th year. Initial values of $S(n) = 6,400,000$, $I(n) = 600,000$, $R(n) = 53,000,000$ and $B_V(n) = B_R(n) = V(n) = 0$, where n is > 4 age group.

Realistic BSVIR

Results

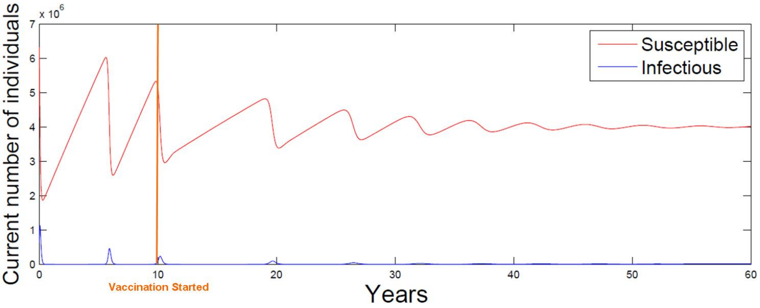


Figure: The current number of infectious and susceptible individuals at each time step. 70% vaccination introduced in 10th year. Initial values of $S(n) = 6,400,000$, $I(n) = 600,000$, $R(n) = 53,000,000$ and $B_V(n) = B_R(n) = V(n) = 0$, where n is > 4 age group.

Realistic BSVIR

Results

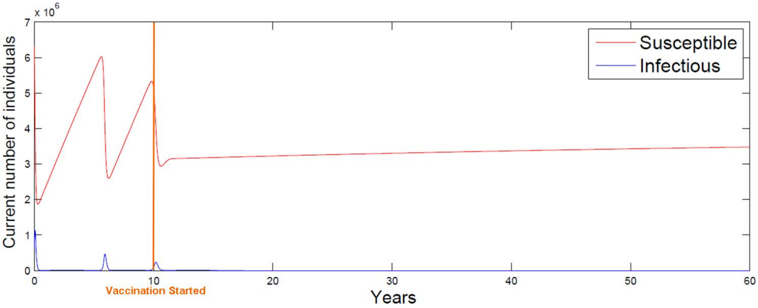


Figure: The current number of infectious and susceptible individuals at each time step. 95% vaccination introduced in 10th year. Initial values of $S(n) = 6,400,000$, $I(n) = 600,000$, $R(n) = 53,000,000$ and $B_V(n) = B_R(n) = V(n) = 0$, where n is > 4 age group.

Realistic BSVIR

Overall cost results

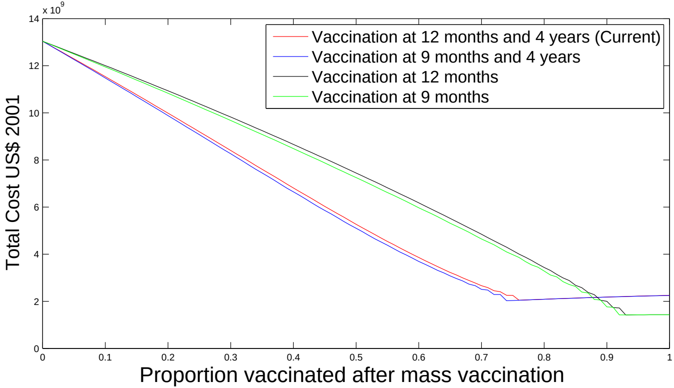


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US $307 (2001 levels) per measles case, US $22.1 (2001 levels) per vaccination and US $2.08 (2001 levels) per associated cost of vaccination.

Realistic BSVIR

Overall cost results

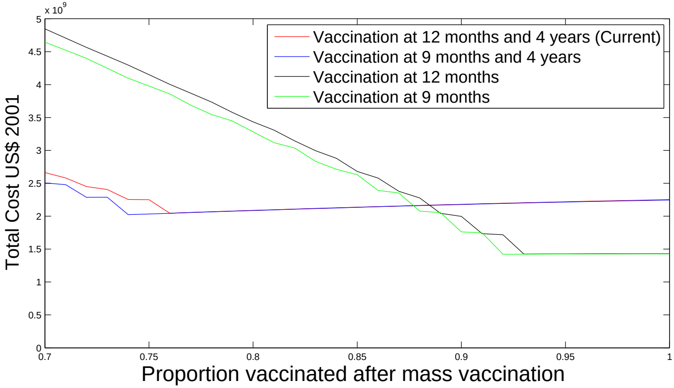


Figure: Total cost of varying proportions of vaccination. The system is run for 50 years after mass vaccination. US $307 (2001 levels) per measles case, US $22.1 (2001 levels) per vaccination and US $2.08 (2001 levels) per associated cost of vaccination.

Realistic BSVIR

Challenges

- Not fully age-stratified
- Serological data not up to date
- Double vaccination schemes independent
- Population assumptions over simplistic
- Economic factors not accounted for
- Lifelong immunity not guaranteed

Overall Results

These models show some general trends :

- It is cheaper in terms of overall cost to over-vaccinated a population than to under-vaccinated a population
- Eradication is possible if over 95% is vaccinated
- Reduction of the initial vaccination to 9 months may have potential cost savings
- Changing to a single vaccination schedule may bring a cost reduction if a high enough proportion of infants are vaccinated

Future Developments

- Age-Stratified Models
- Up to date serological data
- Model mumps and rubella