Administering neonatal vaccination to reduce prevalence of an endemic disease in livestock

Different susceptibility-shaping mechanisms (population turnover, vaccination, waning immunity) can have a large impact on disease dynamics. We will now bring these mechanisms together to investigate a central public health question.

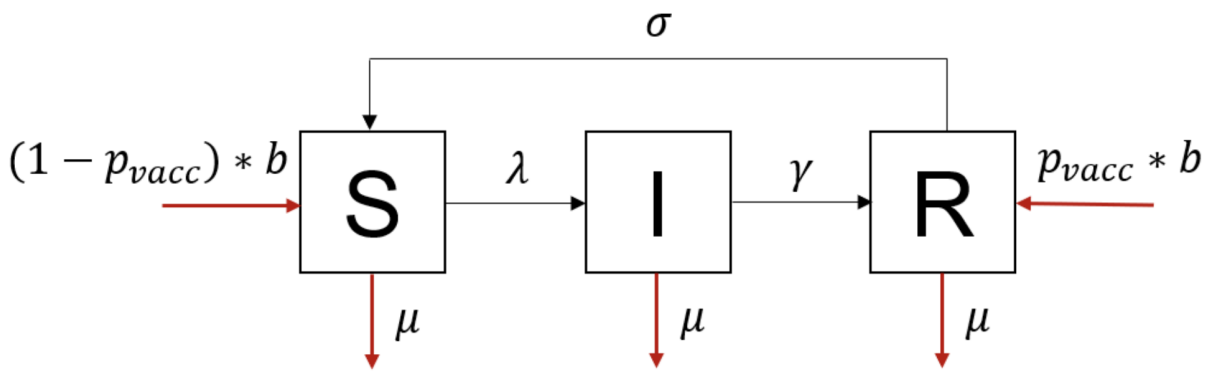
Model Context

A neonatal vaccine has recently become available against an endemic viral infection in livestock. The Ministry of Agriculture has asked you to model the impact of different vaccination scenarios to inform the design of a farm animal vaccination program. They provide you with the following information:

- The infection rate of the disease in this population is 1 day^{-1} and the average duration of the infectious period is 20 days.
- The average lifespan of the population is 3 years.
- The total population size in the country is 300,000 and has not varied over time. The disease is endemic but thought to be relatively rare in this population.
- The vaccine, which has perfect efficacy, is given to a proportion *p_vacc* of newborn animals (that is, it is a neonatal vaccine). It is currently not known whether immunity to the disease and to the vaccine is life-long or wanes over time.

They want you to run the model to endemic equilibrium to inform their vaccination program.

The SIR model structure must be modified to take into account vaccinated births (those going into the recovered compartment), unvaccinated births (those going into the S compartment), waning immunity, and deaths. We know that the initial conditions for the population do not matter (so long as they add up to 300,000 and there is at least one infected individual) as all initial conditions will end up at the same endemic equilibrium with time. The model structure can be visualized as:



From the information given, we can discern the following parameters:

- $\beta = 1$ day^{-1}
- $\gamma = \frac{1}{20} = 0.05$
- N = 300,000 (is stable)
- b = $\frac{1}{3}$years^{-1}
- $\mu = \frac{1}{3}$years^{-1} (population is stable)

- σ depends on the waning immunity, which we have not confirmed

The differential equations we can use to describe this model include:

$$\frac{dS}{dt} = -\lambda S - \mu S + (1 - p_{vacc})bN + \sigma R \tag{1}$$
$$\frac{dI}{dt} = \lambda S - \gamma I - \mu I \tag{2}$$
$$\frac{dR}{dt} = \gamma I - \mu R + p_{vacc}bN - \sigma R \tag{3}$$

Where:

$$\lambda = \beta \frac{I}{N}$$

.

We will first consider a baseline scenario, with no vaccine coverage ($p\_vacc = 0$) and no waning immunity ($\sigma = 0$). We can then build from this baseline scenario to inform the Ministry of Agriculture's policy.

Modeling the baseline scenario (no vaccination) assuming permanent immunity

In this case, we want to find the endemic prevalence of the disease currently assuming permanent immunity.

```
library(deSolve)
library(reshape2)
library(ggplot2)
```

It is given that the infection is an endemic viral infection in livestock. We know that the initial conditions for the population do not matter (see above), so we will choose 5% of the population to be infected (the disease is thought to be relatively rare), 45% to be recovered, and 55% to be susceptible. We will model over the course of 5 years.

```
N <- 300000
initial_number_susceptible <- N * 0.5
initial_number_infected <- N * 0.05
initial_number_recovered <- N * 0.45

times <- seq(from = 0, to = 5, by = 1/365)

initial_state_values <- c(S = initial_number_susceptible,
                          I = initial_number_infected,
                          R = initial_number_recovered)

parameters <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0, pvacc = 0)
```

```
SIR_model <- function(time, state, parameters) {

    with(as.list(c(state, parameters)), {

      N = S + I + R

      lambda <- beta * I / N

      dS <- -lambda * S - mu * S + (1 - pvacc) * b * N + sigma * R

      dI <- lambda * S - gamma * I - mu * I
```

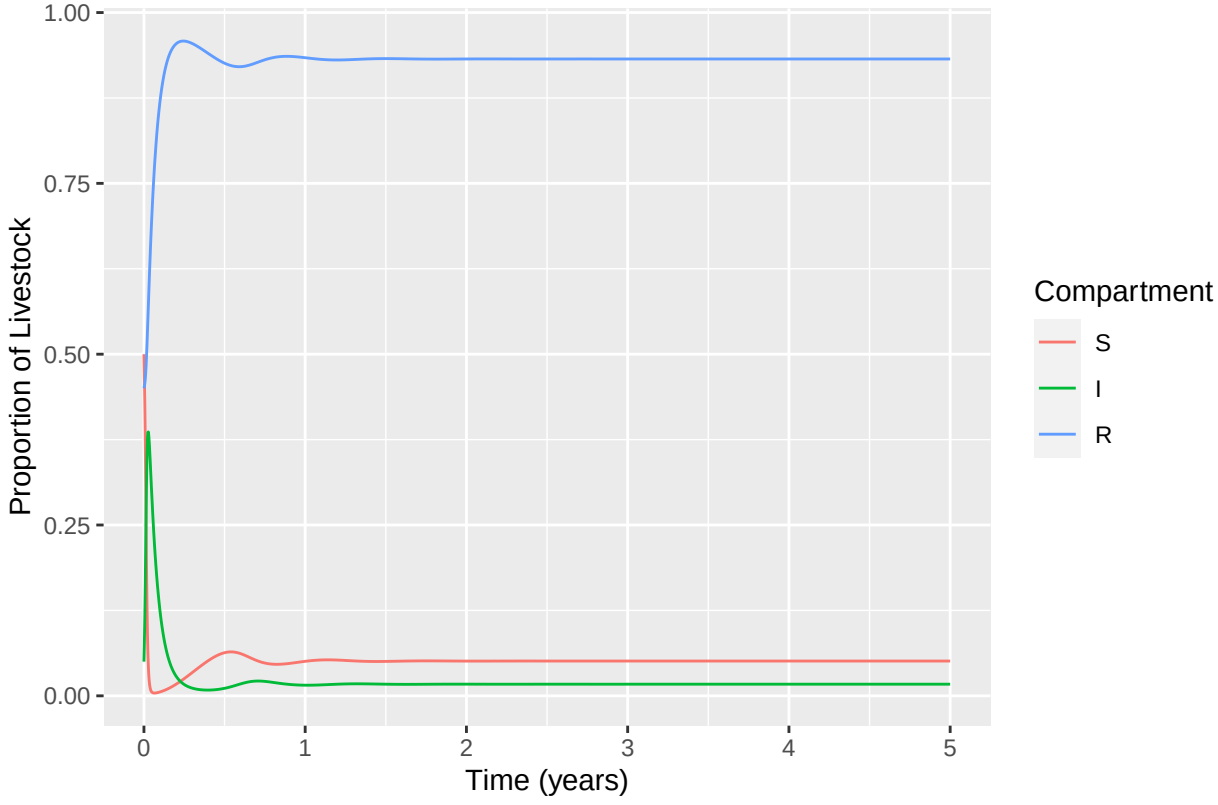
```
      dR <- gamma * I - mu * R + pvacc * b * N - sigma * R

      return(list(c(dS, dI, dR)))
    })
}
```

```
output1 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters))
```

```
output_long1 <- melt(as.data.frame(output1), id = "time")
output_long1$proportion <- output_long1$value/sum(initial_state_values)
ggplot(data = output_long1,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 1: Baseline prevalence of infection, susceptibility and r
```

Figure 1: Baseline prevalence of infection, susceptibility and recovery over



Because the disease seems to have stabilized after 2 years, we can use `output_long` to estimate the endemic prevalence of the disease assuming permanent immunity.

```
output_long1$proportion[round(output_long1$time,0) == 2 & output_long1$variable == "I"][1]
```

```
## [1] 0.01703558
```

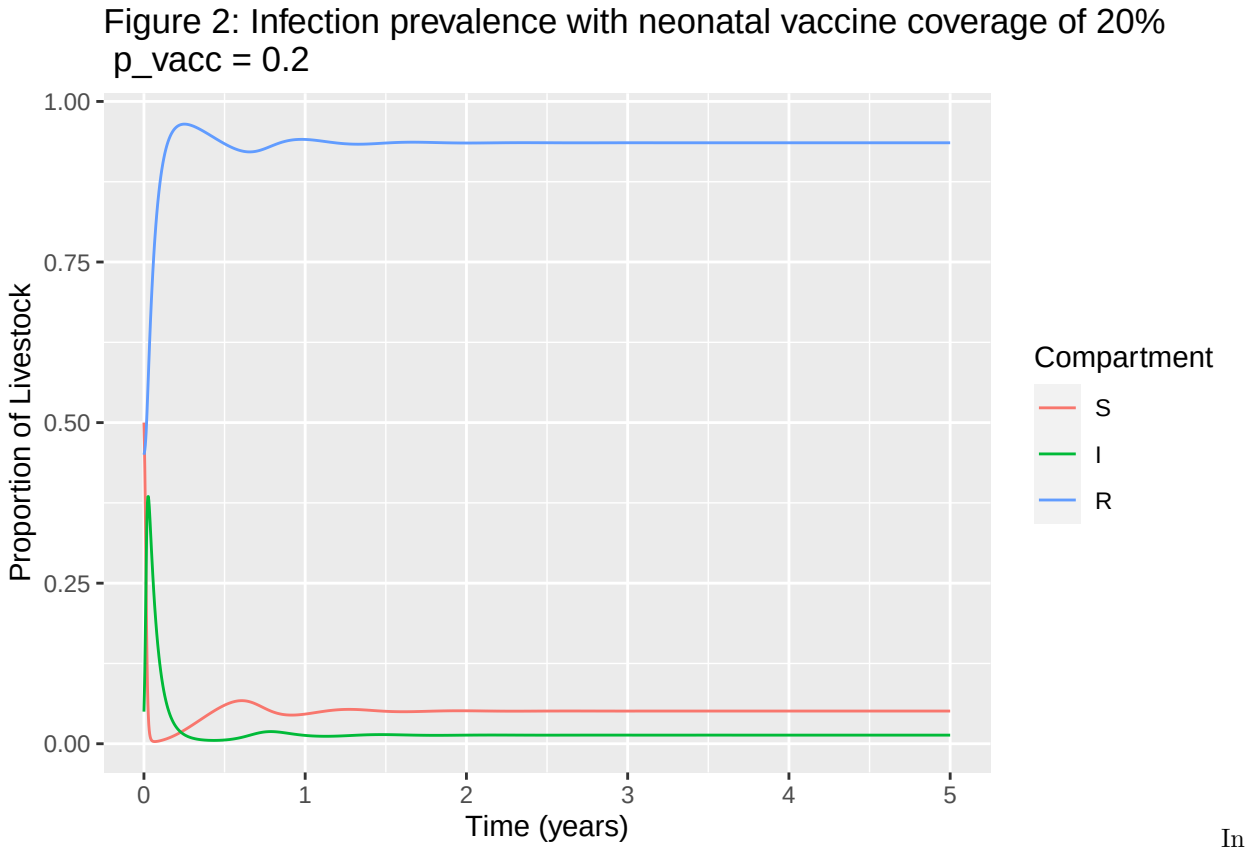
We see that the baseline endemic prevalence is about 1.7%.

Reducing the prevalence to around 0.85% using the neonatal vaccine, assuming permanent immunity

If we wanted to find what proportion of newborn animals the Ministry would need to vaccinate to reduce prevalence by half (assuming lifelong immunity), we can modify our model parameters. Let us first attempt a value of $p\_vacc = 0.2$ to achieve an endemic prevalence of 0.85%.

```
parameters2 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0, pvacc = 0.2)
output2 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters2))

output_long2 <- melt(as.data.frame(output2), id = "time")
output_long2$proportion <- output_long2$value/sum(initial_state_values)
ggplot(data = output_long2,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 2: Infection prevalence with neonatal vaccine coverage of
```



In order to find the endemic prevalence, we use:

```
output_long2$proportion[round(output_long2$time,0) == 2 & output_long2$variable == "I"][1]
```

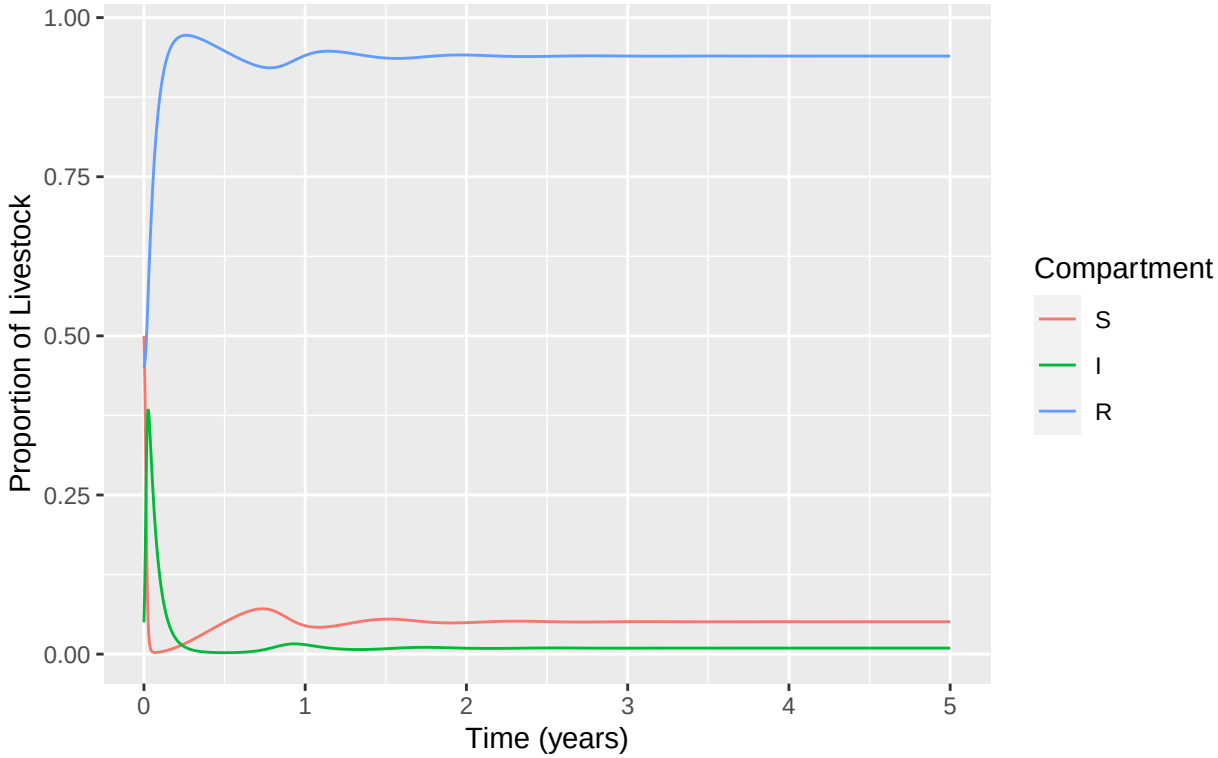
```
## [1] 0.01420778
```

We see a value of $p\_vacc = 0.2$ is not enough. We raise p_vacc to 0.42:

```
parameters3 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0, pvacc = 0.42)
output3 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters3))

output_long3 <- melt(as.data.frame(output3), id = "time")
output_long3$proportion <- output_long3$value/sum(initial_state_values)
ggplot(data = output_long3,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 3: Infection prevalence with neonatal vaccine coverage of
```

Figure 3: Infection prevalence with neonatal vaccine coverage of 42%
p_vacc = 0.42




```
output_long3$proportion[round(output_long3$time,0) == 2 & output_long3$variable == "I"][1]
```

```
## [1] 0.008513821
```

We see that a value of $p\_vacc = 0.42$ decreases the endemic prevalence to nearly 0.85%. The Ministry need only vaccinate around half of newborns to decrease the baseline endemic prevalence by half.

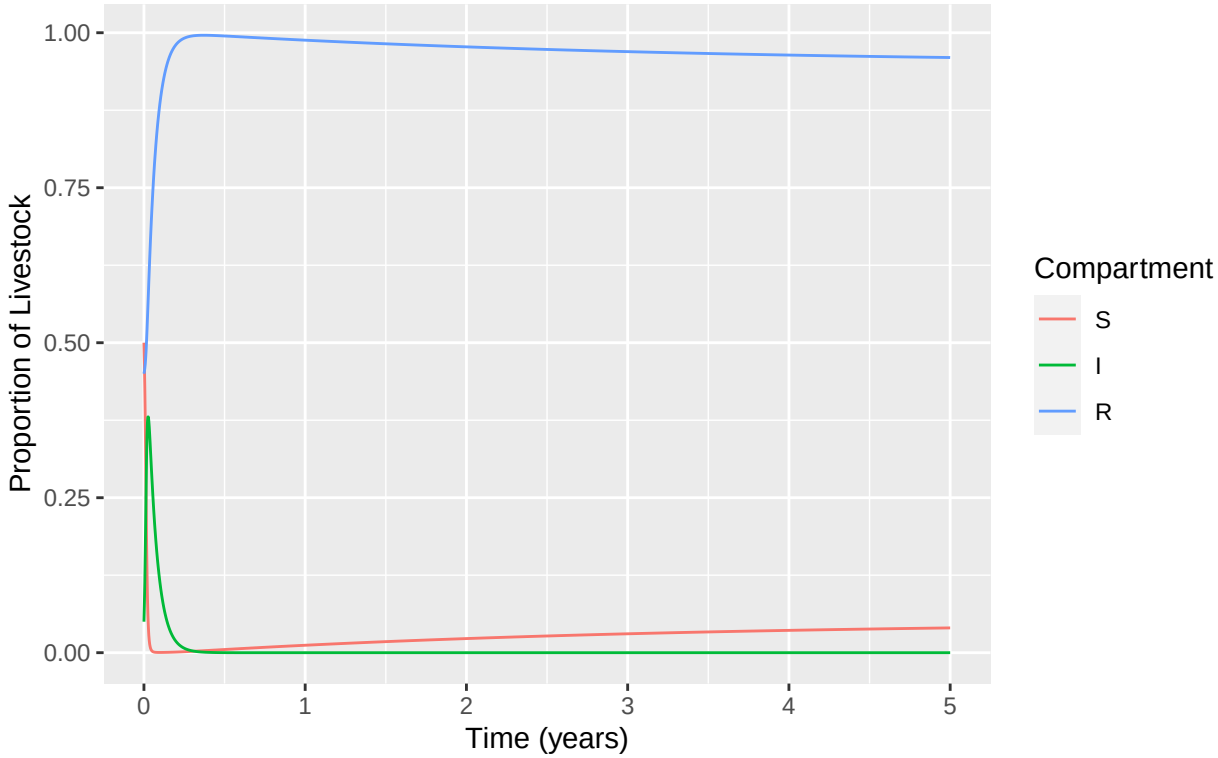
Increasing vaccine coverage to eliminate the infection

Next, we will see whether it is possible to increase the neonatal vaccine coverage to eliminate the infection, assuming lifelong immunity. We'll assume a vaccine coverage of 0.95.

```
parameters4 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0, pvacc = 0.95)
output4 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters4))

output_long4 <- melt(as.data.frame(output4), id = "time")
output_long4$proportion <- output_long4$value/sum(initial_state_values)
ggplot(data = output_long4,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 4: Infection prevalence with neonatal vaccine coverage of
```

Figure 4: Infection prevalence with neonatal vaccine coverage of 95%
p_vacc = 0.95




```
output_long4$proportion[round(output_long4$time,0) == 5 & output_long4$variable == "I"][1]
```

```
## [1] 4.661427e-21
```

We see that at the end of 5 years, the infection essentially dies out, with a prevalence that tends towards zero over time.

Modeling the baseline prevalence and impact of vaccination assuming immunity with an average duration of 1 year

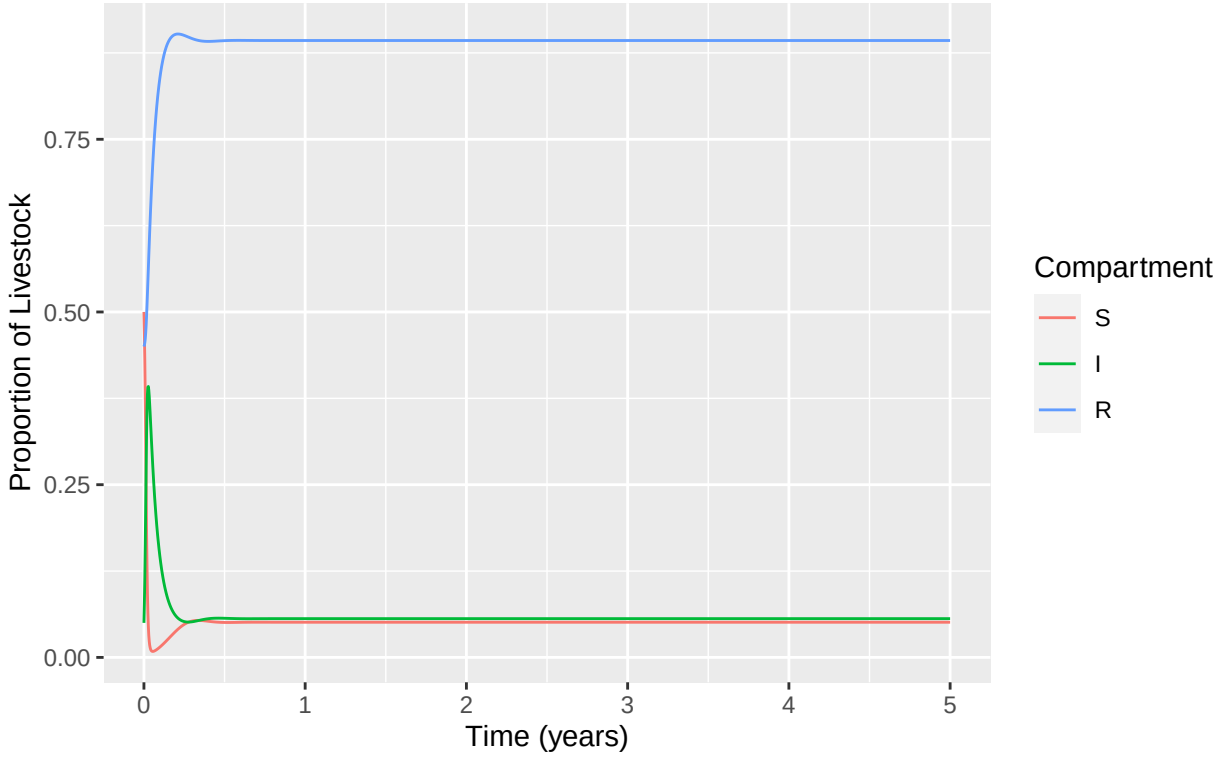
Now, if we assume that the average duration of immunity is only 1 year, we can observe the impact on the proportional reduction in the prevalence with the vaccine coverage above versus the baseline. In essence,

whether a vaccine that delivers immunity for only 1 year is much better than no vaccination at all, assuming waning immunity. In this case, we'll use $p\_vacc = 0.5$ (half of the population). $\sigma = \frac{1}{1} = 1$ year^{-1}.

```
parameters5 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 1, pvacc = 0.5)
output5 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters5))

output_long5 <- melt(as.data.frame(output5), id = "time")
output_long5$proportion <- output_long5$value/sum(initial_state_values)
ggplot(data = output_long5,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 5: Prevalence with waning immunity and vaccine coverage o
```

Figure 5: Prevalence with waning immunity and vaccine coverage of 50%
sigma = 1



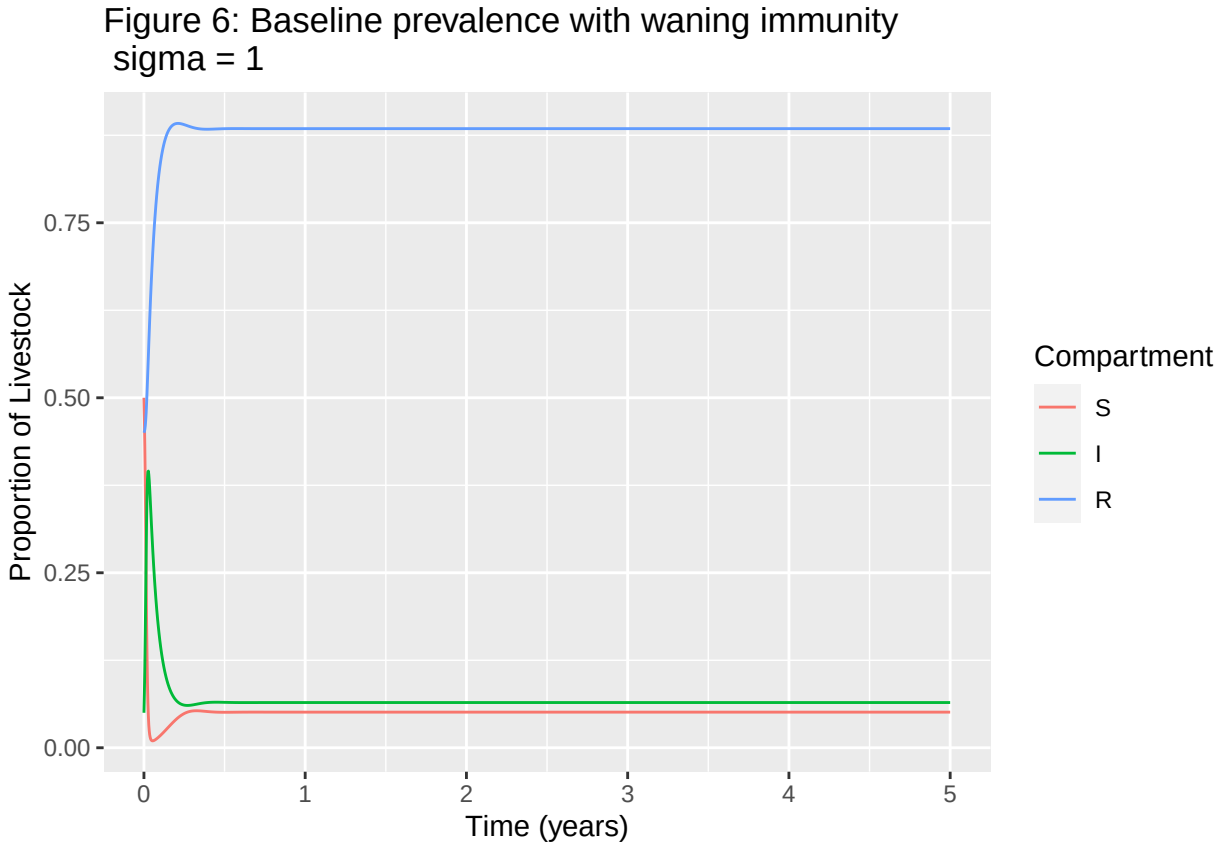

```
waning_vacc <- output_long5$proportion[round(output_long5$time,0) == 5 & output_long5$variable == "I"][
```

We see that about 5.61% is the endemic prevalence in this case.

If we compare this to no vaccine coverage, but with $\sigma = 1$ as well to get a baseline:

```
parameters6 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 1, pvacc = 0)
output6 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters6))
```

```
output_long6 <- melt(as.data.frame(output6), id = "time")
output_long6$proportion <- output_long6$value/sum(initial_state_values)
ggplot(data = output_long6,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 6: Baseline prevalence with waning immunity \n sigma = 1")
```




```
waning_baseline <- output_long6$proportion[round(output_long6$time,0) == 5 & output_long6$variable == "
```

In order to calculate the reduction in prevalence achieved by 50% neonatal vaccine coverage, we can use:

```
1 - waning_vacc / waning_baseline
```

```
## [1] 0.1317056
```

We see if immunity is not permanent (wanes on average of 1 year), a neonatal vaccine coverage of 50% now only leads to a 13% reduction in disease prevalence from the baseline (no vaccine), rather than 50%.

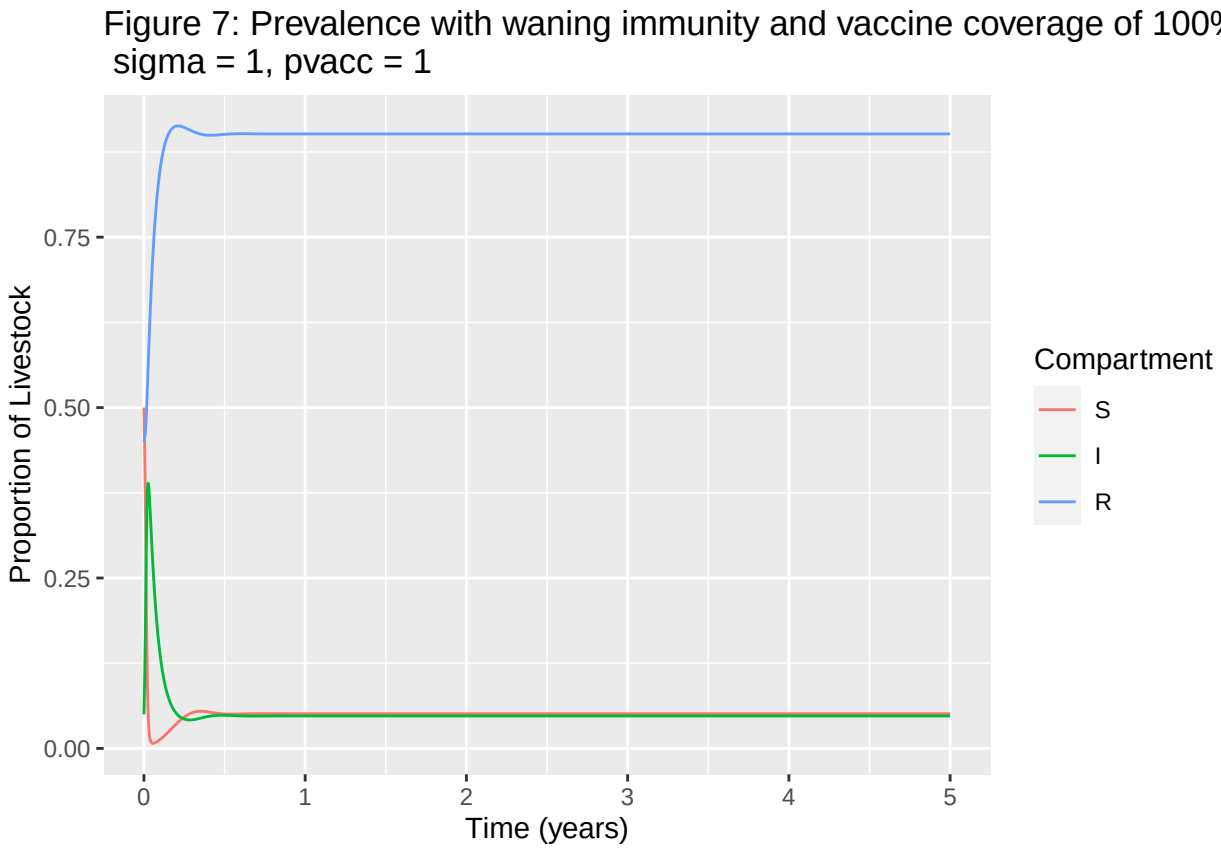
Modeling the impact of vaccination with 100% coverage assuming immunity with an average duration of one year

We can try to increase our vaccine coverage to 100% to observe whether we can eliminate the infection, even if immunity wanes after 1 year.

```
parameters7 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 1, pvacc = 1)
output7 <- as.data.frame(ode(y = initial_state_values,
```

```
                            times = times,
                            func = SIR_model,
                            parms = parameters7))

output_long7 <- melt(as.data.frame(output7), id = "time")
output_long7$proportion <- output_long7$value/sum(initial_state_values)
ggplot(data = output_long7,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 7: Prevalence with waning immunity and vaccine coverage o
```




```
output_long7$proportion[round(output_long7$time,0) == 5 & output_long7$variable == "I"][1]
```

```
## [1] 0.0475974
```

The model suggests that even with 100% coverage of the neonatal vaccine, the endemic prevalence would not reach 0, but would level to about 4.75%.

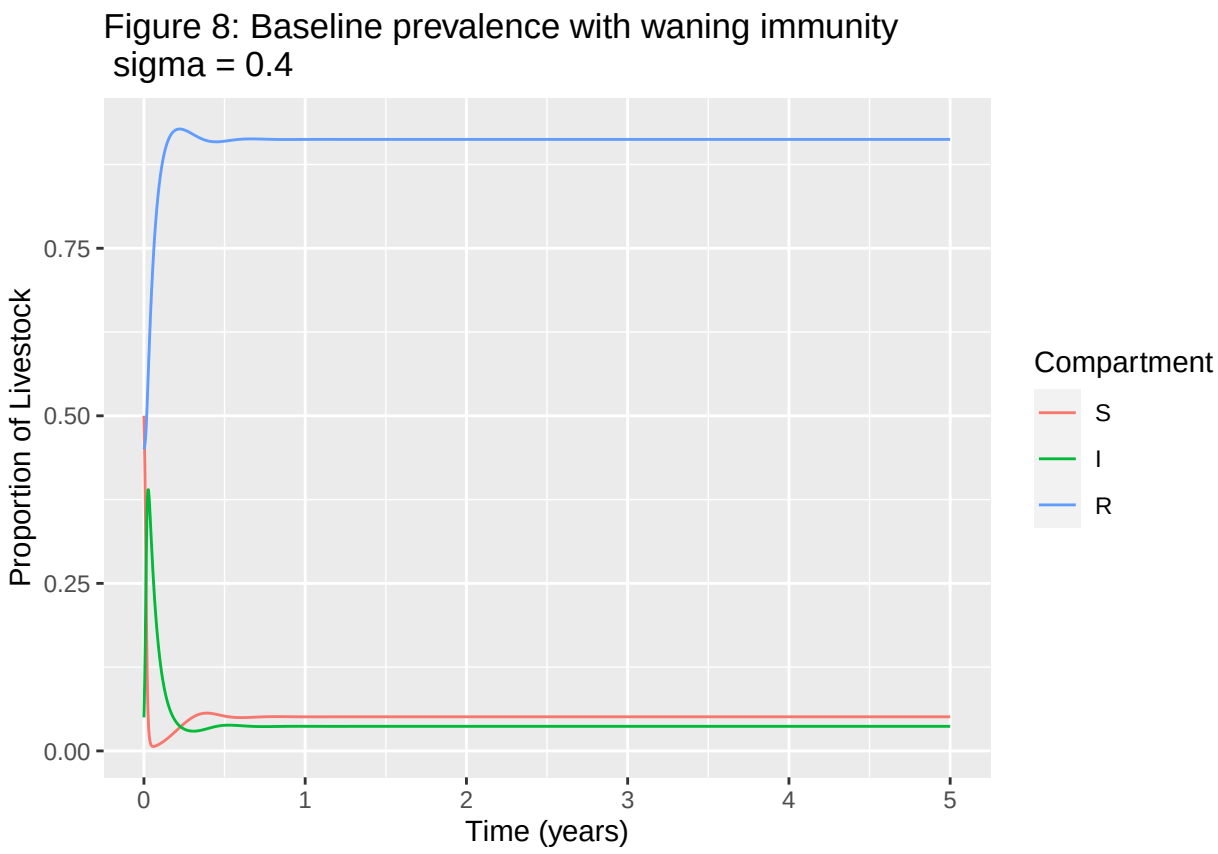
Modelling the baseline prevalence and impact of vaccination with 100% coverage assuming immunity with an average duration of 2.5 years:

If an adjuvant (a vaccine promoter) was given along with the vaccine, that would extend the duration of immunity to 2.5 years on average, what vaccine coverage would be needed to reduce the baseline prevalence by half? Would it be possible to eliminate the disease from the population under these assumptions using neonatal vaccination? These are questions we can answer by modifying our model parameters.

We can first calculate the baseline, where $p\_vacc = 0$ and the duration of immunity is about 2.5 years. σ will now equal $\frac{1}{2.5} = 0.4$ year^{-1}.

```
parameters8 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0.4, pvacc = 0)
output8 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters8))

output_long8 <- melt(as.data.frame(output8), id = "time")
output_long8$proportion <- output_long8$value/sum(initial_state_values)
ggplot(data = output_long8,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 8: Baseline prevalence with waning immunity \n sigma = 0.4
```



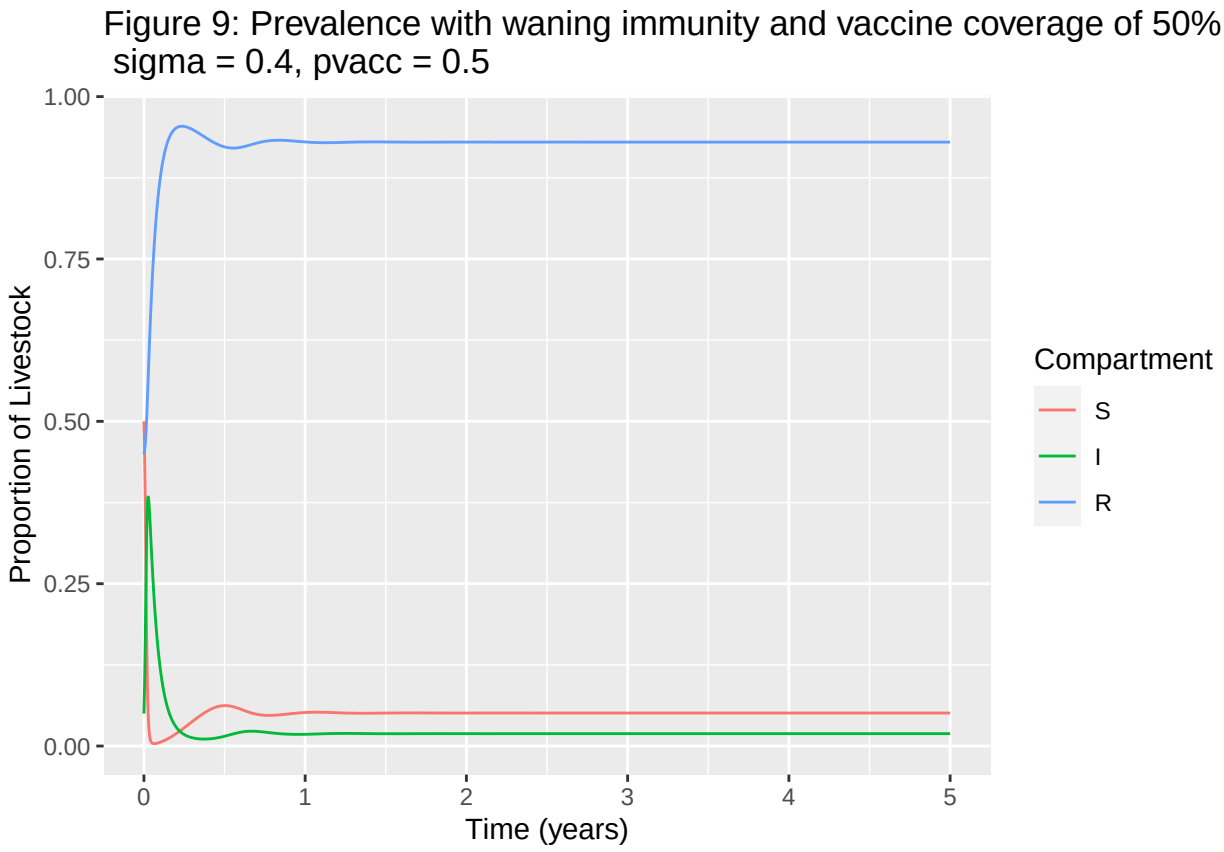

```
waning_baseline_0.4 <- output_long8$proportion[round(output_long8$time,0) == 5 & output_long8$variable =
waning_baseline_0.4
```

```
## [1] 0.03666358
```

We see the baseline with a waning immunity period of 2.5 years is about 3.66%. Now, we can observe the endemic prevalence with a chosen p_vacc. We will begin with $p\_vacc = 1$, and see if we can reduce the endemic prevalence to half of the baseline (to about 1.83%). Additionally, we will also see if we can completely eliminate the disease from the population.

```
parameters9 <- c(beta = 1 * 365, gamma = 0.05 * 365, mu = 1/3, b = 1/3, sigma = 0.4, pvacc = 1)
output9 <- as.data.frame(ode(y = initial_state_values,
                             times = times,
                             func = SIR_model,
                             parms = parameters9))

output_long9 <- melt(as.data.frame(output9), id = "time")
output_long9$proportion <- output_long9$value/sum(initial_state_values)
ggplot(data = output_long9,
       aes(x = time, y = proportion, group=variable, color=variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Proportion of Livestock") +
  labs(colour = "Compartment",title = "Figure 9: Prevalence with waning immunity and vaccine coverage o
```




```
waning_vacc_0.4 <-output_long9$proportion[round(output_long9$time,0) == 5 & output_long9$variable == "I
waning_vacc_0.4
```

```
## [1] 0.01910432
```

The endemic prevalence in this case is about 1.9%.

We see that the even if we increase the neonatal vaccine coverage to 100%, it is impossible to eliminate the disease. This means the neonatal vaccination alone is not enough to completely eliminate the disease from the population as it is still endemic even if every newborn animal is vaccinated. However, by increasing the coverage to 100%, we can reduce the baseline prevalence by about half.

Additional Information to Interpret Results

As stated above, waning immunity strongly influences a variety of policy factors. However, other factors could affect our results. We assumed:

- vaccination done is applied to a proportion *p_vacc* at every time step (in this case, daily)
- immunity from recovery and immunity via vaccination provide the same protection and wane at the same time
- the vaccine is only administered to newborns, so the results might change depending on how different age groups transmit and acquire infection

Overall Recommendations

The modeling analysis done allows us to confirm a few findings. Firstly, neonatal vaccination can substantially reduce the endemic prevalence of the disease if vaccination and recovery provide long-term immunity; these can be clearly seen in Figures 2, 3, and 4. However, the endemic prevalence, required vaccine coverage, and impacts of neonatal vaccination all strongly depend on vaccine efficacy and waning immunity. In Figures 5 and 6, we can see that if long-term immunity is not present (wanes on average of 1 year), a neonatal vaccine coverage of 50% now only leads to a 13% reduction in disease prevalence from the baseline; in addition, in Figure 7 we can see that even if 100% coverage is reached, the endemic prevalence is still around 5%. More research and development should be focused on improving the efficacy of the vaccine to ensure long-term benefits.

In this regard, the modeling results are somewhat inconclusive and highly dependent on the immunity window provided by these vaccines. More research and development should be focused on improving the efficacy of the vaccine to ensure long-term benefits. If a neonatal vaccination is implemented in the population and immunity is found to wane, it may be wise to add an adjuvant to improve the longevity of immunity.