Economics of controlling Johne's disease in New Zealand sheep flocks through vaccination: a web-based decision support tool

Milestone Report

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Summary

Johne's disease is an economically important disease for the New Zealand sheep industry. There is currently a vaccine registered in New Zealand (Gudair ™) that has been shown to reduce mortality and the shedding of bacteria into the environment. Simple cost-benefit analyses indicated that farmers may expect a positive return on investment from vaccination when the annual death rate due to Johne's disease is greater than 1%. However, the actual impact of vaccination is likely to vary due to the time it takes until vaccination has reached an optimal economic return, based on the unique transmission dynamics of Johne's disease in individual flocks. The objective of this study was to develop a simulation model that allows farmers to modify flock management parameters and the extent of OJD in their flock for generating predictions that best reflect the unique circumstances of their farm. An interactive web-based interface for the simulation model was developed using the *shiny* package in R and is freely available through https://epicentre-apps.shinyapps.io/JohnesDiseaseEconomicsSheep/. The results indicate that the relative cost-benefit of vaccination is highly influenced by flock size, clinical incidence of mortality, market values of carcasses, and vaccination costs. Future versions of the model will include more sophisticated methods to estimate the impact of pasture management and the effects of chronic exposure on the susceptibility of sheep to infection.

1. Introduction

Johne's disease is a chronic enteritis caused by *Mycobacterium avium* subsp *paratuberculosis* (MAP) that is present in up to 70% of New Zealand sheep flocks. Infection is usually acquired early in life through vertical transmission, the ingestion of organisms excreted into colostrum or directly onto pasture through faecal contamination. The disease progress slowly and the clinical signs of chronic diarrhea, weight loss, ill-thrift, and poor reproductive performance are usually not seen until sheep reach at least 2 years of age. However, shedding may still occur during the subclinical stages. There are currently no effective treatments for Johne's disease, which results in high mortality rates for clinically affected animals. The disease is particularly difficult to control at the flock level due to the persistence of MAP organisms in the environment and limitations in the diagnostic tests options that are available for sheep flocks.

Gudair™, a killed vaccine marketed by Zoetis, is currently the only ovine Johne's disease vaccine registered for use in New Zealand. In clinical trials, Gudair™ has been shown to reduce mortality and faecal shedding from Johne's disease by at least 90% in infected animals. The company has developed a simple cost-benefit model for vaccination (http://gudair.co.nz/CostBenefits.html) that allows farmers to input their flock size, annual death rate due to Johne's, lambing percentage, and economic values for ewe and lamb carcasses. The model then performs simple calculations to produce a cost-benefit ratio. However, it is likely that the effect of vaccination differs between flocks based on the unique transmission dynamics of Johne's disease. Furthermore, there will likely be a delay before the full effects are observed since the vaccine is typically only used in replacement lambs and will have limited impact on older infected animals. It would therefore be useful for farmers to know how the clinical incidence and mortality will change over time after vaccination has been introduced.

The objective of this study was to develop an interactive simulation model that allows farmers to modify key management parameters to generate predications that are tailored to the unique conditions in their flock. The findings are presented through an interactive web-based application.

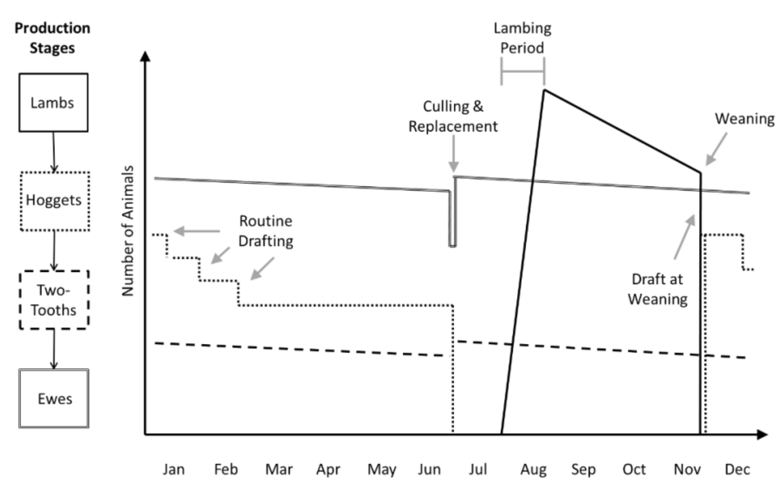
2. Model Description

The simulation model has three components: (1) a demographic component describing the sheep production life cycle, (2) a disease component describing the transmission and clinical effects of Johne's disease within the flock, and (3) a control component describing the impacts of vaccination on the flock. Although the model was developed to represent an average New Zealand sheep farm, the parameters can be modified to reflect the unique situation on individual farms.

Demographic Structure

The model demographic structure was based on a typical 1,500 ewe North Island hill country Romney sheep flock that produced prime lamb for slaughter (Figure 1). The model operated with discrete time steps of one day and explicitly tracked the calendar day of year throughout the simulation. This allowed us to portray seasonal management events in a more realistic fashion than traditional compartmental models. The sheep flock was divided into 4 management groups based on age: lambs (0 to 3 months of age), hoggets (3 to 12 months of age), two-tooths (12 to 24 months of age), and mixed-age ewes (> 24 months of age). It was assumed that mixed-aged ewes and lambs were grazed together during 3 months before an after lambing, and that hoggets and two-tooths were grazed on a separate pasture block.

Figure 1: Diagrammatic representation of management events and transitions between production groups in a typical hill country sheep flock



In the baseline model, the start of the lambing season was set to July 15th and lasted for a period of 30 days. The lambing rate was set at 1.4 lambs born per ewe. Lambs were weaned on November 15th at approximately 3 months of age. We assumed an average mortality rate of 13% between lambing and weaning. At weaning, 20% of prime lambs were immediately drafted for slaughter and the remaining lambs were transferred into the hogget management group. An additional 15% of hoggets were drafted for slaughter every 30 days thereafter until either reaching the threshold number required for replacement or reaching the calendar dates for culling and replacement, which were set at June 15th and June 16th, respectively.

The flock had an annual replacement rate of 25% and it was assumed that replacement animals were all sourced from within the flock when possible. We allowed an additional safety margin of 3.5% when determining how many hoggets and two-tooths to retain as replacements to account for losses due to natural mortality. On the culling date of June 16th, 25% of mixed-age ewes were removed from the flock at random. These were replaced by animals in the two-tooth management group to maintain the flock size at 1,500. Any additional two-tooths beyond the number required for replacements were sold as mutton. In scenarios where there were too few two-tooths for replacement, additional mixed-age ewes were purchased from outside sources and assumed to be susceptible. On the replacement date, the required numbers of hoggets for replacement were transferred into the two-tooth management group and any remaining animals were sold as mutton. The annual mortality rates were fixed at 3% for the hogget and two-tooth groups and at 6% for the mixed-age ewes.

Disease Dynamics

A deterministic compartmental model was used to describe the transition of animals between mutually exclusive disease states (Figure 2). Transition rates and model parameters were retrieved from the literature. Susceptible animals (S) became infected with Johne's disease through contact with MAP organisms in the environment (E) at a rate λ, which was calculated for each production group of animals based on the following equation:

$$\lambda = \left(1.0037 \times \left(1 - e^{(-0.1403 \times \ln(DM))}\right) + 0.0333\right) \times \left(\left(1 - e^{-(0.02 + 0.00121 \times \ln(DM))}\right)\right)$$

where DM represents the number of MAP organisms ingested by each animal each day based on daily dry matter intake. It was assumed that all MAP organisms were shed evenly over the pasture dry matter and that each sheep consumed a percentage of those organisms proportional to the number of sheep on pasture as well as the expected dry matter intake. Separate E compartments were created for ewes and lambs (E_1) and hoggets and two-tooths (E_2) based on the assumption that these groups were grazed separately.

Once an animal became infected with Johne's, a percentage (χ) moved into the paucibacillary progressor state (P). This was proportional to the initial dose of MAP and calculated for each production group as follows:

$$X_{(lambs\ or\ hoggets)} = \frac{1}{(1 + e^{-0.367529 \times (\ln(DM) - 15.99791)}}$$

$$X_{(two-tooths\ or\ ewes)} = \frac{1}{(1 + e^{-0.3771415 \times (\ln(DM) - 22.76194)}}$$

The remaining proportion of animals (1- χ) moved into paucibacillary non-progressor (N) state. The transition from P to the multibacillary state (M) where sheep display clinical signs of Johne's disease occurred at a rate (δ) of 0.002505 per day. The mortality rate of M animals was assumed to be 1.81 times higher than the baseline mortality rates and these animals also gave birth to 12% fewer lambs on average. P and N animals shed MAP organisms into the environment (E) at the rate of 0.1 organisms per day ($\sigma_{P/N}$) while M animals shed organisms at the rate of 1,740 organisms per day (σ_M). The daily rate of MAP decay in the environment (Ψ) was initially set at 0.0002, but later tuned in the simulations to achieve the desired annual deaths due to Johne's disease.

Infected N lambs remained in that compartment until weaning. After weaning, N animals recovered (R) from infection at a rate (γ) of 0.002923 animals per day. Animals that entered the R compartment were assumed to remain in that state until drafting or culling. There were no effects on mortality or lambing rates for animals in the N compartment. All animals regardless of disease state were at equal probability of being removed from the flock during routine drafting or culling events.

The infection state of lambs at birth depended on the infection state of the ewes during the lambing season as shown in Figure 3. All lambs born to S and R ewes entered the S state. Lambs born to ewes in the N and P compartments had a (1 – $\rho_{P/N}$) probability of being S at birth ($\rho_{P/N}$, vertical transmission rate). For the remaining $\rho_{P/N}$ lambs, there was a (1 – χ) probability of becoming N and a χ probability of becoming P. Lambs born to ewes in the M compartments had a (1 – ρ_M) probability of being S at birth. For the remaining ρ_M lambs, there was a (1 – χ) probability of becoming N and a χ probability of becoming P.

Figure 2: Diagrammatic representation of the transition of animals between mutually exclusive disease states for Johne's disease

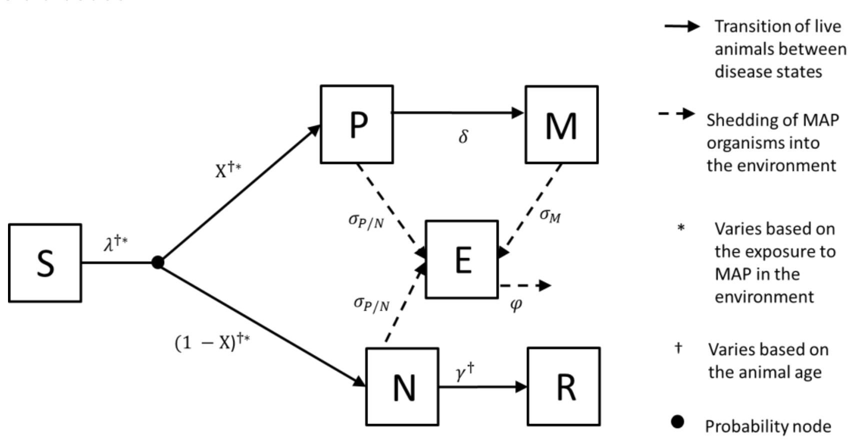
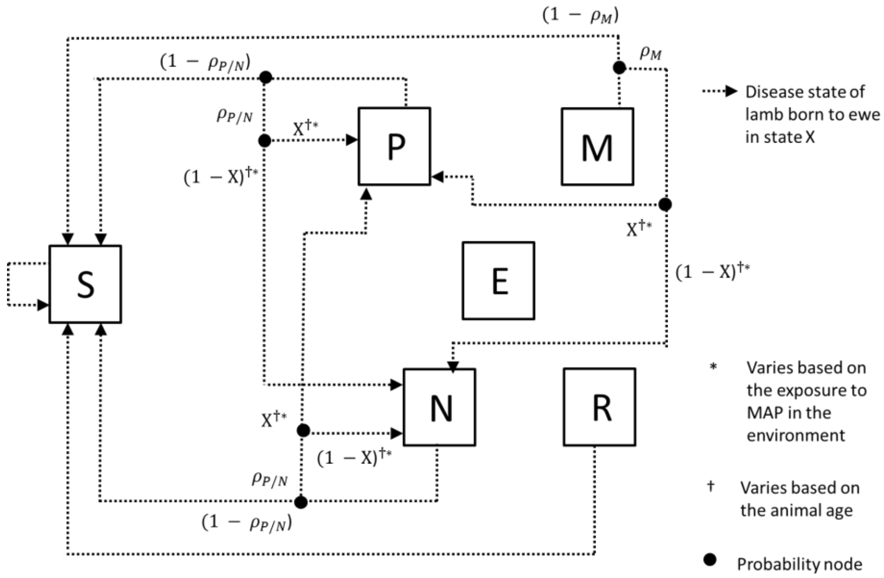


Figure 3: Diagrammatic representation of disease state of lambs born to ewes in each mutually exclusive Johne's disease states



Economic Values

The primary production outputs (benefits) from the flock were measured as the number of prime lamb and mutton carcasses produced over the course of the simulation. The primary losses (costs) were the number of ewe deaths due to Johne's disease, the number of lambs lost through premature ewe death, and the costs of raising or purchasing additional replacement ewes to compensate for the Johne's related deaths. Prime lambs were assigned an average carcass value of $90 per head, while mutton carcasses were valued at $55 per head based on the current price trends reported by Beef&LambNZ. We assumed an average replacement cost of $30 per ewe.

Vaccination Intervention

The model focused on vaccination as the primary strategy for controlling Johne's disease in affected flocks. This was based on expert opinion that testing and culling would not be logistically and financially feasible for the majority of New Zealand sheep operations. Gudair™, a killed vaccine marketed by Zoetis, is currently the only ovine Johne's vaccination registered for use in New Zealand. In clinical trials, Gudair™ has been shown to reduce mortality and faecal shedding from Johne's disease by 70-90% in infected animals. In our model, we assumed that all female lambs (i.e. 50% of lambs born in a season) would receive a single dose of the vaccine at weaning per the label instructions. No booster doses are required and there is no apparent loss in protective immunity over time. Any lambs that were subsequently drafted for slaughter were preferentially removed from the non-vaccinated group. Vaccinated animals were assigned a <1% chance of moving into the progressor track and both the shedding rates and mortality rates of vaccinated animals were reduced by 90%. Although the vaccine causes injection site lesions in 18% of mutton carcasses and 65% of lamb carcasses, there is negligible economic impact on the carcass value The cost of the vaccination was set at $2 per head including labour.

Simulation Conditions

Each simulation model run had an initial 200 year burn-in period to allow the prevalence of Johne's disease and flock demographics to reach an equilibrium state. The model was then run for an additional 20 years to explore the effects on flock production levels under 3 sets of starting conditions: (1) baseline production levels with no Johne's disease in the flock, (2) production levels with Johne's disease in the flock, (3) and production levels after implementing Johne's vaccination in replacement females. The prevalence of infected animals over time was also tracked. The simulation model was initially coded in the C programming language to optimize speed and then converted into an R library to allow easy import of the model results into R for visualization.

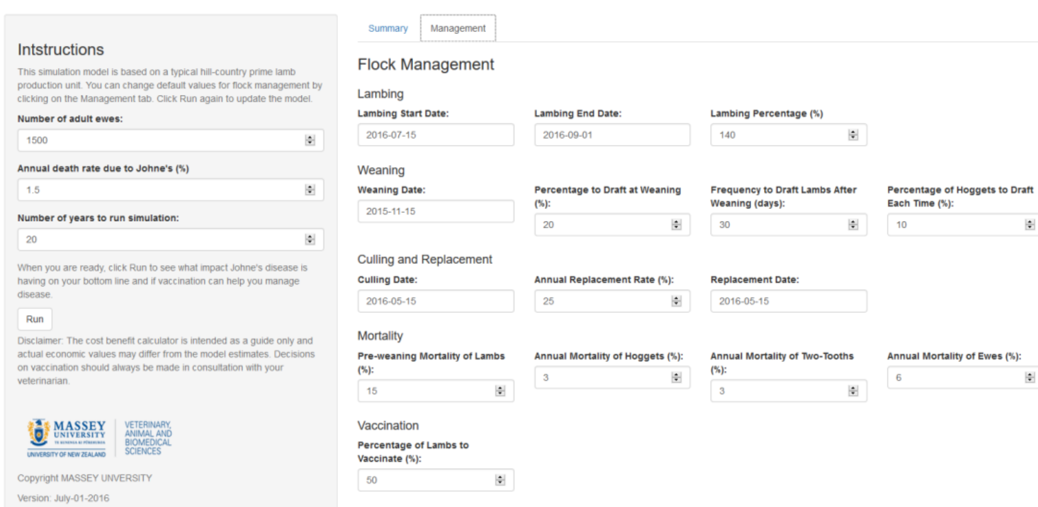
Web-based Interface

We developed a web-based interface for the simulation model using the *shiny* package in R that allows farmers to modify the parameters to match the unique management conditions on their farm. The main advantage to using this approach over traditional spreadsheet-based decision support tools is that we have the ability to update the model in real-time as new information on Johne's disease epidemiology becomes available. This resource can be accessed freely at:
https://epicentre-apps.shinyapps.io/JohnesDiseaseEconomicsSheep/.

3. Results

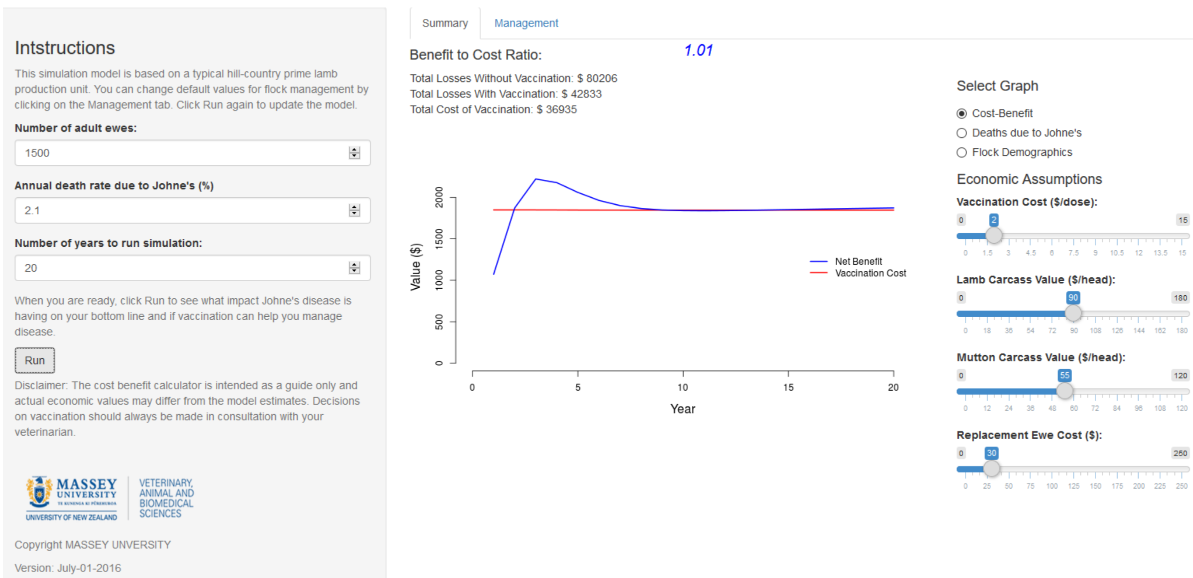
The web-based interface initially asks the user to input values for flock size, annual deaths due to Johnes disease, and the number of years to run the simulation (Figure 4). The user can also change assumptions about flock management including the lambing rates, lambing dates, weaning dates, percentage of prime lambs to draft for slaughter, annual flock replacement rate, baseline mortality rates, and percentage of the lamb crop to vaccinate against Johne's disease. Selecting "Run" cause the underlying simulation model code to run.

Figure 4: Screen capture of the web-based application interface



The model then generates a benefit to cost ratio for the vaccination programme and provides estimates for how much Johne's disease is costing the farmer with and without vaccination (Figure 5). The user can also choose to view changes in the annual mortality due to Johne's disease and the flock demographic structure. Sliders on the right hand side of the screen allows the users to explore the impacts of changing economic values for vaccination costs, lamb and mutton carcass values, and the cost of raising or purchasing additional replacement ewes. Compared with the economic calculator on the Gudair™, website, the simulation model predicts that the annual percentage of deaths due to Johne's disease must be significantly higher before vaccination is economical for controlling Johne's disease in sheep flocks. However, the model is also highly sensitive to changes in assumptions about the economic values.

Figure 5: Screen capture of the simulation model results presented in the web-based interface



4. Discussion

Recent advances in computer science have made it possible for researchers to easily develop interactive tools that allow farmers and veterinarians to utilize the results from complex epidemiological simulation models without having any background in infectious disease modelling. Our web-based interface for the Johne's disease simulation model allows users to modify key parameters to match the unique management situation on their farm and generates a series of outputs that can be used in making animal health decisions. One of the strong advantages of a web-based approach over traditional downloadable Excel spreadsheet models is that we can easily update the underlying model and interface as new information on Johne's disease epidemiology becomes available.

Results from the current simulation model suggest that the mortality rates in infected flocks need to be significantly higher than assumed by the economic calculator on the Gudair™ website before it becomes economical to vaccinate against Johne's. However, it is difficult to make general assumptions given that the results are highly influenced by the management and economic values set in the model. The results must be interpreted with caution as our current simulation model made several simplifying assumptions about the transmission dynamics of Johne's disease in sheep flocks. In order to adjust the annual mortality rate due to Johne's disease, we tuned the parameter describing the survivability of MAP organisms in the environment thereby altering the level of exposure for susceptible sheep. In the real world, this would mimic the combined effects of pasture stocking rates, pasture rotation, and co-grazing of other susceptible species on MAP density in the environment. Based on the results from an ongoing meta-analysis of experimental studies, we might be redesigning the simulation model to track the exposure and infection status of individual animals over time to better predict the disease transmission rates in case the meta-analysis suggests different parameters. Future versions of the model will also build-in the capability for farmers to specify their pasture management practices as this may also provide an alternative means of controlling the disease.