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Assessing the Effect of Vaccination on Disease
Incidence and Severity

by

Gavin Ramsay

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Gavin Ramsay²

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² School of Economics, The University of Queensland, St. Lucia Campus, Brisbane QLD 4072, Australia
Correspondence: Clem Tisdell, Email: c.tisdell@economics.uq.edu.au

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'The overall goal of this project is to develop and evaluate the necessary tools to provide decision-makers with reliable animal health information which is placed in context and analysed appropriately in both Thailand and Australia. This goal will be achieved by improving laboratory diagnostic procedures; undertaking research to obtain cost-effective population referenced data; integrating data sets using modern information management technology, namely a Geographical Information System (GIS); and providing a framework for the economic evaluation of the impact of animal diseases and their control.

A number of important diseases will be targeted in the project to test the systems being developed. In Thailand, the focus will be on smallholder livestock systems. In Australia, research will be directed at the northern beef industry as animal health information for this sector of livestock production is presently scarce.'

For more information on *Research Papers and Reports Animal Health Economics* write to Professor Clem Tisdell (c.tisdell@economics.uq.edu.au) or Dr Steve Harrison, (s.harrison@uq.edu.au) Department of Economics, University of Queensland, Brisbane, Australia, 4072.

Assessing the Effect of Vaccination on Disease Incidence and Severity

ABSTRACT

In this paper the role of acquired immunity in disease control is examined with particular emphasis on vaccination against *B. bovis*. A method is then developed to predict the change in disease incidence that will follow the introduction of a vaccination program. This method involves the extension of the disease prediction model developed in the previous paper to include vaccination. The extended model is then used to estimate the number of cases of disease prevented by vaccination for each age and sex class and each year of the vaccination program. The method is then applied to determine the number of cases of disease prevented by vaccination against *B. bovis*. The information produced is used as an input to determine the production loss avoided due to vaccination against *B. bovis* in a subsequent discussion paper. This paper examines the role of acquired immunity in disease control then outlines the development of a model to predict the effect of vaccination programs on the number of cases of disease. The model is an expanded version of the disease prediction model developed in the previous discussion paper.

Keywords: *Babesia bovis*, livestock disease, livestock vaccinations.

JEL Classifications: Q16

Assessing the Effect of Vaccination on Disease Incidence and Severity

1. Introduction

Vaccination is a common method used to control infectious diseases. Vaccination reduces the number of cases of disease in a herd. In order to determine the benefits of vaccination it is necessary to estimate the number of cases of disease prevented by vaccination.

In this paper the role of acquired immunity in disease control is examined with particular emphasis on vaccination against *B. bovis*. A method is then developed to predict the change in disease incidence that will follow the introduction of a vaccination program. This method involves the extension of the disease prediction model developed in the previous paper to include vaccination. The extended model is then used to estimate the number of cases of disease prevented by vaccination for each age and sex class and each year of the vaccination program. The method is then applied to determine the number of cases of disease prevented by vaccination against *B. bovis*. The information produced is used as an input to determine the production loss avoided due to vaccination against *B. bovis* in a subsequent discussion paper.

2. The Role of Acquired Immunity in Disease Control

Immunity to disease can be acquired as a result of natural exposure to disease or by vaccination. Vaccination is used to induce immunity to a disease agent using either a killed organism, an attenuated or modified organism, or a particular part of an organism which induces protective antibodies. Vaccination is the most commonly used method of animal disease control.

Vaccination can be used to control disease in two ways. Firstly vaccination can be used to protect an individual animal or small group of animals from disease. This is the aim of vaccinating a dog against distemper, thereby greatly reducing the risk of that individual becoming diseased. Vaccination can also be used to control a disease in a herd by reducing

the rate of disease transmission in the herd. By making most of the herd immune, vaccination can be used to prevent a disease from becoming established in the herd (Cleland et al., 1994).

3. Disease Control by Vaccination

Vaccination is the use of an immunogen to induce immunity to a disease agent. Vaccines can be composed of live organisms that are capable of reproducing in the host after inoculation or non-living material that is not capable of reproduction. An outline of the various types of vaccines available and their characteristics is provided by van Dijk et al. (1994). An effective vaccine is one that stimulates long lasting immunity, does not cause side effects in vaccinated animals and is readily available, inexpensive, stable during storage and easy to administer (van Dijk et al., 1994).

Live vaccines usually contain attenuated organisms that have been manipulated in such a way that they no longer produce disease when administered via the route recommended for that vaccine. The genetic basis of attenuation is often poorly understood (van Dijk et al., 1994). Attenuation can be achieved by the selection of mutants by the use of specific culture techniques, genetic reassortment and recombination (van Dijk et al., 1994).

Vaccines in which the immunogen is incapable of replication may contain inactivated organisms in which the immunogenicity of the organism is maintained but the infectivity is destroyed. They may also contain part of an organism that is capable of inducing immunity or a synthetically produced immunogen. Attenuated and inactivated vaccines are the most common vaccines used in livestock disease control. Attenuated vaccines generally provide longer lasting immunity than inactivated vaccines.

In some cases, production effects are seen as a result of vaccination. These effects can be for example, mild transient decreases in milk yield in a large proportion of animals vaccinated, or problems which occur in a small number of animals such as abscesses at the site of vaccination.

The three main factors that determine the effectiveness of a vaccine in reducing the number of cases of disease in a herd are vaccine efficacy, vaccine coverage and the duration of protection afforded by vaccination.

3.1 Vaccine efficacy

Vaccination does not necessarily prevent disease in all animals vaccinated and vaccine efficacy is the ability of the vaccine to prevent disease in vaccinated animals. Vaccine efficacy is defined as the proportion of animals that do not become diseased that would have become diseased had they not been vaccinated. It can be calculated as the rate of disease in unvaccinated animals minus the rate of disease in vaccinated animals expressed as a fraction or percentage of the rate of disease in unvaccinated animals (Martin et al., 1987, p. 132) and is calculated using the formula:

$$VE = \left(\frac{I_u - I_v}{I_u} \times 100 \right) \%$$

where VE is the vaccine efficacy

I_u is the incidence of disease in unvaccinated animals

I_v is the incidence of disease in vaccinated animals

Vaccine efficacy is affected by the proportion of animals vaccinated that are able to mount an effective immune response and the proportion of vaccine doses that are maintained under appropriate conditions and therefore retain potency (Schwabe et al., 1977, p.159). Vaccination may also have the effect of reducing the severity of clinical signs in cases of disease that do occur and, therefore, the level of production loss. This area of efficacy is much more difficult to quantify and has been less studied than that of protection from the occurrence of disease.

3.2 Vaccine coverage

Vaccine coverage can be defined as the proportion of animals in the population that are vaccinated. This would be affected by the proportion of the herd that are mustered and the proportion of mustered animals that have the vaccine appropriately administered (Schwabe et al., 1977, p. 159). The level of immunity of a group of animals to be vaccinated is rarely determined before they are vaccinated.

3.3 Duration of protection

The duration of protection is the length of protection from disease that the vaccine affords. Where vaccination affords only short term protection regular revaccination is needed. An initial vaccination followed some weeks later by a booster vaccination is needed in some cases to produce immunity, for example for protection against bovine ephemeral fever. The duration of protection affects how frequently animals must be vaccinated to maintain protection. However, vaccinal immunity can be boosted by natural exposure to the disease agent and depending on the rate at which this occurs additional vaccinations may not be required to maintain immunity.

3.4 Herd immunity

Herd immunity is the level of acquired immunity in a population. This immunity can be derived from natural infection or vaccination or a combination of both. An important consideration is the level of herd immunity required to prevent a disease from spreading within a population of animals. This is because for a disease to persist in a population the density of susceptible animals exceeds a critical value such that on average each primary case of disease generates at least one secondary case (Anderson and May, 1987).

Anderson and May (1987) examine the use of mathematical models to determine the most effective vaccination strategy to best protect a population from an infectious disease and van Dijk et al. (1994) examine the role of herd immunity with respect to the development of vaccination strategies to control disease in livestock. Cleland et al. (1994) examine the

role of herd immunity in the case of vaccination against foot and mouth disease in Thailand. These authors examine vaccination strategies for the control of contagious diseases and determine that a high level of vaccination coverage is required to prevent disease spread. They also conclude that the level of herd immunity to prevent the establishment of a disease in a herd varies between different diseases.

The role of herd immunity in the case of vector-borne diseases is more difficult to determine because of the variation in the density of the vector population and the ability of some vectors to move from one area to another. In addition information on the importance on vector density is not often available (Rogers, 1992).

4. Vaccination Against *Babesia bovis*

Vaccination is the most commonly used method to prevent disease caused by *B. bovis*. Vaccination for *B. bovis* has been carried out in Australia since the 1890's and became widely used following the establishment of laboratories to promote the production and use of vaccines in 1909 (Mahoney, 1994). The techniques used in Australia to produce vaccines against *B. bovis*, in particular the frozen vaccines, are described by Dalgliesh et al. (1990). These authors also review the development of the vaccine production system and the use of the vaccine to control disease caused by *B. bovis*. This section provides an overview of the vaccine and its use.

Vaccination against *B. bovis* is performed using a live attenuated blood vaccine produced from the blood of infected splenectomised calves (Dalgliesh et al., 1990). The vaccine can be provided in chilled form in which case it must be used within six days of production or as a frozen vaccine that must be stored in liquid nitrogen (Dalgliesh et al., 1990). The frozen vaccine is much more expensive to produce and transport than the chilled vaccine (de Vos et al., 1994), but has the advantage of allowing thorough pre-release checks for efficacy. Within Australia the chilled vaccine is the most used and a stringent set of quality control measures are in place to minimise the risk of contamination of the vaccine with

adventitious agents and ensure reliable infectivity and low virulence of the organisms in the vaccine (Dalglish et al., 1990).

Occasionally disease outbreaks occur in vaccinated herds of cattle (Bock et al., 1992). Investigations of these outbreaks have shown that the failure of vaccination can be due to a variety of factors (Bock et al., 1992), including:

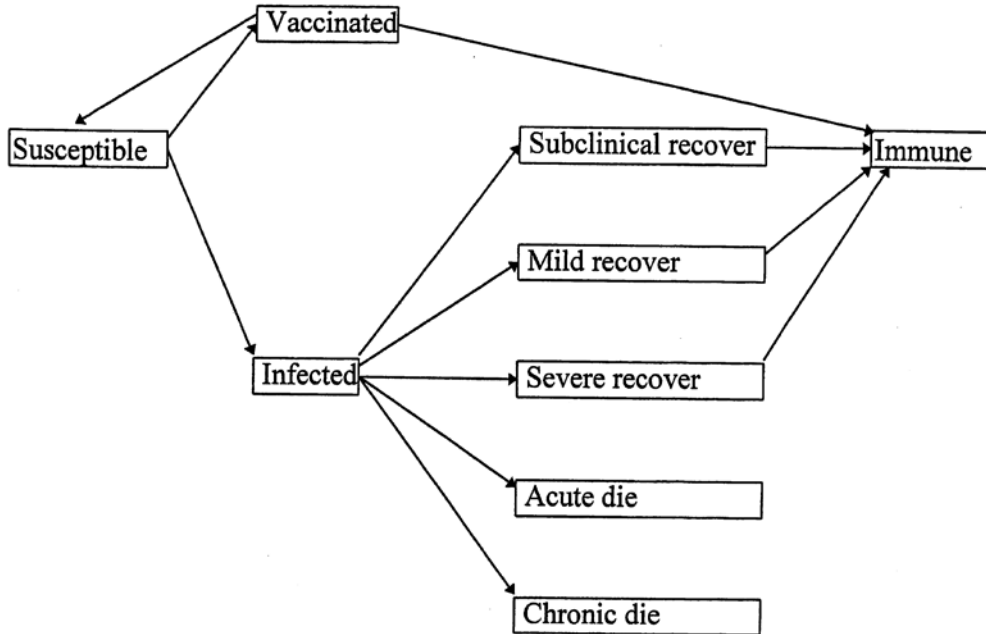
- inherited host factors
- cross immunity between the vaccine strain and the field strain
- the development of virulent breakthrough strains, and
- poor vaccine handling by cattle producers (leading to the situation where enough too few organisms are injected to produce an adequate immune response).

A single vaccination provides long lasting immunity to disease (Dalglish et al., 1990). However, recent studies carried out in Malawi have suggested that immunity declines two years after vaccination in that country (Tjornhehoj et al., 1996). The Tick Fever Research Centre, Wacol, Queensland recommends a single vaccination in young cattle to provide immunity and this is the practice in Central Queensland.

5. Expansion of the Disease Prediction Model to Include Vaccination

In this section, the disease model outlined in Discussion Paper 33 is expanded to include disease control by vaccination. In order to do this an additional state, vaccinated, is included in the disease simulation model. Figure 1 illustrates the modified transition diagram.

Figure 1: Transition diagram for expanded disease prediction/vaccination model



5.1 The effect of vaccination on immunity in the disease prediction/vaccination model

Vaccination increases the proportion of the herd that is immune. In the expanded disease prediction/vaccination model it is assumed that vaccination produces immunity in the same way as subclinical disease caused by natural exposure produces immunity. That is, animals vaccinated become immune without showing any signs of disease or suffering any production losses, and the immunity is long lasting. It is also assumed that vaccination is carried out at the beginning of each year and there is no lag between vaccination and the development of immunity.

5.2 Calculating transition probabilities for the disease prediction/vaccination model

The transition probability from susceptible to vaccinated (P_{sv}) is the probability of an animal being vaccinated. This is calculated using the formula:

$$P_{sv} = P_m \times P_{p/m}$$

where P_m is the probability of being mustered for vaccination and

$P_{p/m}$ is the probability of a mustered animal receiving an appropriate dose of vaccine.

Not all vaccinated animals will become immune to disease and the transition probability from vaccinated to immune (P_{vi}) is defined as the vaccine efficacy, where vaccine efficacy represents the probability of an animal responding with an effective immune response following vaccination.

The transition probability from vaccinated to susceptible (P_{vs}) that is, the probability that an animal will not respond to vaccination with an effective immune response is calculated as:

$$P_{vs} = 1 - P_{vi}$$

5.3 Probability of transition from susceptible to infected state

The transition probability from susceptible to infected state is assumed to be the same as it would be in the absence of the vaccination program. However, it is possible that this probability (as determined by the incidence risk of infection), may change and could either:

- decrease because the proportion of the herd that is susceptible would be greatly reduced by a vaccination program leading to reduced contact between infected and susceptible hosts, or
- increase which may occur where the vaccine is live, transmissible and can revert to virulence, as is the case for *B. bovis* vaccine. However, data is not available to confirm this possibility.

In the disease prediction/vaccination model the transition probabilities from infected to each of the categories of disease susceptibility are assumed to remain the same as those determined to occur without vaccination.

6. Calculating the Number of Cases of Disease Avoided

The aim of determining the change in disease occurrence is to estimate the number of cases of disease that are avoided. In the model developed in this paper the number of cases of disease avoided by a vaccination program is compared with the base level of disease predicted to occur in the absence of vaccination.

The number of cases of disease avoided is calculated as the difference between the number of cases of disease predicted to occur without the vaccination program and the number of cases of disease predicted to occur with a vaccination program. The number of cases of disease avoided by vaccination is calculated for each age and sex class and for each category of disease severity for each year vaccination is carried out.

6.1 Incorporation of vaccination model into a computer spreadsheet

The disease control formulae were entered into a computer spreadsheet using the package Microsoft Excel. The spreadsheet has automatically updated links to the disease prediction model developed in the previous discussion paper. This enables model simulations to be carried out using outputs from the disease prediction model as inputs into the vaccination model thereby producing a disease prediction/vaccination model. Using the spreadsheet model the effect of vaccination programs on the incidence of disease can be rapidly assessed for various levels of age specific seroprevalence and susceptibility of cattle in the herd to disease.

7. Results of Model Simulations to Determine the Effects of Vaccination on the Number of Cases of Disease Caused by *Babesia bovis*

The results of simulation experiments using the model developed in this paper are presented in this section. The experiments are carried out to determine the effects of vaccination programs on the incidence and severity of disease are examined in Sections 7.1, 7.2 and 7.3. In Section 7.1 the effect of vaccination on the proportion of the herd immune is examined for the first, third and seventh year of vaccination programs. In Section 7.2

predictions of the number of cases of disease from which animals recover avoided due to vaccination are examined for each year of vaccination programs. In Section 7.3 predictions of the number of deaths avoided following the introduction of vaccination programs are examined.

In each section two vaccination programs are examined. These are:

- Vaccination program 1 (Vacc 1). In this program animals one year old are vaccinated in each year of the program.
- Vaccination program 2 (Vacc 2). In this program all animals one year old or older are vaccinated in the first year of the program and animals one year old are vaccinated in subsequent years.

In Sections 7.2 and 7.3 predictions of the number of cases of clinical disease from which animals recover that are avoided and number of deaths avoided due to vaccination are examined for each year of the vaccination programs, from year one, the year in which the programs begin to year eight of the vaccination program. Three herds containing cattle with different levels of disease susceptibility are examined. The herds contain cattle that are disease resistant (resistant), disease susceptible (susceptible) or of intermediate susceptibility (intermediate).

Three levels of incidence risk of infection (the transition from susceptible to infected) are examined, namely high, medium and low as were defined in the Discussion Paper 33.

The transition matrix is held constant in these experiments. The initial state vector is the steady state vector without a vaccination program. The results examined are those produced during progress from the initial state vector to the steady state vector with vaccination.

In the simulation experiments vaccination coverage (the transition probability from susceptible to vaccinated) is 0.95 and vaccine efficacy (the transition probability from vaccinated to immune) 0.90. The efficacy selected is lower than the 0.95 used by Bartholomew and Callow (1979) but allows for the possibility of decreased efficacy due to

decreased vaccine viability that may occur under the difficult conditions experienced in Central Queensland.

7.1 Predictions of the effect of Babesia bovis vaccination on the immune status of the herd

In this section the results of simulation experiments to determine the effect of vaccination on immunity in the herd are presented and examined. The effect of vaccination on the level of immunity in the herd varies with the incidence risk of infection, and the vaccination regime used. These effects are presented in Figures 2, 3, and 4.

Where the incidence risk of infection is low as illustrated in Figure 2a Vaccination program 2 produces an immediate high level of immunity in each and every age group vaccinated. This high level of immunity is maintained in subsequent years by the vaccination of yearling animals (Figures 2b and 2c). Vaccination program 1 does not produce a high level of immunity in all age groups until year seven of the vaccination program. This is because the increase in immunity in older animals requires that animals vaccinated as yearlings have moved into older age groups. This is demonstrated by the proportion of the herd immune after three years of the vaccination program as illustrated in Figure 2b. In this case a high proportion of animals are immune in age groups one year old (those vaccinated in year three), two years old (those vaccinated in year two of the vaccination program) and three years old (those vaccinated in year one of the vaccination program) after three years of Vaccination program 1. A lower proportion is predicted to be immune in older age groups. By year seven of the program the animals vaccinated as yearlings in the first year of the vaccination program are seven years old. In this situation each age group in the herd has a high proportion of immune animals as demonstrated in Figure 2c.

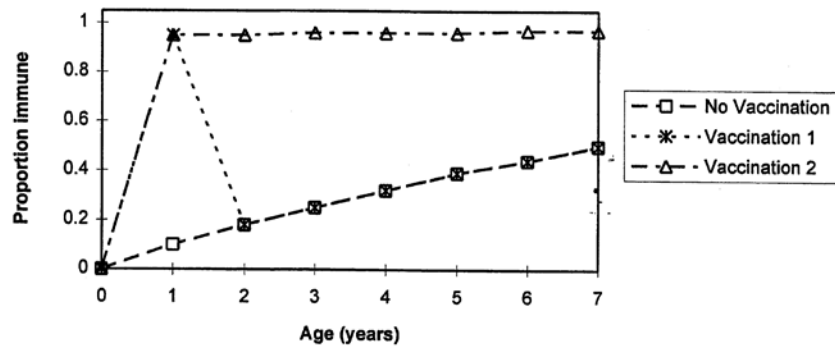
Where the incidence risk of infection is medium Vaccination program two produces a high proportion of immune animals in each age group vaccinated in the first year of the vaccination program (Figure 3a) as is the case where the incidence risk of infection is low. The effect of Vaccination program 1 on the proportion of the herd immune differs from the situation where the incidence risk of infection is low. With a medium incidence risk of

infection the proportion of each age group in the herd immune reaches the same level as achieved under Vaccination program 2 in the third year of the program. This is because the proportion of the herd immune reaches a high level after animals reach four years old in the absence of vaccination (Figure 3c), therefore vaccination has a small effect on the proportion of animals immune in the age groups older than three years.

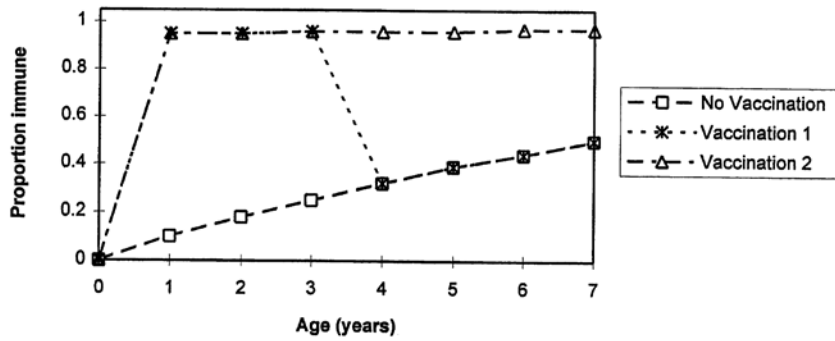
Where the incidence risk is high, the effect of vaccination on the level of herd immunity is predicted to be small and to not vary in subsequent years of the vaccination program for both Vaccination programs 1 and 2 (Figure 4). This is because with a high incidence risk of infection most animals are exposed to *B. bovis* in the first year of life before vaccination is carried out in either of the vaccination programs being examined and almost all animals have been exposed to *B. bovis* by the time they are two years old.

Figure 2: Proportion of the herd immune for each vaccination program and without vaccination with a low incidence risk of infection

2.a First year of vaccination programs



2.b Third year of vaccination programs



2.c Seventh year of vaccination programs

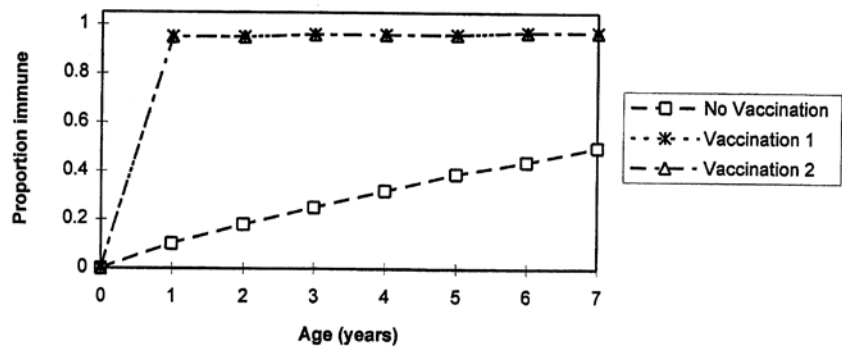
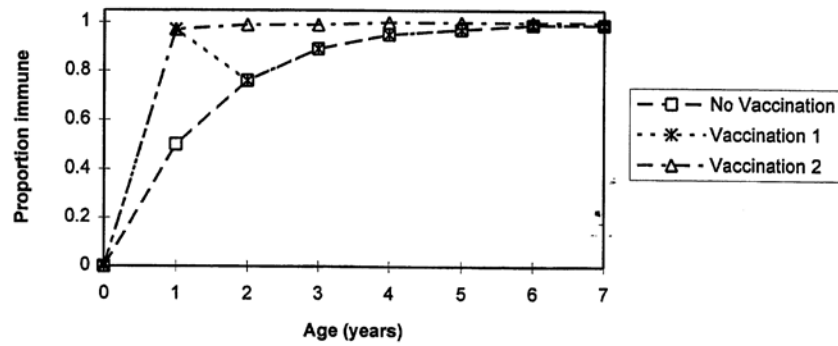
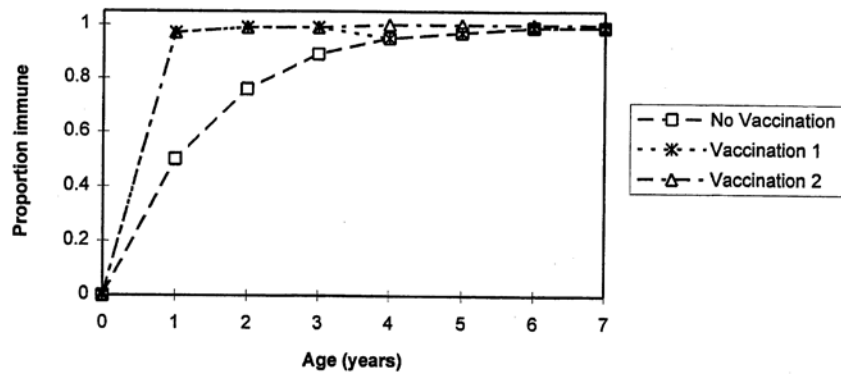


Figure 3: Proportion of herd immune for each vaccination program and without vaccination with medium incidence risk of infection

3.a First year of vaccination programs



3.b Third year of vaccination programs



3.c Seventh year of vaccination programs

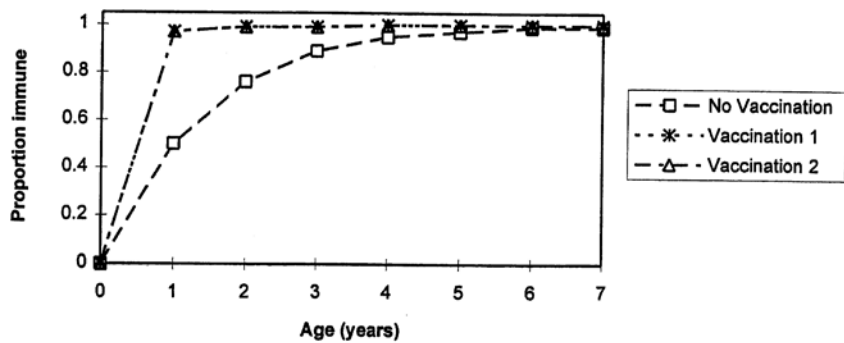
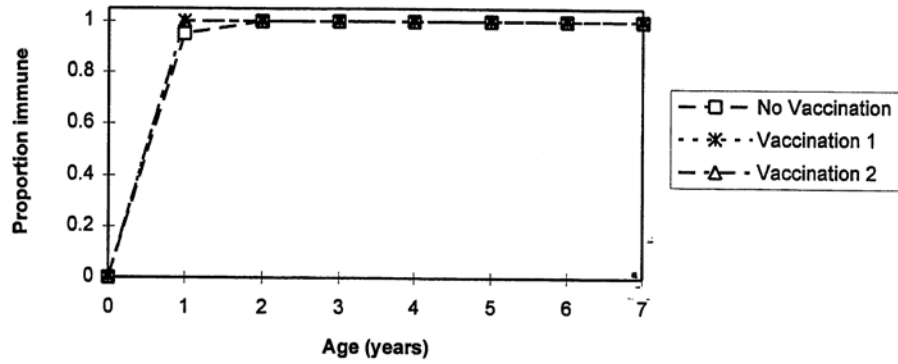


Figure 4: Proportion of herd immune for each vaccination program and without vaccination where the incidence risk of infection is high



The results in this section demonstrate the proportion of the herd immune is affected by the incidence risk of infection, the age at which animals are vaccinated and the number of years since the commencement of the vaccination program. Vaccination has greatest impact on herd immunity where the incidence risk of infection is low and least where the incidence risk of infection is high.

7.2 Predictions of the number of cases of clinical disease with recovery avoided due to *Babesia bovis* vaccination

This section presents and examines the results of simulations to determine the number of clinical cases of disease with recovery avoided by *B. bovis* vaccination. In this section the number of clinical cases of disease avoided consists of the sum of cases of mild clinical disease and severe clinical disease (defined as Categories 2 and 3 the previous discussion paper) avoided. These are calculated separately in the model and are combined for presentation in this section.

The results for herds of each level of disease susceptibility are presented in separate graphs in Figure 5. The effects of the two vaccination programs are presented for each of the three

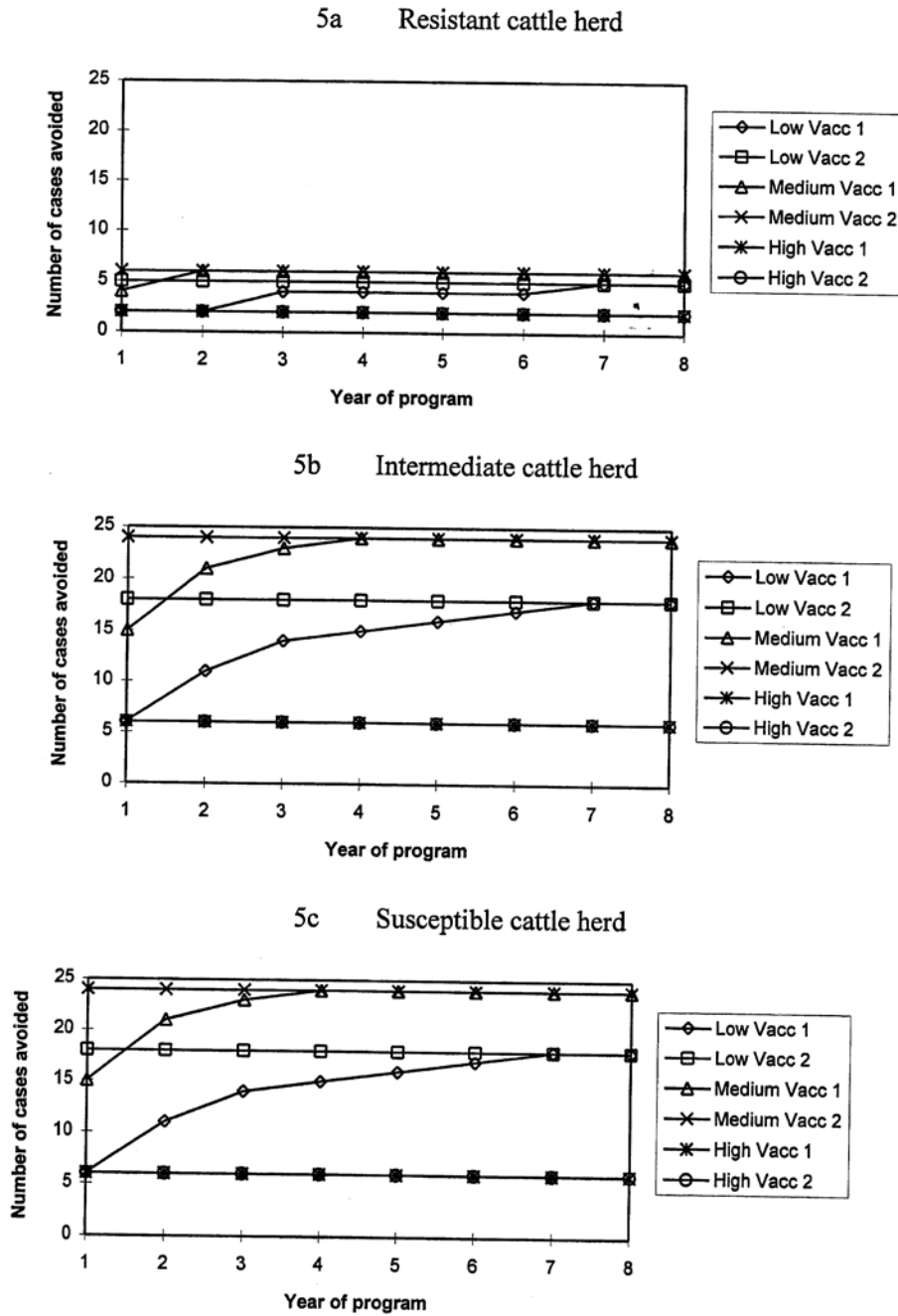
levels of incidence risk of infection, high medium and low. The number of cases of clinical disease with recovery prevented by vaccination is affected by the vaccination program used, the incidence risk of infection and the level of disease resistance of the cattle in the herd. The herds with susceptible and intermediate cattle show similar reductions in the number of clinical cases of disease from which cattle recover while vaccination in the disease resistant herd shows a smaller number of cases prevented.

The number of cases of disease prevented is highest where the incidence risk of infection is medium and lowest when the incidence risk of infection is high. When the incidence risk of infection is low the number of cases prevented by Vaccination program 1 reaches the same level as those avoided by Vaccination program 2 in year seven. Where the incidence risk of infection is medium the number of cases avoided by Vaccination program 1 reaches the same level as those avoided by Vaccination program 2 in year four of the program for susceptible and intermediate herds and in year two for resistant herds. With a high incidence risk of infection there is no difference between the two vaccination programs in the number of cases of clinical disease with recovery avoided.

7.3 Predictions of the number of deaths avoided due to Babesia bovis vaccination

In this section the results of simulations to determine the number of deaths avoided due to *B. bovis* vaccination are presented and examined. The results of the simulations are presented in Figure 6. The results for each level of disease susceptibility are presented in separate graphs in Figure 6. The effects of the two vaccination programs are presented for each of the three levels of incidence risk of infection, high medium and low. The number of deaths avoided is predicted to vary with the vaccination program, incidence risk of infection and the level of innate disease resistance of cattle in the herd.

Figure 5: Number of cases of clinical disease with recovery avoided due to vaccination at three levels of incidence risk of infection and two vaccination programs



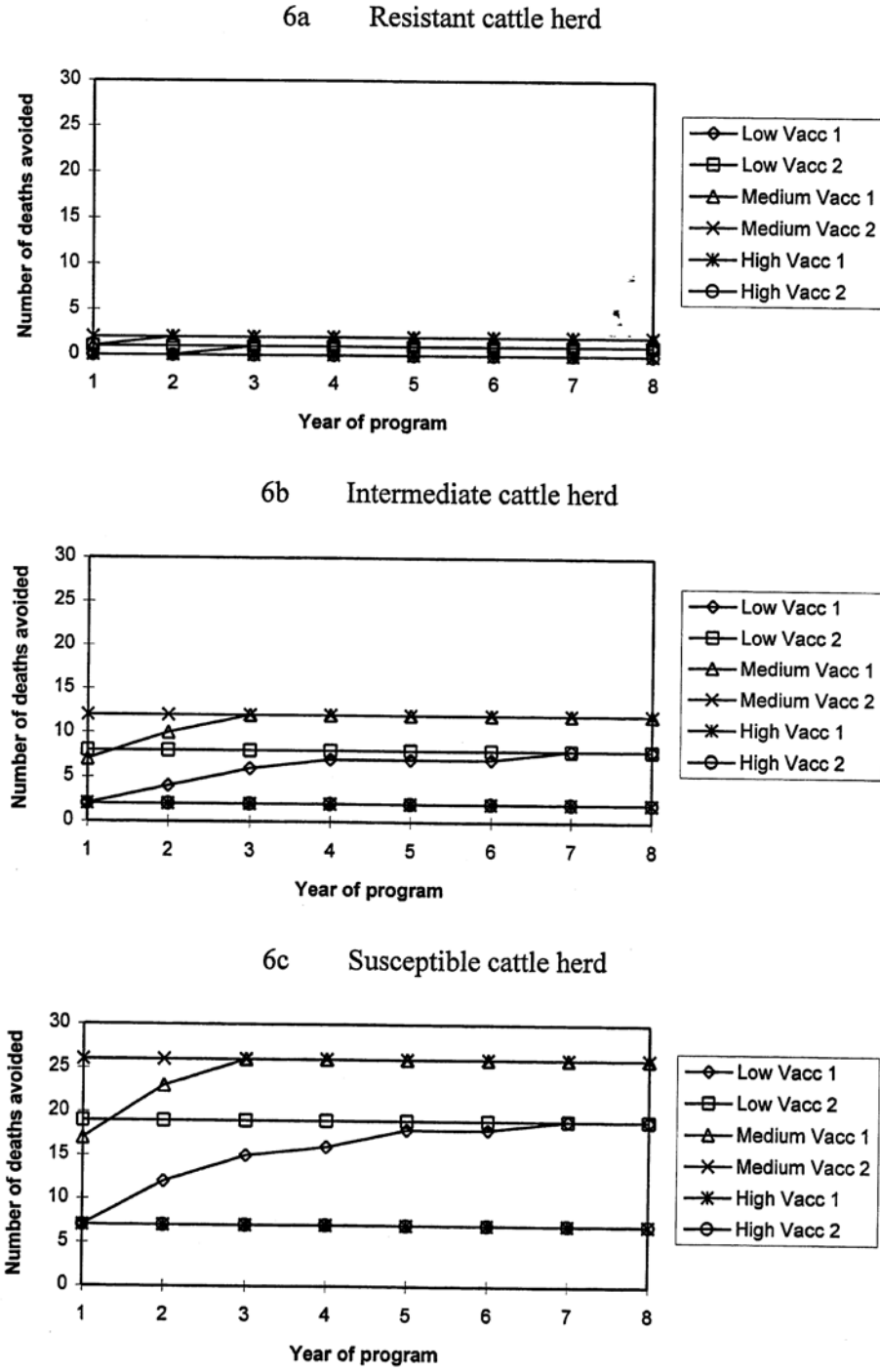
The simulation experiments indicate the largest number of deaths is prevented by vaccination where the incidence risk of infection is medium. Fewest deaths are prevented by vaccination where the incidence risk of infection is high. The number of deaths prevented with a low incidence risk of infection being between the other two. This is related to the results presented in Figure 4 of the previous paper where it is demonstrated that most deaths in animals older than one year are predicted to occur where the incidence risk of infection is medium.

As expected at each level of incidence risk of infection the largest number of deaths is prevented by vaccination in the susceptible herd of cattle. In the herd of disease resistant cattle few deaths are avoided at the three levels of incidence risk of infection examined. In the intermediate herd the number of deaths avoided lies between those predicted for the susceptible and resistant herds.

In the case of Vaccination program 2 the number of deaths avoided reaches its highest level in the first year of the vaccination program and maintains that level. The number of deaths avoided using Vaccination program 1 increases from the first year of the program to reach the level of Vaccination program 2 after period of time. The time before the number avoided using Vaccination program 1 equals the number avoided using Vaccination program 2 varies with the incidence risk of infection.

Where the incidence risk of infection is low the number of deaths avoided due to Vaccination program 1 reaches the level for Vaccination program 2 after the program has been running for seven years. This is because deaths are predicted to occur in all age groups in the absence of vaccination where the incidence risk of infection is low (Figure 5 from the previous paper) and it is seven years before the level of herd immunity is high in all age groups (Figure 2).

Figure 6: Number of deaths avoided due to vaccination at three levels of incidence risk of infection and two vaccination programs



In the case of medium incidence risk of infection the number of deaths avoided due to Vaccination program 1 reaches the level for Vaccination program 2 in the third year of the program. This is because with a moderate incidence risk of infection the number of deaths is predicted to be small in the three year old age group and zero in older age groups in the absence of vaccination as presented in Figure 5 of the Discussion Paper 33.

Where the incidence risk of infection is high the number of deaths avoided by vaccination is low for all levels of disease resistance and in all age groups. Both vaccination programmes are predicted to produce the same results where the incidence risk of infection is high.

8. Summary

This paper examines the role of acquired immunity in disease control then outlines the development of a model to predict the effect of vaccination programs on the number of cases of disease. The model is an expanded version of the disease prediction model developed in the previous discussion paper.

The model developed in this paper provides an effective way to determine the effect of vaccination on herd immunity and predict the number of cases of disease that would be prevented by a vaccination program. Simulations using the model demonstrate that vaccination has greatest impact on the level of immunity in the herd where the incidence risk of infection is low, and least where the incidence risk of infection is high. However, the largest number of cases of disease from which animals recover and deaths are prevented by vaccination where the incidence risk of infection is medium. The same pattern is seen for each of the three levels of disease susceptibility. As expected most cases of disease are prevented by vaccination in cattle that are susceptible to disease and least in resistant cattle.

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