A Stochastic Simulation Model for the Efficacy of Vaccination Against *Mycobacterium avium* subsp. *paratuberculosis* in Dairy Sheep and Goats

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Abstract. We assessed the benefits of vaccination against *Mycobacterium avium* subsp. *paratuberculosis* (MAP) on the average daily milk yield (DMY) of sheep and goat flocks. A stochastic simulation model was used to estimate the DMY pre and post vaccination of the flock replacements. The average DMY increased steadily for the first ten years post vaccination and then reached a plateau. Medians for the DMY were significantly higher post vaccination. The expected difference between the prevalence of MAP infection between and after the initiation of the vaccination program was the most influential factor for the DMY benefits. Vaccination of replacements in a MAP infected flock is expected to improve the overall milk productivity in the long term.

Keywords: Paratuberculosis, milk, vaccination, stochastic simulation.

1 Introduction

Paratuberculosis is a chronic intestinal infection of domestic and wild ruminants, which is caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP). As a result of the progressing MAP infection, infected animals develop reduced productivity, body weight, fertility and, ultimately, die or are prematurely culled. One of the main approaches to reduce the impact of paratuberculosis in sheep and goat flocks is through vaccination of the replacement stock in order to increase their resistance to infection. Vaccination of all sheep in an affected flock has been shown to provide effective disease control in Australia (Windsor, 2006) and underpins the national control program along with a risk-based trading system. Yet, the expected benefits of vaccination in dairy sheep and goats have not yet been quantified. Only scarce and conflicting reports about the direct benefit of vaccination on milk production exist in dairy cows (Juste et al., 2009). Hence, the objective of this study was to assess the expected benefits of vaccination on the milk productivity of dairy sheep and goats.

Proceedings of the 7th International Conference on Information and Communication Technologies in Agriculture, Food and Environment (HAICTA 2015), Kavala, Greece, 17-20 September, 2015.

2 Materials and Methods

A stochastic simulation model was used to assess the expected benefits on the average daily milk yield (DMY) from a vaccination of replacements program. The infection and milk production status of the 200 sheep and goat flock is simulated for 30 years. For the first ten years, the model assumes that vaccination does not take place, while vaccination of the flock replacements starts at the eleventh year and is simulated until the thirtieth year. The yearly assumed replacement rate, the infection rate and the expected average DMY for vaccinated and unvaccinated animals was derived from relevant published literature (Kostoulas et al., 2006; Liapi et al., 2012; Angelidou et al., 2014) and the expert opinion of two authors (EA and LL). Summary of the derived estimates and their corresponding distributions are in Table 1. The model assumes that animals who get infected remain infected for their productive life or until replaced.

Following the primary analysis, sensitivity analysis was performed to assess the impact of different infection rates and DMYs on the expected benefits of vaccination.

The DMY estimates were based on 200 simulations. The model was developed and ran in R. Codes are freely available from the first author upon request.

Table 1. Input parameters for the replacement rate (RR), infection rate (IR) and the average daily milk yield (DMY) for vaccinated and unvaccinated against *Mycobacterium avium* subsp. *paratuberculsosis* sheep and goats.

Input parameter	Parity	Estimate			Distribution
		Min	mode	Max	
RR	All	-	0.17	0.25	beta(17.4, 78.2)
IR unvaccinated	All	0.10	0.15	-	beta(14.5, 77.7)
IR vaccinated	All	-	0.002	0.01	beta(1, 458)
DMY healthy animals	1	0.7	1	1.2	triangular(0.7, 1, 1.2)
	2	0.8	1.3	1.5	triangular(0.8, 1.3, 1.5)
	3	0.8	1.35	1.65	triangular(0.8, 1.35, 1.65)
	>4	0.8	1.25	1.5	triangular(0.8, 1.25, 1.5)
Decrease (%) in DMY infected animals	1	-	5	10	beta(6, 99)
	2	-	10	15	beta(15, 130)
	3	-	15	20	beta(28, 153)
	>4	10	15	-	beta(14, 77)

3 Results

Estimates for the average DMY for a period of 30 years are in Figure 1. For the first ten years the flock did not follow a vaccination program and under endemic disease status the DMY remains fairly similar. Since the initialization of a vaccination of replacements program – year eleven and on – DMY steadily increases. Estimates of the median DMY ten years pre vaccination, the first ten years post vaccination and the last ten years of the vaccination program reveal a significant increase (Figure 2).

Sensitivity analysis revealed that the most influential parameter on the benefits of vaccination was the assumed infection rate in the cohort of vaccinated animals with decreased rates leading to higher and earlier DMY benefits.

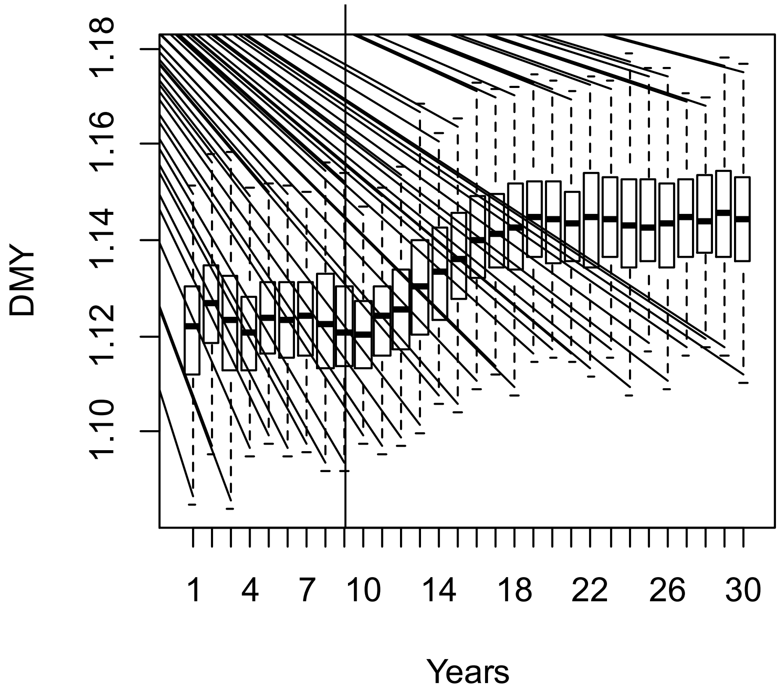

Fig. 1. Predicted average daily milk yield (DMY) in kg before and after commencement of the vaccination of replacements against Mycobacterium avium subsp. paratuberculosis (MAP) in a 200 sheep and goat flock. The vertical line at year 10 marks the initiation of vaccination. Boxes represent inter-quartile ranges and the solid black line at the approximate center of each box is the median; the arms of each box extend to cover the central 95% of the DMY distribution with their ends corresponding to 2.5th and 97.5th percentile.

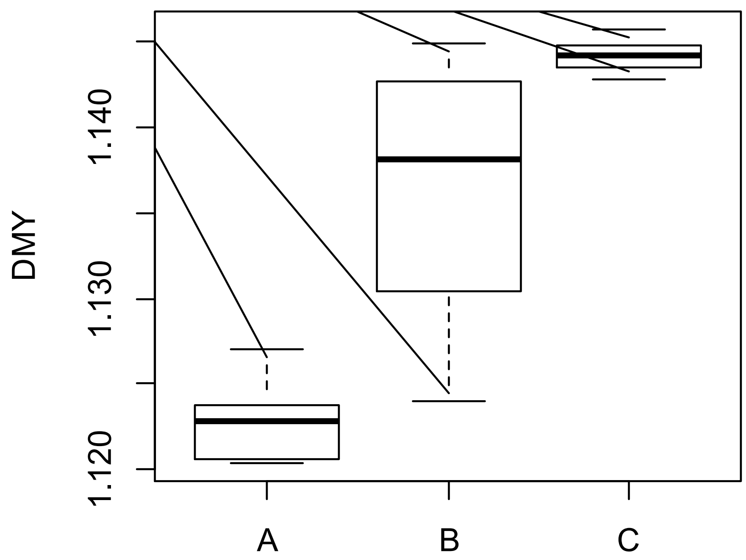

Fig. 2. Predicted median of the DMY ten years pre vaccination against MAP (A), ten years post vaccination (B) and ten to twenty years post vaccination (C).

4 Discussion

In this study we explored the potential benefits of a vaccination of replacements program on the average DMY of dairy sheep and goats. Despite the fact that an overlap was observed between the yearly DMY estimates this was mostly due to the full stochastic approach rather than the absence of actual benefits on the DMY of vaccinated animals. The benefits of vaccination have been masked under the calculation of the average DMY for the whole herd, rather than the calculation of separate DMYs for the vaccinated and unvaccinated animals. Hence, in a flock with 15% true prevalence of MAP infection an average improvement of approximately 12% in the DMY for the vaccinated cohort corresponds to a much lower benefit for the average DMY of the flock. Clearly, the overall DMY gains further decrease in herds/flock with lower prevalence of MAP infection. The latter could also explain the conflicting reports on the direct benefits of vaccination in the milk production of dairy cows (Juste et al., 2009). Still, as indicated by the calculation of median DMYs pre and post vaccination, the long-term benefits from vaccinating the replacement stock are unquestionable.

MAP vaccination constitutes one of the main approaches to reduce the impact of paratuberculosis in sheep and goat flocks. MAP vaccination though not directly preventing from infection, it reduces the occurrence of clinical cases of MAP and MAP excretion from infected animals, thus, cutting off routes to new infections and minimizing MAP-associated direct and indirect production losses (Windsor, 2006). Our model is a first attempt to quantify the positive effect of MAP vaccination on the milk productivity of dairy sheep and goats. Currently ongoing studies that aim to measure the actual benefit in the DMY for vaccinated animals will provide additional real life data and refine our estimates on the improvement of the milk productivity of dairy sheep and goats.

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