The use of vaccination as a response tool for equine Influenza

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Executive summary

The key response activity for controlling or eradicating equine influenza is movement standstill and biosecurity practices (Firestone *et al.* 2013; Garner *et al.* 2011). Modelling is a tool to understanding the value of other response policies including vaccination. Modelling using InterSpread Plus showed that vaccination 7 days or earlier for EI did not greatly improve the efficiency of control. Suppressive vaccination out to a radius of 3km in regions where there is a high density horse population (Auckland and the Waikato) was more effective at control than a national movement standstill only. Where vaccination resources were unlimited increasing the radius of suppressive vaccination out to 5km reduced the time to eradication and the number of infected properties; however, 20% more properties were required to be vaccinated for this scenario. Sensitivity analysis showed that if the local spread parameters were increased by 25% from baseline levels that the number of properties required to be vaccinated could increase by a further 13% and the number of infected properties could increase by 34%. Hence, in response planning disease control authorities need to take account of uncertainty by ensuring that there are more than sufficient resources available for any given scenario.

Introduction

In the event of an incursion of equine influenza (EI) virus into the horse population of New Zealand there will be demands by sectors of the horse industry and the public on the Ministry for Primary Industries to vaccinate horses. Strategic vaccination was used as a tool to assist eradication of EI during the 2007/8 incursion into Australia. There was limited time available for Australian authorities to make critical analysis on the most effective vaccination regime used in the response. Consequently the strategies used by the Australian authorities had not been tested and may have had limited impact on control (Cowled *et al.* 2009, Garner *et al.* 2011).

Queensland and New South Wales used different strategies for control of EI, yet the time taken to eradication was not greatly different between these two Australian states. Analysis of the effectiveness of vaccination was complicated by the strategies changing over time. The New South Wales approach was mainly focused on suppressive vaccination (vaccination of horses around infected premises) in contrast to Queensland's approach that was mainly focused on creating protective buffer zones (Perkins *et al.* 2011). Regardless of its benefit as an eradication tool, vaccination was a key to allowing horse movements necessary for some equine industries to continue to operate (Garner *et al.* 2011). The current Australian response plan for EI includes the use of vaccination as a response tool (Anonymous 2011).

With the benefit of hindsight and ability to carry out analysis using Australian outbreak data it is possible to determine the merits of different vaccination response strategies. Simulation models are one method of examining the affect of a range of control scenarios on specific outcomes, such as the number of infected horse premises. Strategies that have the most significant affect on these outcomes can then be adopted as a disease control policy. Ideally policy is formulated prior to a response as the maximum payoff is likely to occur if response strategies are carried out in a timely manner (Cogger *et al.* 2011).

This paper summarises key findings from results of Australian and New Zealand simulation modelling, as well as other data from the literature. The aim was to inform decision making regarding a response policy for vaccination of horses for EI in the event of an incursion into New Zealand.

Simulation modelling

The Australian outbreak of EI lasted 4 months with approximately 140,000 horses vaccinated as part of control measures (Garner *et al.* 2011). The benefit of vaccination to containment and eradication during this outbreak was questionable given that the number of cases of EI was falling by the time vaccination was initiated (Cowled *et al.* 2009, Garner *et al.* 2011). It is possible that alternative vaccination strategies may have been more effective. These alternative strategies were examined by modelling different scenarios.

Modelling of different Australian outbreak scenarios showed that movement restrictions and biosecurity measures were highly effective in controlling the outbreak (Garner *et al.* 2011). All early vaccination strategies (carried out after 7 days into a control program), where vaccination of horses from high density horse areas were prioritised, reduced the size of the outbreak (Garner *et al.* 2011).

There was a 60% reduction in the number of infected properties and a reduction of 8-9% in the size of the area affected (Garner *et al.* 2011). Where resources for carrying out vaccination were limited, a 1 km suppressive ring vaccination strategy was the most effective strategy (Garner *et al.* 2011). Unfortunately these results cannot be extrapolated to an outbreak scenario in New Zealand as the structure of the horse population, the density of horse properties, local geography and other factors such as climate are very different between Australia and New Zealand.

A stochastic simulation model using InterSpread Plus (Sanson 1993) was used to model outbreak scenarios of EI under New Zealand conditions. The model was parameterised using demographic and movement data collected by Rosanowski (2011) and from data gained from the experience of the Australian EI outbreak. Initial findings from the model did not suggest that vaccination offered any benefit over a national standstill of horse movements (Cogger *et al.* 2011). However, when modelling was carried out with vaccination targeting regions where there was a high density of horses (Auckland and the Waikato) the results supported Australian findings.

It was determined that the use of vaccination in combination with movement restriction was more effective than movement restriction only. A suppressive vaccination strategy (ring vaccination in a zone of 3 km around infected properties) generally was the most effective strategy tested, with regards to the number of infected properties, the number of vaccinated properties (the lowest number being the most optimal) and the duration of the outbreak (Rosanowski 2011).

Comparisons between movement control only and the use of suppressive vaccination as well as movement control showed that the median duration of the outbreak was 51% less when vaccination was carried out (88 vs. 178 days). In addition, there was a 75% reduction in the number of infected properties (793 vs. 3136). The median number of properties where vaccination occurred was 2726.

During the first 10 days of the Australian outbreak of EI most local spread was within 5km of infected properties, with the maximum spread occurring out to a distance of 15.3km (Dhand *et al.* 2013). Over the entire outbreak 83% of infected properties were within 15km of those premises infected through network spread in the first 10 days (Dhand *et al.* 2013). In light of these findings, analysis was carried out using the New Zealand InterSpread Plus model to examine the affect of incorporating these results into local spread parameters. The results indicated that there was some advantage in extending the distance of suppressive vaccination from a ring of 3km to 5km. In this scenario the number of infected properties was reduced by approximately 10% and the duration of the outbreak reduced by approximately two weeks. However, 20% more horses were required to be vaccinated.

Sensitivity analysis showed that if the local spread parameters were increased by 25% from baseline levels that the number of properties required to be vaccinated could increase by a further 13% and the number of infected properties could increase by 34% (Rosanowski 2013). Hence, in response planning disease control authorities need to take account of uncertainty by ensuring that there are more than sufficient resources available for any given scenario.

Development of an agreed vaccination policy and an established relationship with vaccine companies would most likely form part of the conditions necessary to carry out early vaccination. Delays in the start of vaccination would be likely even if a vaccination policy had been agreed upon prior to a response to EI. The reasons for a delay are firstly, because of the need to type the vaccination strain and ensure that any vaccination used provides adequate protection against the field strain and secondly, the time necessary to source available vaccine, ship it to New Zealand and develop appropriate operational procedures to carry out vaccination. Molecular sequencing carried out on the detected EI virus may take between 3-4 days. Subsequently, expert opinion would be sought on the suitability of available vaccines. Initial sourcing of vaccine and negotiations to purchase vaccine could be started immediately, with a final decision made once the suitability of vaccine for use against the field strain was confirmed. It would seem unlikely that even under the most streamlined set of circumstances that vaccination could start prior to a period of 7-10 days elapsing. Despite this, Rosanowski (2011) determined that starting vaccination at 7 days vs. 14 days had no effect on the duration of the epidemic; however, it did reduce the median number of infected properties by 23%.

Conclusions

The key response activity for controlling or eradicating equine influenza is movement standstill and biosecurity practices (Firestone *et al.* 2013; Garner *et al.* 2011). Modelling is a tool to understanding the value of other response policies including vaccination. Modelling using InterSpread Plus showed that vaccination 7 days or earlier for EI did not greatly improve the efficiency of control. Suppressive vaccination out to a radius of 3km in regions where there is a high density horse population (Auckland and the Waikato) was more effective at control than a national movement standstill only. Where vaccination resources were unlimited increasing the radius of suppressive vaccination out to 5km reduced the time to eradication and the number of infected properties; however, 20% more properties were required to be vaccinated for this scenario. Sensitivity analysis showed that if the local spread parameters were increased by 25% from baseline levels that the number of properties required to be vaccinated could increase by a further 13% and the number of infected properties could increase by 34%. Hence, in response planning disease control authorities need to take account of uncertainty by ensuring that there are more than sufficient resources available for any given scenario.

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Appendix

New Vaccination strategies and local spread scenarios for the Equine Influenza control model

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30th May 2013

Summary

Using the Interspread Plus parameters already defined for the New Zealand equine influenza (EI) control model (Rosanowski, 2012), two new vaccination strategies were investigated and a local spread sensitivity analysis was conducted. The two new vaccination strategies were vaccination at a 5 kilometre radius of an infected property (suppressive) and vaccination at a 12 to 15 kilometre band around an infected property (protective). These vaccination strategies were compared to the previously modelled suppressive vaccination at a 3 kilometre radius, protective vaccination at a band between 7 and 10 kilometres and targeted vaccination of racing and breeding properties. All other parameters from the previous model (Rosanowski, 2012) remained unchanged.

The sensitivity analysis utilised the model with a vaccination strategy at a radius of 5 kilometres and consisted of four scenarios; baseline with local spread probabilities up to 7.5 kilometres, baseline plus local spread probabilities up to 15 kilometres, 25% increase local spread probabilities compared to the baseline and 25% decrease in the local spread probability compared to the baseline. The local spread characteristics in the EI control model by Cogger (2010) were not investigated.

For the vaccination strategies and local spread scenarios, three outcomes were investigated; the duration of the outbreak, the number of infected properties and the number of vaccinated properties. Data were summarised using quartiles, minimums and maximums. Significance was assessed using the Kruskal Wallis analysis of variance comparing the different vaccination strategies or local spread scenarios. Boxplots were created for each outcome.

Suppressive vaccination at a radius of 5 kilometres was the most effective strategy as this strategy had the shortest duration of the outbreak and the fewest infected properties during the

outbreak. Suppressive vaccination at a radius of 3 kilometres resulted in the fewest vaccinated properties. The duration of the outbreak, the number of infected properties, and the number of vaccinated properties all varied significantly by vaccination strategy (P<0.001).

In the sensitivity analysis, the scenario with a 25% reduced local spread had an outbreak with a shorter duration, fewer infected properties and fewer vaccinated properties compared to the other scenarios. There was a significant difference between scenarios and each of the outcome variables (P<0.01). The Baseline plus 15 kilometres scenario had a shorter outbreak duration, greater number of infected and vaccinated properties compared to the Baseline strategy. However the trends identified by of the scenarios included in the sensitivity analysis were consistent.

Description of parameters

Vaccination strategies

Table 1: Vaccination strategies modelled using InterSpread Plus simulation modelling

Strategy	Type	Description	Level
Vaccination[a]			
	Suppressive	Vaccination of all premises with horses in a radius of a known infected property	3 km radius 5 km radius
	Protective	Vaccination of all premises with horses in a band around a known infected property	7 to 10 km band 12 to 15 km band
	Targeted	Vaccination of breeding and training operations within a radius of a known infected property	20 km radius

[a] All vaccination strategies implemented with movement restriction

Sensitivity analysis

Sensitivity analysis on local spread characteristics was run on four different models. The Baseline scenario was the model where suppressive vaccination started at 14 days at a 5 kilometre radius and the local spread characteristics of this model are shown in Table 2. The baseline model was based on the Australian EI outbreak (EI Report, Firestone paper). Descriptions of the four models are found in Table 3.

Table 2: The probability of infection through the Baseline local spread scenario of equine influenza, based on the distance from an infected property and days since property was infected, used in the equine influenza InterSpread Plus model.

Distance from an infected property	Days since property was infected					
	1 and 2	3 and 4	5 and 6	7	8 and 9	10 onward
≤1,000 metres	0	0.0500	0.0400	0.0300	0.0200	0.0001
1,000 metres to 3,000 metres	0	0.0040	0.0030	0.0020	0.0010	0.0001
3,001 meters to 5,000 metres	0	0.0020	0.0010	0.0010	0.0010	0.0001
5,001 metres to 7,500 metres	0	0.0009	0.0004	0.0003	0.0001	0.0001

Table 3: Local spread scenarios modelled using Interspread Plus simulation modelling

Local spread scenario	Description
Baseline	Suppressive vaccination, starting at 14 days at a 5 km radius, local spread up to 7.5 km.
Baseline plus 15 km	Suppressive vaccination, starting at 14 days at a 5 km radius. Plus local spread at 15 kilometres. From days 3 to 7, the probability of local spread was 0.0001. From day 8 until 10, local spread probability decreased to 0.00001
Baseline -25%	Suppressive vaccination, starting at 14 days at a 5 km radius. Local spread up to 7.5 km reduced by 25% of the Baseline model
Baseline +25%	Suppressive vaccination, starting at 14 days at a 5 km radius. Local spread up to 7.5 km increased by 25% of the Baseline model

Results

Duration of the outbreak

Table 4: Descriptive statistics for the duration of an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Vaccination strategy	Distance of application	Duration of outbreak					
		Minimum	25th	Median	75th	Maximum	P value[a]
Suppressive[b]							
	3 km radius	47	76	89	108	179	<0.001
	5 km radius	28	67	75	82	119	
Protective[c]							
	7 to 10 km band	33	75	85	99	157	
	12 to 15 km band	46	81	96	120	179	
Targeted[d]							
	20 km radius	82	114	136	175	180	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Vaccination in a ring around an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[d] Vaccination of all properties involved in the racing industry (training and breeding) in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection

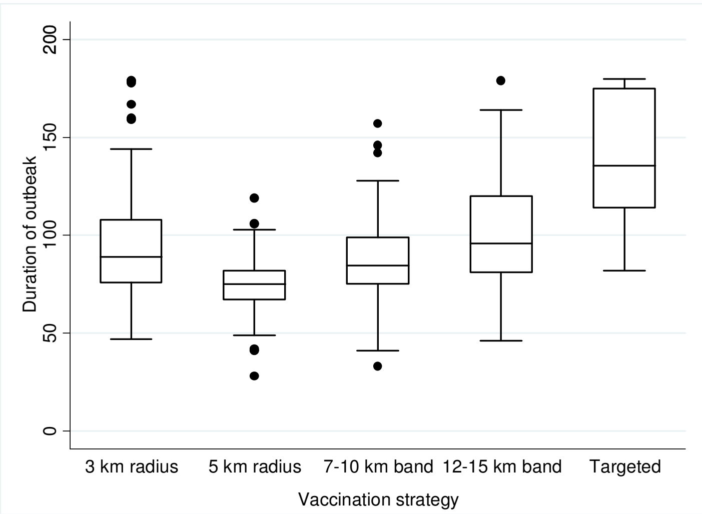

Figure 1: Boxplot for the duration of an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Number of infected properties

Table 5: Descriptive statistics for the number of infected properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Vaccination strategy	Distance of application	Number of infected properties					
		Minimum	25th	Median	75th	Maximum	P value[a]
Suppressive[b]							
	3 km radius	44	350	608	1053	2658	<0.001
	5 km radius	20	267	538	964	2675	
Protective[c]							
	7 to 10 km band	30	367	619	1244	2826	
	12 to 15 km band	134	529	848	1314	2855	
Targeted[d]							
	20 km radius	328	1975	2148	2342	3355	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Vaccination in a ring around an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[d] Vaccination of all properties involved in the racing industry (training and breeding) in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection

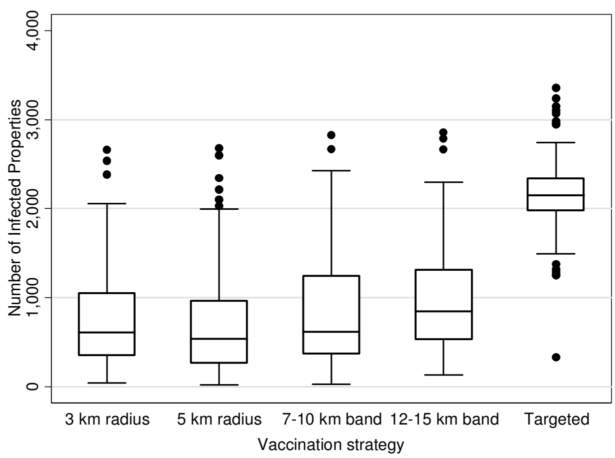

Figure 2: Boxplot for the number of infected properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Number of vaccinated properties

Table 6: Descriptive statistics for the number of vaccinated properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Vaccination strategy	Distance of application	Number of vaccinated properties					P value[a]
		Minimum	25th	Median	75th	Maximum	
Suppressive[b]							
	3 km radius	352	1725	2547	3450	4883	<0.001
	5 km radius	316	1904	3216	4259	5884	
Protective[c]							
	7 to 10 km band	541	2817	3953	5644	7017	
	12 to 15 km band	898	3531	5251	6509	7753	
Targeted[d]							
	20 km radius	785	1493	1653	1715	2006	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Vaccination in a ring around an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[d] Vaccination of all properties involved in the racing industry (training and breeding) in a radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection

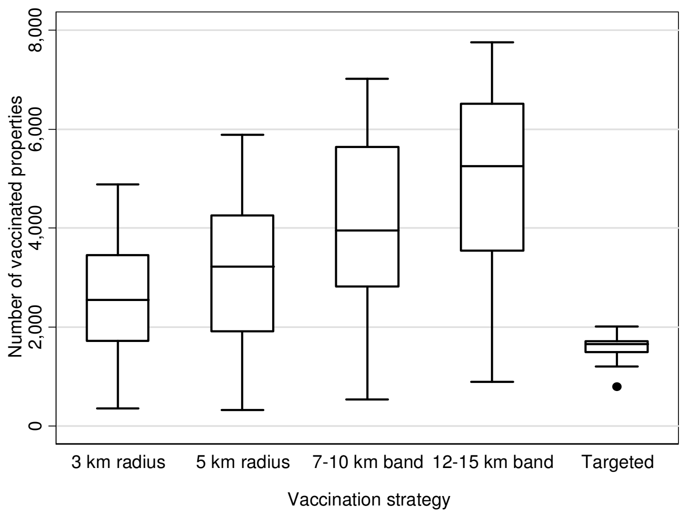

Figure 3: Boxplot for the number of vaccinated properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Sensitivity analysis

Table 7: Descriptive statistics for the duration of an equine influenza outbreak by local spread scenario. Data from an InterSpread Plus model with 90 iterations per scenario and seed property located in the Waikato.

Local spread scenario	Duration of outbreak (days)					
	Minimum	25th	Median	75th	Maximum	P value[a]
Baseline[b]	28	67	75	82	119	<0.01
Baseline + 15km[c]	5	67	74	88	108	
Baseline -25%[d]	1	48	60	69	98	
Baseline +25%[e]	13	73	80	93	168	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a 5km radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Same scenario as the Baseline, but including a local spread parameter at 15 km
[d] Local spread characteristics reduced by 25% compared to the Baseline scenario
[e] Local spread characteristics increased by 25% compared to the Baseline scenario

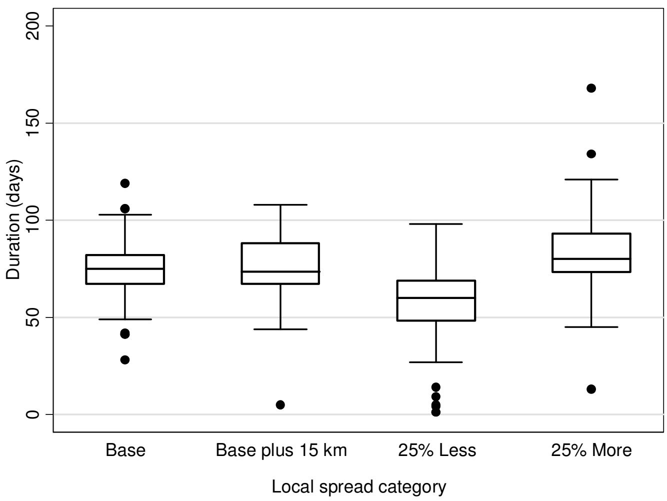

Figure 4: Boxplot for the duration of an equine influenza outbreak by local spread scenario. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Table 8: Descriptive statistics for the number of infected properties in an equine influenza outbreak by local spread scenario. Data from an InterSpread Plus model with 90 iterations per scenario and seed property located in the Waikato.

Local spread scenario	Number of infected properties					
	Minimum	25th	Median	75th	Maximum	P value[a]
Baseline[b]	20	267	538	964	2675	<0.01
Baseline + 15km[c]	2	297	581	1219	2929	
Baseline -25%[d]	1	62	279	600	1593	
Baseline +25%[e]	3	456	823	1372	2970	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a 5km radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Same scenario as the Baseline, but including a local spread parameter at 15 km
[d] Local spread characteristics reduced by 25% compared to the Baseline scenario
[e] Local spread characteristics increased by 25% compared to the Baseline scenario

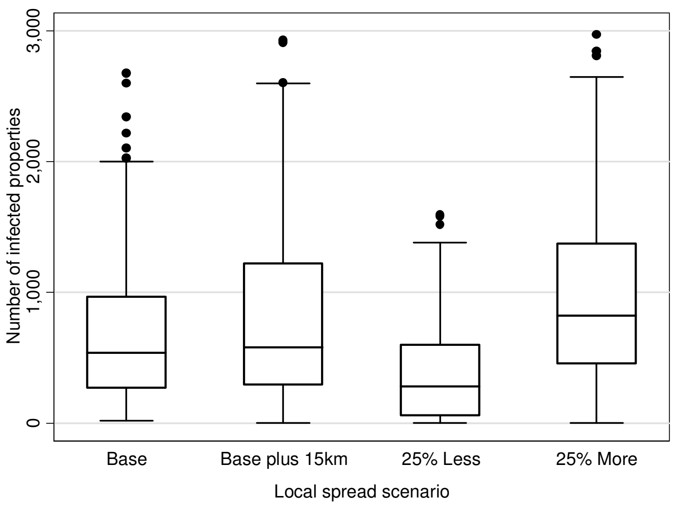

Figure 5: Boxplot for the number of infected properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.

Table 9: Descriptive statistics for the number of vaccinated properties in an equine influenza outbreak by local spread scenario. Data from an InterSpread Plus model with 90 iterations per scenario and seed property located in the Waikato.

Local spread scenario	Number of vaccinated properties					
	Minimum	25th	Median	75th	Maximum	P value[a]
Baseline[b]	316	1904	3216	4259	5884	<0.01
Baseline + 15km[c]	119	2141	3438	4986	6031	
Baseline -25%[d]	281	814	2270	3625	5666	
Baseline +25%[e]	141	2785	3693	4580	5955	

[a] Kruskal-Wallis analysis of variance
[b] Vaccination in a 5km radius of an infected property starting 14 days after official detection, strategy included movement restriction starting on the first day of EI detection
[c] Same scenario as the Baseline, but including a local spread parameter at 15 km
[d] Local spread characteristics reduced by 25% compared to the Baseline scenario
[e] Local spread characteristics increased by 25% compared to the Baseline scenario

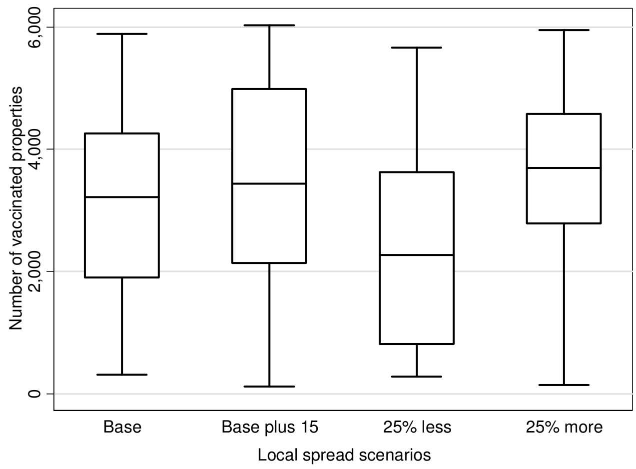

Figure 6: Boxplot for the number of vaccinated properties in an equine influenza outbreak by control strategy. Data from an InterSpread Plus model with 90 iterations per control strategy and seed property located in the Waikato.