

# The equine influenza epidemic in Australia: Spatial and temporal descriptive analyses of a large propagating epidemic

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## ABSTRACT

Australia experienced a large outbreak of equine influenza in August 2007. Nearly 10 000 premises were infected during the epidemic. We used spatial and temporal analytical techniques to describe the epidemic, to quantify important descriptors of the epidemic, and to generate hypotheses about how the epidemic progressed and which control tools assisted in eradication. Spatio-temporal epidemic curves revealed three phases in the epidemic: dispersal, local spread and disease fade out. Spatial dispersal of infection rapidly declined immediately after national movement restrictions were introduced. The epidemic peak had passed before emergency vaccination could have induced substantial immunity in the equine population. Thirty seven clusters of epidemiologically linked premises were delineated using an interpolated surface of date of onset of clinical signs, geographic data and location of infected premises. These clusters were analysed individually to parameterise key epidemic measures: cumulative incidence, incidence rate, effective reproduction rate, nearest neighbour spread distances, epidemic length and the number of infected premises. These measures were summarised by landscape (rural versus peri-urban location) and standardised by disease management zone. Compared to rural areas, peri-urban areas appeared to have a higher density of equine premises (4.66 premises km<sup>-2</sup> versus 0.80 premises km<sup>-2</sup>), longer epidemics (95 days versus 87 days), more infected premises (393 versus 339) and a shorter spread distance (1.27 km versus 2.38 km). However, effective reproduction rates (2.04 versus 1.99), cumulative incidence (27.4 versus 26.9) and incidence rates (1.36 versus 1.54) were similar. The relative impact of vaccination and national movement restrictions in controlling this epidemic needs further investigation.

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## 1. Introduction

Equine influenza (EI) is caused by an influenza A virus (family *Orthomyxoviridae*). Infection of equidae is characterised by respiratory disease (Myers and Wilson, 2006). EI is distributed across most of the world and only eight OIE member countries that conduct surveillance for EI have never reported EI (OIE, 2008a). In August 2007 Australia – which had been previously free of EI –

experienced a large outbreak that was associated with imported horses (Callinan, 2008). Despite a rapid and effective eradication campaign that limited the spread of the infection to just two eastern states (New South Wales [NSW] and Queensland [Qld]), nearly 10 000 premises were infected during the epidemic. Following the last EI case in December 2007, extensive surveillance programs were unable to detect the virus in the Australian equine population, confirming the successful eradication of EI. Australia regained its EI free status in December 2008, after declaring it had met OIE guidelines for freedom from EI (OIE, 2008b; Cowled et al., 2008, unpublished report).

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The program to eradicate EI was a coordinated national response involving cooperation between Commonwealth (national) and State governments and industry. There were many facets to the control program including:

1. Movement restrictions which were initially applied nationally and aimed to prevent further dispersion of EI by equine movements or congregations at events. After the initial national movement standstill, infected states implemented restricted and controlled zones to assist management of equid movements. This system was modified later to allow a more flexible risk-based zoning approach (see below).
2. Public awareness and communication.
3. A risk-based zoning system was implemented based on the risk that EI was present in an area. A restricted area (or red zone) was an infected area where equid movements were prohibited. A special restricted area (or purple zone) was a defined part of an infected area with high horse densities and where active spread of infection was considered inevitable. This zone allowed equid movements within the zone but not outside the zone. A control area (amber zone) was an area of low risk of infection adjacent to an infected area where enhanced surveillance and movement restrictions were also imposed. A protected area (green zone and white zone) was an area assessed to be free from EI.
4. Laboratory testing for eradication and proof of freedom was extensive with more than 100 000 laboratory tests conducted.
5. Disease tracing and surveillance.
6. Enhanced biosecurity to prevent long range movement of the virus and reduce local spread.
7. Emergency vaccination of approximately 136 000 horses, most of which were in NSW or Qld.

These measures contained and ultimately eradicated the epidemic, but it is important to determine which control tools were the most useful.

Post-outbreak analysis of epidemics is necessary to understand how diseases spread, thus leading to improved contingency plans for managing future outbreaks. In particular, analysis of data from the Australian EI epidemic offers a rare opportunity to explore the spread of a highly contagious disease in a fully susceptible population. Such an analysis may also provide insights for managing important outbreaks of other highly contagious emergency diseases.

Analysis of infectious disease data may be relatively straightforward in circumstances where the epidemic is confined to a small, well-described susceptible population and the causative organism is known. In these cases, knowledge of the susceptible population, infected individuals and epidemiological tracing data allows disease spread mechanisms to be rapidly identified and control measures to be quickly implemented. However, in the event of an extensive epidemic, such as the EI epidemic in Australia, where many thousands of premises were rapidly infected across large areas of a country, comprehensive data is rarely available in a timely fashion. In this situation, resources for tracing and epidemiological investigations

can be rapidly overwhelmed and only limited data may be available. However, available data will usually include locations of infected premises (IP) or animals (spatial data, with varying accuracy) and the date that clinical signs of disease began or were reported (temporal data).

A substantial amount of research has been conducted on methods of analysing spatial and temporal disease data (Ward and Carpenter, 2000; Kulldorff and Nagarwalla, 1995; Thulke et al., 2005; Stevenson et al., 2008; Ward et al., 2008; Farnsworth and Ward, 2009). Spatial and temporal analysis can be used to describe epidemics, can assist in generating hypotheses about disease causation and can be used to investigate relevant control techniques (Ward and Carpenter, 2000). For example, a recent outbreak of highly pathogenic avian influenza was described with various geostatistical methods to generate important disease dispersal hypotheses, for example that initial introduction was by water birds and subsequent spread was by the movement of domestic poultry (Ward et al., 2008; Farnsworth and Ward, 2009).

The objective of this study was to analyse data from the Australian EI epidemic using a range of spatial and temporal methods to:

1. describe spatial and temporal trends;
2. quantify important epidemic descriptors; and
3. generate hypotheses about disease spread and the effect of major control tools.

## 2. Methods

### 2.1. General approach

This study first focused on describing the epidemic spatially and temporally. Based on common spatial and time characteristics, we divided epidemiologically linked IPs into clusters of diseased premises. We then analysed these individual clusters to estimate key epidemiological parameters. Finally, clusters were pooled, based on commonality of region and standardised for different management zone, to provide summary statistics.

### 2.2. Data

There were three datasets used in this analysis: a dataset of IPs, a dataset of vaccinated premises and a dataset of the horse population at risk. These datasets were created from data supplied by the NSW and Qld governments. The dataset of IPs was based on IPs in the NSW and Qld government emergency animal disease recording systems in March 2008, several months after the epidemic had finished. During the response, premises were recorded as infected if they had clinical evidence of infection and laboratory testing confirmed disease. Additionally, during the peak of the epidemic when veterinary resources were limited, a premises could be classified as infected if it was in close proximity to a known premises that was infected or had appropriate risk factors (such as known contact with an IP) and clinical signs consistent with EI. During this study, additional IPs were identified from interpretation of suspect premises lists and historical laboratory results. For

example, premises with positive serology results demonstrating a prior history of infection, but that had never been declared an IP, and no history of having moved equids during the epidemic (under a permit application process) were added to the official list of IPs.

There were 9609 IPs recorded in the dataset, 6313 from NSW and 3296 from Qld. Each IP had an outbreak location ( $x$  and  $y$  coordinates representing the property centroid) and in 95% of cases, an estimated date of onset of clinical signs. Estimated dates of onset of clinical signs were generally obtained through histories provided via owner interviews or veterinary clinical observations (together 80% of cases). For records without this information, dates of onset of clinical signs were estimated by subtracting 1 day from the date that an IP was declared (15% of cases), assuming that a 1 day lag time existed between the start of clinical signs on a premises and declaration of an IP (Evan Sergeant Pers. Com., September 2007, Nina Kung Pers. Com., January 2009). The remaining 5% of IPs had no date associated with their record. Vaccination datasets from NSW and Qld were organised to represent the number of premises vaccinated by day of the epidemic in both NSW and Qld. Vaccination data from Qld only extended until 17 November 2007, although vaccination continued after this time.

The third dataset contained locations and equid numbers for equine premises in NSW and Qld. Before the 2007 outbreak, a useable dataset on the distribution and density of horses did not exist in Australia. However, detailed information was required to manage the EI response and both NSW and Qld disease control centres compiled databases of equine premises during the epidemic. Sources for the databases included: records from routine state veterinary service based population surveys (collected before the epidemic), industry databases, all equine premises recorded in the emergency animal disease recording systems, entries from an online registration system, information from emergency vaccination databases and, various ad hoc sources such as telephone directories or information gathered via the permit process for equid movements during the epidemic. Both the population and IP datasets were cleaned to remove many duplicates, wrongly geocoded locations and typographical errors. Other geographic data was sourced from the Topo 250K data set (Geoscience Australia, 2006).

### 2.3. Software and programming

Data manipulation and analyses were conducted within the MapInfo®, MapBasic® and VerticalMapper® software environments (available from Pitney Bowes Mapinfo, <http://www.mapinfo.com/products/applications/mapping-and-analytical-applications>). These software environments together represent a sophisticated and customisable geographical information system (GIS). Specifically, VerticalMapper® and MapInfo® were used to interpolate and visualise data to delineate clusters. Purpose built applications were written in MapBasic® code and implemented in MapInfo® to analyse cluster data. In all analyses, the Albers Australian conic (AGD84) projection option in MapInfo was used.

### 2.4. Spatial and temporal overview of the epidemic

An epidemic curve was created by plotting the number of premises on which equids first displayed clinical signs for each day of the epidemic on the  $Y$  axis, and day of the epidemic on the  $X$  axis. The day clinical signs were first reported was used, rather than the date of confirmation of diagnosis to avoid reporting bias (Gibbens and Wilesmith, 2002). The change in the size of the infected area over time was also calculated. The area infected was estimated by creating a minimum convex hull (MCH) that encompassed all infected premises for every 2 days of the epidemic. A MCH is a convex polygon which encompasses a collection of point locations (Mapinfo Corporation, 2006). The increase in the infected area from one 2-day time period to the next was calculated by subtracting the MCH area from the preceding MCH area. Negative values were recorded as zero (i.e. no increase). The epidemic curve was divided into three phases, based on a visual inspection of the epidemic curve and the MCH series. Descriptive statistics were estimated for each phase.

Separate epidemic curves for both NSW and Qld were also generated. These curves included polygons that represented the earliest estimated date that equines vaccinated on premises during the emergency vaccination program may have developed immunity. That is, the polygon recorded the number of premises on which equines were vaccinated each day of the epidemic, but the polygon was shifted forward 14 days to represent the delay from vaccination date to early immunity. Fourteen days was chosen to offset vaccination day, since limited research has confirmed that the level of antibodies rise markedly in vaccinated naïve horses 14 days after the first vaccination (Minke et al., 2007). Additionally, horses challenged 2 weeks after a single vaccination had markedly reduced clinical signs of EI with no detectable virus excretion (Toulemonde et al., 2005). The representation of epidemic curves against vaccine-induced immunity assisted examination of the temporal relationship between the epidemic curve and the effect of emergency vaccination.

An epidemic curve was also generated using clusters as the epidemiological unit of interest. This histogram recorded the number of new clusters arising over time. Specifically, the date that the equids on the first IP in a cluster began showing clinical signs was recorded as the start date for a cluster. The number of clusters in which equids displayed clinical signs each day was plotted against a time axis in a similar fashion to the premises level epidemic curve.

The mean centre (Ward and Carpenter, 2000) of the epidemic was calculated by day and plotted over the epidemic region by epidemic phase. Simply, each day, the mean centre was calculated as the mean  $x$  coordinate and the mean  $y$  coordinate of all IPs.

### 2.5. Identifying epidemic clusters

Interpolation using kriging (Ward et al., 2008), and in some circumstances the identification of potential geographic barriers/aids to the spread of disease, were used to delineate clusters of epidemiologically linked premises.

Firstly, semivariogram analysis was conducted to parameterise the kriging model. A semivariogram is a plot of the semivariance (inverse autocorrelation) of all pairs of locations at a series of defined distances, the lag distance (Ward et al., 2008). The semivariance expresses the degree of relationship (for example, epidemic day or disease prevalence) between points on a surface (Northwood Technologies Inc., 2001). A semivariogram of the number of days between first diagnosis of the epidemic outside quarantine (24 August 2007) and the onset of clinical signs at a premises was generated. Simply, several lag distances and a number of lags were used and several statistical models were investigated to identify an optimal semivariogram for modelling (Ward et al., 2008). Parameters were estimated from this semivariogram and used as input for interpolation using kriging. The resulting interpolated surface was then displayed as a continuous, graduated colour surface of outbreak day across the region of the epidemic, with infected premises, and in some circumstances geographic features, overlaid in the GIS. In this manner, common colours in a region indicated commonality in the date that clinical signs were first reported by premises in that region, and could be interpreted as a disease cluster with potentially a common source.

Next, several steps were used to divide the complete set of IPs into clusters of epidemiologically linked IPs. IPs that were further apart than the range (a parameter from semivariogram analysis which identifies the distance beyond which the value of some attribute at points are spatially independent), with no intervening IPs, were considered not to belong to the same cluster. Groups of

IPs that overlaid a common colour region or a logical progression of colours formed spatio-temporal clusters of disease. Logical patterns of colour at a cluster most commonly comprised a progression of colour outwards from an outbreak start site (for example like a “bullseye”), representing the spread of the local epidemic across the landscape over time. Where the interpolated surface was insufficient to delineate a disease cluster (for example where an apparently illogical progression of colour [i.e. outbreak dates] occurred within a potential cluster), further examination of geographic data representing potential barriers to the spread of disease (areas of low horse density, such as national parks, mountainous regions and urban regions) and potential aids to the spread of disease (peri-urban areas, rural land use areas or roads) were overlaid on the outbreak map within the GIS. These then helped to divide or combine IPs into one or more clusters, or contributed to a decision to leave an IP as an isolated IP, not part of a cluster.

#### 2.6. Parameters calculated by cluster

Parameter estimates were calculated for individual clusters. Table 1 lists the descriptive parameters quantified for each cluster and the method of calculation.

#### 2.7. Parameter estimates for clusters pooled by common region and management zones

During the epidemic, EI occurred in two distinct landscapes: (1) peri-urban regions close to major popula-

**Table 1**

Descriptive parameters quantified for each cluster of disease during a spatial and temporal descriptive analyses of the equine influenza epidemic in Australia (August 2007).

Parameter	Method of calculation
Cumulative incidence	The proportion of the total premises at risk that became IPs. A MCH was created around all IPs in a cluster at the conclusion of the epidemic. The population at risk was determined by selecting all premises within the MCH. The proportion of all premises infected was reported for the entire epidemic as cumulative incidence. 95% confidence intervals for cumulative incidence calculated based on the normal approximation to the binomial distribution (Thrusfield, 2005).
Epidemic length	Last estimated date of onset of clinical signs—the first date of onset of clinical signs (days).
Effective reproduction rate ( $R_T$ )	The number of secondary cases produced in a host population not consisting entirely of susceptible individuals (Anderson and May, 1992). The mean of the number of premises each IP transmitted infection to was calculated for each cluster, using a nearest neighbour method (Ward et al., 2009). For each new IP, potential source premises were identified within the cluster by searching for premises that were infectious 2 days before clinical signs were displayed by the IP. All IP were considered infectious for 10 days. Time assumptions were based on a 2 day incubation period and a 7–10 day infectious period with these estimates derived from within published ranges (AVMA, 2006). 95% confidence intervals calculated as for means = mean $\pm$ t (estimated standard error of the mean) (Thrusfield, 2005).
Geographic centre of cluster	The geographic centre of the cluster was calculated as the mean of both the x and y coordinates (Ward and Carpenter, 2000).
Incidence rate (per animal year at risk)	(Number of IPs/((population at risk – 1/2 number of IPs) $\times$ epidemic length)) $\times$ 365 (Dohoo et al., 2003). 95% confidence intervals for incidence rates for clusters of >100 premises were calculated with a Poisson distribution based method which accounts for the complex nature of the denominator, after Thrusfield (2005). For clusters of <100 premises, tabulated confidence intervals of Altman et al. (2000), quoted in Thrusfield (2005) were used.
Premises density	The total number of premises within the MCH was divided by the total area of the MCH.
Spread distance	Estimated spread distance was calculated with nearest neighbour methods (see above for $R_T$ ). The Euclidean distance between newly infected premises and the infecting premises was calculated and the mean of all such distances calculated for each cluster. 95% confidence intervals calculated as for means = mean $\pm$ t (estimated standard error of the mean) (Thrusfield, 2005).

tion centres and (2) surrounding towns in rural areas. A peri-urban area was classified as a zone within 20 km of the boundary of a metropolitan city (population > 50 000). A cluster was classified as peri-urban if any of its IPs fell within a peri-urban area. Rural clusters were all other clusters that did not fit this criterion.

The EI epidemic was managed in two distinct ways within portions of both the peri-urban and rural landscapes, designated as either a “red zone” or as a “purple zone” (see Section 1). Red zones were generally in lower density horse populations in NSW, but included all infected areas in Qld (including high density horse areas). The purple zone was declared in infected areas of NSW with generally high horse densities. It is unlikely that parameters estimated without adjusting for the control zones would be valid. The zones are displayed in Fig. 1.

Summary adjusted parameters for both peri-urban and rural clusters were generated via the following steps:

1. Parameters were estimated for each cluster identified (see Table 1).
2. Clusters were categorised into one of four pools (red zone rural, red zone peri-urban, purple zone rural and purple zone peri-urban).
3. Mean cluster parameters for each pool were calculated to produce an overall crude parameter estimate for each of the pools.

4. Four pools were combined to two pools using direct adjustment (Thrusfield, 2005) to summarise parameters for the two regions (peri-urban versus rural). That is, the rural red zone and rural purple zone were combined to produce rural parameter estimates and the peri-urban red zone and peri-urban purple zone were combined to produce peri-urban parameter estimates. Direct adjustment was used to combine pools to reduce the possible confounding effect of differences in zone management or other characteristics and allow a valid comparison between rural and peri-urban regions. The standard population was the total population of the four pools. The specific values in each pool were weighted by the frequency of the parameter in the standard population.

### 3. Results

#### 3.1. Spatial and temporal overview

The epidemic was assumed to begin with the first reported clinical signs of EI at the Eastern Creek Quarantine station (17 August 2007) and was assumed to end 130 days later with the first reported clinical signs on the last premises in Queensland reported to be infected (25 December 2007). The epidemic curve (Fig. 2) peaked on 1 October 2007 (276 IPs).

The spatio-temporal epidemic curve can be divided into three phases, which we refer to as dispersal, local spread

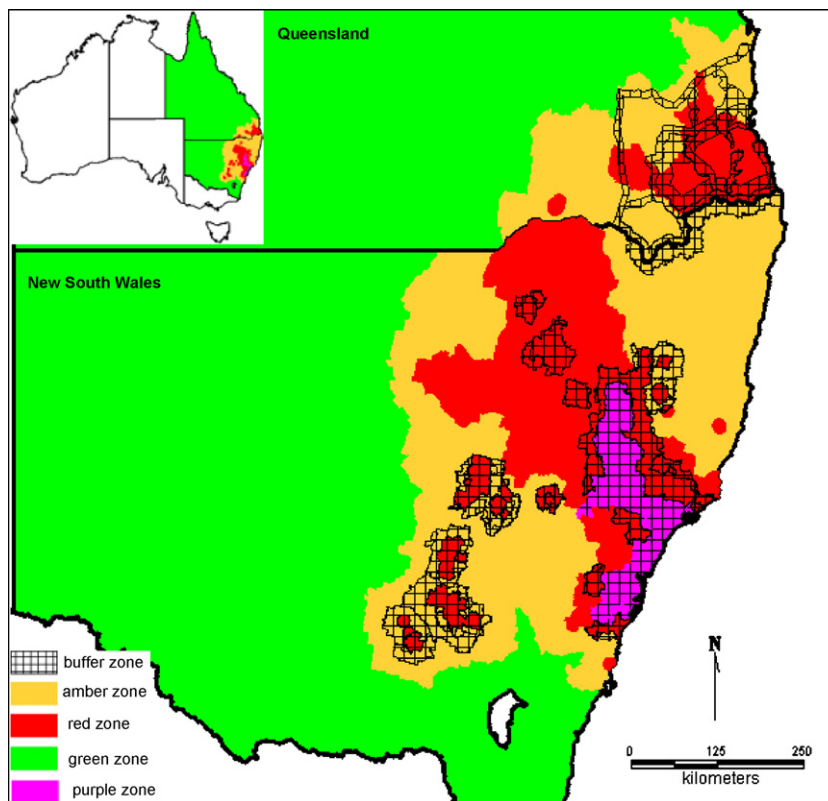


Fig. 1. The peak area of infection during the Australian equine influenza epidemic. There were green, amber, red and purple zones declared during the Australian EI epidemic. The red and purple zones were structured to contain all infected premises in Australia. The hatched zones represent buffer zones where vaccination frequently occurred.

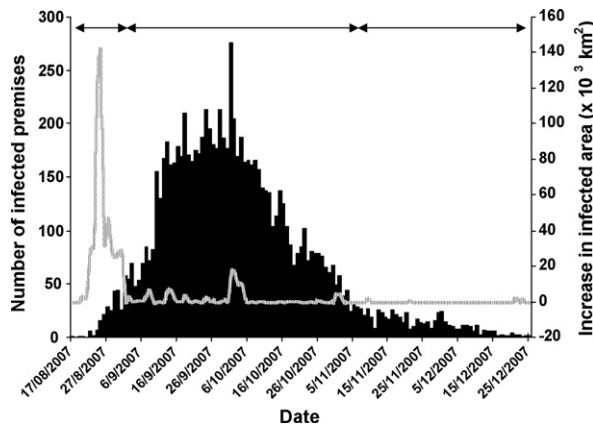


Fig. 2. The spatio-temporal epidemic curve for the Australian equine influenza epidemic. The vertical columns represent the number of new infections by estimated first clinical signs each day, whilst the polygon represents the increase in the total area of infected land every 2 days. Each phase of the epidemic is represented by an arrow (with arrows from left to right indicating dispersal, local spread and epidemic fade-out phases).

and epidemic fade-out phases. These phases are summarised in Table 2. The dispersal phase extended from the start of the epidemic until the initial spatial spread of infection ended, as indicated by the flattening of the spatial polygon (Fig. 2). This phase was characterised by relatively few new IPs, but a very large expansion in the area of land infected, largely associated with movement of infected horses before implementation of the response program. The local spread phase extended from the end of the dispersal phase until the completion of the descending part of the epidemic curve. This phase was characterised by a large increase in the number of new IPs, with little increase in the area of infected land. The epidemic fade-out phase included that part of the epidemic curve representing decrease and secondary peaks. It was characterised by low numbers of new cases at a gradually declining incidence rate.

The NSW and Qld epidemic curves had both peaked before substantial vaccine-induced immunity could have developed in equines vaccinated on the earliest premises to be vaccinated. See Fig. 3.

The mean centre of the epidemic was found within NSW each day of the epidemic. In the dissemination phase,

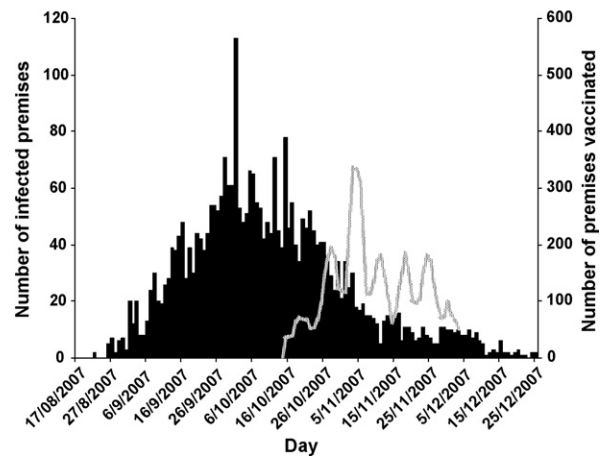
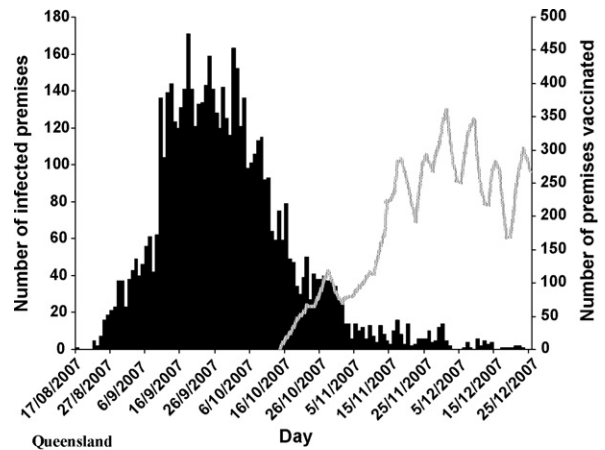


Fig. 3. Epidemic curves and vaccine-induced immunity for the equine influenza epidemic in New South Wales and Queensland, Australia. The vertical columns represent new infections by day of the epidemic. The polygon represents the daily tally of premises vaccinated during the emergency vaccination program, shifted forward 2 weeks to represent the delay between vaccination and early immune response. Note: Queensland vaccination data was only available till November 17, 2007.

the mean centre shifted radically and without apparent pattern across several hundred kilometres. However, during the local spread phase, and in the fade-out phase the mean centre moved systematically (i.e. mean centres

Table 2

The three phases of the Australian equine influenza epidemic (August 2007) as characterised by the spatio-temporal epidemic curve during a spatial and temporal descriptive analyses.

Epidemic phase	Date range	Increase in infected premises during phase (%) <sup>a</sup>	Increase in infected area during epidemic phase (%) <sup>b</sup>	Epidemiological characteristics
Dispersal	17/8/07–1/9/07	2.5	83%	Spatial dispersal of incubating cases with relatively few infected premises.
Local spread	2/9/07–11/11/07	91.5	16.9%	Local spread within infected regions with little spatial dispersal.
Epidemic fade out	12/11/07–25/12/07	6	0.1%	Declining new infections, some continuing spread to local susceptible populations.

<sup>a</sup> Total infected premises numbered 9609, of which 9086 had an estimated time of first clinical signs and are included on the epidemic curve and in analyses for this table.

<sup>b</sup> Total area infected was 291 490 km<sup>2</sup> as calculated with a minimum convex hull.

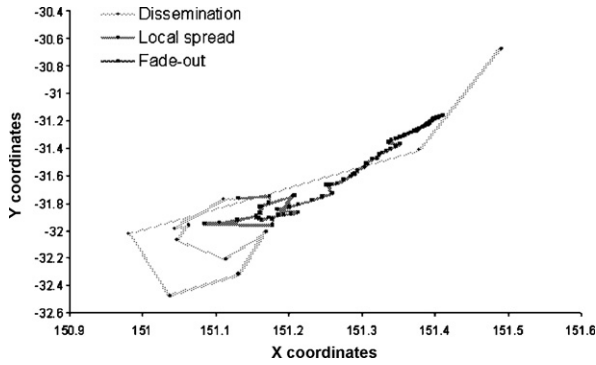


Fig. 4. The change in location of the epidemic mean centre during the Australian equine influenza epidemic.

produced a smooth line over time), in a north easterly direction towards Qld (see Fig. 4).

3.2. Cluster identification

We used a quadratic semivariogram model to approximate the empirical semivariogram in order to inform kriging. The quadratic model used 14 lags and a lag size of 40 km (with the sill suggesting a range of approximately 225 km). That is, beyond approximately 225 km, the onset

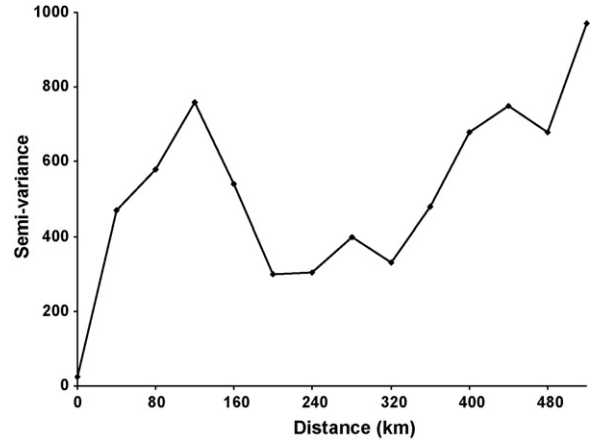


Fig. 5. Empirical semivariogram of the day of onset of clinical signs of equine influenza in the Australian epidemic in 2007.

day of clinical signs on IPs was apparently independent. Fig. 5 represents the empirical semivariogram. The interpolated map of onset day revealed a large number of premises that were infected early during the epidemic but apparently did not result in a local cluster. These can be seen in Fig. 6 as premises located in blue regions with no

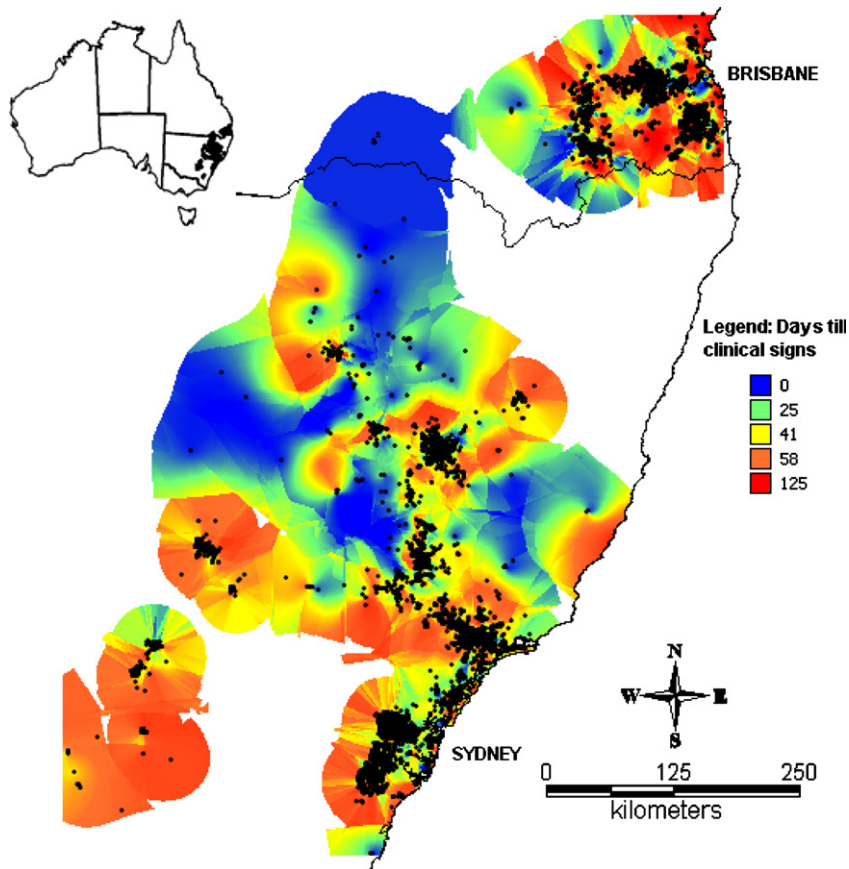


Fig. 6. Outbreak map of day of infection and spatial location of infected premises. Blue regions are areas containing a premises infected early in the epidemic. Red regions contain premises infected later in the outbreak. Black circles represent infected premises.

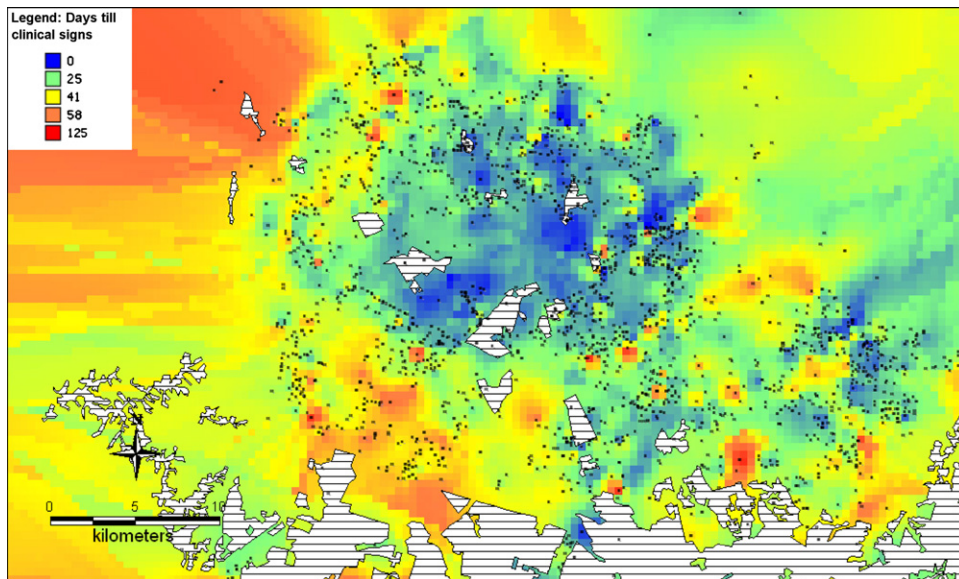


Fig. 7. A cluster in the Sydney region identified through a logical progression of infection date outwards from the centre of the cluster. The black dots represent infected premises. The cluster is bounded on the south and east by the Sydney peri-urban areas as shown by white/lined polygons.

complex colour arrangement surrounding them and few IPs; these were generally in rural areas. However, the interpolated surface also revealed the converse, with groups of premises surrounded by complex colour patterns (indicating a diversity of infection dates). Examination of these localities at a finer scale indicated that many distinct clusters are present (Fig. 7). Fig. 7 shows a typical progression of colour (or time) across a cluster, demonstrating early infection in the centre of the cluster, and later infection dates as the cluster expanded from that location.

The interpolated map and geographic layers assisted in the identification of 20 disease clusters in NSW and 17 clusters in Qld. These clusters contained 97% of all IPs that had a recorded date of first clinical signs. The remaining IPs with a recorded date of first clinical signs did not fit into any of these clusters. Fig. 8 shows the number of new

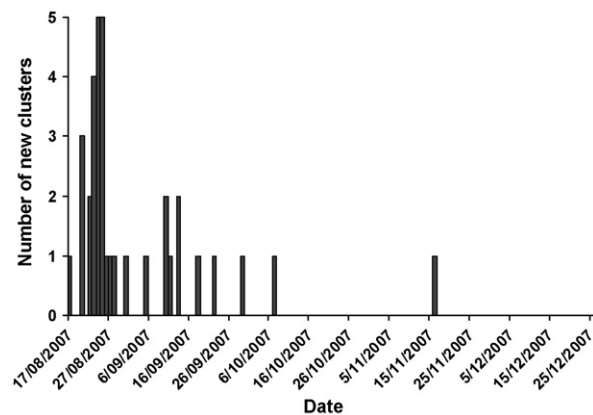


Fig. 8. A cluster epidemic curve. The histogram plots the number of clusters over time and demonstrates that most clusters appeared in the early dispersal phase of the epidemic.

clusters appearing over time; most clusters appeared during the initial dissemination phase of the epidemic.

### 3.3. Parameter estimates

Estimates of parameters for each cluster varied greatly for some parameter types, but were relatively uniform for others. For example, the numbers of IPs ranged from 3 to 1902, and the epidemic lasted from 37 to 124 days in different clusters. Densities of equine premises at cluster locations ranged from 0.35 to 5.23 equine premises  $\text{km}^{-2}$ . Incidence rates ranged from 0.39 to 6.61 cases per animal year, and cumulative risk ranged from 6 to 47%. Spread distances ranged from 0.57 to 15.57 km. However, estimates of the effective reproduction rate ( $R_T$ ) were relatively constant and were approximately 2 for most clusters. Parameter estimates for individual clusters are listed in Appendix 1. Summary parameter estimates for the four types of clusters pooled by management zone and geographic region type are listed in Table 3. Parameter estimates for rural versus peri-urban locations, standardised for disease control zones are listed in Table 4. Standardised peri-urban cluster parameters demonstrated that equine populations in peri-urban regions were denser and more numerous than in rural areas. These peri-urban equine populations underwent longer, more extensive epidemics with shorter spread distances of disease.

## 4. Discussion

This descriptive analysis indicates that the EI epidemic in Australia in 2007 consisted of three key phases. The first phase (dispersal) was characterised by substantial spatial dispersal of relatively few infected horses. Indeed, 81% of the total infected area was determined by less than 300 IPs (3% of the final IP tally) in the several days immediately

**Table 3**

Parameter estimates for four pools differentiated on location (peri-urban and rural) and management (red or purple zone) during a spatial and temporal descriptive analyses of the equine influenza epidemic in Australia (August 2007).

Zone and management category	Premises density (premises/km <sup>2</sup> )	R <sub>T</sub>	Epidemic length (days)	Number of infected premises	Incidence rate (cases per horse year)	Cumulative incidence (%)	Spread distance (km)
Rural purple zone	0.39	2.05	99	496	1.09	25.5	2.11
Peri-urban purple zone	5.96	2.09	91	432	1.40	25.3	1.40
Rural red zone	1.48	1.91	67	79	2.30	28.5	2.82
Peri-urban red zone	2.5	1.96	101	328	1.29	29.9	1.05

before the first diagnosis of EI in Australia. Many of these introductions resulted in the seeding of infection within local horse populations through horse movements that later led to the development of substantial clusters of disease. Much of the spread in this period has been attributed to several horse events held immediately before EI was confirmed (ESG, 2009). However, spatial dispersal rapidly decreased and had largely ceased by 1 September 2007. The principal control measures implemented within the eradication program to this stage was a national equine standstill (implemented 25 August 2007). This suggests that one of the key steps in controlling the epidemic was the movement standstill, which prevented further dispersal of horses incubating infection. Thus, many large populations of equines in Australia, such as in the nearby state of Victoria, never became infected with EI virus. This highlights the critical importance of immediate movement restrictions of susceptible species during emergency eradication campaigns for highly contagious transboundary diseases.

The second phase of the epidemic (local spread) was characterised by limited spatial dispersal of infection, but a very large increase in the number of infected premises. Simply, whilst movement restrictions largely prevented the dispersal of infection to new areas, localised infection of susceptible equine premises in already infected areas continued. 'Local spread' could have involved many transmission mechanisms and has been discussed by Davis et al. (2009). However, despite the success of the movement controls at reducing large scale spatial dissemination (or expansion of the infected area as measured with a MCH), it is important to note that some new clusters of disease developed in susceptible populations *within* the infected area through local biosecurity breakdowns (for example resulting in fomite spread) during the local spread phase.

It was during this second phase of the epidemic that emergency vaccination was introduced as a control tool. The vaccine used was a canary pox vectored recombinant vaccine for EI expressing the hemagglutinin genes for influenza H3N8 strains (A/eq/Kentucky/94 and A/eq/New-

market/2/93) (ProteqFlu; Merial Australia Pty Ltd.). Vaccine strategies varied between regions during the epidemic, but largely concentrated on establishing buffers of vaccinated equines around disease clusters in NSW and extensive buffers of vaccinated equines at some distance from the nearest IP in Qld. Additionally, blanket vaccination in some infected regions and vaccination to protect high socio-economic value horses was practiced in both NSW and Qld (with some high socio-economic value horses vaccinated in other Australian states). Vaccination began on 29 September 2007, but the first round of vaccinations (i.e. the first vaccination in the immunisation course) was not substantially complete until 15 November 2007. Assuming that immunity had begun to develop 2 weeks following the first vaccination or injection (Toulemonde et al., 2005; Minke et al., 2007), the earliest date that immunity may have begun to develop in vaccinated horse populations was 13 October to 29 November 2007 (2 weeks after the first round of vaccination was conducted). Whilst individual variability in the development of immunity is likely, a conservative point estimate of time to earliest immunity was used to ensure simplicity in this broad level descriptive analysis.

The role that vaccination played in the containment and eradication of EI in Australia is unclear. However, an examination of the temporal overlap of earliest immunity following vaccination, in relation to the individual epidemic curves for NSW and Qld suggests that the peak of the epidemic had already been reached before substantial immunity from vaccination could have developed. That is, the epidemic had peaked (18 September 2007 in NSW and 1 October 2007 in Qld) and was in decline before vaccine-induced immunity could have begun to develop in the earliest premises to be vaccinated (13 October 2007). However, any inferences could only be tentative because group and individual characteristics are not necessarily the same and ecological fallacy is possible (Selvin, 1958; Thrusfield, 2005). Further research has occurred in this area, specifically examining the likely effect of earlier vaccination on the epidemic (Garner Pers. Com., August 2009) and has been submitted for publication.

**Table 4**

Parameter estimates for rural and peri-urban landscapes during a spatial and temporal descriptive analyses of the equine influenza epidemic in Australia (August 2007). Estimates were directly standardised by contribution of red zone and purple zone infected premises in the total infected premises population.

Zone category	Premises density (premises/km <sup>2</sup> )	R <sub>T</sub>	Epidemic length (days)	Number of infected premises	Incidence rate	Cumulative incidence (%)	Spread distance (km)
Rural	0.80	1.99	87	339	1.54	26.9	2.38
Peri-urban	4.66	2.04	95	393	1.36	27.4	1.27

The epidemic mean centre remained in NSW for the entire epidemic. This was partly due to the total numbers of IP being greater in NSW, but partly because premises in Qld were limited to the southern portion of the state. However, the pattern of change in mean centres during the epidemic indicates the relative influence of various infected equine populations over time. During the initial dissemination phase, the mean centre of the epidemic fluctuated widely across NSW. This indicated that the addition of relatively few IPs each day during the dissemination phase of the epidemic strongly influenced the mean centre. As the epidemic progressed into the local spread phase and heavy concentrations of horses became infected in the NSW purple zone, the mean centre focused within the Hunter Valley region of NSW. Later as the local spread phase continued and as the fade-out phase began, the mean centre shifted north and east towards the Southern Qld region, indicating the continuing nature of the epidemic around south east Qld relative to the rapidly fading epidemic in NSW.

This descriptive analysis also aimed to summarise data and estimate parameters that might be useful for future modelling studies. Epidemiological tracing of horses in the early phase of the epidemic from two key known horse events (at Maitland and Narrabri) before the control program began revealed that up to 61 and 37 premises respectively may have become infected from horses moved from these two locations (ESG, 2009, unpublished report). Based on these data this would suggest a very high premises level basic reproductive rate ( $R_0$ ) in the early phases of the epidemic due to super-spreading events (Lloyd-Smith et al., 2005). However, we estimated much lower premises level effective reproduction rates ( $R_T$ ) for clusters over the course of the epidemic.  $R_T$  is much lower than  $R_0$  because of the effect of increasing immunity throughout an epidemic and control measures (Anderson and May, 1992).  $R_T$  estimates varied between 1.99 and 2.4 for rural and peri-urban regions. Thus, we estimated that on average each IP infected two other premises during the epidemic. By examining the confidence intervals around individual clusters (Appendix 1) it is obvious that there was little variation around these estimates, indicating that super-spreading events (Lloyd-Smith et al., 2005) were overall rare throughout the epidemic. In other words, once the control program had been implemented, there were few instances of an IP infecting large numbers of other premises. The apparent lack of large scale spread from individual premises following the initiation of the national control program indicates that the measures put in place (including movement restrictions, disinfection and biosecurity precautions) were highly effective in reducing the spread of infection.

Spread distances estimated in this descriptive analysis can inform contingency plans for future epidemics of equine disease in Australia. During the epidemic (and in current contingency plans for EI; AHA, 2007) restricted areas were declared around infected premises to reduce the risk of spread of EI. Restricted areas were structured to establish a buffer of at least a 10 km from an IP to surrounding non-infected areas. Our analysis indicates that 95% of spread distances were less than 10 km in all but

one cluster, Barmedman. Long distance spread at Barmedman was largely associated with the movement of harness racing horses before the local epidemic was diagnosed and therefore before movement restrictions. This implies that the size of the restricted area was adequate. Clearly in these situations, closing down race meetings and events at which horses mix is also a key measure that will help limit dispersion of disease.

It is important to note that the nearest neighbour method (Table 1; Ward et al., 2008) used to estimate spread distance and  $R_T$  in this study has some important assumptions which may introduce biases into the resulting estimates. This method assumes that the shortest possible spread distances occur within a cluster, potentially underestimating parameters if the nearest neighbour was not the source of an infection for a premises. For example, this method cannot account for longer distance movements associated with deliberate spread. Whilst there was generally good compliance with the control campaign, deliberate spread did occur in some situations (Kevin Cooper, NSW DPI, Pers. Comm., March 2009). Also, the nearest neighbour method cannot take into account possible between cluster spread; this bias would result in spread distance being underestimated if significant inter-cluster spread occurred. Conversely, spread distance might be overestimated if undetected IPs were present in a cluster. Missing IPs may lead to distant IPs in a cluster being assigned as the source for a new IP, despite an undiagnosed, more local IP being responsible for the infection. Additionally reporting anomalies meant that some IPs may have been misclassified resulting in inaccurate estimates of spread distances. For example, the existence of a small number of horses (e.g. stallions) that left an IP under permit and subsequently were shown to be seropositive (but recovered) at their new premises may have resulted in some premises being misclassified as IPs (Kevin Copper, NSW DPI, Pers. Comm., March 2009). Additionally, some IPs may have been misclassified when they were diagnosed in the absence of laboratory results as occurred during the peak of the epidemic.

Another parameter of interest in this study was the cumulative incidence over the course of each cluster's epidemic. These values are lower than may intuitively be expected for such a contagious disease but are consistent with similar low cumulative incidences observed in other epidemics of contagious transboundary diseases such as the Foot-and-Mouth disease epidemic in the United Kingdom in 2001 (Gibbens et al., 2001). Partially, this may be explained by spatial disconnectedness between premises, limiting the spread of infection. However, reductions in movements between premises and other biosecurity interventions may have played a role in limiting risk. It is important to note though, that these estimates may be biased downwards if the population database had significant undetected replication of horse premises, due to common entries in the different components that comprised the final population database.

Parameter estimates were standardised with respect to the proportion of red or purple zone IPs in the peri-urban or rural landscapes. This was to reduce potential confounding associated with differences in zone management

and other landscape characteristics. The differences indicate that, as expected, peri-urban landscapes had denser and larger populations of equine premises. Peri-urban clusters had a longer epidemic duration and shorter spread distances. Perhaps surprisingly there appeared little difference between the incidence rate, cumulative incidence and  $R_T$  between rural and peri-urban regions.

## 5. Conclusion

It appeared that movement restrictions contributed greatly to the control of EI in Australia in 2007 by restricting spatial dissemination and seeding of susceptible populations of equines. It appears that vaccination may have only had a minor role in eradicating the disease and there is therefore a need for further research to evaluate the role vaccination played in containing and eradicating EI. Parameter estimates from the spatio-temporal analyses can inform future contingency plans. Parameter estimates may also prove useful as input parameters for future modelling studies of emergency animal diseases.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.prevetmed.2009.08.006](https://doi.org/10.1016/j.prevetmed.2009.08.006).

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