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Review of 20 years of human acute Q fever notifications in Victoria, 1994–2013

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Objective To describe the epidemiological and clinical features of acute Q fever in Victoria from 1994 to 2013.

Design Retrospective case series and spatiotemporal analyses of human notification data.

Methods Records for all confirmed cases of Q fever in Victoria notified between 1994 and 2013 were reviewed. Clinical and epidemiological features of the cases were described and spatiotemporal analysis undertaken for all cases potentially acquired within Victoria.

Results A total of 659 confirmed acute Q fever cases were notified over the study period. Cases decreased at a rate of 4.2% per annum (95% confidence interval (CI):0.9, 7.4%). Notification rates decreased among abattoir workers and related occupations by 10.9% per annum (95% CI: 6.5, 15.0%), whereas those among dairy farmers rose by 14.9% per annum (95% CI: 4.7, 26.0%). The mean age of cases increased over the study period while the ratio of male to female cases decreased. Spatiotemporal analysis suggested endemic transmission, with 55% of cases associated with abattoirs and related businesses and a further 30% considered to have acquired the infection locally. In addition to abattoir-associated

clusters, important foci for local acquisition included South and East Gippsland, Wodonga and an outbreak centred on a dairy goat farm west of Melbourne.

Conclusions There has been a reduction in cases of acute Q fever in Victoria over the past 20 years and a changing epidemiology with respect to age, sex and acquisition source. Epidemiological and spatiotemporal analyses suggest a low level of endemic transmission within the state, with multiple foci of increased zoonotic transmission.

Keywords *Coxiella burnetii*; public health; Q fever; surveillance; spatiotemporal analysis; zoonosis

Abbreviations ABS, Australian Bureau of Statistics; CFT, complement fixation test; CI, confidence interval; DHHS, Department of Health and Human Services; ERP, estimated resident population; IFA, immunofluorescence assay; Ig, immunoglobulin; IQR, interquartile range; NQFMP, National Q Fever Management Program; SA1, Statistical Area Level 1.

Q fever is a widespread zoonosis and emerging infectious disease, recently notable because of a large outbreak in the Netherlands, 2007–2012.[1] The disease was first recognised in Brisbane, Australia,[2] with the causative agent, *Coxiella burnetii*, identified in 1937 by Australian scientist Frank Macfarlane Burnet, and the understanding of its biology advanced through the development, testing and production of the only licensed human vaccine for Q fever (Q-Vax®, Seqirus Limited, VIC, Aust).

Infection with *C. burnetii*, a strict intracellular bacterium, causes symptoms in approximately 40% of human cases, with the majority experiencing an acute flu-like illness. The most common route of infection is inhalation of aerosolised infectious organisms excreted by infected animals, particularly around the time of parturition in ruminants, or from contaminated environmental dust particles.[3] A single bacterium of this species is sufficient to cause demonstrable infection in just under half of those humans exposed.[4] This, combined with an ability to survive for long periods in the environment, is important in the epidemiology of *C. burnetii* infection in humans.

Rates of Q fever in in the human population in Australia have traditionally been among the highest in the world,[5] with a 10-year (2004–13) mean annual national rate of 1.9 cases/100,000 population.[6] The highest rates of Q fever notifications (> 50 cases/100,000 population) are reported in south-west Queensland and north-west New South Wales.[5] Victoria's 10-year mean annual rate is 0.5 cases/100,000 population.[6]

Although it has previously been stated that Q fever is not endemic in Victoria,[7,8] only two studies address this issue. In 1972, a serological survey found only 0.5% of 1576 Victorian dairy cattle to be positive with the complement fixation test (CFT).[9] The only serological survey undertaken in humans was conducted in 2001–02, as part of the National Q Fever Management Program (NQFMP).[10] Preexisting immunity to *C. burnetii* was detected in 5% of farmers in Victoria, compared with 15% and 21% for farmers in NSW and Queensland, respectively; immunity was similar for abattoir workers from all three states (11–13%), likely reflecting the interstate movement of animals to slaughter.

Given this paucity of prior research, we reviewed the epidemiological and clinical information available for all confirmed human cases of acute Q fever recorded in Victoria

over a 20-year period (1994–2013), with a particular focus on the evidence for local acquisition of infection within Victoria.

Materials and methods

In Victoria, Q fever is a notifiable condition for humans; however, it is not notifiable in animals.[11] This study included all confirmed human cases of acute Q fever notified to the Victorian Department of Health and Human Services (DHHS) from 1 January 1994 to 31 December 2013, according to the nationally agreed case definition.[12]

In each case notified to DHHS, the person affected is interviewed by a public health officer. A semi-structured telephone interview aims to identify the probable source of infection, which then leads to the instigation of public health actions to modify ongoing exposure risks, particularly in workplace settings. Travel outside of Victoria is routinely recorded, as is exposure to animals or high-risk settings (shearing sheds, hunting etc.). Additional details are often recorded, such as contact with or recent acquisition of stock from interstate. Clinical information is recorded from the interviewee, medical practitioner and hospital discharge summaries.

We prepared epidemic curves and assessed them for trend, firstly by aggregating by month and year, and into 5-year periods, and preparing frequency cross-tabulations and calculating summary statistics, then by constructing univariable linear, negative binomial and logistic regression models, where appropriate, in the R statistical package version 3.2.3.[13] 'Occupational categories' were grouped following the NQFMP[10] and a categorical variable was used to represent the presumed 'Site of acquisition', coded in consideration of data (and uncertainties) obtained in the case interviews, as follows:

- 'potentially acquired overseas', if there was mention of travel outside Australia in the incubation period
- 'interstate outbreak-linked', if the case was epidemiologically linked to an interstate outbreak
- 'potentially acquired interstate', if there was mention of travel interstate (and a possible exposure site) in the incubation period
- 'associated with local abattoir or related business' (including rendering, tanneries, butchers and from investigated outbreaks at factories handling carcases/byproducts)
- 'other (presumed locally acquired)', if none of the above were documented.

Time-series were plotted, by 'Site of acquisition', first excluding cases considered to be 'potentially acquired overseas' or 'interstate outbreak-linked', then repeated further excluding cases 'potentially acquired interstate' and 'local abattoir or related business associated'. Data were de-identified prior to geocoding based on reported exposure site (or residential address if exposure site was unknown), then aggregated for further spatiotemporal analyses by Statistical Area Level 1 (SA1) units. SA1s are the smallest geographic areas defined in the Australian Statistical Geography Standard (Australian Bureau of Statistics [ABS]) for which annual estimated resident population (ERP) data were available, albeit only

for 2001–13 (based on ABS, Customised report, 2014), so ERP for the preceding 7 years were exponentially extrapolated.

To investigate the spatial pattern of risk of infection over time, risk surfaces were estimated, in 5-year periods, using Gaussian kernel density estimation,[14] implemented in R with edge effect correction using the 'spatstat' library.[15] Risk surfaces are 3-dimensional plots comprising grid cells of regular dimensions (here 5 × 5 km) covering a landscape. In this analysis, colour shading was used to represent the estimated density of cases acquired per cell divided by the estimated population at risk per cell as the third dimension. To make use of the case and ERP data, available aggregated by SA1, spatially-weighted random distributions of each population were prepared, as suitable for kernel density surface estimation, by disaggregating case and ERP data to random point locations by SA1. The amount of smoothing (bandwidth) applied (14 km) in estimating surfaces was selected as the mean of those calculated for case and ERP point data using isotropic leave-one-out least-squares cross-validation.[16]

Space–time clusters of acute Q fever were also detected using the space–time scan statistic[17] in SatScan version 9.3.1. Because the expected number of cases in each SA1 was assumed to follow a Poisson distribution, scanning was undertaken for elliptical clusters (of the centroids of SA1s) with dimensions up to 25% of the study area and 25% of the period, time precision of 1 year and no penalty for non-compact spatial clusters, with sensitivity analyses undertaken to test the effect of dimension parameters on the outputs. Likelihood ratio test statistics and corresponding P-values were calculated for each detected cluster by 999 Monte Carlo simulations run in parallel on the Victorian Life Sciences Computation Initiative Peak Computing Facility. Identified space–time clusters were considered statistically significant if they had a Monte Carlo simulation-derived P-value < 0.05.

Results

A total of 728 cases of confirmed Q fever were identified. Of these, 69 were excluded from further analysis for the following reasons: chronic Q fever (37); interstate resident (17); not consistent with case definition (13); and lack of information on electronic database with no hardcopy file available (2).

Epidemiology of confirmed Q fever cases

Between 1994 and 2013, 659 cases of acute Q fever in Victorian residents were analysed (mean annual notification rate: 0.75 cases/100,000 population), with the subjects having a median age of 38 years (interquartile range [IQR]: 28–48) (Table 1). Males accounted for 84% of cases, 85% (557 cases) were acquired secondary to occupational exposure and 45% (299 cases) were associated with an outbreak (e 2 epidemiologically linked cases).

A total of 12 cases were excluded from the spatiotemporal analysis, on the basis of being considered 'potentially overseas acquired' or 'interstate outbreak-linked'. Of the remaining 647 cases, there was mention of interstate travel during the incubation period for 85 cases (13%) and 364 cases (56%) mentioned a likely exposure at a Victorian abattoir or related business (Figure 1). The remaining 198 cases were presumed to be locally acquired infections

(Figure 1). Of these, 124 made mention of a farm exposure, 19 mentioned other animal-related exposures (including hunting various wildlife, as well as veterinary and other stock-handling across a variety of Victorian locations). The remaining 55 cases were classified as locally acquired with no known source.

The crude count of cases decreased by 4.2% per annum over the study period (95% CI: 0.9, 7.4% per annum). For each year studied, the proportion of males reporting infection decreased by 1.0% (95% CI: 0.5, 1.5%) while the mean age increased by 0.5 years (95% CI: 0.3, 0.6). Occupationally acquired cases decreased by 5.4% per annum (95% CI: 1.7, 8.9). Cases in abattoir workers and related occupational groups (tanners, wool classers and shearers) decreased by 11.5% per annum (95% CI: 7.0, 15.7%). Counts of cases 'potentially acquired interstate' and 'presumably locally acquired' remained constant until 2013, when a large, point-source outbreak occurred at a goat dairy farm. Excluding the cases associated with the goat dairy farm outbreak in 2013, counts of acute Q fever cases among dairy farmers rose by 14.9% per annum (95% CI: 4.7, 26.0%). Cases among non-dairy cattle and sheep farmers remained relatively constant across the study period (P = 0.61). Cases among dairy farmers (excluding the goat dairy outbreak) peaked between September and October (coinciding with key calving periods in Victoria's dairy districts). Cases among beef cattle and sheep farmers had a wider peak between July and October, whereas abattoir workers experienced two peaks (in June and November).

Reported outbreaks

There were 59 outbreaks detected, the largest of which are described in Supplementary Table 1. The proportion of outbreak-associated acute Q fever cases decreased 2.0% per annum over the study period (95% CI: 1.3, 2.6%). Throughout the 1990s, abattoirs contributed to > 90% of outbreak cases; however, for the period 2009–13, 66% (21/32) of outbreak-associated cases were linked to farms, with the single goat-related outbreak in this period contributing most of these cases.

Spatiotemporal analysis (for Victorian-acquired Q fever cases)

Risk maps by 5-year time period are presented in Figure 2 based on different inclusion criteria, including and excluding abattoir-associated and potentially interstate acquired cases (n = 647 and n = 198, respectively). Between 1994 and 2003, including abattoir-associated and potentially interstate acquired cases resulted in a clustered pattern across much of populated Victoria. As abattoir-associated cases declined throughout the study period, the risk maps became increasingly comparable for both the group with presumably locally acquired infection and the group containing locally acquired, abattoir and potentially interstate acquired infections. Several foci of increased risk were constantly observed throughout the study period in the south-east and east of the state (Gippsland region) and at several sites along the New South Wales border. Most of the other smaller foci were explained by reported outbreaks and abattoir-associated clusters.

Statistically significant space–time clusters are presented in Table 3 and Figure 3. When cases of interstate infection or at an abattoir or related business were excluded there were five clusters: one in Golden Plains shire, representing the 2013–14 outbreak associated with a

dairy goat farm, three in Gippsland and one in Wodonga, corresponding closely with the foci identified in the kernel density mapping. This provides evidence for *C. burnetii* endemicity in at least these locations. When potentially interstate-acquired cases and those associated with local abattoirs or related business were included, a further 11 statistically significant spatiotemporal clusters were observed (Figure 3).

Clinical parameters of confirmed Q fever cases

Clinical data was unreliably recorded prior to 2004. There were no statistically significant differences in the data when the two 5-year periods (2004–08 and 2009–13) were compared; overall counts for this 10-year period are presented in Table 2. Rare clinical manifestations reported to the DHHS included seven cases of splenomegaly (one with splenic rupture), six of orchitis and three of myocarditis/pericarditis.

Discussion

This large retrospective case series provided an update on the epidemiological and clinical features of acute Q fever in Victoria. A previous Victorian tertiary hospital case series (prior to the availability of Q-Vax), including 111 cases from 1962 to 1981, reported infections for which 99% of cases were in males and 92% of them were abattoir workers.[18] Data presented here are in keeping with the 2009 report from NSW,[19] where a decrease was observed in the overall number of confirmed cases of acute Q fever, particularly in abattoir workers and related outbreak settings, as well as an increase in the proportion of cases in females. A recently published national review of Q fever notifications data[20] reported an increase in the numbers of females and increased age of subjects in notified cases. Many of these epidemiological changes could be attributed to the success of the NQFMP (2001–02) in vaccinating high-risk workers,[5] particularly those working in abattoirs; the Australian Q Fever Register (https://www.qfever.org) was established in 2001 to store voluntarily submitted information on the Q fever immune status of individuals and subsequent interventions that maintain adequate vaccination rates for abattoir workers. Farmers were not the specific targets of this program. Given that the majority of infections continue to be secondary to occupational exposure (80% between 2009 and 2013), these represent preventable cases, suggesting that the targeted vaccination program should be expanded.

Because in 30% of human cases there was no travel history or any other plausible interstate or international exposure (i.e. not attributed to an interstate outbreak or contact with interstate animals, which may occur through an abattoir or related business), this study provided epidemiological evidence of the endemicity of *C. burnetii* in Victoria. Numbers of cases notified among dairy farmers rose dramatically over the study period (three cases in the decade to 2003 compared with 23 in the subsequent decade, peaking in 2008, with a further 18 cases associated with the dairy goat outbreak). Possible explanations for this rise include changes in reporting practices and/or awareness among dairy farmers following the NQFMP or a change in risk for this group of farmers. Surveillance data suggest the majority of dairy farms are primarily cattle; however, sheep, goat and other possible livestock were not routinely excluded and may act as confounders.

A community outbreak in Wodonga in 2006 was attributed to a local abattoir (DHHS unpubl. data). The investigation of the 2013–14 outbreak in Golden Plains shire associated with a dairy goat farm has been reported elsewhere.[21] Gippsland holds 35% of Victoria's dairy cattle, 20% of the state's beef cattle and 55% of its domesticated goats. Seven small (d 3 cases) farm-associated outbreaks (out of 10 in the past 20 years) have been reported in this region: six were associated with cattle farms and one with a goat farm.

Ruminants are presumably the main source of infection in Gippsland, although environmental contamination by wildlife has been raised as a possible explanation for cases of infection in people with no direct animal contact.[22,23] Infection of stock in Gippsland may be occurring through direct contact with infected stock, importation of infected stock from interstate and elsewhere in Victoria, transmission on fomites or via environmental contamination. Local native wildlife may also be providing a reservoir for infection,[22–27] which spills over into ruminants, thereby exposing people. Serological surveys of livestock and wildlife in Victoria would clarify the public health and production risks.

Estimates from the Netherlands' outbreak suggest that only 7.9% of acute Q fever infections were notified to public health services.[28] In France, this value has been shown to be influenced by clinician awareness and testing practices;[29] therefore, it may well be lower in Victoria. With 55 of 647 potentially locally acquired cases (8.5%) in which no plausible exposure could be identified at interview there is a need to consider acute Q fever as a differential diagnosis even without traditional risk factors reported. Of these 55 cases, 19 resided in metropolitan Melbourne and had no mention of potential rural exposure at interview. Although the recall of exposure may be an issue, this nonetheless raises the possibility of previously unrecognised urban sources, or transmission of infectious organisms on vehicles or products transferred from rural to urban environments.

Variation in methods of case finding, diagnostic testing, reporting and surveillance data make it difficult to compare clinical features across publications. The hospitalisation rate of 53% was higher than the historical rate in France (2%)[29] and recent rate of 20% in the Netherlands, but in keeping with the initial outbreak rate of 50% in 2007 for the Netherlands[1] and that of a small enhanced surveillance case series from NSW.[19] The largely sporadic nature of cases and lower level of clinical awareness in Victoria may suggest that mild cases remain undiagnosed, while those who are diagnosed are more severely unwell, contributing to the higher hospitalisation rate. The slightly higher than expected proportion of chronic cases (5%), which were excluded from further analysis, may also suggest under-ascertainment of mild acute cases.

Study limitations

The retrospective nature of this case series limited the data to that collected as part of routine surveillance. There is, therefore, a high likelihood of under-reporting of clinical signs, symptoms and parameters reliant on diagnostic specimens and an inherent level of subjectivity in the classification of cases based on retrospective analysis of available epidemiological and clinical data. In almost 50% of cases, confirmation was based on laboratory definitive evidence; of the remaining 50% based on laboratory suggestive evidence, in two-thirds there was a high titre of specific immunoglobulin (Ig) M, suggesting

that non-specific false-positive results were less likely. However, given that IgM may remain persistently elevated for some time following infection, and that in some cases there was a low specific IgM titre combined with relatively non-specific clinical case definition, a few cases may be misclassified as acute Q fever. Previous state-level analyses of 'enhanced risk factor data' (as described by Sloan-Gardner et al.[20]) have been restricted to NSW and Queensland, and have been limited by missing data, particularly for occupational and animal exposure variables. The data analysed here were largely complete for these risk factors, enabling a deeper understanding of the changing epidemiology of Q fever in Victoria.

Conclusions

The number of notified cases of acute Q fever in Victoria has steadily decreased over the period 1994–2013. This analysis provided further evidence for the increasing relative importance of non-abattoir-related contact with animals and the need to consider the risk of Q fever outside traditional at-risk occupations. The spatial distribution of acute Q fever notifications was previously widespread across Victoria, but there has been a progressive reduction in cases associated with abattoirs and related businesses. The number of cases considered to have acquired the infection locally suggests endemicity of *C. burnetii* within the state; spatial analysis demonstrates several, potentially long-standing foci notable for regular zoonotic transmission to humans and many other areas with very low levels of transmission to humans. Further research should be undertaken to inform public health action and increase the awareness of risks among the general public, veterinary and medical practitioners in Victoria, which should in turn improve vaccination uptake and clinical recognition of infection, thereby reducing the future effect of Q fever in this state.

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Conflict of interest and sources of funding

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Supplementary Table 1. Detail on the largest (e 5 associated cases) of 59 outbreaks of Q fever in Victoria between 1994 and 2013

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Figure 1. Time-series of confirmed Q fever cases in Victoria, 1994–2013, by reported place of acquisition.

Figure 2. Risk surfaces of Q fever in Victoria, by 5-year period, excluding cases considered to be 'potentially acquired overseas' or 'interstate outbreak-linked' (n = 647), and for the subset of cases (n = 198) where there was also no mention of interstate travel during the incubation period and no association with an abattoir or related business. Shading represents the proportional risk of acute Q fever, derived by dividing the case count per 5 × 5 km grid cell by the estimated population at risk of infection for that cell. Relative increased risk of acquiring acute Q fever according to location can be inferred by the degree of shading: the darker the shading the higher the risk.

Figure 3. Locations in Victoria where, between 1994 and 2013, the risk of acquiring acute Q fever was significantly higher than expected based on statewide acquisition data, as determined by the space–time scan statistic. These spatiotemporal clusters are presented for all cases, excluding those considered 'potentially acquired overseas' or 'interstate outbreak-linked' (n = 647) and for the subset of cases (n = 198) where there was also no mention of interstate travel during the incubation period and no association with an abattoir or related business. Small clusters are represented by points at their centroid.

Table 1. Trends in the demographics of confirmed human Q fever cases in Victoria between 1994 and 2013, by 5-year period

	Time period			
	1994–98	1999–2003	2004–08	2009–13
No. of cases	237	175	124	123
No. of male cases (%)	213 (90)	150 (86)	95 (77)	93 (76)
Median age (IQR)	34 (27, 44)	37 (26, 49)	42 (30, 51)	43 (30, 57)
Occupational exposure (%)	211 (89)	158 (90)	90 (73)	98 (80)
Outbreak associated (%)	143 (60)	75 (43)	38 (31)	43 (35)
Overseas acquired	4	3	2	1
Occupational group[a]				
Abattoir worker	166 (70)	107 (61)	50 (40)	31 (25)
Beef cattle/sheep farmer	11 (5)	17 (10)	16 (13)	15 (12)
Dairy farmer	1 (0)	2 (1)	12 (10)	29 (24)
Farmer unspecified	8 (3)	13 (7)	8 (6)	11 (9)
Shearer	11 (5)	10 (6)	0 (0)	5 (4)
Stock related	4 (2)	7 (4)	3 (2)	6 (5)
Tanner/wool classer	10 (4)	2 (1)	1 (1)	1 (1)
Other	26 (11)	17 (10)	34 (27)	25 (20)
Site of acquisition[b]				
Potentially overseas	4 (2)	3 (2)	2 (2)	1 (1)
Interstate outbreak	0 (0)	0 (0)	0 (0)	2 (2)
Potentially interstate	17 (7)	29 (17)	18 (15)	21 (17)
Local abattoir & related	176 (74)	108 (62)	50 (40)	30 (24)
Other (presumed local)	40 (17)	35 (20)	54 (44)	69 (56)
Farm	22	24	29	49
Animal-handling	6	3	5	5
Unknown sources	12	8	20	15

Numbers in parentheses are column percentages.

[a]Classified per the National Q Fever Management Program: 'Abattoir workers' includes contractors attending abattoirs, 'Dairy farmers' includes cattle and goat dairy farmers.

[b]'Local abattoir & related' includes rendering, tanneries, butchers and cases from outbreaks at factories handling carcases/byproducts; 'Other (presumed local): Animal-handling' includes hunters, veterinarians and others with exposure to livestock, as well as council workers exposed to deceased animals.

IQR, interquartile range.

Table 2. Clinical parameters of confirmed Q fever cases in Victoria between 2004 and 2013

Parameter	n (%)
Total no. of cases	247
Hospitalised cases	132 (53)
Not stated	15 (6)
Reported clinical parameters[a]	
Hepatitis	86 (35)
Pneumonia	20 (8)
Other	
Headache	119 (48)
CNS symptoms	10 (4)
Haematological derangements	23 (11)
No symptoms reported	16 (6)
Treated	210 (85)
Tetracycline	204 (83)
Macrolide	3 (1)
Fluoroquinolone	3 (1)
Not treated	22 (9)
Not stated	15 (6)
Laboratory evidence of diagnosis	
Culture	1 (<1)
PCR assay	10 (4)
Seroconversion	78 (32)
Rising titre	34 (14)

Specific IgM[b]	123 (50)
High titre	88 (36)
Low titre	35 (14)
Not stated	1 (<1)

[a]Hepatitis: jaundice, hepatomegaly or elevation of liver function tests more than twice the upper limit of normal; respiratory symptoms: cough, pneumonia, shortness of breath; CNS symptoms: confusion, delirium, meningitis, need for lumbar puncture; haematological derangement: splenomegaly, leucopenia, thrombocytopenia; acute renal impairment: elevated creatinine.

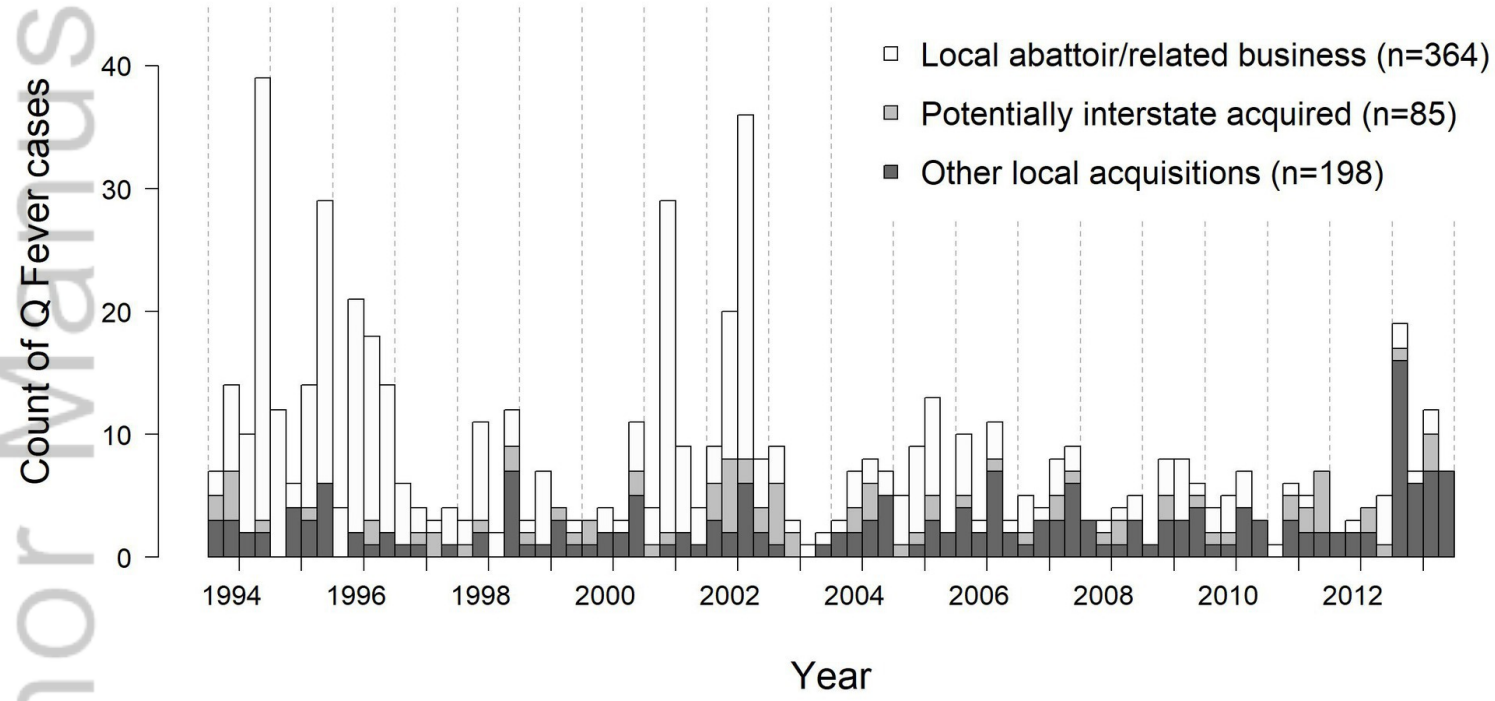
[b]High titre: immunofluorescence assay (IFA) total phase 2 (Ph2) Ig > 200 or CFT Ph2 Ig > 10; low titre: total Ph2 Ig not stated, IFA < 200, CFT < 10 or enzyme immunoassay testing.

CFT, complement fixation test; CNS, central nervous system; Ig, immunoglobulin.

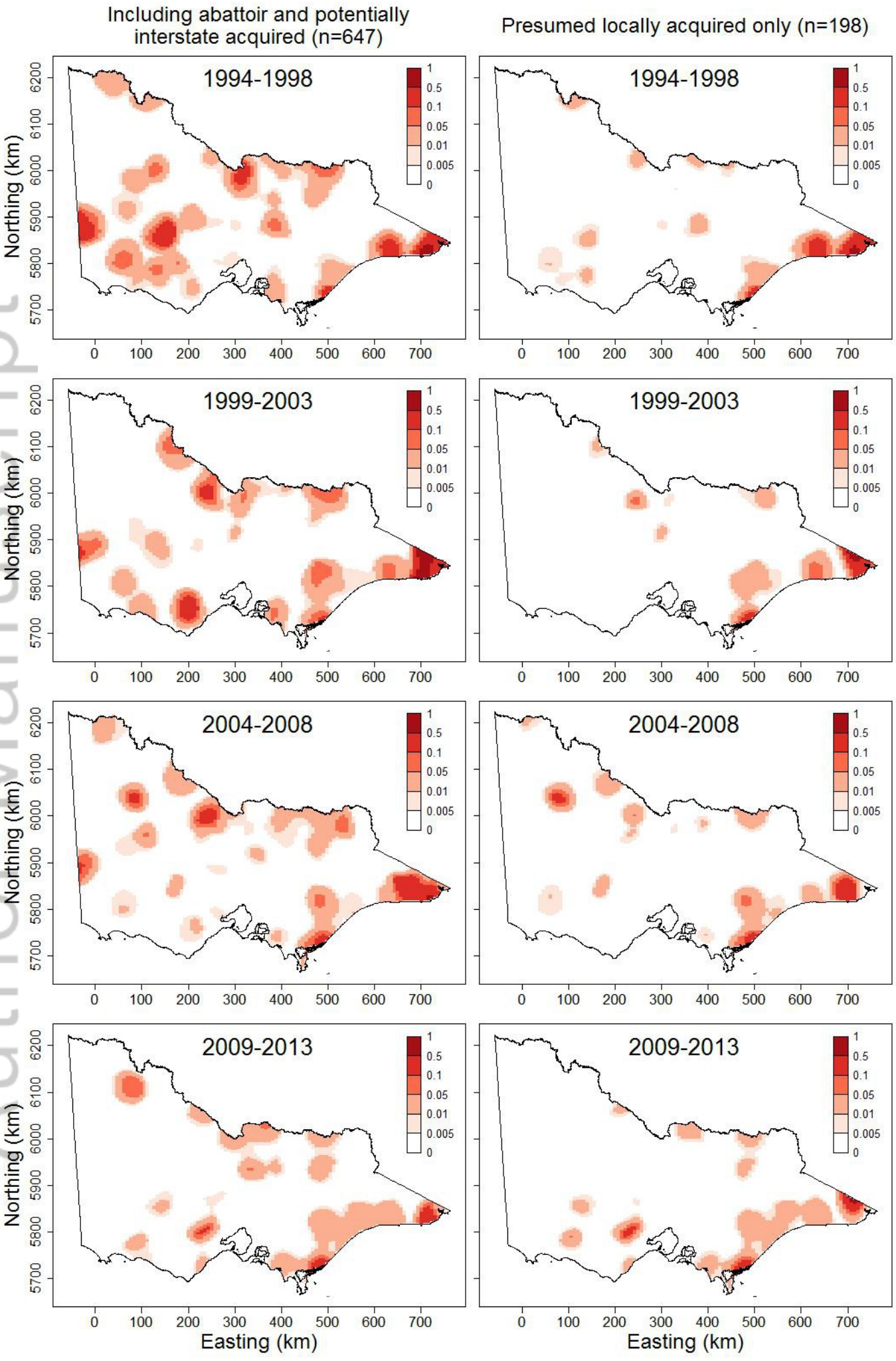
Table 3. Five most statistically signification clusters of Q fever cases in Victoria, 1994–2013, detected using the space–time permutation scan statistic on data aggregated by Statistical Area 1 and annually, by model run

Model run	Cluster location	Time frame	No. of cases		Likelihood ratio test statistic	P value[a]
			Observed	Expected		
Excluding cases considered to be 'potentially acquired overseas' or 'interstate outbreak-linked' (n = 647)	Melbourne – west	1994–98	39	0.02	262.7	< 0.001
	Colac	2002	28	< 0.01	247.0	< 0.001
	Wodonga	1998–2002	33	0.01	231.7	< 0.001
	Kyabram	1994	26	< 0.01	210.4	< 0.001
	Golden Plains	2013	19	< 0.01	151.1	< 0.001
Also excluding cases 'potentially acquired interstate' and 'local abattoir or related business associated' (n = 198)	Golden Plains	2013	19	< 0.01	174.2	< 0.001
	South-east Gippsland	2007–11	16	0.17	49.7	< 0.001
	Wodonga	2002–06	9	0.04	39.8	< 0.001
	Orbost	1998–2002	6	< 0.01	38.9	< 0.001
	Mallacoota	1995	3	< 0.01	18.1	0.023

[a]P-values obtained by re-estimating likelihood ratio test statistic for each detected cluster on 999 Monte Carlo simulations of the dataset under the null hypothesis of spatial and temporal randomness. Standard Monte Carlo critical values estimated for Run 1 as 18.22, 19.24 and 19.43, for P = 0.05, P = 0.01 and P = 0.001, respectively. For Run 2 as 17.35, 19.04 and 19.44, for P = 0.05, P = 0.01 and P = 0.001, respectively.



avj_12704_f1.jpeg



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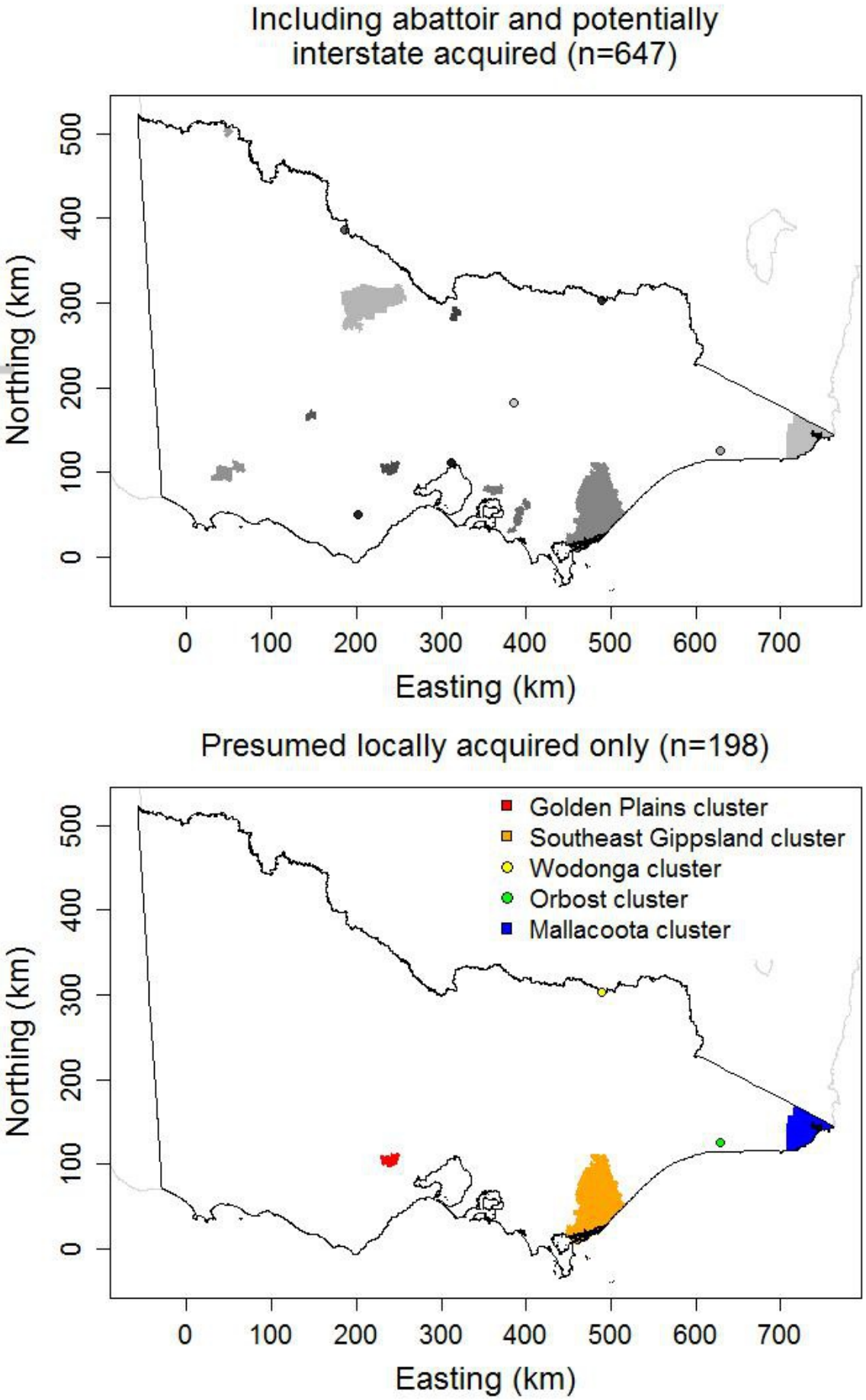

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