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Socioeconomic, geographic and climatic risk factors for canine parvovirus infection and euthanasia in Australia

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ABSTRACT

Infection of canids with canine parvovirus (CPV) can result in severe, often fatal disease. This study aimed to examine climatic, socioeconomic and geographic risk factors for CPV infection and CPV-associated euthanasia in Australia. Australian veterinary hospital responses (534; 23.5 %) to a national veterinary survey of CPV case occurrences and euthanasias in 2016 were used. Severe caseloads (> 40 cases per annum) were reported by 26 (11 %) hospitals (median 60 cases; IQR 50–110). Case reporting, case numbers, and without-treatment euthanasia were significantly associated with disadvantage across all Socio-Economic Index for Areas quintiles ($p < 0.0001$) – the greater the disadvantage, the more reports. Strong negative correlations were found between case numbers and the Index of Relative Socioeconomic Disadvantage ($r_{SP} = -0.3357$, $p < 0.0001$) and also between euthanasia and the Index of Education and Occupation ($r_{SP} = -0.3762$, $p < 0.0001$). Hospitals in more remote areas were also more likely to report cases and to euthanize without treatment ($p < 0.0001$). Of the climate variables, temperature of the hottest month was most strongly positively correlated with case numbers ($r_{SP} = 0.421$, $p < 0.0001$), and lower annual rainfall was associated with more case-reporting hospitals ($p < 0.0001$). These results confirm that socioeconomic disadvantage is a significant risk-factor for CPV infection and outcome, and high temperature may also contribute to risk.

1. Introduction

Canine parvovirus (CPV) is a small non-enveloped single-stranded DNA virus of the genus *Carnivore Protoparvovirus* that first emerged in the mid-to-late 1970s, with a global pandemic occurring shortly after (Hoelzer and Parrish, 2010). Subsequent capsid mutations have led to a number of strains currently circulating globally, classified as CPV-2a, 2b and 2c (Mylonakis et al., 2016). All current strains are able to infect a range of carnivores and felids (Shackelton et al., 2005). Although infections can be subclinical, CPV can cause gastroenteritis, dehydration, immune suppression and death, and disease typically occurs in dogs under 6 months of age. Adults can also be affected (Allison et al., 2014; Altman et al., 2017; Ling et al., 2012; Mylonakis et al., 2016). Euthanasia is the leading cause of death from CPV in Australia (Ling et al., 2012) with 20,000 CPV cases estimated annually and higher reporting in rural and remote areas and lower socioeconomic regions (Kelman et al., 2019). The reasons for this distribution are not fully understood, however lack of vaccination or an incomplete vaccination course due to affordability issues in these areas is one suggested explanation (Brady et al., 2012; Kelman et al., 2019; Zourkas et al., 2015). Breed, stress, co-infection with other pathogen(s), immunosuppression, and geographic region are reported predisposing factors for infection (Goddard and Leisewitz, 2010; Kalli et al., 2010; Mylonakis et al., 2016). Breed-susceptibility may relate to hereditary immunodeficiency in some animals (Day, 1999). Stress due to co-pathogen infection, weaning, and overcrowding can lead to suppressed immunity and higher risk of clinical infection (Brunner and Swango, 1985). Weaning and intestinal co-pathogen infection can also predispose to infection due to dysbiosis with increased enterocyte turnover and higher mitotic rate, increasing susceptibility to CPV due to its predilection for rapidly dividing cells (Houston et al., 1996; O'Sullivan et al., 1984). Season, rainfall and temperature have also been reported as risk factors for infection, although no definitive relationship between these factors and infection has been established. The canine breeding cycle, with more puppies born in spring and summer, might explain one aspect of seasonal disease occurrence. (Castro et al., 2007; Horner, 1983; Houston et al., 1996; Kalli et al., 2010; Rika-Heke et al., 2015). Epidemiological studies have been limited until recently by a lack of reliable and suitable data, and an absence of national representative data (Brady et al., 2012). The aim of this study was to determine from national data the association between socioeconomic, geographic, and climatic risk factors and CPV infection, and CPV-associated euthanasia rates.

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2. Materials and methods

2.1. Data sources

We previously reported the sample population, and survey design of a national survey of veterinary hospitals, conducted to describe the geographic distribution of CPV-related disease across Australia, and the financial impact on pet owners (Kelman et al., 2019). For the current study, we utilized this same survey data and analyzed the relationship between CPV case numbers and euthanasia rates against climate, socioeconomic determinants, and remoteness of the areas surveyed. Our previous study had obtained data for 2015 and 2016, and due to equivocal findings, only 2016 data was used for the current study. Survey respondents were asked to report their annual rate of euthanasia, both for CPV cases without treatment being attempted, and for those patients euthanized despite treatment having been commenced; both outcomes were analyzed in the present study.

Socioeconomic data was sourced from the Australian Bureau of Statistics 2016 Australian Census as a Socio-Economic Indexes for Areas (SEIFA) data cube (http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/2033.0.55.0012016?OpenDocument). Relative socio-economic advantage and disadvantage are broadly defined in terms of people's access to material and social resources, and their ability to participate in society. (Australian Bureau of Statistics, 2018a). Indices reported included Relative Socio-economic Disadvantage (IRSD), Relative Socio-economic Advantage and Disadvantage (IRSAD), Education and Occupation (IEO), and Economic Resources (IER). IER ranks areas by summarizing variables related to financial aspects of relative socio-economic advantage and disadvantage. IEO ranks areas by variables relating to the professional qualifications and skills of people and the level of employment. IRSD ranks by variables reflecting the level of disadvantage in an area, ignoring indicators of advantage. IRSAD ranks areas from most disadvantaged to most advantaged, reflecting all variables (Australian Bureau of Statistics, 2018a).

Remoteness data was sourced from the 2016 Australian Census as a Remoteness Area (RA) data cube (http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1270.0.55.005July%202016?OpenDocument) where postcodes, categorized by RA codes were each assigned to one of five RA classes: Major Cities of Australia, Inner Regional Australia, Outer Regional Australia, Remote Australia, Very Remote Australia. RAs represent relative proximity to an urban center and relative access to services (Australian Bureau of Statistics, 2018b).

Climate data was sourced from selected weather stations of the Australian Bureau of Meteorology (BOM) for: daily maximum, minimum and average temperature (calculated by averaging the daily maximum and minimum); monthly mean of mean, maximum and minimum daily air temperatures; total daily and monthly rainfall. All Australian BOM weather stations were downloaded from http://www.bom.gov.au/climate/data/stations/ and those active with a complete dataset during 2016 were selected. This data was then linked to an ABS Postal Areas ASGS Ed 2016 Digital Boundaries Shapefile (ESRI Format) downloaded from http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1270.0.55.003July%202016?OpenDocument. ArcGIS was used to determine those weather stations that were closest to each postcode corresponding with a responding veterinary hospital in our survey. Temperature and rainfall data were obtained from 208 and 465 unique weather stations, respectively.

2.2. Data management

Survey data, BOM data and ABS data were all managed in Microsoft® Excel for Mac version 16.16.10. Only data from 2016 were analysed. Data from our national veterinary CPV survey were separated into two datasets: all hospitals (including those survey hospitals that reported no CPV cases in 2016) and CPV-reporting hospitals only. An additional 'caseload severity' category was also created to sort hospitals according to the number of CPV cases reported in 2016, and to reflect the severity of their caseload. Categories were designed to consider the likelihood of litters of puppies presenting with CPV and the inflating effect that litters would have on case numbers, since infections in each litter likely originate from a single source of infection. The categories were:

- low (< 6) – several individual cases of CPV or 1 or 2 litters with 2–3 affected puppies, probably representing individual exposure but not outbreak conditions;
- mild (6–15) – higher numbers of individual cases of CPV or several litters of 2–3 puppies infected, representing some possible local disease spread and a small but limited epidemic;
- moderate (16–40) – several dozen individual cases or multiple litters of 2–3 puppies infected, representing an epidemic with further spread or possibly several epidemics over the course of a year;
- severe (40 +) – large numbers of litters and/or individual cases, or ongoing endemic conditions

Socioeconomic data was accessed as both scores (ranks) and deciles for each of the socioeconomic indexes. Deciles were converted into quintiles for further analysis.

For the Remoteness Area data from the ABS, the classes Remote Australia and Very Remote Australia were combined due to insufficient numbers (three only) of Very Remote Australian suburbs for analysis. For correlations, Remoteness Area codes (0,1,2,3) were used.

Climate data from the BOM were cleaned and sorted. Eight weather stations had incomplete data, and these were replaced with the next closest station with a complete dataset, as identified manually from the BOM website. From the climate data, the following climate measures

Table 1
Descriptive data for climatic quintiles associated with veterinary hospitals surveyed in national canine parvovirus survey, Australia, 2016.

Climate Variable	Quintile	Climate value			
		Min	Max	Median	Interquartile range
Total Annual Rainfall	1	301.0	623.9	557.4	472.8 - 604
	2	624.9	717	693.6	655.5 - 715.1
	3	718.4	799.1	778.8	754.8 - 788.2
	4	800.8	1017	856.8	822.2 - 951.4
	5	1026	2839.4	1334.8	1107.6 - 1411.4
Highest Daily Rainfall	1	21.4	38.4	36.1	31.8 - 36.6
	2	38.6	49.8	46	41.4 - 49.2
	3	51	72.2	60.6	54.7 - 62.9
	4	74.4	120.6	88	83.5 - 98.5
	5	120.8	263.6	141.2	130.2 - 175.0
Highest Monthly Rainfall	1	80.8	113.4	102	91.6 - 107.6
	2	113.6	142.2	129.4	119.9 - 139.6
	3	143	172.8	156	149.6 - 159.4
	4	178.6	279.4	242.2	193.4 - 264.8
	5	280.4	807.4	348.6	307.1 - 443.8
Annual mean temperature, measured by annual mean of monthly mean of mean daily temperatures	1	5.2	15.4	14.3	13.8 - 14.9
	2	15.4	17.7	16.6	16.1 - 17.1
	3	17.7	18.5	18.2	17.7 - 18.4
	4	18.5	21.6	19.3	18.8 - 20.4
	5	21.7	28.9	24.1	22.4 - 25.9
Highest monthly temperature, measured by monthly mean of daily maximum temperatures	1	13.8	28.2	26.2	24.1 - 27.3
	2	28.4	30.8	29.7	29.0 - 30.2
	3	30.9	32.1	31.8	31.3 - 32
	4	32.2	33.4	32.6	32.3 - 33.2
	5	33.5	39.7	34.5	33.9 - 36.3
Lowest monthly temperature, measured by monthly mean of daily minimum temperatures	1	−1.8	4.0	3.0	1.1 - 3.3
	2	4.1	5.8	4.7	4.3 - 5.4
	3	5.9	7.1	6.4	6.2 - 6.8
	4	7.2	9.8	7.9	7.5 - 9.0
	5	10	19.8	13	11.8 - 16.3

Table 2
Descriptive data for Socioeconomic Indexes For Areas (SEIFA) scores, associated with all veterinary hospitals surveyed in national canine parvovirus survey, Australia, 2016.

SEIFA Variable	Remoteness Area	SEIFA score value					Kruskal-Wallis One-Way Analysis of Variance		Spearman Rank Correlation	
		N	Min	Max	Median	Interquartile range	Mean rank	P-value	R	P-value
Index of Relative Socioeconomic Disadvantage (IRSD)	Combined	534	719	1127	1011.5	972 - 1062	267.5	< 0.0001	−0.5840	< 0.0001
	Major Cities of Australia	314	719	1127	1045.5	1005.8 - 1081	341.5[abc]			
	Inner Regional Australia	135	776	1119	981	954 - 1005	185.3[ad]			
	Outer Regional Australia	68	808	1037	956	927.75 - 988	121.1[bd]			
	Remote Australia	17	843	1045	976	933 - 991	139.4[c]			
Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD)	Combined	534	743	1179	999	955 - 1065	267.5	< 0.0001	−0.6284	< 0.0001
	Major Cities of Australia	314	743	1179	1049.5	999.5 - 1097.3	348.2[abc]			
	Inner Regional Australia	135	813	1121	964	932 - 986	171.8[a]			
	Outer Regional Australia	68	811	1052	936.5	913 - 966.5	115.4[b]			
	Remote Australia	17	870	1013	964	933.5 - 971	145.8[c]			
Index of Economic Resources (IER)	Combined	534	792	1167	1003	968 - 1045	267.5	< 0.0001	−0.4445	< 0.0001
	Major Cities of Australia	314	792	1167	1027	992 - 1066	321.8[abc]			
	Inner Regional Australia	135	826	1142	982	962 - 1008	217.5[ad]			
	Outer Regional Australia	68	821	1040	970	945 - 988.5	153.1[bd]			
	Remote Australia	17	828	1024	957	909.5 - 987.5	120.1[c]			
Index of Education and Occupation (IEO)	Combined	534	771	1195	996	946 - 1083	267.5	< 0.0001	−0.5880	< 0.0001
	Major Cities of Australia	314	771	1195	1050.5	989.75 - 1108.3	342.5[abc]			
	Inner Regional Australia	135	812	1148	958	926 - 989	181.7[ad]			
	Outer Regional Australia	68	832	1045	928	916.25 - 959.75	119[bd]			
	Remote Australia	17	919	992	948	936 - 973.5	157.3[c]			

Superscript denotes statistically significant different mean rank.

Table 3
Australian canine parvovirus case numbers and euthanasia rates, 2016, reported by caseload severity.

Caseload severity (cases)	Number of Canine Parvovirus Cases in 2016			Kruskal-Wallis One-Way Analysis of Variance		Without Treatment Euthanasia rate		Kruskal-Wallis One-Way Analysis of Variance		Despite Treatment Euthanasia rate		Kruskal-Wallis One-Way Analysis of Variance	
	N	Median	Interquartile range	Mean rank	P-value	Median	Interquartile range	Mean rank	P-value	Median	Interquartile range	Mean Rank	P-value
Low (< 6)	116	2.0	1.0 - 3.0	58.5[ab]	< 0.0001	12.5	0.0 - 50.0	93.7[ab]	< 0.0001	0.0	0.0 - 18.0	111.1	0.0812
Mild (6-15)	49	10.0	7.0 - 12.2	141.0[ab]		30.0	13.7 - 50.0	134.4[a]		5.0	0.0 - 10.0	116.3	
Moderate (16-40)	46	25.0	20.0 - 30.0	188.5[a]		50.0	27.5 - 70.0	159.0[b]		10.0	1.0 - 10.0	139.6	
Severe (40+)	26	60.0	50.0 - 110.0	224.5[b]		27.5	14.2 - 60.0	132.2		5.0	1.0 - 10.0	123.0	

Superscript denotes statistically significant different mean rank.

for each reporting veterinary hospital's postcode were calculated: total annual rainfall; highest daily rainfall; highest monthly rainfall; annual mean temperature (measured by annual mean of monthly mean of mean daily temperatures); highest monthly temperature (measured by monthly mean of daily maximum temperatures); lowest monthly temperature (measured by monthly mean of daily minimum temperatures). Climate data was also converted into quintiles for analysis.

2.3. Data analysis

All statistical analysis was performed using Statistix® version 10.0 (Analytical Software, Tallahassee, FL), except a Stepwise Logistic Regression performed using SPSS (IBM SPSS Statistics 24). Significance was $p < 0.05$ for all statistical analyses. Frequency distributions were generated for SEIFA index quintiles (IRSD, IRSAD, IER and IEO), remoteness areas and climate variable quintiles. Descriptive statistics were calculated for SEIFA quintiles, remoteness areas, and caseload severity categories, with respect to CPV case numbers and CPV-related euthanasia rates (without treatment or despite treatment). Descriptive statistics were also calculated for climate variable quintiles, with respect to climate value and also CPV case numbers. Chi-squared test for independence was performed for CPV case occurrence (yes vs no) for all categories. Kruskal-Wallis One-Way Analysis of Variance was calculated for CPV case numbers and euthanasia rates for each category, and Dunn's All-Pairwise Comparisons Test was performed on mean rank scores for all statistically significant results. Spearman Rank Correlation was used to determine the relationship between continuous measured data. Scatter plots were generated for euthanasia rate versus IEO score and CPV caseload versus IRSD score; Loess smooth fitted curves were created using an alpha of 0.75 and linear degree. Logistic regression was used to identify socioeconomic, remoteness and climate predictors of CPV case reporting by hospitals. Predictor variables were chosen from each predictor category as that variable most highly associated (Chi-squared statistic) with CPV case-reporting hospitals. As there was a strong association with all SEIFA variables, for this category the variable with the highest correlation (Spearman Rank correlation statistic) with CPV case numbers was chosen. The best-fitting model was identified using stepwise logistic regression and P-to-enter 0.05 and P-to-remove 0.10. Maps displaying CPV case numbers in relation to remoteness area were generated using ArcGIS® version 10.2 (ESRI).

3. Results

In total, 534 veterinary hospitals responded to the survey and 237 of these reported CPV cases during the 2016 calendar year. Total annual rainfall reported for climatic quintiles varied considerably (301 mm to 2839 mm). Highest daily rainfall ranged from 21.4 mm to 263.6 mm, highest monthly rainfall ranged from 80.8 mm to 807.4 mm. Annual mean temperature ranged from 5.2 °C to 28.9 °C. Average maximum temperature for the hottest month (mean of daily maximums) ranged from 13.8 °C to 39.7 °C. Average minimum temperature for the coldest month (mean of daily minimums) ranged from -1.8 °C to 4.0 °C (Table 1). The remoteness area category, "Major Cities of Australia", had the highest and lowest SEIFA index scores, and the highest median across all indices. The mean rank SEIFA score for "Major Cities of Australia" was also significantly higher than all other categories across all indices. The lowest median SEIFA scores were for Outer Regional Australia (956, 936.5 and 928 for IRSD, IRSAD and IEO, respectively) and Remote Australia for IER (957). There was a moderate to high correlation between remoteness area codes and SEIFA index scores, the strongest being IRSAD ($r_{SP} = -0.6284$, $p < 0.0001$), (Table 2).

3.1. Caseload severity a risk factor for euthanasia without treatment

The greatest number of hospitals (49 %, 116/237) reported low numbers of cases ("low caseload" category; median 2.0, IQR 1.0–3.0),

Table 4
Veterinary hospitals reporting canine parvovirus cases and case numbers, reported by Socioeconomic Indexes for Areas (SEIFA), 2016.

		Veterinary hospitals with CPV case occurrence in 2016							Number of Canine Parvovirus Cases in 2016, from hospitals that reported cases						
		Frequency		Hospitals seeing CPV cases (%)								Kruskal-Wallis One-Way Analysis of Variance		Spearman Rank Correlation	
Variable	Quintile	Yes	No		Chi2	DF	P-value	OR	N	Median	IQR	Mean rank	P-value	R	P-value
Index of Relative Socioeconomic Disadvantage (IRSD)	1	51	18	73.9	95.36	12	< 0.0001	13.95	51	12.5	3.0 - 30.0	144.1[a]	< 0.0001	−0.3357	< 0.0001
	2	64	36	64.0				8.75	64	4.5	2.0 - 25.0	123.9[b]			
	3	63	53	54.3				5.85	63	6.0	2.0 - 19.0	127.4[c]			
	4	33	62	34.7				2.62	33	3.5	1.0 - 10.0	105.3[d]			
	5	26	128	16.9				1.00	26	1.0	1.0 - 2.0	54.9[abcd]			
Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD)	1	49	19	72.1	88.02	12	< 0.0001	9.31	49	12.5	3.5 - 30.0	141.9[a]	< 0.0001	−0.3117	< 0.0001
	2	68	33	67.3				7.44	68	6.5	2.0 - 29.0	126.2[b]			
	3	56	50	52.8				4.04	56	10.0	3.0 - 20.0	128.4[c]			
	4	28	65	30.1				1.56	28	4.5	2.0 - 9.8	101.4			
	5	36	130	21.7				1.00	36	2.0	1.0 - 5.8	73.2[abc]			
Index of Economic Resources (IER)	1	59	29	67.0	48.93	12	< 0.0001	6.56	59	10.0	4.0 - 26.0	139.5[a]	0.0027	−0.2695	< 0.0001
	2	66	55	54.5				3.87	66	9.0	2.0 - 22.0	126[b]			
	3	55	63	46.6				2.81	55	4.0	2.0 - 20.0	114.3			
	4	30	63	32.3				1.53	30	4.5	1.0 - 15.2	106.3			
	5	27	87	23.7				1.00	27	2.0	1.0 - 8.0	80.8[ab]			
Index of Education and Occupation (IEO)	1	57	22	72.2	111.3	12	< 0.0001	11.61	57	12.0	3.5 - 28.0	138.6[a]	< 0.0001	−0.3185	< 0.0001
	2	78	30	72.2				11.66	78	8.0	3.0 - 25.0	133.7[b]			
	3	47	52	47.5				4.05	47	5.0	2.0 - 20.0	115.4[c]			
	4	26	63	29.2				1.85	26	3.0	1.0 - 10.0	98.1			
	5	29	130	18.2				1.00	29	1.0	1.0 - 5.0	65.7[abc]			

Superscript denotes statistically significant different mean rank.
Chi2 = Chi squared statistic, DF = degrees of freedom, OR = odds ratio.

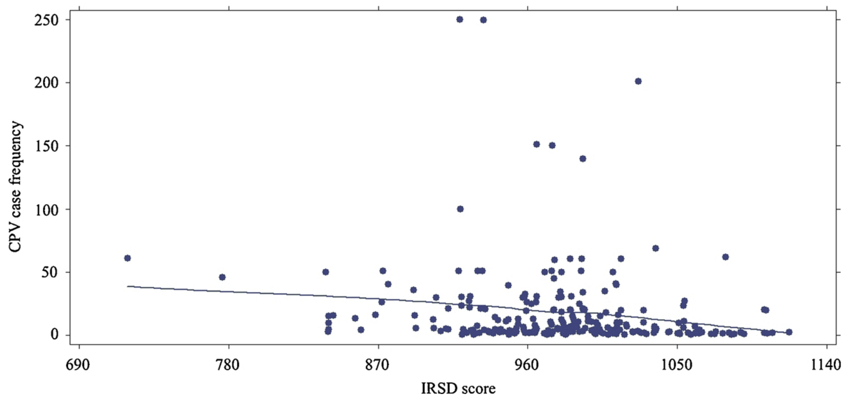

Fig. 1. Scatter plot of canine parvovirus cases reported per veterinary hospital in 2016 vs Index of Relative Socioeconomic Disadvantage score. A Loess smooth fitted curve has been overlaid, using an alpha of 0.75 and linear degree.

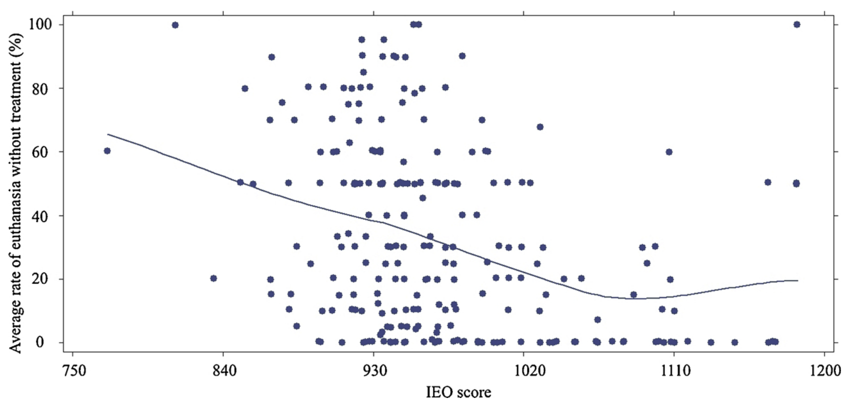

Fig. 2. Scatter plot of canine parvovirus without-treatment euthanasia rate reported per veterinary hospital in 2016 vs Index of Education and Occupation score. A Loess smooth fitted curve has been overlaid, using an alpha of 0.75 and linear degree.

Table 5
Australian canine parvovirus euthanasia rates, reported by Socioeconomic Indexes for Areas (SEIFA), 2016.

		Without Treatment Euthanasia rate						Despite Treatment Euthanasia rate					
				Kruskal-Wallis One-Way Analysis of Variance		Spearman Rank Correlation				Kruskal-Wallis One-Way Analysis of Variance		Spearman Rank Correlation	
Variable	Quintile	Median	Interquartile range	Mean rank	P-value	R	P-value	Median	Interquartile range	Mean rank	P-value	R	P-value
Index of Relative Socioeconomic Disadvantage (IRSD)	1	50.00	15.00 - 75.00	146.6[ad]	< 0.0001	−0.3224	< 0.0001	10.0	0.0 - 20.0	139	0.0841	−0.1711	0.0061
	2	27.50	10.00 - 50.00	123.8[b]				4.5	0.0 - 10.0	117.2			
	3	30.00	5.00 - 60.00	125.7[c]				5.0	0.0 - 10.0	118.2			
	4	10.00	0.00 - 30.00	86.5[d]				2.0	0.0 - 10.0	108			
	5	5.00	0.00 - 30.00	78[abc]				0.0	0.0 - 10.0	100.4			
Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD)	1	50.00	15.00 - 66.25	142.4[a]	< 0.0001	−0.3176	< 0.0001	10.0	0.0 - 15.0	133.3	0.1508	−0.1632	0.009
	2	30.00	10.00 - 50.00	128.7[b]				5.0	0.0 - 11.5	123.9			
	3	30.00	5.00 - 57.50	124.2[c]				5.0	0.0 - 10.0	118.6			
	4	17.50	0.00 - 50.00	99.5				0.0	0.0 - 13.8	103.1			
	5	5.00	0.00 - 28.75	75.9[abc]				0.0	0.0 - 10.0	103.3			
Index of Economic Resources (IER)	1	33.00	10.00 - 60.00	130.8	0.0028	−0.2678	< 0.0001	10.0	0.0 - 20.0	133.9	0.0396	−0.1933	0.0019
	2	45.00	10.00 - 62.50	137[a]				5.0	0.0 - 13.5	127.8			
	3	25.00	1.00 - 50.00	111.9				2.0	0.0 - 10.0	101.2			
	4	10.00	0.00 - 42.50	96.8				4.0	0.0 - 10.2	115.1			
	5	15.00	0.00 - 30.00	88.4[a]				0.0	0.0 - 10.0	105.5			
Index of Education and Occupation (IEO)	1	50.00	15.00 - 70.00	146.4[a]	< 0.0001	−0.3762	< 0.0001	10.0	0.5 - 19.0	138.2[a]	0.0397	−0.1817	0.0036
	2	31.50	9.75 - 57.75	130.4[b]				4.5	0.0 - 10.0	116.8			
	3	25.00	1.00 - 50.00	111.8				8.0	0.0 - 10.0	119.6			
	4	20.00	0.00 - 30.00	89.1				1.0	0.0 - 10.0	109.5			
	5	0.00	0.00 - 27.50	73[ab]				0.0	0.0 - 7.8	94.7[a]			

Superscript denotes statistically significant different mean rank.

while 11 % of hospitals (26/237) reported over 40 cases ("severe caseload" category; median 60.0, IQR 50.0–110.0). There was a significant difference for the without-treatment euthanasia rate between the low severity group, and the mild and moderate groups ($p < 0.0001$), but not for the despite-treatment euthanasia rate across any groups. The moderate severity group had the highest without-treatment euthanasia rate (median 50 %, IQR 27.5–70.0), and the low severity group had the lowest euthanasia rate (median 12.5 %, IQR 0.0–50.0%) (Table 3).

3.2. Socioeconomic disadvantage a risk factor for CPV case occurrence and euthanasia

The number of hospitals reporting CPV cases was significantly different across the quintiles of all SEIFA indices, with the Index of Education and Occupation (IEO) showing the greatest difference ($\chi^2 = 111.3$, df = 12, $p < 0.0001$). Hospitals from the most disadvantaged IEO quintile were 11.61 times more likely ($p < 0.0001$) to report CPV cases than from the least disadvantaged (57/79 versus 29/159, respectively, Table 4).

There was also a significant difference and moderate negative correlation between all SEIFA index quintiles and CPV case numbers — the less disadvantaged the area, the less CPV cases reported. The greatest difference was for the Index of Relative Socioeconomic Disadvantage (IRSD), where the least disadvantaged quintile differed in mean rank from every other quintile. This index also had the strongest negative correlation between CPV case numbers and SEIFA rank score (r_{SP} = –0.3357, $p < 0.0001$), with the most disadvantaged quintile hospitals reporting a median of 12.5 cases per annum (IQR 3.0–30.0) compared to the least disadvantaged quintile's median of 1.0 case per annum (IQR 1.0–2.0). (Table 4, Fig. 1).

The without-treatment euthanasia rate also differed significantly between the quintiles of all SEIFA indices, and also showed a significant moderate negative correlation. The highest correlation was for the Index of Education and Occupation (IEO) (r_{SP} = –0.3762, $p < 0.0001$), reflecting the higher the disadvantage, the higher the number of patients euthanized for CPV without treatment (Fig. 2). For this index, the median without-treatment euthanasia rate for the most-disadvantaged area hospitals was 50 % (IQR 15.0–70.0), compared to the least-disadvantaged area hospitals (0 %; IQR 0.0–27.5) (Table 5).

The despite-treatment euthanasia rate was only significantly different for the Index of Economic Resources (IER) and IEO ($p = 0.0396$ and 0.0397, respectively). There was a mild negative correlation between SEIFA rank score and despite-treatment euthanasia rate for all indices (Table 5).

3.3. Remoteness a risk factor for CPV case occurrence and euthanasia without treatment

There was a significant difference in the frequency of hospitals reporting CPV cases, between remoteness areas ($\chi^2 = 81.82$, df = 3, $p < 0.0001$), with hospitals in more remote areas more likely to report cases. Hospitals in the category Remote Australia were 11.61 times more likely to report cases than those in the category Major Cities of Australia.

Hospitals in areas of greater remoteness were not only more likely to report CPV cases, but also reported higher numbers of CPV cases (represented graphically for hospitals in New South Wales and

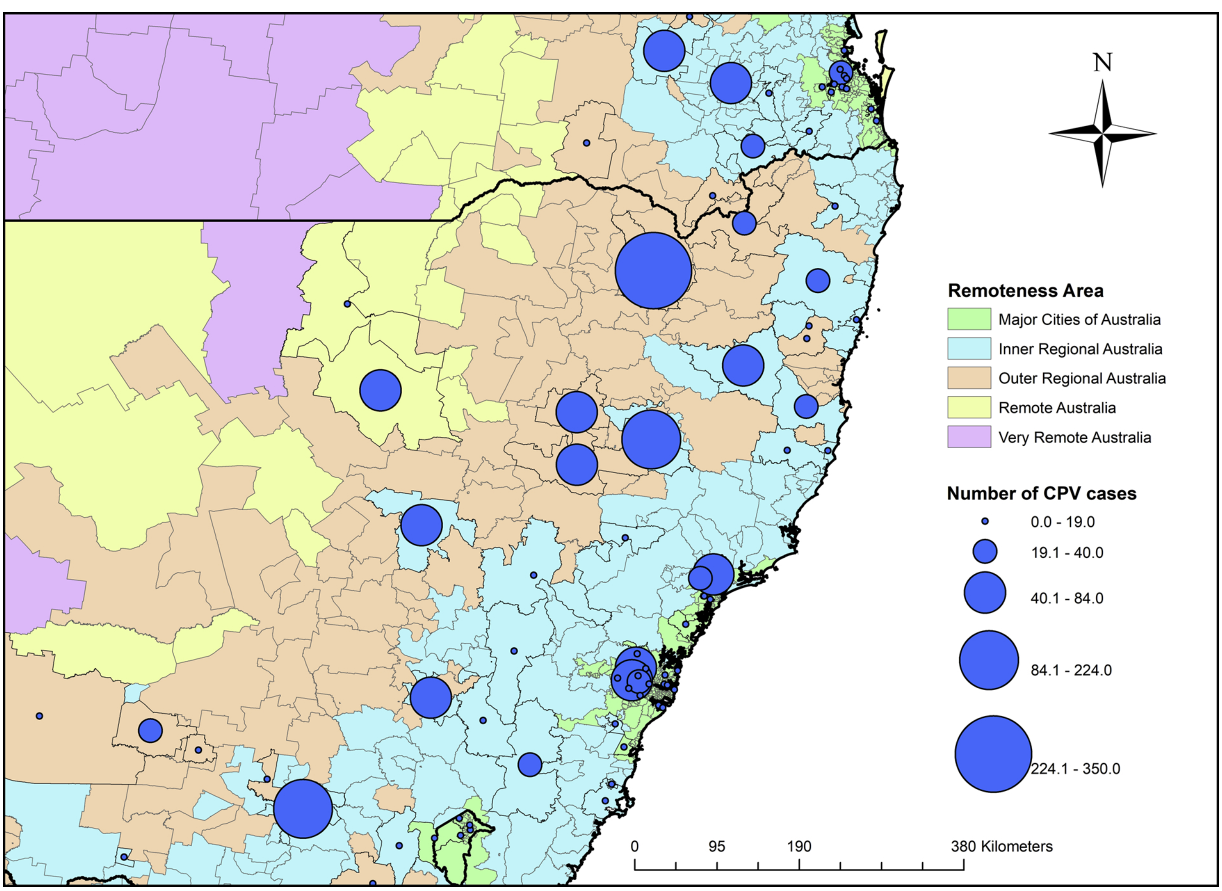

Fig. 3. Frequency of Australian canine parvovirus cases, mapped against Australia Bureau of Statistics Remoteness Areas (RA), in the states of New South Wales and Southeast Queensland, 2016.

Table 6
Australian veterinary hospitals reporting canine parvovirus cases and case numbers, reported by Remoteness Areas (RA), 2016.

Remoteness Area Category	Veterinary hospitals with CPV case occurrence in 2016						Number of Canine Parvovirus Cases in 2016, from hospitals that reported cases				
	Frequency		Hospitals seeing CPV cases (%)							Kruskal-Wallis One-Way Analysis of Variance	
	Yes	No		Chi2	P-value	Odds ratio	N	Median	Interquartile range	Mean Rank	P-value
Major Cities of Australia	90	224	28.7	81.82	< 0.0001	1.00	90	3.0	1.0 - 10.0	93.4[ab]	< 0.0001
Inner Regional Australia	82	53	60.7			3.85	82	5.5	2.0 - 20.2	119.7	
Outer Regional Australia	51	17	75.0			7.47	51	13.0	4.0 - 30.0	148.8[a]	
Remote Australia	14	3	82.4			11.61	14	20.0	10.4 - 50.0	170.8[b]	

Superscript denotes statistically significant different mean rank.

southeast Queensland; Fig. 3). Outer Regional Australia hospitals reported a median of 13 CPV cases in 2016 (IQR 4.0–30.0) and Remote Australia hospitals reported a median of 20 cases (IQR 10.4–50.0). Both were significantly higher than Major Cities of Australia hospitals (median 3.0; IQR 1.0–10.0) ($p < 0.0001$; Table 6).

The without-treatment euthanasia rate differed significantly for the remoteness areas ($p < 0.0001$), but not the despite-treatment euthanasia rate ($p = 0.1003$). The median without-treatment euthanasia rate for Major Cities of Australia hospitals was 10 % (IQR 0–36.0), which differed significantly to each of the other remoteness areas; the highest being Outer Regional Australia with a median of 50 % (IQR 12.5–62.5). (Table 7).

3.4. Climate – lower rainfall a risk factor for CPV case occurrence

There was a significant difference in the frequency of hospitals reporting CPV cases across the quintiles for each of the rainfall variables measured, with Total Annual Rainfall the most significant ($\chi^2 = 24.10$, df = 4, $p = 0.0001$). The lowest rainfall quintile was 2.16 times more likely to report cases than the highest quintile.

CPV case numbers were only statistically different between the quintiles for the variable “highest monthly rainfall” ($p = 0.0229$), however pairwise comparisons did not demonstrate any differences between pairs of mean rank scores (Table 8).

3.5. Climate – high temperature a risk factor for CPV case occurrence

There was a significant difference in the frequency of hospitals reporting CPV cases for the quintiles of “highest monthly temperature” ($\chi^2 = 94.96$, df = 4, $p < 0.0001$) and “lowest monthly temperature” ($\chi^2 = 41.61$, df = 4, $p < 0.0001$), but not for “annual mean temperature” ($\chi^2 = 8.03$, df = 4, $p = 0.0904$). Hospitals in the highest quintile for “highest monthly temperature” had a 14.25 times greater risk of reporting CPV than those in the lowest quintile.

There was a significant difference between quintiles for CPV case numbers reported, for the variables “highest monthly temperature” ($p < 0.0001$) and “annual mean temperature” ($p = 0.0087$) but not for “lowest monthly temperature” ($p = 0.0534$). There was a moderate correlation between highest monthly temperature and CPV cases – the higher the hottest month’s temperature, the more cases reported ($r_{SP} = 0.421$, $p < 0.0001$). The median annual caseload for a hospital in the highest quintile was 26.0 (IQR 6.0–50.0) compared to only 3.0 cases for the lowest quintile (IQR 2.0–8.0). A similar but weaker correlation was found for annual mean temperature ($r_{SP} = 0.2142$, $p = 0.0009$; Table 9).

3.6. Stepwise logistic regression demonstrated socioeconomic disadvantage the best-fitting model for CPV case prediction

Within predictor categories, variables most highly correlated with CPV case numbers were IRSD score, RA code, maximum temperature and minimum temperature. The best-fitting model for predicting CPV case reporting by hospitals, identified using stepwise logistic regression contained IRSD decile ($p < 0.0001$), maximum temperature quintile ($p < 0.0001$) and minimum temperature quintile ($p = 0.002$). This model produced a % correct classification of 76.8, and an R^2 of 0.371.

4. Discussion

Using data from a large national survey that broadly represented veterinary hospitals across Australia, we found that significant risk factors for CPV case-occurrence were lower socioeconomic index, high temperature, low rainfall and greater remoteness. Risk factors for euthanasia were lower socioeconomic index, remoteness and caseload severity. However, for remoteness and caseload, a significant risk was only present for euthanasia without treatment.

Table 7
Australian canine parvovirus euthanasia rates, reported by Remoteness Areas (RA), 2016.

	Without Treatment Euthanasia rate				Despite Treatment Euthanasia rate			
			Kruskal-Wallis One-Way Analysis of Variance				Kruskal-Wallis One-Way Analysis of Variance	
Remoteness Area Name	Median	Interquartile	Mean rank	P-value	Median	Interquartile	Mean rank	P-value
Major Cities of Australia	10.0	0.0 - 36.0	90[abc]	< 0.0001	1.5	0.0 - 20.0	115.5	0.1003
Inner Regional Australia	30.0	11.5 - 52.5	131.3[a]		8.0	0.0 - 10.0	131	
Outer Regional Australia	50.0	12.5 - 62.5	142.8[b]		5.0	0.0 - 10.0	113.6	
Remote Australia	40.0	17.2 - 60.0	146.5[c]		0.5	0.0 - 6.2	90.7	

Superscript denotes statistically significant different mean rank.

Approximately half the case-reporting hospitals (49 %, 116/237) reported five or less cases annually (median 2.0, IQR 1.0–3.0), suggesting that local population immunity in these areas is sufficiently high to prevent high caseloads. Seroprevalence studies in these regions would help to clarify this. In areas in which hospitals reported > 15 cases per annum, insufficient population immunity is a likely contributor to caseloads. If improved vaccination programs could be introduced to these areas, case numbers could probably be reduced. Currently, there are no documented reports of the success of targeted vaccination programs in areas where CPV seroprevalence is recognized to be low, despite our understanding that CPV vaccines are highly effective in preventing disease. It may also be that dogs in remote areas are more likely to be free-roaming or have greater contact with other dogs (Mustiana et al., 2015), resulting in faster disease transmission.

Social disadvantage has been suggested previously as a risk factor for CPV (Brady et al., 2012; Brunner and Swango, 1985). Our multivariate analysis of national data demonstrated this was also a significant variable in our study, confirming this finding. An association between CPV case occurrence and socioeconomic status might be due to vaccine affordability (Brady et al., 2012; Zourkas et al., 2015) or reduced accessibility to veterinary facilities, (Brady et al., 2012; Freiwald et al., 2014) however scientific evidence to support this has been lacking. A perceived lack of affordability of vaccination has been recognized. A 2017 UK study reported that 25 % of owned dogs and 35 % of owned cats had not had a primary vaccination course, and that 20 % of UK dog and cat owners believed that vaccinations were 'too expensive'; a 2011 USA survey reported similar results (Burns, 2013; "Pets at risk as vaccinations decline," 2017). These reports highlight a socioeconomic gap between the need for pet ownership and the ability of pet owners to afford or prioritize paying for pet healthcare. Reduced prophylactic pet healthcare due to financial constraints or other social factors could also increase risk for gastrointestinal co-pathogens such as hookworm, roundworm, tapeworm, giardia, *Cryptosporidium parvum*, canine enteric coronavirus, and canine distemper virus which have been identified as risk-factors for CPV disease (Carman and Povey, 1982; de Castro et al., 2007; Denholm et al., 2001; Duijvestijn et al., 2016; O'Sullivan et al., 1984; Pollock, 1982; Pratelli et al., 1999; Smith et al., 1980; Zicola et al., 2012). For example, an Argentinian study found an increasing gradient of contamination of sidewalks by canine faeces and an increase in faecal parasites, as socioeconomic status decreased (Rubel and Wisnivesky, 2005). Stress, immune suppression, and overcrowded unsanitary environments are also reported CPV predisposing factors and could be confounders of a socioeconomic link (Brunner and Swango, 1985; Goddard and Leisewitz, 2010; Hoskins, 1997).

A rural predisposition for CPV cases has been reported previously in Australia (Zourkas et al., 2015) and high CPV-seroprevalence has also been reported in rural regions in other countries (Acosta-Jamett et al., 2015; Belsare and Gompper, 2013; Orozco et al., 2014). Potential risk factors for CPV cases in rural regions could include reduced access to veterinary services and reduced vaccination rates, due to a shortage of rural veterinarians (Australian Veterinary Association, 2019), and longer travel distances leading to increased difficulty in maintaining consistent vaccination coverage. The relationship between geographical remoteness and vaccination rates has not been investigated. National surveillance of companion animal vaccination rates and seroprevalence rates could be useful in helping identify areas where population immunity is lacking and disease risk is therefore increased.

We found an association between areas of lower rainfall (annual, highest daily or highest monthly) and higher occurrence of CPV-reporting hospitals. This strengthens the findings of a previous Australian study (Rika-Heke et al., 2015) that found a significant negative cross-correlation between parvovirus occurrence and rainfall 4–6 months previously, suggesting that an extended dry period resulted in more cases. Taken together, these results suggest that periods of reduced rainfall might contribute to environmental persistence of CPV, increasing the risk of exposure of an individual.

We identified, for the first time, a strong association between high temperature in the hottest month of the year, and higher annual CPV case reporting and case numbers. While previous studies have examined seasonality of cases, relationships with ambient temperature have not been examined. Seasonality as a risk factor for CPV cases has been reported in New Zealand (Horner, 1983), Canada (Houston et al., 1996) and Brazil (Castro et al., 2007) (spring and summer); in Colorado, USA (Studdert et al., 1983) (summer and autumn); and in Australia (autumn and spring) (Ling et al., 2012). A spring/summer predilection for cases might reflect breeding patterns — more puppies born during this period — and also movement of animals during vacation periods to shows and boarding kennels (Horner, 1983). Our finding of a strong association between CPV cases and maximum temperature in the hottest month of the year suggests that animal factors and short-term transmission might play a more important role in disease spread than environmental viral contamination and persistence (Gordon and Angrick, 1986). Our results also suggest that higher environmental temperature alone is inadequate to prevent environmental viral persistence and transmission. Virus may persist in shaded, humid environments long enough to continue propagating outbreaks observed (Gordon and Angrick, 1986; Pollock, 1982). In-vitro and environmental studies on viral longevity suggest that moisture content is a potentially important factor for survival, as where dehydration was noticed, titer reduction and loss of infectivity was evident (Pollock, 1982). A USA environmental study conducted between December 1982 and August 1983, examined CPV-infected feces buried in soil 25 cm deep at various locations of direct sunlight, complete shade and partial shade. CPV infectivity in all but 3 sites had dropped to non-infectious levels by 5 months and only one shaded site remained infectious at 7 months (Gordon and Angrick, 1986). We also found an association between lowest minimum temperature of the coldest month, and higher case reporting. This might reflect survivability of the virus in colder environmental conditions. Epidemiological studies of seasonal patterns over several years in local, endemic regions have never been published and would be useful to provide insight into individual microclimates and specific local risk factors.

Euthanasia is the leading cause of CPV-related death in Australia,

Table 8
Rainfall risk factors for canine parvovirus occurrence in veterinary hospitals and case numbers, in 2016. Odds ratios were only calculated for significant ($p < 0.05$) risk factors.

		Veterinary hospitals with CPV case occurrence in 2016							Number of CPV cases in 2016, from hospitals that reported cases						
		Frequency		Hospitals seeing CPV cases (%)					Kruskal-Wallis One-Way Analysis of Variance					Spearman Rank Correlation	
Variable	Quintile	Yes	No		Chi2	DF	P-value	OR	N	Median	IQR	Mean rank	P-value	R	P-value
Total Annual Rainfall	1	65	44	59.6	24.10	4	0.0001	2.16	47	5.0	2.0 - 22.5	119.4	0.1586	−0.0743	0.2544
	2	47	65	42.0				1.06	48	6.0	2.0 - 19.8	119.7			
	3	54	47	53.5				1.68	47	9.0	2.0 - 27.0	128.2			
	4	36	71	33.6				0.74	51	6.0	2.0 - 25.0	128.7			
	5	35	70	33.3				1.00	44	3.0	2.0 - 9.5	96.8			
Highest Daily Rainfall	1	60	52	53.6	17.68	4	0.0014	1.69	52	5.0	2.0 - 15.0	114.1	0.4779	0.0306	0.6392
	2	55	47	53.9				1.71	45	10.0	3.0 - 22.5	130.3			
	3	52	64	44.8				1.19	45	4.0	1.0 - 23.5	105.8			
	4	29	69	29.6				0.62	48	7.0	2.0 - 23.8	123.2			
	5	41	65	38.7				1.00	47	7.0	2.0 - 20.0	122			
Highest Monthly Rainfall	1	60	47	56.1	20.50	4	0.0004	1.87	47	5.0	2.0 - 15.0	106.5	0.0229	0.1117	0.0861
	2	48	60	44.4				1.17	48	4.0	2.0 - 15.0	108.3			
	3	58	48	54.7				1.77	47	13.0	3.0 - 34.0	144.3			
	4	34	73	31.8				0.68	49	4.0	2.0 - 14.0	108.5			
	5	38	68	35.8				1.00	46	8.0	2.0 - 21.25	128.3			

Superscript denotes statistically significant different mean rank.
Chi2 = Chi squared statistic, DF = degrees of freedom, OR = odds ratio.

with national euthanasia rates between 24 % and 41 % of CPV cases (Kelman et al., 2019; Ling et al., 2012). CPV infection or infectious contact was also cited as the reason for euthanasia of 45 % of puppies in RSPCA animals shelters in Queensland in 2014 (Hemy et al., 2017). To examine CPV risk factors for euthanasia in this study, we collected data on euthanasia rates without treatment, versus where treatment for disease had commenced and a decision for euthanasia was later made, since different factors would likely influence either decision. We hypothesized that clients with severe financial constraints would be more likely to elect euthanasia without attempting treatment (Kelman et al., 2019). In the current study we identified a strong association between social disadvantage and without-treatment euthanasia rate, across all SEIFA indices. The decision to euthanize a dog diagnosed with CPV infection is also likely be influenced by the severity of clinical disease. Severe cases of CPV are considered painful (Mylonakis et al., 2016; Prittie, 2004; Sos, 1983) and prognosis can be poor (Prittie, 2004; Schoeman et al., 2013). This can lead a veterinarian to recommend euthanasia on humane grounds, or for the pet owner to elect for this course, with or without such a recommendation.

With an increased risk of euthanasia for socioeconomically-disadvantaged clients, veterinarians need to carefully assess suspected CPV cases of these clients to reduce the risk of mis-informed euthanasia decisions. The availability of PCR and immunochromatography tests has made detection of CPV infection easier for clinicians. However, given that 80 % of infections may be subclinical, mild or transient (Parrish et al., 1982; Pollock, 1981; Prittie, 2004; Sos, 1983), this also increases the risk of a misdiagnosis of CPV disease where etiology may involve pathogens other than CPV (Freisl et al., 2017; Kelman et al., 2019). For the despite-treatment euthanasia rate, the correlations were still significant although not as strong. This suggests that for those clients who elect to treat cases, socioeconomic factors are less of a determinant in the decision to subsequently elect for euthanasia, but still play a role.

The average cost to treat a CPV case in Australia is $1500 (Kelman et al., 2019). In a 2011 Chicago pet-owner survey, those in the lowest income demographic were less likely to spend > $1000 on their pets, despite the same level of attachment reported as higher demographics (Freiwald et al., 2014). In a 2011 USA survey, 29.3 % of dog owners who did not visit a veterinarian cited a lack of affordability as the reason (Burns, 2013). A recent USA study demonstrated that households in the highest income category (> $70 K) spent 114 % more on pet care than the lowest income category (< $20 K) (Einav et al., 2016). We previously found a moderate correlation ($r_{SP} = 0.1739$, $p = 0.0053$) between cost of CPV treatment and rate of euthanasia without treatment (Kelman et al., 2019). These findings all support that affordability to treat CPV disease is likely an important reason for euthanasia, especially for socioeconomically disadvantaged dog owners.

Remoteness was also significantly associated with increased euthanasia without-treatment ($p < 0.0001$) but not despite-treatment ($p = 0.1003$). This could be due to the increased difficulty to accessing veterinary services, including limited treatment options and reduced access to 24-h emergency and specialist care facilities required for more severe CPV cases. Caseload severity was also significantly associated with increased euthanasia without-treatment ($p < 0.0001$) but not euthanasia despite-treatment ($p = 0.0812$), which suggests that veterinarians or clients are more likely to attempt to treat CPV cases when they have had less experience with the disease. It is also possible that in low-risk environments that CPV is not suspected initially, and supportive treatment started before a diagnosis is made. In this scenario, patient improvement could encourage ongoing treatment in a patient that will recover, where euthanasia may otherwise have been elected if CPV was diagnosed pre-treatment.

The limitations of this study include that some case reporting figures were estimated by survey respondents, and we did not ascertain the degree of diagnostic testing performed to confirm cases, which may lead to inaccuracy of some data. It has previously been reported that

Table 9
Temperature risk factors for canine parvovirus occurrence in veterinary hospitals and case numbers, in 2016. Odds ratios were only calculated for significant ($p < 0.05$) risk factors.

		Veterinary hospitals with CPV case occurrence in 2016							Number of CPV cases in 2016, from hospitals that reported cases						
		Frequency		Hospitals seeing CPV cases (%)								Kruskal-Wallis One-Way Analysis of Variance		Spearman Rank Correlation	
Variable	Quintile	Yes	No		Chi2	DF	P-value	OR	N	Median	IQR	Mean rank	P-value	R	P-value
Annual mean temperature*	1	49	60	45.0	8.03	4	0.0904		47	4.0	1.0 - 13.0	96.8[a]	0.0087	0.2142	0.0009
	2	40	67	37.4					48	5.0	2.0 - 23.0	116.8			
	3	57	51	52.8					47	6.0	2.0 - 21.0	122.5			
	4	40	66	37.7					50	4.0	2.0 - 19.2	112.9			
	5	51	53	49.0					45	15.0	4.5 - 32.5	147.6[a]			
Highest monthly temperature**	1	32	77	29.4	94.96	4	< 0.0001	1.00	47	3.0	2.0 - 8.0	93.9[ad]	< 0.0001	0.421	< 0.0001
	2	33	83	28.4				0.96	49	2.0	1.0 - 10.0	85.1[be]			
	3	35	74	32.1				1.14	46	6.0	2.0 - 20.0	119.6[c]			
	4	60	50	54.5				2.89	52	10.0	3.2 - 23.0	134.9[de]			
	5	77	13	85.6				14.25	43	26.0	6.0 - 50.0	165.1[abc]			
Lowest monthly temperature***	1	71	37	65.7	41.61	4	< 0.0001	2.81	47	7.0	2.0 - 30.0	125.2	0.0534	−0.0175	0.7883
	2	55	53	50.9				1.52	49	8.0	2.0 - 30.0	130.4			
	3	44	64	40.7				1.01	48	4.5	2.0 - 17.8	108.5			
	4	26	83	23.9				0.46	48	3.5	2.0 - 11.5	98.4			
	5	41	60	40.6				1.00	45	9.0	2.5 - 23.0	133.2			

Superscript denotes statistically significant different mean rank.
Chi2 = Chi squared statistic, DF = degrees of freedom, OR = odds ratio.
* Measured by annual mean of monthly mean of mean daily temperatures.
** Measured by monthly mean of daily maximum temperatures.
*** Measured by monthly mean of daily minimum temperatures.

72.4 % of CPV cases recorded by veterinarians were based on diagnostic testing (Zourkas et al., 2015), and a similar occurrence is probably likely for our study. As the survey was voluntary and prospective, reporting bias may have resulted in under-reporting or over-reporting of cases, especially for hospitals estimating results. Only cases seen by veterinarians were accepted so it is likely that actual numbers are higher, particularly for communities where veterinary attendance rates are low. Only annual data were recorded in our survey, however CPV cases have been reported to occur with some seasonality (Brady et al., 2012; Duijvestijn et al., 2016; Horner, 1983; Houston et al., 1996; Ling et al., 2012; Zhao et al., 2016), which may account for lower correlations in some of our findings. Due to a lack of dog population data for the categories analyzed, we were unable to estimate disease incidence or prevalence in this analysis. Despite these limitations, the benefit of our study design was to be able to achieve a "snapshot" of CPV case occurrence and risk factors across Australia and to gain broadly representative data for the nation, for the first time.

5. Conclusions

With euthanasia without treatment being the highest cause of death from CPV, accurate communication of prognosis in dogs with mild CPV-associated disease may safeguard against unnecessary euthanasia decisions in future. This may be especially important for socio-economically-disadvantaged clients where euthanasia risk is highest. The correlation between CPV cases and socioeconomics also highlights that social issues and affordability are likely major factors in the spread of this disease, and suggests that discounted vaccination programs for disadvantaged persons could help to reduce disease occurrence, and should be considered in endemic regions.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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