Epidemiology of methicillin resistant Staphylococcus species carriage in companion animals in the Greater Brisbane Area, Australia

Hester Rynhoud (✉ h.rynhoud@uq.edu.au)  
University of Queensland  https://orcid.org/0000-0002-9491-5118

Erika Meler  
University of Queensland

Justine S Gibson  
University of Queensland

Rochelle Price  
University of Queensland

Tina Maguire  
University of Queensland

Trisha Farry  
University of Queensland

Emma Bennett  
University of Queensland

Josephine Hartono  
University of Queensland

Ricardo J Soares Magalhães  
University of Queensland

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Abstract

**Background:** Methicillin resistant *Staphylococcus* species such as *S. aureus* (MRSA) and *S. pseudintermedius* (MRSP) can be involved in life-threatening multidrug resistant infections in companion animals. Knowledge of methicillin resistant *Staphylococcus* (MRS) carriage and factors influencing carriage in companion animals from South East Queensland is limited. Nasal and rectal swab samples were collected from dogs, cats and horses upon admission or within 24 hours of hospitalisation to several primary accession and referral veterinary practices between November 2015 and December 2017. MRSA and MRSP were identified using standard microbiological (Brilliance selective medium) and molecular (*mecA* gene PCR) methods. Risk factors associated with methicillin resistant *Staphylococcus* (MRS) carriage were quantified using Bernoulli logistic regression models. A Bayesian geostatistical model was developed to predict the probability of MRS carriage in Brisbane and surrounding areas.

**Results:** Our results indicated that while the prevalence of MRSP carriage in dogs was 8.7% (35/402) no MRSP was isolated from cats (0/69) and horses (0/60); no MRSA was isolated in any species. MRSP carriage in dogs was significantly associated with previous hospitalisation, previous bacterial infection, consultation type, average precipitation, and human population density. Our predictive map of MRSP carriage indicated that the probability of carriage was highest along the coastal areas of Greater Brisbane, particularly Brisbane city, Sunshine Coast and Gympie areas.

**Conclusions:** This study determined that MRSP carriage in dog populations from South East Queensland is geographically clustered and associated with both clinical and environmental factors.

**Background**

Methicillin resistant *Staphylococcus aureus* (MRSA) and methicillin resistant *S. pseudintermedius* (MRSP) are important opportunistic pathogens in human and veterinary medicine and their broad range of antimicrobial resistance can hinder treatment in people and animals (1). Methicillin resistant *S. aureus*, a predominant human pathogen, has gained attention in the veterinary community due to its detection in healthy and diseased dogs, cats and horses (2, 3). In contrast, MRSP is commonly isolated from dogs and cats but has been rarely identified in horses and human infections (4). Both MRSA and MRSP can exist commensally on the skin, nares and intestinal tract of animals and humans but can also become opportunistic pathogens (5). Case reports have shown risks for zoonotic transmission for both MRSA and MRSP (6, 7). The first case of a non-invasive infection due to zoonotic transmission was identified in a human with otitis externa who had the same strain of *S. pseudintermedius* (previously *S. intermedius*) as the carriage isolates from her pet dog (8).

Methicillin resistant *S. aureus* carriage in humans and MRSP carriage in dogs can be risk factors for infections (9–11). Studies have shown that decolonisation of methicillin resistant and susceptible *S. aureus* in human surgical patients reduce their risk for developing health care-associated infections (12–14). MRSP carriage was also shown to be a risk factor for surgical site infections in dogs (9). However,
carriage of *Staphylococcus* may persist despite systemic antibiotic treatments and after successfully treating a MRSP infection (15). Finally, to show the impact of carriage not only in animals but also in humans, case reports can be found in the literature of animals with no clinical signs acting as reservoirs of bacteria for recurring infections in their owner. A mupirocin resistant MRSA infection in people was linked back to the family dog and further reoccurrence of the infection was prevented by decolonisation of MRSA from the dog's nares (16). Investigating the epidemiology of MRSA and MRSP carriage in companion animals is therefore a critical step to understand the possible implications for human and animal health.

Identifying populations at higher risk of carriage or infection and their determinants is critical information to target infection control strategies. For example, Chusri, Chongsuvivatwong (17) utilised spatiotemporal analyses to identify clusters of *Acinetobacter baumannii* infections within and between ward outbreaks in a human hospital indicating the need to improve infection control practices. Spatial studies regarding companion animals have focused more on disease distribution in communities rather than hospitals (18, 19). Worthing, Abraham (20) described the geographical distribution of clinical MRSP isolates based on multilocus sequence typing (MLST) types across Australia; however, their study did not explore risk factors that could explain the spatial distribution and geographical clustering. The literature is lacking information overall regarding the spatial patterns of MRS carriage in animals.

In this study we, aimed to quantify the epidemiology of MRSA and MRSP carriage in dogs, cats, and horses in South East Queensland by identifying potential risk factors and the geographical distribution of at-risk areas.

**Methods**

**Target population and study design**

The target population of the study included companion animals presenting to veterinary clinics in South East Queensland. Samples from 402 dogs, 69 cats and 60 horses were collected with owner’s consent at six collaborating clinics and/or hospital between November 2015 and December 2017 in Brisbane, Queensland, Australia. These included two private referral hospitals, two veterinary teaching hospitals, and two general practice clinics. The inclusion criteria included animals that had not been hospitalised for more than 24 hours to reduce the likelihood of isolating hospital associated MRS. Nasal and rectal swabs were collected from animals at the time of consultation or within 24 hours of admission. Studies have reported better detection of staphylococci using two samples; and that rectal swabs were better for MRSP and nasal for MRSA detection (15, 21). A mixture of healthy and diseased animals were sampled (Supplementary Table 1).

**Sample processing**

Once samples were collected, the transport media swabs were stored at 4 °C. They were transported to the laboratory for processing within five days from collection. All swab (larger M40 and smaller E-swabs)
samples were initially incubated aerobically in Mueller Hinton broth containing 6.5% NaCl (w/v) overnight (Thermo Fisher Scientific, Thebarton, South Australia, Australia). Staphylococcus isolation and identification was achieved using routine microbiological tests including selective MRSA 2 Brilliance™ agar (Thermo Fisher Scientific), Gram staining, catalase and coagulase testing. *S. aureus* colonies culture as a dark denim blue colour, and *S. pseudintermedius* colonies a lighter denim blue colour on MRSA 2 Brilliance agar. Both organisms are gram positive, catalase and coagulase positive. A multiplex PCR was performed to distinguish between MRSA and MRSP (22). Methicillin resistance was determined phenotypically by performing disk diffusion antimicrobial sensitivity tests using 1 µg oxacillin or 30 µg cefoxitin following CLSI guidelines (23). Resistance was also determined genotypically by the presence of the *mecA* gene using polymerase chain reaction (PCR) (24).

**Risk factor data**

Animal demographic and clinical history data up to 12 months prior to sampling was extracted from each animal’s medical record and stored in a MS Excel database. Recorded data included signalment, household geographical location, previous medication use, previous bacterial infections, previous hospital visits, hospitalisation, and surgeries (Table 1).
Table 1
Variables included in univariable logistic regression analysis

| Variables                      | Details                                                                                                                                                                                                 |
|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Individual Factors**         |                                                                                                                                                                                                       |
| 1 Species                      | Dogs, cats and horses                                                                                                                                                                                  |
| 2 Age (years)                  | $\leq 1, 1–3, 4–6, 7–9, \geq 10$                                                                                                                                                                     |
| 3 Sex                          | Female or male                                                                                                                                                                                          |
| 4 Breed                        | Herding, Sporting, Non-Sporting, Working, Hounds, Terriers, Toy and mixed                                                                                                                                  |
| 5 Neuter status                | Desexed or entire                                                                                                                                                                                        |
| 6 Location of sampling         | Clinic A-F                                                                                                                                                                                              |
| 7 Prior bacterial infection    | Yes/no                                                                                                                                                                                                  |
| 8 Prior visit to clinic        | Yes/no                                                                                                                                                                                                  |
| 9 Prior hospitalisation        | Yes/no                                                                                                                                                                                                  |
| 10 Prior surgery               | Yes/no                                                                                                                                                                                                  |
| 11 Chemotherapy                | Yes/no                                                                                                                                                                                                  |
| 12 Antimicrobial combination   | Combinations of the time periods in which drugs were taken. Antimicrobial use was recorded for 5 intervals (day of sampling, 1 month prior, 1–3 months prior, 3–6 months prior and 6–12 months prior to sampling). By combining the use over the 5 time intervals we created a variable summarising usage patterns e.g. 10000 means that antimicrobials were used on day of sampling but not in any of the 12 months prior. |
| 13 Corticoid combination       | Same as antimicrobial combination                                                                                                                                                                       |
| 14 Consultation type           | General practice, internal medicine, dermatology, surgery, healthy                                                                                                                                       |
| **Environmental and Demographic Factors** |                                                                                                                                                                                                 |

| Variables | Details |
|-----------|---------|
| 15        | Urban vs Rural | Whether animals residential address was in an urban or rural area (30) |
| 16        | Socio-economic indexes for areas | Deciles representing indexes of relative socio-economic advantage and disadvantage in 2016. |
| 17        | Average Precipitation (mm) | Values extracted from map |
| 18        | Average Temperature (°C) | Values extracted from map |
| 19        | Elevation (m) | Values extracted from map |
| 20        | Human Population | Values extracted from map |

Data on potential socioeconomic and environmental risk factors (Table 1) for carriage were obtained from available maps and linked to each household coordinate using a geographic information system (QGIS version 2.18.12, and ArcMap version 10.6.1) (25).

Socio-Economic indexes for areas (SEIFA) data were retrieved from the Australian Bureau of Statistics (26). SEIFA data were provided for greater Brisbane postcodes as deciles ordered from lowest (1) to highest (10) scores. SEIFA deciles were extracted for each animal street address by performing a spatial join with the postcode of their place of residence. Due to the distribution of the SEIFA scores in the sample population every two decile categories were merged. Further to that, relevant environmental maps were downloaded from: average temperature and precipitation maps (with a resolution of ~ 1 km²) were retrieved from WorldClim version 2 (27) for the elevation map (with a resolution of ~ 0.8 km²) were retrieved from DIVA-GIS (28), human population density from 2017 (with a resolution of 3 arc approximately 100 m at the equator) was obtained from the WorldPop project site (29) and the urban extents grid was obtained from the Global Rural-Urban Mapping Project, version 1 (30).

**Statistical analysis**

Statistical analyses for this study were divided into three phases. First, we performed Bernoulli logistic regression to provide insights into the association between methicillin resistant *Staphylococcus* (MRS) spp. carriage and predictors (individual-level and, socioeconomic and environmental). The Akaike information criterion (AIC) was used as an indicator of the model fit. The lower AIC is an indication of a better fitted model. Second, we then tested for the presence of residual spatial autocorrelation in MRS carriage probability using semivariograms. Finally, we developed a spatial prediction model of MRS carriage using a Bernoulli geostatistical model with the Bayesian statistical software, OpenBUGS version 3.2.3 rev 1012 (Medical Research Council Biostatistics Unit, Cambridge, UK and Imperial College London, London, UK).

*Risk factors for methicillin resistant Staphylococcus spp. carriage*
Risk factors for MRS carriage were evaluated using univariable and multivariable Bernoulli logistic regression models for each species with MRS carriage as the outcome of interest. Location of sampling was included as a random effect in both univariable and multivariable analyses to account for multiple observations at the same clinics and to standardise error. All other factors were included as fixed effects. Firstly, univariable models were used to identify any association between the risk factors and MRS carriage based on a conservative \( p \)-value of 0.20. Pearson’s correlation coefficient was used to test for any correlation between variables. Risk factors that had a \( p \)-value of 0.20 or less in the first phase were then included in a manual backward stepwise variable selection process in a multivariable logistic regression analysis. Confounders were identified by assessing the impact of their removal on the coefficients of the remaining variables. If the coefficient of one variable changed by more than 25% when a variable was eliminated, then it was considered a confounder and put back into the multivariable model. Risk factors included in the final multivariable model with a \( p \)-value of 0.05 or less were termed significant in this study.

Two multivariable models were created, one model including demographic and clinical factors only and one including demographic, clinical and environmental factors (average land temperature, average precipitation, elevation, human population density, socio-economic status and urban vs rural location data). Regression statistical analyses were performed using the statistical software Stata version 13.1 (Stata Corporation, College Station, TX, USA).

**Analysis of residual geographical clustering of methicillin resistant Staphylococcus species**

Semivariograms of the residuals from the final multivariable models (including and excluding environmental factors) were used to quantify the extent of geographical clustering of MRSA or MRSP carriage in dogs after accounting for all risk factors in the final Bernoulli logistic regression model (31). The semivariogram is a graphical representation of the variation in observations between all pairs of dogs located at a series of defined separating distances. The semivariogram is defined by three parameters including the nugget, the partial sill and the range. The nugget is the spatially unstructured variation which represents the natural random variation, very small-scale spatial variability or measurement error. The partial sill is the spatially structured variance which can represent the tendency for geographical clustering. The range is an indication of the size of clusters as it represents the separating distance at which spatial autocorrelation ceases to occur. The proportion of the variance that is spatially structured was estimated by dividing the partial sill by the sum of the partial sill and nugget. This measure indicates the role of location in explaining the variation in MRSA and MRSP carriage in dogs in the greater Brisbane area (also known as the propensity for geographical clustering). Residual semivariograms were produced using the geoR package in R version 3.4.1 (The R foundation for statistical computing, Vienna, Austria).

**Spatial risk prediction of methicillin resistant Staphylococcus species and model validation**

A model-based geostatistical model of MRS carriage in client owned dogs was built using OpenBUGS version 3.2.3 rev 1012. A total of 391 individual observations were included in the analysis. Initial
covariates included sex and age categories (<1 y, 1–4 y, >4–7 y, >7–10 y and >10 y) as fixed effects, and the average values of precipitation, temperature, elevation and human population density extracted at the home address of dog owners as a spatial random effects. Environmental variables were standardised by subtracting the mean and dividing by the standard deviation. A predictive model was run with the age sex combination that had a higher influence on carriage (being a female and age categories >7–10 y and >10 y). The outputs of the Bayesian models are distributions termed ‘posterior distributions’, which represent the uncertainty associated with the parameter estimates. Posterior means predictions and standard deviations of the mean prediction were categorised and mapped using ArcMap version 10.6.1 (ESRI 2018). The model’s ability to correctly predict carriage was analysed using the receiver operating characteristic (ROC) analysis in Stata. The carriage status of 391 observations were compared to the posterior mean estimates of carriage in the learning phase of the model.

Results

Prevalence of methicillin resistant Staphylococci

The MRSP prevalence in dogs was 8.7% (35/402), 0% in cats (0/69) and 0% in horses (0/60). Of the dogs who carried MRSP, 9% (3/35) were infected (one with a skin abscess and severe alopecia, one with toxoplasmosis, and one with an infected eye); 9% (3/34) were healthy with no recorded disease; 11% (4/35) had unknown health statuses and 71% (25/35) had non infectious diseases. No MRSA was isolated. There were equal numbers of nasal (n = 26) and rectal (n = 26) positive results. Fifteen dogs (out of a total of 35) were MRSP positive from both nasal and rectal swabs.

Fifty-one percent of MRSP negative (187/367) and positive (18/35) dogs were female, where 48% (175/367) of MRSP negative and 40% (14/35) of MRSP positive were male. Seventy-three percent (267/367) of MRSP negative and 63% (22/35) of MRSP positive dogs were neutered where 26% (95/367) and 29% (10/35) were entire. Fifteen percent (55/376) of MRSP negative and 6% (2/35) of MRSP positive dogs were under one year old. Twenty percent of MRSP negative (75/367) and positive dogs (7/35) were between one and four years old. Twenty two percent (81/367) of MRSP negative and 14% (5/35) of MRSP positive dogs were between four and seven years old. Twenty two percent (80/367) of MRSP negative and 29% (10/35) of MRSP positive dogs were between seven and ten years old. Nineteen percent (69/367) of MRSP negative and 23% (8/35) of MRSP positive dogs were over ten years old. The age of 2% (7/367) and the sex and neuter status of 1% (5/376) were unknown for MRSP negative dogs. The age, sex and neuter status of nine percent (3/35) of positive dogs were unknown.

Three clinics out of the six yielded patients’ positive for MRSP. Forty percent (14/35) were from one referral hospital, 34% (12/35) were from a teaching hospital and 26% (9/35) were from the other referral hospital. The carriage rate in the one referral hospital was 5% (14/102), 14% (12/249) in the teaching hospital, and 31% (9/29) in the other referral hospital. No MRSP was isolated from the animals sampled in the two general practices.

Risk factors for methicillin resistant MRSP carriage
Only dog data were analysed as there was no MRSP carriage identified in cats and horses sampled in this study. The univariable screening ($p < 0.2$) determined that sex, neuter status, prior clinic visit, prior bacterial infection, prior hospitalisation, prior surgery, chemotherapy, consultation type, urban or rural location, and all environmental and demographic factors should be retained in the full regression model (Table 2). The overall p-value for categorical variables was not reported due to unbalanced data where at least one category had less than five positive cases. In these cases, if the p-value of at least one category was smaller than 0.20 then it was included in the full regression model. The final multivariable model including environmental factors; i.e. urban and rural data, elevation, temperature, precipitation, and human population density resulted in a better fit to the data [i.e. lower Akaike information criterion (AIC) ($AIC = 163$) compared to the model with demographic and clinical factors only ($AIC = 173$)].
Table 2
Univariable analysis of associations between methicillin resistant Staphylococci carriage in dogs and individual/environmental factors.

| Variable                      | Odds Ratio (95% Confidence Interval) | P value |
|-------------------------------|--------------------------------------|---------|
| Age (years)                   |                                      |         |
| < 1                           | reference                            |         |
| > 1 to 4                      | 1.05 (0.95–1.16)                     | 0.315   |
| > 4 to 7                      | 1.02 (0.96–1.09)                     | 0.484   |
| > 7 to 10                     | 1.08 (0.92–1.26)                     | 0.338   |
| > 10                          | 1.07 (0.95–1.20)                     | 0.242   |
| Sex                           |                                      |         |
| Male                          | reference                            |         |
| Female                        | 1.01 (1.00–1.03)                     | 0.044   |
| Breed                         |                                      |         |
| Working dogs                  | reference                            |         |
| Toy                           | 1.18 (0.72–1.93)                     | 0.515   |
| Terriers                      | 1.94 (0.82–4.63)                     | 0.133   |
| Gundogs                       | 1.76 (0.48–4.63)                     | 0.394   |
| Hounds                        | 1.44 (0.46–4.53)                     | 0.533   |
| Utility                       | 3.04 (1.53–6.03)                     | 0.001   |
| Non Sporting                  | 1.05 (0.33–3.27)                     | 0.94    |
| Crosses                       | 1.35 (0.45–4.04)                     | 0.592   |
| Neuter status                 |                                      |         |
| Entire                        | reference                            |         |
| Neutered                      | 0.98 (0.96–1.01)                     | 0.161   |
| No prior visit to clinic      | reference                            |         |
| Prior visit to clinic         | 1.06 (1.00–1.12)                     | 0.053   |
| No prior bacterial infection  | reference                            |         |
| Prior bacterial infection     | 1.12 (1.00–1.26)                     | 0.058   |
| Variable                                      | Odds Ratio       | P value |
|-----------------------------------------------|------------------|---------|
| **No prior hospitalisation**                  | reference        |         |
| **Prior hospitalisation**                     | 1.08 (1.03–1.14) | 0.003   |
| **No prior surgery**                          | reference        |         |
| **Prior surgery**                             | 1.06 (1.01–1.11) | 0.025   |
| **Not on chemotherapy**                       | reference        |         |
| **Currently on chemotherapy**                 | 1.29 (0.88–1.87) | 0.181   |
| **Antimicrobial combination**                 | **reference**    |         |
| **No antimicrobials**                         | reference        |         |
| A                                             | 1.10 (0.95–1.27) | 0.193   |
| B                                             | 1.06 (0.93–1.21) | 0.374   |
| C                                             | 1.02 (0.88–1.18) | 0.800   |
| D                                             | 1.10 (0.89–1.35) | 0.368   |
| E                                             | 1.12 (0.93–1.35) | 0.229   |
| **Corticoid combinations**                    | **reference**    |         |
| **No corticoids**                             | reference        |         |
| A                                             | 1.02 (1.01–1.04) | 0.004   |
| B                                             | 0.93 (0.88–0.98) | 0.010   |
| C                                             | 0.93 (0.86–0.98) | 0.010   |
| D                                             | 1.16 (0.87–1.54) | 0.341   |
| E                                             | 1.16 (0.87–1.55) | 0.311   |
| **Consult types**                             |                  |         |
| **General practice**                          | reference        |         |
| **Internal medicine**                         | 1.13 (0.99–1.30) | 0.078   |
| **Dermatology**                               | 1.19 (1.17–1.20) | <0.001  |
| **Surgery**                                   | 1.03 (0.93–1.14) | 0.567   |
| **Healthy**                                   | 0.99 (0.98–1.01) | 0.225   |
| **Urban**                                     | reference        |         |
| Variable                       | Odds Ratio (95 Confidence Interval) | P value |
|-------------------------------|------------------------------------|---------|
| Rural                         | 1.04 (0.99–1.10)                   | 0.092   |
| Average precipitation (mm)    | 1.00 (1.001–1.005)                 | < 0.001 |
| Average temperature (°C)      | 1.04 (1.00–1.08)                   | 0.031   |
| Average elevation(m)          | 1.00 (1.00–1.00)                   | 0.052   |
| Human population              | 1 (1–1.01)                         | < 0.001 |

**Socio-economic Status (10 Deciles)**

| Decile          | Odds Ratio (95 Confidence Interval) | P value |
|-----------------|------------------------------------|---------|
| 1 and 2         | reference                           |         |
| 3 and 4         | 1.86 (0.694–4.978)                  | 0.217   |
| 5 and 6         | 1.63 (0.159–16.641)                 | 0.679   |
| 7 and 8         | 4.98 (1.352–18.193)                 | 0.016   |
| 9 and 10        | 5.43 (2.829–10.403)                 | < 0.001 |

Dogs were used as the unit of analysis and the location of sampling as a random effect. P < 0.2 is considered significant.

†Antimicrobial combinations categories:

A = dogs received antimicrobials on day of sampling and 1 month prior, some dogs received antimicrobials up to 12 months prior to sampling, B = dogs received antimicrobials on sampling day but not 1 month prior and some dogs had antimicrobials between 1 and 12 months prior to sampling, C = dogs received no antimicrobials on sampling day but did a month prior and some dogs received antimicrobials 2 to 12 months prior to sampling, D = dogs received no antimicrobials on day of sampling and 1 month prior and some did 2 to 12 months prior, E = dogs received no antimicrobials up to 6–12 months before sampling.

‡Corticoid combinations categories:

A = dogs received corticoids on day of sampling and 1 month prior, some dogs received corticoids up to 12 months prior to sampling, B = dogs received corticoids on sampling day but not 1 month prior; and some dogs had corticoids between 1 and 12 months prior to sampling, C = dogs received no corticoids on sampling day but did a month prior and some dogs received corticoids 2 to 12 months prior to sampling, D = dogs received no corticoids on day of sampling and 1 month prior and some did 2 to 12 months prior, E = dogs received no corticoids up to 6–12 months before sampling.

The multivariable model adjusted for environmental factors revealed that dogs carrying MRSP had higher odds of experiencing prior bacterial infections and hospitalisation within the year before sampling than MRSP negative dogs [Odds Ratio (OR):1.73 (1.18–2.56), p = 0.005 and OR: 2.55 (1.24–5.24), p = 0.011, respectively] (Table 3). MRSP positive dogs had higher odds of presenting to the dermatologist and internal medicine specialist [OR: 4.40 (2.01–9.62), p < 0.001] and OR: 2.32 (1.15–4.71), p = 0.019, respectively] compared to MRSP negative dogs. Dogs carrying MRSP had higher odds of residing in
locations with increased average precipitation and human population density than MRSP negative dogs [OR: 1.02 (1.00–1.05), p = 0.022 and OR: 1.03 (1.01–1.05), p = 0.01, respectively]. Despite SEIFA being significant in the univariable model this variable lost statistical support in the final multivariable model and was not retained.
Table 3
Multivariable analysis of associations between methicillin resistant Staphylococci carriage in dogs and individual/environmental factors.

| Variable                    | Excluding environmental variables | Including environmental variables |
|-----------------------------|-----------------------------------|-----------------------------------|
|                             | OR (95% CI)                       | P > z                             | OR (95% CI)                       | P > z                             |
| Age (years)                 |                                    |                                   |                                   |                                   |
| < 1                         | reference                          |                                   | reference                          |                                   |
| > 1 to 4                    | 2.12 (0.35–2.86)                   | 0.414                             | 3.15 (0.42–23.8)                   | 0.266                             |
| > 4 to 7                    | 1.16 (0.12–1.14)                   | 0.899                             | 1.44 (0.16–12.91)                  | 0.746                             |
| > 7 to 10                   | 2.17 (0.24–9.33)                   | 0.489                             | 2.16 (0.29–16.25)                  | 0.455                             |
| > 10                        | 1.86 (0.50–6.89)                   | 0.351                             | 2.07 (0.62–6.87)                   | 0.237                             |
| Sex                         |                                    |                                   |                                   |                                   |
| Male                        | reference                          |                                   | reference                          |                                   |
| Female                      | 1.43 (0.69–3)                      | 0.339                             | 1.11 (0.67–1.84)                   | 0.676                             |
| No prior bacterial infection| reference                          |                                   | reference                          |                                   |
| Prior bacterial infection    | 1.82 (1.70–1.95)                   | < 0.001                           | 1.73 (1.18–2.56)                   | 0.005                             |
| No prior hospitalisation    | reference                          |                                   | reference                          |                                   |
| Prior hospitalisation       | 2.19 (1.18–4.05)                   | 0.012                             | 2.55 (1.24–5.24)                   | 0.011                             |
| No prior chemotherapy       | reference                          |                                   | reference                          |                                   |
| Prior chemotherapy          | 5.12 (0.84–1.12)                   | 0.076                             | 4.00 (0.56–28.53)                  | 0.166                             |
| Antimicrobial combination†  |                                    |                                   |                                   |                                   |
| No antimicrobials            | reference                          |                                   | reference                          |                                   |
| A                           | 1.58 (0.48–5.21)                   | 0.456                             | 1.13 (0.28–4.59)                   | 0.867                             |
| B                           | 1.1 (0.25–4.91)                    | 0.902                             | 0.68 (0.11–4.4)                    | 0.687                             |
| C                           | 0.85 (0.07–0.69)                   | 0.902                             | 0.68 (0.03–15.64)                  | 0.812                             |
| Variable                  | Excluding environmental variables | Including environmental variables |
|--------------------------|-----------------------------------|-----------------------------------|
|                          | OR (95% CI)                       | OR (95% CI)                       |
|                          | P > z                             | P > z                             |
| D                        | 1.29 (0.28–6.01)                  | 1.25 (0.18–8.83)                  |
|                          | 0.743                             | 0.824                             |
| E                        | 2.82 (0.55–4.48)                  | 2.55 (0.37–17.39)                 |
|                          | 0.215                             | 0.339                             |

**Corticoid combinations ‡**

| Corticoid combinations | Excluding environmental variables | Including environmental variables |
|------------------------|-----------------------------------|-----------------------------------|
|                        | OR (95% CI)                       | OR (95% CI)                       |
|                        | P > z                             | P > z                             |
| No corticoids          | reference                         | reference                         |
| A                      | 0.49 (0.12–1.99)                  | 0.68 (0.13–3.55)                  |
|                        | 0.318                             | 0.652                             |
| B                      | omitted                           | omitted                           |
| C                      | omitted                           | omitted                           |
| D                      | 1.12 (0.5–2.53)                  | 1.96 (0.74–5.2)                  |
|                        | 0.784                             | 0.179                             |
| E                      | 1.31 (0.07–5.08)                  | 1.72 (0.1–28.5)                  |
|                        | 0.856                             | 0.705                             |

**Consult types**

| Consult types            | Excluding environmental variables | Including environmental variables |
|--------------------------|-----------------------------------|-----------------------------------|
|                         | OR (95% CI)                       | OR (95% CI)                       |
|                         | P > z                             | P > z                             |
| General practice        | reference                         | reference                         |
| Internal medicine       | 2.8 (1.58–4.94)                  | 2.32 (1.15–4.71)                  |
|                         | < 0.001                           | 0.019                             |
| Dermatology             | 5.65 (3.38–9.47)                  | 4.40 (2.01–9.62)                  |
|                         | < 0.001                           | < 0.001                           |
| Surgery                 | 1.56 (0.22–11)                    | 1.12 (0.16–8.01)                  |
|                         | 0.655                             | 0.911                             |
| Average temperature (°C) |                                   | 0.82 (0.02–43.69)                 |
| Average elevation (m)    |                                   | 1 (0.98–1.02)                     |
| Average precipitation (mm) |                                 | 1.02 (1.00–1.05)                   |
|                         |                                   | 0.022                             |
| Human population        |                                   | 1.03 (1.01–1.05)                   |
|                         |                                   | 0.01                              |
| AIC                     | 173                               | 163                               |

**Health Status**

| Health Status        | Dogs | Cats | Horses |
|----------------------|------|------|--------|
| Unknown              | 44 (11%) | 10 (14%) | 8 (13%) |
| Infectious disease   | 39 (10%) | 11 (16%) | 4 (7%) |
| Non infectious disease | 211 (52%) | 20 (29%) | 14 (23%) |
| Variable                  | Excluding environmental variables | Including environmental variables |
|--------------------------|-----------------------------------|----------------------------------|
|                          | OR (95% CI) | P > z     | OR (95% CI) | P > z     |
| Non diseased             | 108 (27%)  | 28 (41%)  | 34 (57%)    |            |
| Total                    | 402        | 69        | 60          |            |

Supplementary Table 2. The posterior estimates for parameters in the learning phase of the Bayesian geostatistical model.

| Model Parameters | Posterior Mean | Posterior Standard deviation | 95% Credible Interval |
|------------------|----------------|-----------------------------|-----------------------|
| Female           | 2.259          | 3.744                       | (-0.7388–13.51)       |
| Age 1–4 years    | 4.979          | 7.131                       | (-0.6496–24.22)       |
| Age > 4–7 years  | 2.173          | 5.449                       | (-4.419–18.23)        |
| Age > 7 to 10 years | 5.252      | 7.442                       | (-0.7229–25.28)       |
| Age > 10 years   | 5.873          | 8.545                       | (-0.7485–27.07)       |
| Average precipitation (mm) | 2.657      | 3.946                       | (-2.134–13.61)        |
| Average temperature (°C) | 17.37     | 27.27                       | (-0.3244–96.97)       |
| Average elevation (m) | 8.378     | 15.13                       | (-1.634–55.42)        |
| Human population density | 0.1444    | 1.133                       | (-2.744–2.896)        |

Dogs were used as the unit of analysis and the location of sampling as a random effect. P < 0.05 is considered significant.

†Antimicrobial combinations categories:

A = dogs received antimicrobials on day of sampling and 1 month prior, some dogs received antimicrobials up to 12 months prior to sampling, B = dogs received antimicrobials on sampling day but not 1 month prior and some dogs had antimicrobials between 1 and 12 months prior to sampling, C = dogs received no antimicrobials on sampling day but did a month prior and some dogs received antimicrobials 2 to 12 months prior to sampling, D = dogs received no antimicrobials on day of sampling and 1 month prior and some did 2 to 12 months prior, E = dogs received no antimicrobials up to 6–12 months before sampling.

‡Corticoid combinations categories:
| Variable                                                                 | Excluding environmental variables | Including environmental variables |
|-------------------------------------------------------------------------|-----------------------------------|-----------------------------------|
|                                                                        | OR (95% CI)                       | OR (95% CI)                       |
|                                                                        | P > z                             | P > z                             |
| A = dogs received corticoids on day of sampling and 1 month prior,     |                                   |                                   |
| some dogs received corticoids up to 12 months prior to sampling, B =   |                                   |                                   |
| dogs received corticoids on sampling day but not 1 month prior,        |                                   |                                   |
| and some dogs had corticoids between 1 and 12 months prior to         |                                   |                                   |
| sampling, C = dogs received no corticoids on sampling day but did a    |                                   |                                   |
| month prior and some dogs received corticoids 2 to 12 months           |                                   |                                   |
| prior to sampling, D = dogs received no corticoids on day of sampling  |                                   |                                   |
| and 1 month prior and some did 2 to 12 months prior, E = dogs           |                                   |                                   |
| received no corticoids up to 6–12 months before sampling.              |                                   |                                   |

Spatial dependence and geographical risk prediction of MRSP carriage

The residual semivariogram for the model excluding environmental factors showed clustering of MRSP carriage with an average cluster size of 5.52 km and 47% propensity for clustering, after adjusting for the environmental factors average clusters increased to 6.23 km and the propensity for clustering increased to 69% (Fig. 1 and Table 4).

Table 4
The nugget, partial sill and range for residual semivariograms including and excluding environmental data.

| Redidual semivariogram parameters | Multivariable model excluding environmental data | Multivariable model including environmental data |
|----------------------------------|-------------------------------------------------|-------------------------------------------------|
| Nugget                           | 0.007114502                                     | 0.005247965                                     |
| Partial Sill                     | 0.006379589                                     | 0.011837460                                     |
| Propensity for clustering (%)    | 47                                              | 69                                              |
| Range (km)                       | 5.52                                            | 6.23                                            |

During the learning phase of our geographical model of MRSP carriage risk we found that female dogs over the age of 7 years old (combined 7–10 years and >10 years age categories) had a higher probability of MRSP carriage compared to other sex/age groups thereby providing a justification for our predictive analysis to be performed for this age/sex combination (Supplementary table 1). Our predictive map revealed that the probability of MRSP carriage rates was highest along the coast, ranging from 50% to over 70% (Fig. 2). Areas predicted to have a higher probability of MRSP carriage (>50% to >70%) include suburbs belonging to the Brisbane City Council, Sunshine Coast Regional Council, Gympie Regional Council and Gold Coast City areas. Lower carriage rates were estimated further inland, ranging from under 10–20%. Standard deviations associated with the predicted means were between 0.24 and 0.28 in the high-risk areas in Brisbane City and Sunshine Coast areas. The standard deviations were higher (0.28–0.32) in areas where predicted carriage was high in the Northern and Southern ends of the map (Noosa Shire, Gympie region and Gold Coast City). The ROC analysis revealed a ROC area of 0.99940 with 95% confidence intervals 0.99841 to 1.0 indicating a very good discriminatory ability of the model.

Discussion
This study is the first to analyse the prevalence, associated risk factors and geographical distribution of MRS carriage in South East Queensland, Australia. We identified a carriage rate of 8.7% for MRSP and 0% for MRSA in dogs. No MRS was isolated in cats or horses. These findings are in agreement with a recent study in two Sydney veterinary hospitals that isolated MRSP from 8% of veterinary personnel owned dogs and 7% of general canine hospital admissions (32). Other studies in non-clinical Australian settings have yielded much lower MRSP carriage estimates; only one MRSP was isolated from 117 healthy dogs in Victoria (33) and no MRSP on dogs from remote Aboriginal communities in Western Australia and New South Wales (34, 35). While the Victorian and Sydney study did not detect MRSA in cats or dogs, the two studies on dogs from remote Aboriginal communities in Western Australia and New South Wales identified MRSA in 2.6% of the dogs (34, 35). MRSA has been detected in Australian horses (3.7%) (2) so perhaps the lack of MRSA isolation in horses could be explained by the small sample size and single sampling location in this study, indicating the need to enrol more horses from multiple locations in future carriage investigations.

Our results also agree with existing literature from others countries where carriage rates of MRSP in dogs ranged between 3–34% for studies reported from Spain, Finland, Iran and Canada (15, 36–38). MRSP is isolated less often in cats with carriage prevalence between 4–19% as reported in the United States, Brazil and Iran (38, 39, 40). There is currently no MRSP carriage being reported in horses; however, it has been identified from clinical infections (41–43). The low isolation rate of MRSA in dogs and cats was also expected. The reported prevalence of MRSA carriage in dogs ranges between 0.5–9% in Canada, Portugal and the United Kingdom (6, 44–46). A lower prevalence of MRSA ranging between 0–4% has been reported in cats from Brazil, Portugal and the United Kingdom (6, 46, 47). MRSA reported in horses is 2–5% in Canada and the United Kingdom (46, 48).

Our findings suggest that MRSP carriage in dogs is associated with previous history of health-care contact including prior hospitalisation, prior bacterial infection and consultation type. The causal link between MRSP carriage and previous hospitalisation and prior bacterial infection is likely to be confounded by the frequency and length of stay. Indeed, previous studies on risk factors for MRS infections had demonstrated an increased risk linked to more frequent and longer admissions to veterinary clinics (37, 49, 50). This can partly be explained by the increase the likelihood of being exposed and colonised by nosocomial bacteria such as MRS as a function of longer periods spent in healthcare settings or the influence of treatments. Specific consultation types, internal medicine and dermatology, seemed to influence carriage. MRS positive dogs that visited dermatologists had odds twice as high as MRS positive dogs attending internal medicine consultations. Resistant staphylococci are predominately a skin pathogen and are frequently treated by dermatologists (51). Dogs visiting dermatologists are more likely to have a history of persistent MRS infections and increased exposure to antibiotics and corticoids, which could increase the likelihood of MRS isolation from these animals (52). Another point to consider is that higher risks of carriage associated with hospitalisation and dermatology/internal medicine visits do not necessarily mean that transmission is occurring at these locations as dogs visiting these facilities usually experience underlying diseases that expose them to antimicrobials which may facilitate resistance in methicillin susceptible S. pseudintermedius already carried on their skin. This is supported
by our finding that dogs with previous bacterial infections had higher odds of carriage. A previous study also indicated that MRSP carriage was higher in dogs that had pyoderma either previously or during sampling (52).

Our analysis is the first to reveal important ecological risk factors associated with MRSP carriage. Precipitation and human population was shown to influence MRSP carriage in dogs suggesting that the environment may play an important role on MRSP in dogs. Our results indicate that increased precipitation is a risk factor for MRSP carriage. Wang, Towers (53) found that average temperature and humidity was significantly associated with S. aureus skin and soft tissue infections in children under 19 years. MRS carriage was significantly associated with temperature and elevation in the univariable analysis (p < 0.20) in our study, but this association was lost after accounting for individual and environmental factors in the final multivariable analysis. The Bayesian analysis, however, revealed that they had a stronger effect on carriage (Supplementary table 2) compared to precipitation and human population. These results indicate a need to investigate further to determine whether temperature and elevation do in fact influence MRSP carriage in dogs. Even though temperature was not significantly associated with MRSP carriage in our dog population, precipitation might serve as a proxy for humidity in this case. Perhaps moisture is influencing the occurrence of bacterial colonisation or infections. In our study, another environmental factor influencing carriage was human population density. High human population could function as a proxy of a higher pet dog population density. Crowds have been known to be at higher risk of bacterial infections, and so the higher density in human and associated dog populations could result in higher skin contact rates between individuals thus facilitating the dissemination of MRSP through the population (54).

Our findings also demonstrate that MRSP is highly clustered in southeast Queensland. After adjusting for individual, clinical and ecological risk factors our results still indicated the presence of residual spatial autocorrelation in MRSP carriage with average cluster sizes of 6 km. The propensity for clustering increased from 47–69% when environmental variables were included in the analysis. This result indicates that MRSP transmission is likely to be spatially structured and could be driven by other environmental or behavioural factors not included in our models. MRSP can be transmitted between and persist in household pets and can survive in the environment for prolonged periods of time (55). These factors could result in transmission in the community outside of the hospital environment such as dog parks or beaches. Indeed, our predictive probability of MRSP carriage map (Fig. 2) indicates that there is higher risk of carriage along the eastern coast of Queensland from the Gold Coast to the Sunshine Coast. Risk also increases north along the coast, which is where average precipitation and temperature are higher too. These high-risk areas included the Brisbane City council, Sunshine Coast council, Noosa Shire, and Gympie regional council. Surveillance strategies associated with MRS in companion animals in South East Queensland should target these areas first. The uncertainty in the spatial prediction (as measured by the standard deviation (SD)) associated with the Brisbane and Sunshine Coast high-risk areas are low (SD: <0.20 to 0.26), which indicates a higher level of certainty associated with these results. The areas with high uncertainty (SD: >0.34) surrounding the predictions were linked to the northern areas, including Noosa Shire and Gympie, where predicted carriage was between 50 and over 70%. Higher uncertainty (SD:
>0.28–0.3) was also associated with the Gold Coast area where there was a high predicted risk of carriage. These areas should be targeted by future sampling studies to fill the gap in knowledge.

The results of our study should be interpreted in light of some limitations. First, there could be bias associated with the clinical sample of individuals we had available for our study. The inclusion of dogs presenting to referral and teaching hospitals might not be entirely representative of a typical dog population. Further, medical records are characterised by incomplete information, which could have contributed to the lack of data for areas found to be associated with high predictive uncertainty for MRSP carriage in South East Queensland such as the Gold Coast and Northern Sunshine Coast. Future studies should aim to investigate MRS carriage in companion animals in this part of Australia. Nevertheless, the findings from this study are useful to uncover the landscape epidemiology of MRS carriage in Australian dogs. Second, the ecological nature of our model could have contributed to a lack of statistical support for the socioeconomic variable which as previously been postulated to be an important factor in antimicrobial resistant bacteria epidemiology, including MRSA (56, 57). While SEIFA scores were significant at the univariable analysis the fact that the SEIFA scores were available at the postcode level could have contribute to the loss of statistical support due to presence of regression dilution bias (58). Further studies should consider obtaining detailed information of owners SES to account for the variation in MRSP risk identified in this study. In addition, our results indicate that our model failed to account for all the residual geographical clustering of MRSP and future studies should consider adjustment for additional finer-scale factors that could influence MRSP carriage status in dogs such as in-house pet contacts, presence of an MRSP infected dog, use of disinfectants at home, as well as human carriage.

**Conclusions**

In conclusion, MRSP carriage in dog populations of Brisbane and surrounding areas contrasts with other Australian findings but is within the range of previous published studies worldwide. The associated risk factors include prior bacterial infection, prior hospitalisation, consultation types, average precipitation and human population density. Clustering of 6 km is evident in Brisbane and surrounding areas and higher risk of carriage was found along the coast, particularly Brisbane city, Sunshine Coast and Gympie areas.

**Abbreviations**

MRSA
Methicillin resistant *Staphylococcus aureus*

MRSP
Methicillin resistant *Staphylococcus pseudintermedius*

MRS
Methicillin resistant *Staphylococcus*

PCR
Polymerase Chain Reaction
Declarations

Ethics approval and consent to participate

This research was approved by the Animal Ethics Unit from the University of Queensland (The University of Queensland AnimalEthicsSVS/487/15/KIBBLE). Written consent was obtained from all participants.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

EM, JSG, and RSM designed the study and were major contributors in writing the manuscript. RP and TM helped with microbiological and molecular sample processing. TF, EB, and JH collected samples and animal clinical history data. HR aided in the collection and processing of samples and clinical histories. HR and RSM analysed the data. All authors read and approved the final manuscript.

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Figures
Residual geographical clustering of MRSP carriage in the greater Brisbane area based on the multivariable logistic regression models excluding and including environmental factors.
*One decimal degree at the equator is approximately 111km.

**Figure 1**

Residual semivariograms of probability of MRSP carriage in Greater Brisbane
Figure 2

Predicted mean carriage rates of MRSP within Queensland and the associated standard deviation map. The predicted mean carriage is a representation of the probability of carriage and the standard deviation indicates the uncertainty surrounding the predicted means. Queensland locality boundaries were created by the © State of Queensland (Department of Natural Resources, Mines and Energy) 2018. Updated data available at http://qldspatial.information.qld.gov.au/catalogue//. This material is licensed under a Creative Commons - Attribution 4.0 International licence (https://creativecommons.org/licenses/by/4.0/).