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## Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in dogs and cats: a case-control study

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**Abstract** – Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in dogs and cats were investigated in an unmatched case-control study. A total of 197 animals from 150 veterinary practices across the United Kingdom was enrolled, including 105 MRSA cases and 92 controls with methicillin-susceptible *S. aureus* (MSSA) infection. The association of owners and veterinarian staff with the human healthcare sector (HCS) and animal-related characteristics such as signalment, antimicrobial and immunosuppressive therapy, and surgery were evaluated as putative risk factors using logistic regression. We found that significant risk factors for MRSA infection were the number of antimicrobial courses ( $p = 0.005$ ), number of days admitted to veterinary clinics ( $p = 0.003$ ) and having received surgical implants ( $p = 0.001$ ). In addition, the odds of contact with humans which had been ill and admitted to hospital ( $p = 0.062$ ) were higher in MRSA infected pets than in MSSA controls. The risk factors identified in this study highlight the need to increase vigilance towards identification of companion animal groups at risk and to advocate responsible and judicious use of antimicrobials in small animal practice.

**methicillin-resistant *Staphylococcus aureus* infection / risk factor / dog / cat / case-control study**

### 1. INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) remains an important nosocomial pathogen by contributing to health and economic burdens on human patients and

health-care systems (HCS) worldwide [49, 50]. In humans, contact with HCS facilities is commonly documented as an independent risk factor for MRSA carriage or infection [21, 23, 27, 31]. Also, the selection pressure exerted by the use of antimicrobial therapy is a well documented risk factor, especially with the use of cephalosporins and fluoroquinolones

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[24, 42, 48, 51]. Additionally, overcrowding and understaffing leads to the failure of MRSA control programmes in human hospitals which could be contributing to the spill-over of infection to the community [13].

For many years, MRSA was considered only a human pathogen. It has now become an increasingly urgent problem in veterinary medicine, with infections being reported in companion and food animal species (i.e. dogs, horses, cats, pet birds, cattle and pigs) [7, 28, 44]. In late 2003 and early 2004, it became apparent that MRSA infection in the UK was much more widespread in dogs and cats than previously thought [36]. Worldwide there is an increase in the number of reported MRSA clinical infections in veterinary practices which suggests that either there is increased awareness about MRSA infection in veterinary practices – leading to increased diagnosis and detection – or companion animals such as dogs, cats and horses, have become increasingly exposed and susceptible to MRSA and are now a potential reservoir of infection to humans [11, 32, 38].

Given the close social interaction between companion animals and humans it is expected that contact with human carriers such as at home or at the veterinary practice would be linked to MRSA acquisition by a pet. Also, the transmission of MRSA strains between different host species has previously been described in the context of households (i.e. between owners and their pets) and veterinary practices (i.e. between veterinary personnel and pets) [11, 32, 41, 47]. Mucosal carriage of MRSA in otherwise healthy attending veterinary staff, owners and human-health care workers has been demonstrated in numerous studies [12, 21, 26, 29, 32, 39, 43, 45, 46]. Transfer between humans and animals has been corroborated by typing studies which showed that MRSA from dogs and cats were typically identical to hospital-associated lineages dominant in the particular countries [6, 33, 40].

To the best of our knowledge, human-related risk factors associated with MRSA infection in dogs and cats have not been adequately investigated. Their identification may facilitate the

design of appropriate infection control and prevention strategies in veterinary practices with additional benefits for public health. This would allow a better understanding of MRSA epidemiology in these species which would inform revision of the current recommendations for the control of this important zoonotic agent in humans by including animal-related control measures. We hypothesise that the risk of MRSA infection in dogs and cats is determined by factors of the companion animals' clinical history and the contact with humans associated with the HCS.

This study aims to identify risk factors for MRSA infection in dogs and cats by investigating animal-related characteristics such as signalment (e.g. species, sex, age, and body weight), medication and veterinary intervention and in-contact human association with the HCS.

## 2. MATERIALS AND METHODS

### 2.1. Study groups and data collection

An unmatched population-based case-control study was conducted including dogs and cats with MRSA infection (cases) and those with methicillin-susceptible *S. aureus* (MSSA) as controls. Previous case-control studies in humans and animals have often used subjects with MSSA infection/colonization as a control group since it is considered a justifiable assumption that these individuals come from the same source population as MRSA cases [19, 22, 24, 27].

We used a population database available at one of the largest diagnostic laboratories currently operating in the UK (IDEXX Laboratories, Wetherby, UK) to minimize selection biases that could arise from difficulties in enumeration of the source population. Animals were identified from clinical specimens submitted to the veterinary laboratory for bacterial culture and antimicrobial susceptibility testing. Samples had been submitted by veterinary surgeons across the UK between October 2005 and October 2007 as part of their diagnostic investigations into suspected bacterial infection. For all consecutive *S. aureus* isolations during that period (single submissions from different animals) laboratory staff requested permission from the submitting veterinary surgeon to pass on practice details and animal

identification to the authors. The authors then invited the veterinary surgeons to participate in the study and study material (consent forms, questionnaires, swabs) were sent to the practice. The veterinary surgeons were asked to recruit up to four volunteering people (ideally two veterinary staff, two pet owners) in contact with the respective infected animal. Where close contact with more than four volunteering people was identified, study material was provided for an additional two humans. Participants were asked to complete a questionnaire on healthcare-associations and submit a nasal swab. Validated questionnaires were used to gather information on direct or indirect contact with human health care system facilities (i.e. work within the human healthcare sector, contact with healthcare workers or people with known MRSA carriage or infection, participant's health status including antimicrobial therapy, visits to healthcare facilities) for the 6-month period prior to enrolment. Methods and detailed results of the human nasal swabbing are described separately [30].

Animal medical histories were requested for each animal covering the 6-month period prior to *S. aureus* isolation.

## 2.2. Ethics

The sampling procedures in animals and in humans had been approved by the Royal Veterinary College Ethics Committee and the National Research Ethics Service (NRES) (formerly Central Office for Research Ethics Committees), respectively. Following their written consent, participants would code their nasal swab prior to laboratory submission. Consent forms with participants' details and coded swab results were collected by the authors who informed all participants of their nasal swab results in writing together with a recommendation to discuss any positive results with their doctors. Owners' details were deleted from their animal's medical histories if they were not participating.

## 2.3. Culture of samples

All clinical samples from animals and subsequent human nasal swabs (as described in [30]) were initially processed by IDEXX Laboratories. Staphylococcal isolation and identification was based on a combination of routine microbiological tests, automated speciation and antimicrobial susceptibility testing (Vitek2, bioMérieux, Hazelwood, MO, USA) and by latex agglutination testing for the detection of

penicillin-binding protein 2' (Oxoid, Basingstoke, UK). Animal and human *S. aureus* were subsequently confirmed at the Royal Veterinary College phenotypically (colony morphology assessment, Gram staining, slide and tube coagulase tests, DNase test, Voges–Proskauer reaction, lactose and trehalose fermentation) and genotypically using demonstration of the species-specific thermonuclease gene (*nuc*) by polymerase chain reaction (PCR) [8]. MRSA were identified from growth on mannitol salt agar (Oxoid) supplemented with 6 mg/L of oxacillin (Sigma-Aldrich, Gillingham, UK) and confirmed by disc diffusion tests with methicillin (5 µg, Oxoid) on Mueller–Hinton agar (Oxoid) incubated for 24 h at 30 °C following the Clinical and Laboratory Standards Institute guidelines [14], and by molecular confirmation of the presence of *mecA* by PCR [10]. All *S. aureus* isolates were typed based on characterisation of their lineage-specific restriction modification system (RM) [15].

## 2.4. Statistical analysis

All statistical analyses were carried out using the statistical software Stata SE Version 9.2 (Stata Corporation, College Station, TX, USA). Data were collected for 12 animal-related variables from pets' medical histories (Tab. I) and for 19 human healthcare-related variables from questionnaires (Tab. II). The statistical analysis was carried out in two phases using *S. aureus* infection status of the animal (i.e. MRSA case or MSSA control) as the outcome variable of interest.

Firstly, all putative human-healthcare-association and all animal related risk factors were screened using univariable logistic regression for statistical association with animal MRSA infection status based on a liberal *p*-value of 0.20 in the likelihood-ratio test.

Secondly, all risk factors significant in the screening phase were considered for inclusion through a manual backward stepwise variable selection process in a multivariable logistic regression analysis. The criterion for removal of risk factors was based on statistical considerations using the likelihood ratio test with a significance level of  $p > 0.05$ .

The impact of clustering of cases and controls by veterinary practice was assessed in the univariable and in the multivariable analysis by including "veterinary practice postal code" as a random effect using the XTLOGIT command in Stata estimating the statistical significance of intraclass correlation coefficient,  $\rho$ . The final model was assessed for potential

**Table 1.** Univariable analysis of associations between MRSA infection status (i.e. MRSA case and MSSA control) in 181 dogs and cats and attributes of their clinical history (based on available medical records) during the 6 months prior to sample submission, using animal as the unit of analysis and veterinary practice as a random effect. For variables with two categories the *p*-value is provided where as for variables with more than two categories an overall *p*-value based on a Wald-test is provided.

| Variable level  | MRSA<br><i>n</i> (%) | MSSA<br><i>n</i> (%) | OR    | 95% CI      | <i>p</i> -value | Overall<br><i>p</i> -value |
|---|----------------------|----------------------|-------|-------------|-----------------|----------------------------|
| <b>Species</b>  |                      |                      |       |             |                 |                            |
| Dogs  | 70 (70.71)           | 47 (57.32)           | Ref.  |             |                 |                            |
| Cat   | 29 (29.29)           | 35 (42.68)           | 0.5   | 0.20–1.23   | 0.131           |                            |
| <b>Sex</b>  |                      |                      |       |             |                 |                            |
| Female  | 49 (49.50)           | 37 (45.12)           | Ref.  |             |                 |                            |
| Male  | 50 (50.50)           | 45 (54.88)           | 0.83  | 0.35–1.98   | 0.67            |                            |
| <b>Age in years</b>                                   |                      |                      |       |             |                 |                            |
| < 2   | 22 (23.91)           | 21 (26.58)           | Ref.  |             |                 | 0.749                      |
| 2 to 5  | 26 (28.26)           | 17 (21.52)           | 1.07  | 0.28–4.16   | 0.919           |                            |
| 5 to 9  | 20 (21.74)           | 23 (29.11)           | 0.6   | 0.16–2.31   | 0.455           |                            |
| > 9   | 24 (26.09)           | 18 (22.78)           | 1.19  | 0.31–4.59   | 0.798           |                            |
| <b>Body weight</b>                                    |                      |                      |       |             |                 |                            |
| < 15 kg   | 39 (43.33)           | 44 (58.67)           | Ref.  |             |                 |                            |
| > 15 kg   | 51 (56.67)           | 31 (41.33)           | 2.03  | 0.81–5.08   | 0.13            |                            |
| <b>Number of visits to veterinary practice*</b>       |                      |                      |       |             |                 |                            |
| Once  | 8 (8.16)             | 16 (19.51)           | Ref.  |             |                 | 0.126                      |
| 2 to 4  | 29 (29.59)           | 26 (31.71)           | 2.73  | 0.69–10.87  | 0.154           |                            |
| > 5   | 61 (62.25)           | 40 (48.78)           | 3.79  | 1.05–13.75  | 0.043           |                            |
| <b>Number of days admitted to veterinary practice</b> |                      |                      |       |             |                 |                            |
| None  | 8 (8.08)             | 30 (36.58)           | Ref.  |             |                 | 0.001                      |
| 1   | 28 (28.28)           | 38 (46.34)           | 3.82  | 0.96–15.30  | 0.058           |                            |
| > 1   | 63 (63.64)           | 14 (17.07)           | 35.41 | 6.04–207.55 | 0.001           |                            |
| <b>Number of antimicrobial courses</b>                |                      |                      |       |             |                 |                            |
| None  | 8 (8.09)             | 25 (30.49)           | Ref.  |             |                 | 0.01                       |
| 1   | 31 (31.31)           | 24 (29.27)           | 6.06  | 1.50–24.50  | 0.011           |                            |
| 2   | 30 (30.30)           | 23 (28.05)           | 5.37  | 1.34–21.52  | 0.018           |                            |
| > 3   | 30 (30.30)           | 10 (12.20)           | 19.75 | 3.41–114.44 | 0.001           |                            |
| <b>Topical antimicrobial therapy</b>                  |                      |                      |       |             |                 |                            |
| No  | 65 (65.66)           | 58 (70.73)           | Ref.  |             |                 |                            |
| Yes   | 34 (34.34)           | 24 (29.27)           | 1.53  | 0.57–4.09   | 0.394           |                            |
| <b>Systemic glucocorticoid therapy</b>                |                      |                      |       |             |                 |                            |
| Yes   | 16 (16.16)           | 17 (20.73)           | Ref.  |             |                 |                            |
| No  | 83 (83.84)           | 65 (79.27)           | 1.23  | 0.40–3.75   | 0.722           |                            |
| <b>Surgical implant</b>                               |                      |                      |       |             |                 |                            |
| No  | 71 (71.72)           | 80 (97.56)           | Ref.  |             |                 |                            |
| Yes   | 28 (28.28)           | 2 (2.44)             | 49.4  | 4.38–556.60 | 0.002           |                            |
| <b>Duration of infection*</b>                         |                      |                      |       |             |                 |                            |
| < 2 months  | 72 (72.73)           | 48 (58.54)           | Ref.  |             |                 |                            |
| > 2 months  | 27 (27.27)           | 34 (41.46)           | 0.45  | 0.17–1.19   | 0.106           |                            |
| <b>Concurrent chronic disease*</b>                    |                      |                      |       |             |                 |                            |
| No  | 61 (61.62)           | 38 (46.34)           | Ref.  |             |                 |                            |
| Yes   | 38 (38.38)           | 44 (53.66)           | 0.36  | 0.12–1.01   | 0.053           |                            |

Ref.: reference category; OR: odds ratio; CI: confidence interval.

\* Number of visits to veterinary practice: number of outpatient visits in 6 months prior to swab; Duration of infection: duration of clinical signs compatible with infection at sampling site; Concurrent chronic disease: chronic non-communicable conditions not associated with MRSA or MSSA infection. These included, but were not limited to endocrinopathy, heart disease, degenerative joint disease.

confounders amongst the removed variables by individually assessing their impact on the coefficients of the included variables. If the coefficient of one these variables changed by more than 25%, the eliminated variable was assumed to be a confounder and forced back into the model. We also assessed the coefficient of determination, *R*-squared, of the main effects model. Biologically meaningful first-order interaction terms were also tested for statistical significance. The goodness-of-fit of the final multivariable model was tested using the Hosmer–Lemeshow test [20].

### 3. RESULTS

#### 3.1. *S. aureus* infection in dogs and cats

Bacteriological results and questionnaire information were available for 197 dogs and cats from a total of 150 practices (Fig. 1) corresponding to 105 MRSA cases and 92 MSSA controls; most practices (79%,  $n = 119$ ) contributed one animal, 18 practices contributed two animals each, 10 practices three animals each and 3 practices four animals each. The reasons for refusal among submitting veterinary surgeons were concerns about time commitment and stigma effect on the private practice, while for owners it was the perceived inconvenience of the investigators' requests. With respect to human survey participation, aiming at least one human participant per animal, we were able to obtain 77% participation for MRSA cases and 74% for MSSA control animals. On average, each MRSA case and each MSSA control had 3 participating in-contact humans; more precisely, 6 in-contact humans were available for 2 animals, 5 for 4 animals, 4 for 82 animals, 3 for 41 animals, 2 for 55 animals and 1 in-contact human for each of 13 animals. Assuming that a maximum of 788 human participants could have participated, the overall human participation percentage was 76.5% (94.2% for veterinary staff, 54.6% for pet owners). In addition, clinical histories were collected for a total of 181 animals, corresponding to 99 MRSA cases and 82 MSSA controls. Reasons given for non-participation of veterinary staff included time concerns or a very short contact history with the pet (e.g. animal

visiting practice once while on holidays, attending veterinary staff left practice). Analysis of animal clinical histories has shown that 76% (137/181) of animals enrolled had used at least one course of beta-lactam antimicrobial in the last 6 months preceding the sampling whilst fluoroquinolones had been used in 28% (51/181) of animals and 84% (43/51) of these had also been administered at least one course of beta-lactam antimicrobial.

#### 3.2. Univariable analysis

We investigated the strength of association between the infection status of dogs and cats enrolled in the study with (1) factors related to their recent clinical history and (2) in-contact person factors (i.e. their links to the HCS facilities).

At a  $p \leq 0.20$ , MRSA infection status in animals was associated with 8 animal medical history related factors (Tab. I) and 6 in-contact person factors (Tab. II).

#### 3.3. Multivariable analysis

The final multivariable model was based on 176 records. The following variables were retained significant at a  $p < 0.05$ : “Number of antimicrobial courses”, “Number of days admitted to the veterinary practice”, “Ongoing infection”, “Surgical implant”, and an interaction term between “Contact with at least two ill humans” and “Contact with at least one human admitted to hospital” (Tab. III). The inclusion of “veterinary practice postal code” as a random effect into the final multivariable model did not improve model fit. The goodness-of-fit of the final multivariable model to the data, as assessed by the Hosmer–Lemeshow goodness of fit test, was adequate ( $p = 0.764$ ).

### 4. DISCUSSION

This study provides for the first time a comprehensive investigation of risk factors for MRSA infection in dogs and cats from first opinion practices and their human in-contacts.

**Table II.** Univariable analysis of associations between MRSA infection status (i.e. MRSA case and MSSA control) in 197 dogs and cats and attributes of their in-contact humans with respect to links to human health-care system (HCS) facilities, during the 6 months prior to sample submission, using animal as the unit of analysis and veterinary practice as a random effect.

| Variable level  | MRSA <i>n</i> (%) | MSSA <i>n</i> (%) | OR   | 95% CI    | <i>p</i> -value |
|---|-------------------|-------------------|------|-----------|-----------------|
| At least one human in-contact works at HCS                      |                   |                   |      |           |                 |
| No  | 68 (64.76)        | 54 (58.70)        | Ref. |           |                 |
| Yes   | 37 (35.24)        | 38 (41.30)        | 0.77 | 0.37–1.59 | 0.476           |
| At least two human in-contacts work at HCS                      |                   |                   |      |           |                 |
| No  | 96 (91.43)        | 80 (86.96)        | Ref. |           |                 |
| Yes   | 9 (8.57)          | 12 (13.04)        | 0.64 | 0.20–2.01 | 0.446           |
| At least one human in-contact was ill                           |                   |                   |      |           |                 |
| No  | 43 (40.95)        | 29 (31.52)        | Ref. |           |                 |
| Yes   | 62 (59.05)        | 63 (68.48)        | 0.64 | 0.30–1.36 | 0.249           |
| At least two human in-contacts were ill                         |                   |                   |      |           |                 |
| No  | 86 (81.90)        | 67 (72.83)        | Ref. |           |                 |
| Yes   | 19 (18.10)        | 25 (27.17)        | 0.55 | 0.23–1.30 | 0.174           |
| At least one in-contact human has been visited by HCS workers   |                   |                   |      |           |                 |
| No  | 54 (51.43)        | 57 (61.96)        | Ref. |           |                 |
| Yes   | 51 (48.57)        | 35 (38.04)        | 2    | 0.89–4.49 | 0.092           |
| At least two in-contact humans have been visited by HCS workers |                   |                   |      |           |                 |
| No  | 88 (83.81)        | 81 (88.04)        | Ref. |           |                 |
| Yes   | 17 (16.19)        | 11 (11.96)        | 1.67 | 0.58–4.82 | 0.346           |
| At least one in-contact human lives with ill person             |                   |                   |      |           |                 |
| No  | 90 (85.71)        | 84 (91.30)        | Ref. |           |                 |
| Yes   | 15 (14.29)        | 8 (8.70)          | 1.9  | 0.61–5.98 | 0.271           |
| At least one in-contact human has been admitted to hospital     |                   |                   |      |           |                 |
| No  | 40 (38.10)        | 51 (55.43)        | Ref. |           |                 |
| Yes   | 65 (61.90)        | 41 (44.57)        | 2.48 | 1.15–5.35 | 0.021           |
| At least two in-contact humans have been admitted to hospital   |                   |                   |      |           |                 |
| No  | 89 (84.76)        | 78 (84.78)        | Ref. |           |                 |
| Yes   | 16 (15.24)        | 14 (15.22)        | 1.04 | 0.39–2.77 | 0.936           |
| At least one in-contact human has been to GP                    |                   |                   |      |           |                 |
| No  | 11 (10.48)        | 5 (5.43)          | Ref. |           |                 |
| Yes   | 94 (89.52)        | 87 (94.57)        | 0.43 | 0.10–1.75 | 0.236           |
| At least two in-contact humans have been to GP                  |                   |                   |      |           |                 |
| No  | 37 (35.24)        | 28 (30.44)        | Ref. |           |                 |
| Yes   | 68 (64.76)        | 64 (69.56)        | 0.73 | 0.32–1.64 | 0.45            |
| At least three in-contact human have been to a GP               |                   |                   |      |           |                 |
| No  | 69 (65.71)        | 61 (66.30)        | Ref. |           |                 |
| Yes   | 36 (34.29)        | 31 (33.70)        | 1.19 | 0.54–2.58 | 0.668           |
| At least one in-contact human has been to a dentist             |                   |                   |      |           |                 |
| No  | 13 (12.38)        | 15 (16.30)        | Ref. |           |                 |
| Yes   | 92 (87.62)        | 77 (83.70)        | 1.56 | 0.53–4.53 | 0.418           |
| At least two in-contact humans have been to a dentist           |                   |                   |      |           |                 |
| No  | 50 (47.62)        | 53 (57.61)        | Ref. |           |                 |
| Yes   | 55 (52.38)        | 39 (42.39)        | 1.9  | 0.84–4.30 | 0.124           |
| At least three in-contact humans have been to dentist           |                   |                   |      |           |                 |
| No  | 79 (75.24)        | 76 (82.61)        | Ref. |           |                 |
| Yes   | 26 (24.76)        | 16 (17.39)        | 1.79 | 0.73–4.36 | 0.201           |

Continued on next page

**Table II.** Continued.

| Variable level  | MRSA <i>n</i> (%) | MSSA <i>n</i> (%) | OR   | 95% CI    | <i>p</i> -value |
|---|-------------------|-------------------|------|-----------|-----------------|
| At least one in-contact human has been to a nursing home          |                   |                   |      |           |                 |
| No  | 77 (73.33)        | 63 (68.48)        | Ref. |           |                 |
| Yes   | 28 (26.67)        | 29 (31.52)        | 0.76 | 0.34–1.70 | 0.508           |
| At least one in-contact human has taken antimicrobials            |                   |                   |      |           |                 |
| No  | 42 (40)           | 32 (34.78)        | Ref. |           |                 |
| Yes   | 63 (60)           | 60 (65.22)        | 0.76 | 0.36–1.61 | 0.466           |
| At least two in-contact humans have taken antimicrobials          |                   |                   |      |           |                 |
| No  | 84 (80)           | 66 (72.53)        | Ref. |           |                 |
| Yes   | 21 (20)           | 25 (27.47)        | 0.57 | 0.23–1.41 | 0.222           |
| At least one in-contact human has taken immunosuppressant therapy |                   |                   |      |           |                 |
| No  | 87 (82.86)        | 82 (90.11)        | Ref. |           |                 |
| Yes   | 18 (17.14)        | 9 (9.89)          | 2.04 | 0.70–5.95 | 0.19            |

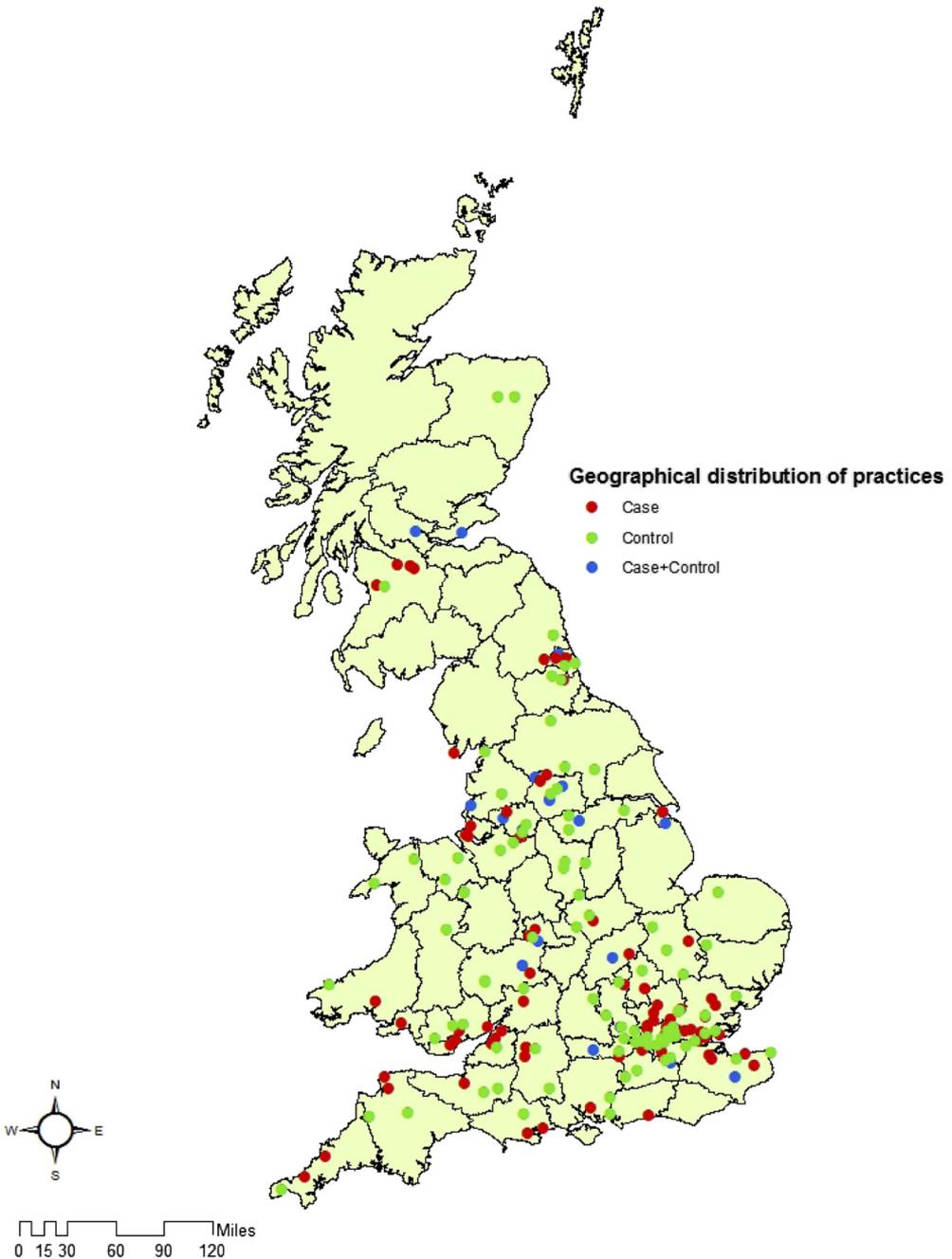
Ref.: reference category; OR: odds ratio; CI: confidence interval; GP: general practitioner.

We identified the following risk factors: number of antimicrobial courses, number of days admitted to the veterinary practices, ongoing infection (for less than 2 months), surgical implant, and contact with humans who had been ill and had been admitted to hospital. These risk factors broadly mirror those described for MRSA infections in humans which suggests that the aetiology of staphylococcal infections is likely to be similar in these hosts.

Responsible and judicious use of antimicrobials is an essential part of an ethical approach to improving companion health and welfare [25]. This includes avoiding empirical antimicrobial therapy (i.e. therapy initiated on the basis of observation of clinical signs and patient history only) without confirmation of diagnosis by laboratory or other methods. The use of repeated antimicrobial therapy has been previously identified as a risk factor for inducing selection pressures in favour of MRSA strains in humans [24, 42, 48, 51]. Our results suggest that dogs and cats with MRSA infections are more likely to have received more than three courses of antimicrobials within the 6 months prior to isolation of MRSA than MSSA controls. This observed association may be a consequence of repeated empirical therapy and selection in favour of MRSA strains; alternatively, if animals had MRSA, it is likely that practitioners attempted multiple antimicrobial courses to treat infection. These results are consistent with a recent study in 3 veterinary referral hospital in the USA where

specific antimicrobial drugs were identified as significant risk factors for MRSA infection in dogs [22].

The use of certain types of antimicrobial drugs (namely, cephalosporins and fluoroquinolones) has been shown to contribute to selection of MRSA strains in humans [17, 48] and has been found to be a risk factor for MRSA infection in dogs [22]. Recently there have been calls for banning of use of these antimicrobials by veterinary practitioners as a means for reducing selection pressures and alleviating MRSA infection burden in humans [4, 34]. In our study the use of fluoroquinolones, which are known to be ineffective against UK hospital MRSA and may contribute to selection, was limited when compared to the usage of beta-lactam antimicrobials and they were often used in combination with at least one course of beta-lactam antimicrobial. However, due to the low variability of antimicrobial usage in our sample our findings do not provide sufficient evidence to inform whether specific antimicrobial practice usage profiles in the UK are associated with increased risk of MRSA infection and therefore further studies are needed in this domain. Regula et al. have investigated the antimicrobial usage profiles of eight mixed veterinary practices (small animals and large-animals) in Switzerland and found that veterinarians judiciously used the antimicrobials of highest importance for the treatment of humans (i.e. fluoroquinolones, third- and fourth-generation cephalosporins and



**Figure 1.** Geographical distribution of 150 practices enrolled in the study during October 2005 to October 2007 for which complete georeference information was retrieved. Practices contributing an MRSA case, an MSSA control or both are depicted as red (black), green (grey) and blue (dark) dots, respectively. (For a color version of this figure, please consult [www.vetres.org](http://www.vetres.org).)

**Table III.** Risk factors for MRSA infection in dogs and cats retained in the final multivariable logistic regression model based on 176 records using animal as the unit of analysis ( $R^2 = 0.35$ ). For variables with two categories the  $p$ -value is provided where as for variables with more than two categories an overall  $p$ -value based on a Wald-test is provided.

| Variable Level  | OR    | 95% CI      | $p$ -value | Overall $p$ -value |
|---|-------|-------------|------------|--------------------|
| Number of antimicrobial courses                                 |       |             |            | 0.005              |
| None  | Ref.  |             |            |                    |
| 1   | 4.45  | 1.26–15.77  | 0.021      |                    |
| 2   | 5.78  | 1.54–21.65  | 0.009      |                    |
| > 3   | 17.31 | 3.59–83.48  | < 0.001    |                    |
| Number of days admitted   |       |             |            | 0.003              |
| None  | Ref.  |             |            |                    |
| 1   | 1.32  | 0.44–3.97   | 0.619      |                    |
| > 1   | 5.27  | 1.62–17.10  | 0.006      |                    |
| Duration of infection   |       |             |            |                    |
| < 2 months  | Ref.  |             |            |                    |
| > 2 months  | 0.20  | 0.08–0.53   | 0.001      |                    |
| Surgical implant  |       |             |            |                    |
| No  | Ref.  |             |            |                    |
| Yes   | 32.98 | 4.59–236.86 | 0.001      |                    |
| At least two human in-contacts were ill (A)                     |       |             |            |                    |
| No  | Ref.  |             |            |                    |
| Yes   | 0.11  | 0.02–0.78   | 0.027      |                    |
| At least one in-contact human has been admitted to hospital (B) |       |             |            |                    |
| No  | Ref.  |             |            |                    |
| Yes   | 1.48  | 0.62–3.55   | 0.381      |                    |
| Interaction term: A*B   | 8.51  | 0.85–85.16  | 0.062      |                    |

Ref.: reference category; OR: odds ratio; CI: confidence interval.

macrolides), as recommended by prudent usage guidelines [35]. Furthermore, for the protection of human health, ongoing joint activities of the World Organization for Animal Health (OIE), Food and Agricultural Organization of the United Nations (FAO) and World Health Organization (WHO) have led to the elaboration of numerous international guidelines on responsible and judicious use of antimicrobial agents in animals [18, 34]<sup>1,2</sup>. An important spin-off from

this consultative process was the establishment of a Codex Alimentarius Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance which primarily seeks to define a list of critical antimicrobials used in human and food animal veterinary medicine. However, similar efforts are still absent in the context of companion animal veterinary medicine both at national and international level.

The results of our study also suggest that MRSA infected dogs and cats are five times more likely than MSSA infected pets to have been admitted to the veterinary practice for a duration of more than one day. In humans, length of stay as measured by number of days admitted to hospital has been identified as a risk factor for MRSA infection as well as a result of MRSA infection [1, 16]. Because animals were not examined for MRSA carriage or infection prior to admission to the respective veterinary practice the results cannot explain whether

<sup>1</sup> FAO/WHO/OIE, WHO global principles for the containment of antimicrobial resistance in animals intended for food, 2000. Available from [http://whqlibdoc.who.int/hq/2000/WHO\\_CDS\\_CSR\\_APH\\_2000.4.pdf](http://whqlibdoc.who.int/hq/2000/WHO_CDS_CSR_APH_2000.4.pdf) [cited 25 March 2010].

<sup>2</sup> Codex-Alimentarius, Code of practice to minimize and contain antimicrobial resistance, 2005. Available from [http://www.codexalimentarius.net/download/standards/10213/CXP\\_061e.pdf](http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf) [cited 25 March 2010].

MRSA infection prolonged admission or whether MRSA infection was a result of prolonged length of stay at the practice.

The linkage of owners and veterinarians to HCS facilities has been suggested as a pathway through which animals are exposed to MRSA strains [9, 32]<sup>3</sup>. We have identified nosocomial linkage factors of in-contact humans (i.e. exposure to HCS facilities) which were associated with MRSA infection in dogs and cats. Previous visits or admission to hospital are well-known risk factors for human acquisition of MRSA in the hospital setting [2, 5, 12, 27, 31, 37]. Our results suggest that the odds of contact with at least two ill in-contact humans and the hospitalization of at least one in-contact person is eight times as likely in MRSA infected pets as it is in MSSA controls. Although this result was marginally significant ( $p = 0.062$ ), it suggests human exposure to HCS may contribute to the epidemiology of MRSA infection in dogs and cats. If hospitalization of in-contact humans indeed has an effect on MRSA infection of dogs and cats, having this information could lead to modified practice management procedures prior to admission of the animal to surgery.

The results of our study, particularly for human in contact factors, have to be interpreted cautiously taking into account that, only 70% of MRSA cases and MSSA controls had information about in-contact humans. Although, this human participation percentage was similar or better when compared to previous studies in veterinary staff [3]<sup>4</sup>, this level of attrition may have contributed to insufficient power for identifying significant associations between these factors and MRSA infection in dogs and cats.

<sup>3</sup> Oughton M.T., Dick H.L., Willey B.M., Brown S., McGeer A., Kreiswirth B.N., et al., Methicillin Resistant *Staphylococcus aureus* (MRSA) as a cause of infections in domestic animals: evidence for a new humanotic disease? Interscience Conference on Antimicrobial Agents and Chemotherapy Chicago, 2001.

<sup>4</sup> Robinson D., Hooker H., Royal College of Veterinary Surgeons – The UK veterinary profession in 2006; 2006. Available from [http://www.rcvs.org.uk/Shared\\_ASP\\_Files/UploadedFiles/97D3DAF0-9567-4B2F-9972-B0A86CFB13C7\\_surveyprofession2006.pdf](http://www.rcvs.org.uk/Shared_ASP_Files/UploadedFiles/97D3DAF0-9567-4B2F-9972-B0A86CFB13C7_surveyprofession2006.pdf) [consulted 10 September 2009].

In summary, control efforts for reducing MRSA infection in dogs and cats should be aimed at reducing MRSA transmission amongst veterinary personnel and within-practice environmental contamination through promotion of enhanced personal and practice hygiene, and client education. This could be combined with increased vigilance of animal groups at risk identified in this study, e.g. admitted patients and implant patients, and contact with recently hospitalised humans which is expected to have an impact on the reduction of within-practice MRSA infection and transmission. In addition, responsible and judicious use of antimicrobials at the veterinary practice level should be urgently advocated to significantly mitigate the risk for dogs and cats developing MRSA infection. This would mean the early sampling of infections in risk groups, avoidance of empirical use of antimicrobial agents and use of antimicrobial therapy based on known sensitivity.

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