THESIS

SURVEILLANCE AFFECTING INFECTION CONTROL IN A VETERINARY TEACHING HOSPITAL

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ABSTRACT

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Healthcare-associated infections (HCAI) are poorly understood in veterinary medicine. Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) is an increasingly reported pathogen of dogs. Consequently, there are increasing concerns regarding treatment difficulties and propagation of antibiotic resistance. The first study seeks to estimate the burden of MRSP carriage among dogs presenting to the Colorado State University Veterinary Teaching Hospital (CSU-VTH).

This study enrolled 243 canine patients across 3 different hospital services upon admission to the VTH and 155 canine patients across 3 different hospital services that received paired samples at two different time points. The 3 hospital services were Community Practice (healthy patients), Dermatology (patients with skin disease) and Surgical Oncology (patients with a higher risk of acquiring an infection during visit).

The estimated prevalence of MRSP carriage at enrollment and follow-up was 4%. For enrollment samples, no patients enrolled through Community Practice carried MRSP, while 8% of Dermatology patients and 3% of Surgical Oncology patients were MRSP carriers. For paired samples, carriage persistence was only seen for patients enrolled through Dermatology.

Results of this study showed that the prevalence of MRSP carriers among dogs presenting to the CSU-VTH falls within ranges previously published. MRSP

colonization was seen most commonly among dogs with skin disease and least commonly among healthy dogs.

The second study focuses on surveillance for HCAIs via patient temperatures stored in the electronic medical record (EMR) system of a VTH. Little work has been done in veterinary medicine on surveillance of HCAIs in a VTH. The EMR system contains patient temperature data for each visit. This study explores the association between fevers after admission and known risk factors for HCAIs (e.g. duration of stay in the hospital, critical care involvement).

This study included all medical records corresponding to canine visits from the period of January 1, 2012 to June 30, 2015. After selecting for visits of ≥ 1 night and removing missing data, 6,254 unique canine visits remained. Visits were classified into type of case (Medicine, Surgery, Oncology, Other) and whether criticial care (ECC) was involved). Length of stay was determined based on admission and discharge date. A visit that produced a fever after admission was a visit where the animal had a normal rectal temperature (≤102.5°F) upon admission and subsequently produced a fever (>102.5°F) after admission. The cumulative incidence of fevers after admission was calculated. Odds ratios (OR) between fevers after admission and case type and ECC involvement and duration of stay in the hospital were calculated via multivariable logistic regression.

The estimated cumulative incidence of fevers after admission was 9%. Results of multivariable regression showed that a negative association existed between Medicine-type cases, Oncology-type cases and long duration of hospitalization (>2 days).

This study shows that fevers after admission are associated with known risk factors for HCAIs and may be useful in a syndromic approach to HCAI surveillance. This study did not explore the association between HCAI and fevers after admission.

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1 Review of Literature

1.1 Staphylococcus pseudintermedius and methicillin-resistance

1.1.1 Overview

Bacteria of the genus *Staphylococcus* are commensals of the skin and mucous membranes of both humans and animals. Under favorable conditions, some *Staphylococcus* spp. may become pathogenic (Morris, Boston, O'Shea, & Rankin, 2010). *Staphylococcus* spp. exhibit a species predilection, with *Staphylococcus aureus* the main staphylococcal pathogen (Chiller, Selkin, & Murakawa, 2001; Fredricks, 2001) of humans and *Staphylococcus pseudintermedius* the main commensal/pathogen of dogs (Bannoehr & Guardabassi, 2012). In dogs, *Staphylococcus* spp. have been known to cause infections of the skin, ears, surgical sites/wounds and urinary tract (van Duijkeren et al., 2011; Weese & van Duijkeren, 2010). The most common staphylococcal pathogen of dogs is *S. pseudintermedius*, and is also a commensal of canine mucous membranes and skin (Bannoehr & Guardabassi, 2012; Hartmann, White, West, Walker, & DeBoer, 2005). *S. pseudintermedius* is not a normal commensal of humans (Guardabassi, Loeber, & Jacobson, 2004), but has been reported to be able to colonize (Morris et al., 2010; Paul, Moodley, Ghibaudo, & Guardabassi, 2011) and cause infection in humans (Campanile et al., 2007; Somayaji, Priyantha, Rubin, & Church, 2016; Talan, Goldstein, Staatz, & Overturf, 1989).

1.1.2 History of S. pseudintermedius

Historically, routine diagnostic bacteriology for *Staphylococcus* spp. hinged upon the coagulase test, classifying all coagulase-positive *Staphylococcus* spp. (CPS) as *S. aureus* (Devriese et al., 2005). Coagulase-negative *Staphylococcus* spp. (CNS) were considered non-pathogenic and ignored as potential causes of disease. In 1976, Hajek, based on isolates from pigeons, dogs, minks and horses, reported the discovery of a new species within the genus *Staphylococcus*, noting heterogeneities within the *S. aureus* group. Hajek called this new species *S. intermedius* with microbiological features that, up until 1976, was considered to be characteristic of *S. aureus* (Hajek, 1976). For 30 years, *S. intermedius* was considered a common cause of skin and soft tissue infections in dogs (Allaker, Lloyd, & Bailey, 1992; Allaker, Lloyd, & Simpson, 1992; Cox et al., 1988; Devriese & De Pelsmaecker, 1987; Medleau, Long, Brown, & Miller, 1986; Werckenthin, Cardoso, Martel, & Schwarz, 2001).

Since Hajek's discovery, other microbiological features were discovered providing further differentiation of the CPS spp. (Devriese et al., 2005). *Staphylococcus hyicus* was discovered in 1978 (Devriese et al., 1978). *S. delphini* was discovered in 1988 (Varaldo, Kilpper-Balz, Biavasco, Satta, & Schleifer, 1988), *S. schleiferi* subsp. *coagulans* was discovered in 1990 (Igimi, Takahashi, & Mitsuoka, 1990) and *S. lutrae* was discovered in 1997 (Foster, Ross, Hutson, & Collins, 1997). *S. pseudintermedius* was discovered in 2005 (Devriese et al., 2005) based on molecular characterization. Biochemical identification of some staphylococcal species, particularly coagulase-negative Staphylococci with routine testing is a challenge requiring automated systems

involving performance of extensive phenotypic testing and molecular identification (Devriese et al., 2005).

S. delphini isolates and *S. pseudintermedius* strains have the same phenotypic characteristics. *S. intermedius* (Devriese et al., 2005; Varaldo et al., 1988) came to be known as the *S. pseudintermedius* group (SIG). Molecular methods are required to differentiate *S. delphini, S. intermedius* and *S. pseudintermedius* (Sasaki et al., 2007a). Thus, prior to the description of *S. delphini* and *S. pseudintermedius*, routine diagnostic bacteriologic isolates identified as *S. intermedius* could have been any member of the SIG. Species from which the bacteria was isolated provided valuable information as to which member of the SIG the isolate truly belonged, e.g. isolates from a dolphin would most likely be *S. delphini*. In 2007, it was shown that the majority of *S. intermedius* isolated from dogs were *S. pseudintermedius*, leading to the convention in nomenclature that all SIG isolates identified via routine methods from dogs are identified as *S. pseudintermedius* (Devriese, Hermans, Baele, & Haesebrouck, 2009; Sasaki et al., 2007b). This allows for the presumptive identification of *S. pseudintermedius* without further molecular testing to differentiate it from the other SIG members (Devriese et al., 2009).

1.1.3 S. pseudintermedius as a commensal

S. pseudintermedius is a commensal of healthy canine skin and mucous membranes (Bannoehr & Guardabassi, 2012). It has been isolated from various anatomical sites of healthy dogs, including the nasal vestibulum, external auditory canal, anal mucosa and on the skin surface and hair coat (Griffeth, Morris, Abraham, Shofer, & Rankin, 2008). Genetic diversity of *S. pseudintermedius* colonizing healthy

dogs is often high (Paul et al., 2011). The most common colonization sites for MRSP in dogs appear to be the pharynx/oral cavity, rectum/perineum (Paul et al., 2011; Rubin & Chirino-Trejo, 2011) and nasal vestibulum (Devriese & De Pelsmaecker, 1987)

1.1.4 S. pseudintermedius as a pathogen

S. pseudintermedius causes opportunistic disease when the physical or immunological barriers to infection are lowered due to alterations in the skin barrier (due to predisposing factors such as atopic dermatitis), medical and surgical procedures and/or immunosuppressive disorders (Bannoehr & Guardabassi, 2012). *S. pseudintermedius* is involved in canine pyoderma, otitis, wound and surgical infections and abscesses (van Duijkeren et al., 2011; Weese & van Duijkeren, 2010). Since *S. pseudintermedius* is a normal commensal of canine skin and mucous membrane flora, infections by *S. pseudintermedius* are opportunistic and infection itself not transmissible by direct contact between healthy and diseased dogs (Bannoehr & Guardabassi, 2012).

Pathogenicity of *S. pseudintermedius* does not appear to be related to strain. Non-diseased dogs seem to carry a genetically diverse population of *S. pseudintermedius* in various anatomical sites (Bannoehr & Guardabassi, 2012; Fazakerley, Williams, Carter, McEwan, & Nuttall, 2010; Pinchbeck et al., 2006). Genetic diversity appears to decrease in dogs with superficial bacterial folliculitis (Pinchbeck et al., 2006) and atopic dermatitis (Fazakerley et al., 2010).

In humans, colonization by *S. aureus* is a risk factor for subsequent infection by *S. aureus*. However, in dogs, the relationship of colonization and *S. pseudintermedius* infection is unclear. Non-methicillin resistant *S. pseudintermedius* strains isolated at the site of skin infection were found via pulsed-field gel electrophoresis to be identical to

those found at colonization site(s) on the same patient (Fazakerley et al., 2010; Pinchbeck et al., 2006; A. Sasaki et al., 2005).

1.1.5 Methicillin-resistant *S. pseudintermedius*

Prior to the emergence of methicillin-resistance, *S. pseudintermedius* was susceptible to beta-lactam antibiotics (Weese & van Duijkeren, 2010). However, since 2006, reports of methicillin resistance among *S. pseudintermedius* have been increasing (van Duijkeren et al., 2011). Methicillin-resistance is conferred upon *S. pseudintermedius*, as it is with *S. aureus* via acquisition of the *mecA* gene. This gene encodes an altered penicillin-binding-protein-2a (PBP2a) that is present in the cell wall. PBP2a confers *in vivo* resistance to all beta-lactam antibiotics because this class cannot bind to the bacterial call wall to exert its bacteriocidal effects (Berger-Bächi & Rohrer, 2002; Hartman & Tomasz, 1984; Kwon et al., 2005; van Duijkeren, Box, Heck, Wannet, & Fluit, 2004). Reports from Europe and North America show that MRSP isolates are commonly resistant to various classes of antimicrobials (Gold, Cohen, & Lawhon, 2014; Nienhoff et al., 2011), including fluoroquinolones, lincosamides, macrolides, aminoglycosides, sulfonamides and chloramphenicols (Gold et al., 2014; Nienhoff et al., 2011). Therapeutic options may be limited, however, effective topical therapies and/or systemic therapies are often still available.

Dogs may be contaminated, colonized or infected with MRSP. When a dog is contaminated with MRSP, the bacteria have not invaded tissue,are not replicating and can be easily washed off. Often, only one culture of the dog is positive, while subsequent cultures are negative (van Duijkeren et al., 2011). When a dog is persistently colonized with MRSP, the bacteria have become a part of the microbial flora

of the dog. Dogs that are colonized with MRSP are called “carriers” (van Duijkeren et al., 2011). As such, colonization and carriage are used interchangeably. In colonized individuals, bacteria are not prompting an immune response, and not necessarily causing observable clinical signs.or immune reactions (van Duijkeren et al., 2011). Distinguishing between MRSP contamination and colonization of a patient requires multiple samples to be taken from a patient. Colonization sites include groin, mouth, anus, head and mucosa (Griffeth et al., 2008), with the anal region and nasal mucosa being the most frequently colonized sites (Fazakerley et al., 2009; Weese & van Duijkeren, 2010). The anal region seems to be the most heavily colonized (Devriese & De Pelsmaecker, 1987). When a dog is infected with MRSP, the bacteria have invaded a body site, is multiplying and causing observable clinical signs (van Duijkeren et al., 2011).

1.1.6 Epidemiology of MRSP

Frequency of isolation of MRSP from dogs with active skin infections in the United States has increased dramatically in the last decade (Frank, Kania, Kirzeder, Eberlein, & Bemis, 2009; Jones, Kania, Rohrbach, Frank, & Bemis, 2007; Kania et al., 2004), with prevalence at 0% (0/210) prior to 1986 (Medleau et al., 1986), 3.5% (2/57) from 1999 to 2001 (Kania et al., 2004) and 7% (4/59) from 2005 to 2006 (Griffeth et al., 2008). Prevalence of methicillin-resistance among *S. pseudintermedius* isolates from clinical samples submitted to a veterinary diagnostic laboratory increased from 5% in 2001 to 30% in 2007 (Bemis, Jones, Frank, & Kania, 2009). Prevalence of MRSP colonization in healthy dogs has been reported to range from 2% to 6% (Detwiler, Bloom, Petersen, & Rosser, 2013; Hanselman, Kruth, & Weese, 2008). Reports as high

as 16% have been reported (Epstein, Yam, Peiris, & Epstein, 2009). MRSP colonization prevalence varies with geographic region, e.g. 1.5% (3/200, Slovenia, 2005) (Vengust, Anderson, Rousseau, & Weese, 2006), and 16.7% (6/36, Hong Kong, 2008) (Epstein et al., 2009). MRSP colonization prevalence in northern Colorado, among shelter dogs, has been estimated to be 3% (6/200, United States, 2009) (Gingrich, Kurt, Hyatt, Lappin, & Ruch-Gallie, 2011).

MRSP transmission occurs via animal-to-animal contact (van Duijkeren et al., 2011; Guardabassi, Schwarz, & Lloyd, 2004; Harvey & Noble, 1998; van Duijkeren et al., 2011; Zubeir et al., 2007). Humans may also transmit MRSP from one patient to another (van Duijkeren et al., 2011; Guardabassi et al., 2004; van Duijkeren et al., 2011; Zubeir et al., 2007). While rare, human infections with MRSP have been reported (Campanile et al., 2007; Gerstadt, Daly, Mitchell, Wessolossky, & Cheeseman, 1999; Kempker, Mangalat, Kongphet-Tran, & Eaton, 2009; Somayaji et al., 2016; Starlander, Börjesson, Grönlund-Andersson, Tellgren-Roth, & Melhus, 2014; Stegmann, Burnens, Maranta, & Perreten, 2010). MRSP has also been isolated from household environments with actively infected animals (van Duijkeren et al., 2011).

Although active MRSP infections resolve with appropriate topical and/or systemic therapy, MRSP may persist in colonization sites (e.g. nose, mouth, rectum, axilla or perineal regions) for as long as 6 months post-therapy (Laarhoven et al., 2011). Healthy patients presenting for wellness checks may also carry MRSP asymptomatically in various colonization sites (e.g. nose, rectum) (Beck, Waisglass, Dick, & Weese, 2012; Gingrich et al., 2011; Griffeth et al., 2008; Nienhoff et al., 2011). Colonized patients

may be a source of MRSP environmental contamination increasing the risk for nosocominal colonization or infection of canine patients (Beck et al., 2012).

1.1.7 Treatment and Control of MRSP

There is no indication that MRSP is more virulent than methicillin-susceptible *S. pseudintermedius* (MSSP), though resolution may take longer with MRSP (Frank et al., 2009). While bacterial culture and susceptibility is always recommended (Hillier et al., 2014) and basing treatments on culture and susceptibility results allows for prudent use of antimicrobials, initial treatments may begin based on clinical assessment of risk for resistance. For instance, for cases of superficial bacterial folliculitis at low risk of resistance, it is recommended that beta-lactams or clindamycin are used if culture and susceptibility is not an option. However, if resistance is suspected due to history or lack of response, then treatment should be based on culture and susceptibility (Frank & Loeffler, 2012; Hillier et al., 2014). Situations that would warrant culture and susceptibility include failure to respond to appropriate antimicrobial treatment and a history of multidrug resistant infection in the dog or a pet from the same household as the dog. Resistant infections by *S. pseudintermedius* should be suspected when initial treatments fail or in patients with prior exposure to many antimicrobial classes (Hillier et al., 2014).

Anecdotal evidence exists for treatment success with chloramphenicol (Bryan et al., 2012). Adverse effects include gastrointestinal upset and weight loss as well as hindlimb muscle weakness (Bryan et al., 2012; Frank & Loeffler, 2012). Chloramphenicol is an inhibitor of the cytochrome P450 3A isoenzymes leading to potential drug toxicity (Pai, Momary, & Rodvold, 2006). Other adverse effects include

liver toxicity and bone marrow suppression (Greene, Hartmann, & Calpin, 2006). Routine monitoring of dogs on chloramphenicol should be performed, including blood screening for inappetant dogs or dogs that exhibit substantial weight loss (Frank & Loeffler, 2012; Greene, 2013). Its use is limited largely by human health concerns. While rare, exposure to chloramphenicol may lead to aplastic anemia in humans, a potentially fatal condition. Use of chloramphenicols should be accompanied by strict adherence to handling precautions (Greene, 2013).

Rifampicin is an effective treatment against *Staphylococcus* spp. and has great tissue penetration (Frank, 1990). Against MRSP strains, however, rifampicin may be ineffective (Kadlec, Duijkeren, Wagenaar, & Schwarz, 2011). One adverse effect of rifampicin therapy is hepatotoxicity (Bajwa, Charach, & Duclos, 2013; Frank, 1990). Patients should be monitored for concurrent increases in hepatic enzyme activity (Bajwa et al., 2013; Frank & Loeffler, 2012). Other clinical signs include thrombocytopenia, hemolytic anemia, anorexia, vomiting and diarrhea (Frank & Loeffler, 2012). Body secretions, such as urine, feces, saliva and tears may be red-orange (Frank & Loeffler, 2012). Rifampicin is an inducer of cytochrome P450 3A isoenzymes which can potentially lead to subtherapeutic levels (Baciewicz, Self, & Bekemeyer, 1987; Pai, Momary, & Rodvold, 2006).

Amikacin, historically, has not been commonly used in treating skin infections due to its parenteral administration, which is less acceptable to clients (Frank & Loeffler, 2012) and potential for nephrotoxicity and ototoxicity. Usage has been increasing due to MRSP, however (Frank & Loeffler, 2012).. Nephrotoxicity is the major potential adverse effect and (Frank & Loeffler, 2012). Meticulous monitoring for signs of acute kidney

injury, e.g. renal casts, glycosuria and azotemia, is extremely important when using amikacin, and can often deter the use of amikacin (Noli & Morris, 2011). Use of amikacin should be based on culture and susceptibility results that show no other antibiotics would be effective (Frank & Loeffler, 2012) and if topical therapy options are exhausted or impossible.

Tetracycline resistance is common in both MSSP and MRSP (Frank & Loeffler, 2012). Tetracycline resistance is conferred by the *tet(K)* and *tet(M)* genes (Frank & Loeffler, 2012). The *tet(K)* gene confers resistance to tetracycline but not doxycycline or minocycline (Frank & Loeffler, 2012). The *tet(M)* gene confers resistance to tetracycline, doxycycline and minocycline (Frank & Loeffler, 2012). Susceptibility of both tetracycline and minocycline should be performed. Resistance to minocycline indicates the presence of the *tet(M)* gene, implying the organism is resistant to tetracycline, doxycycline and minocycline. Minocycline may be considered a therapeutic option if doxycycline resistance is present, as it is generally well tolerated. In MRSA, doxycycline resistance can be induced by pre-incubation with tetracycline or doxycycline (Schwartz et al., 2009; Trzcinski, Cooper, Hryniewicz, & Dowson, 2000). It is not known if this is the case for MRSP (Frank & Loeffler, 2012).

Clindamycin is considered a first-line antibiotic in treating pyoderma in dogs (Bloom & Rosser, 2001; Frank & Loeffler, 2012; Littlewood, Lakhani, Paterson, Wood, & Chanter, 1999;Scott, Beningo, Miller, & Rothstein, 1998) and is a good choice for MRSP that is susceptible to clindamycin due to fewer adverse effects (Frank & Loeffler, 2012). However, clindamycin-susceptible MRSP is uncommon, and interpretation of susceptibility results can be complicated by inducible clindamycin resistance (Ganiere,

Medaille, & Mangion, 2005). Inducible clindamycin resistance should be suspected when the organism is resistant to erythromycin *in vitro* but susceptible to clindamycin. A "D-Test" (double-disc diffusion test) can be performed to determine if inducible clindamycin resistance is present. The D-test tests for clindamycin-resistance among staphylococci by placing erythromycin discs in close proximity to a clindamycin disc. Clindamycin-resistance is indicated by a "D" shaped zone of inhibition around the clindamycin-disc.

Fluoroquinolone-resistance among MRSP strains is common. As such, it may be considered a poor treatment option for MRSP (Perreten et al., 2010). However, in susceptible cases, fluoroquinolones may be preferable to rifampicin and amikacin due to adverse side effects given fewer adverse side effects. Population consumption of fluoroquinolones are associated with isolation of MRSA in humans (Venezia, Domaracki, Evans, Preston, & Graffunder, 2001; Weber, Gold, Hooper, Karchmer, & Carmeli, 2003) and, while unproven, may be the case for MRSA infection in dogs (Frank & Loeffler, 2012). It is not known if fluoroquinolones select for MRSP (Frank & Loeffler, 2012). Due to the risks and lack of therapeutic effect against MRSP infections, it is recommended that antibiotics of the fluoroquinolone class be reserved for deep infections associated with Gram-negative organization, and not for staphylococcal infections (Frank & Loeffler, 2012) .

Although, linezolid has been used successfully in the treatment of methicillin-resistant staphylococci (Murphy, 2008), and some commercial laboratories may present data for linezolid and vancomycin, these drugs are considered last-resort treatments for human MRSA patients, and use in veterinary medicine is strongly discouraged. No

reports have been published regarding the use of linezolid to treat MRSP infections in dogs in a clinical setting (Frank & Loeffler, 2012). Less evidence exists for vancomycin in the treatment of these organisms in dogs (Frank & Loeffler, 2012).

Topical therapy may be used as a sole therapy or in conjunction with systemic therapy for superficial staphylococcal pyoderma (involving the epidermis and hair follicle) and otitis externa in methicillin-susceptible or methicillin resistant infections (Frank & Loeffler, 2012; Loeffler, Cobb, & Bond, 2011; Loeffler et al., 2007). Topical therapy alone may not be able to resolve deep pyoderma (staphylococcal infection of the skin involving the dermis and/or subcutis). Shampoos that have demonstrated therapeutic responses in dogs with superficial bacterial folliculitis include those that contain chlorhexidine, benzoyl peroxide or ethyl lactate (Frank & Loeffler, 2012). Effective options for focal lesions include chlorhexidine spray, mupirocin ointment, benzoyl peroxide gel, fusidic acid or nisin (Frank & Loeffler, 2012; Werner & Russell, 1999). MRSP isolates appear to be largely susceptible to mupirocin and fusidic acid, however, resistance have been identified (Loeffler et al., 2008). Although undocumented, it is possible that staphylococcal organisms may develop resistance to topical antimicrobials, including chlorhexidine, and fusidic acid (Frank & Loeffler, 2012). Prudent use of topical therapies is always advised (Frank & Loeffler, 2012) , in particular with mupirocin and fusidic acid, given known resistance. However, there is less concern over chlorhexidine and benzoyl peroxide (Borio et al., 2015). Decolonization of MRSP in dogs (as is done with MRSA in humans) is neither practiced nor generally recommended and is controversial due to lack of studies supporting this practice (Frank & Loeffler, 2012) .

Veterinary hospital infection control practices regarding MRSP involve hand and environmental hygiene. Hand and environmental hygiene minimize the potential of unrecognized carriers and contaminated hands and objects (humans and animals) spreading the organism between patients (Frank & Loeffler, 2012). For MRSA, colonization in dogs resolved spontaneously through regular kennel cleaning alone (Loeffler et al., 2010). Although less is known about longitudinal carrier status in MRSP, this highlights the importance of environmental hygiene. Healthy dogs in contact with MRSP infected pets also show higher MRSP colonization rates (36%) (van Duijkeren et al., 2011). As such, isolation procedures within a veterinary setting for MRSP infected animals may be a necessary precaution (Frank & Loeffler, 2012). Isolation procedures include the use of barrier nursing precautions (protective aprons, overshoes, gloves) and limiting staff contact (van Duijkeren et al., 2011).

1.1.8 Zoonotic risk

Human colonization and infection by MSSP and MRSP are uncommon and is most likely due to the host predilection of *S. pseudintermedius* spp. to canines (van Duijkeren et al., 2011). Human cohabitation with dogs with deep pyoderma that are actively infected with MSSP appears to be associated with *S. pseudintermedius* colonization in humans (Guardabassi et al., 2004). However, MSSP colonization of this group of humans was short-term and resolved with the resolution of purulent lesions of the dog (Guardabassi et al., 2004). Human colonization by MSSP may also be associated with members of the veterinary profession (Hanselman, Kruth, Rousseau, & Weese, 2009; van Duijkeren et al., 2011). Infections with MSSP have been associated with dog bite wounds (Kelesidis & Tsiodras, 2010; van Duijkeren et al., 2011),

bacteremia (Somayaji et al., 2016; Vandenesch et al., 1995), brain abscess (Atalay, Ergin, Cekinmez, Caner, & Altinors, 2005), pneumonia (Gerstadt et al., 1999), ear infections (Kikuchi et al., 2004), varicose leg ulcers (van Duijkeren et al., 2011), surgical site infections and an infected implantable defibrillator (Riegel et al., 2011; van Duijkeren et al., 2011). Findings for human MRSP colonization appear to be similar (Hanselman et al., 2009; Sasaki et al., 2007a; van Duijkeren et al., 2008) and appears to be associated with members living in a household with an MRSP positive dog and/or members of the veterinary profession (van Duijkeren et al., 2011). While rare, MRSP in humans (Somayaji et al., 2016) has been associated with bacteremia in cancer patients (Campanile et al., 2007), pneumonia (Gerstadt et al., 1999) and post-operative sinus infections (Kempker et al., 2009). A cluster of wound infections by MRSP occurring in a human tertiary hospital has also been reported (Starlander et al., 2014).

1.2 Healthcare-associated infections in veterinary teaching hospitals

1.2.1 Impact of HCAIs in human and veterinary medicine

Much work has been performed on the impact of HCAIs in human medicine. Studies in human medicine would suggest that HCAIs cause a significant medical and financial toll among patients, the hospital and the healthcare system (Calfee, 2012). It is estimated that the overall direct medical costs of HCAIs in U.S. human hospitals ranges from $28 billion to $45 billion per year (Calfee, 2012; Scott, 2009). Estimates for cost per infection for surgical site infections range from $10,443 (2005 dollars) to $25,546 (2002 dollars) per infection (Scott, 2009). Cost per infection for central line-associated bloodstream infections ranged from $5,734 (2003 dollars) to $22,939 (2003 dollars) per infection (Scott, 2009). The cost for ventilator-associated pneumonias

ranged from $11,897 (1999 dollars) to $25,072 (2005 dollars) per infection (Scott, 2009). And the cost for catheter-associated urinary tract infections was estimated to be approximately $758 per infection (Scott, 2009).

Based on data submitted to the National Nosocomial Infection Surveillance (NNIS) system of the Centers for Disease Control (CDC) in 2002, >1.7 million HCAIs occur in hospital patients per year (Calfee, 2012; Klevens et al., 2007). These results would further suggest that approximately 5% of patients admitted to a hospital develop an infection during hospitalization. In 2002, there were 98,000 deaths due to HCAI (Klevens et al., 2007), placing HCAI within the top ten causes of death in the United States (Calfee, 2012). A study that further examined HCAI as the cause of death among unexpected in-hospital deaths, 31% were possibly or probably related to HCAI (Morgan, Lomotan, Agnes, McGrail, & Roghmann, 2010). This suggests that many of these patients did, in fact, die due to HCAI instead of dying with HCAI (Carrico & Ramírez, 2007). One study estimated that approximately 45% to 69% of these HCAI events are preventable (Umscheid et al., 2011).

There are fewer studies regarding the health and economic impacts of HCAIs in veterinary hospitals. This may be attributed to the fact that veterinary infection control is a relatively new discipline (Burgess & Morley, 2015). HCAI events in both small animal (Cherry et al., 2004; Weese & Armstrong, 2003) and large animal veterinary hospitals (Castor, Wooley, Shotts, Brown, & Payeur, 1989; Dallap Schaer, Aceto, & Rankin, 2010; Goehring, Landolt, & Morley, 2010; Hartmann, Callan, McGuirk, & West, 1996; Konkle, Nelson, & Lunn, 1997; Madewell et al., 1995; Schott II et al., 2001; Seguin et al., 1999; Steneroden, Van Metre, Jackson, & Morley, 2010; Tillotson et al., 1997; Ward

et al., 2005; Weese et al., 2006) have been reported and have caused significant consequences, including longer visit durations (13 months) (Seguin et al., 1999), hospital closures (Goehring et al., 2010; Schott II et al., 2001; Tillotson et al., 1997; Weese & Armstrong, 2003) and facility renovations (Dallap Schaer et al., 2010; Tillotson et al., 1997) and euthanasia of patients (Dallap Schaer et al., 2010; Goehring et al., 2010; Hartmann et al., 1996; Konkle et al., 1997; Schott II et al., 2001; Steneroden et al., 2010; Tillotson et al., 1997). Multidrug resistance has been associated with the causative agents implicated in several veterinary HCAI outbreaks (Dallap Schaer et al., 2010; Hartmann et al., 1996; Schott II et al., 2001; Seguin et al., 1999; Ward et al., 2005; J. S. Weese et al., 2006). Additionally, zoonotic infections have also been reported during HCAI outbreaks (Cherry et al., 2004; Konkle et al., 1997; Schott II et al., 2001; Seguin et al., 1999; Weese et al., 2006).

Economic impacts were only reported for two studies. Renovations to facilities were reported to cost $550,000 (Tillotson et al., 1997) in one study and lost revenue due to hospital closure, staged reopening, decreased caseload, facility remediation and decontamination and hospital coverage of patient bills was estimated at $4.12 million (Dallap Schaer et al., 2010) for another study. The pathogen involved in both of these outbreaks of HCAIs was *Salmonella*.

1.2.2 Syndromic surveillance for HCAI

Syndromic surveillance can be defined as the use of health-related data, such as non-specific indicators of disease, that precede diagnosis to signal with sufficient probability the occurrence of a case or outbreak that warrants a health response (Dorea, Sanchez, & Revie, 2011; Henning, 2004; Ruple-Czerniak et al., 2013). These

non-specific measures of disease can include clinical signs (e.g. IV catheter site inflammation, urinary tract inflammation, acute respiratory disorders, gastrointestinal disorders, surgical site inflammation and fevers of unknown origin) (Ruple-Czerniak et al., 2013) or other pre-diagnosis health-related measures, such as pharmacy sales, presenting complaint upon presentation to the hospital or laboratory test orders (Dorea et al., 2011).

Several advantages exist for syndromic surveillance. Syndromic surveillance makes use of pre-diagnostic data that, while less specific than a confirmatory diagnosis is often reported more frequently and can be utilized in a real-time analysis and interpretation (Dorea et al., 2011). While the data may not be representative of the disease burden in the entire population, the assumption is that syndromic surveillance data are sensitive to disease fluctuations in the population (Dorea et al., 2011; Yahav & Shmueli, 2007). This may provide an early, albeit weak, signal of an HCAI event (Yahav & Shmueli, 2007).

Syndromic surveillance systems can be utilized to understand risk factors for HCAI events across multiple hospitals. A syndromic surveillance study to estimate baseline rates for HCAIs in small animal critical care units of veterinary referral hospitals used the following syndromes: IV catheter site inflammation, urinary tract inflammation, acute respiratory disorders, gastrointestinal disorders, surgical site inflammation and clinical or microbiological evidence of septicemia (Ruple-Czerniak et al., 2013). Positive associations existed between the syndromes and increased duration in the hospital, undergoing surgery and placement of a urinary catheter (Ruple-Czerniak et al., 2013). The study also concluded that syndromic surveillance systems can be standardized

across multiple hospitals for effective data collection of HCAI rates and risk factors for occurrence (Ruple-Czerniak et al., 2013).

1.2.3 The electronic medical record and patient rectal temperatures as a tool for surveillance

The electronic medical record (EMR) is a relatively new technology in veterinary medicine. There is little reported about the use of EMR systems in veterinary hospitals. One study performed in 1996 reported that completeness and accuracy of data entered were so inadequate such that the intended research on post-operative complications following elective surgeries using data stored in the EMR was impossible (Pollari, Bonnett, Allen, Bamsey, & Martin, 1996). At the current time, several VTHs have fully transitioned over to the use of EMR systems. This full transition implies the storage of all medical data, including patient histories, clinician assessments, physical exam data, diagnostic and laboratory data, procedures data and treatment data. The full transition also implies the use of the EMR system as the primary interface for the clinician to enter patient data into the hospital database. However, no recent studies exist that describe the usage, completeness and accuracy of the data stored in these EMR systems.

The use of EMR data for HCAI surveillance has many advantages. Surveillance utilizing EMR data bypasses the need for paper records. Collection of patient data via chart review requires an extended amount of time and labor and lends itself to error (Wright et al., 2009). In human medicine, all EMR systems that allow for automated surveillance report a time-savings benefit (Wright, 2008). In human medicine, reductions in time and labor as a result of automated surveillance have been reported to be as high as 60% for surgical-site infection surveillance efforts (Chalfine et al., 2006).

Reductions in time spent on bloodstream infection surveillance and urinary tract infections have also been reported (Wright, 2008). In one study, automated surveillance detected 24% more HCAI when compared with traditional practitioner-based surveillance (Evans et al., 2009). Another study reported that voluntary physician reports of HCAI were only 59% sensitive while automated surveillance sensitivity was reported to be 91% (Bouam, Girou, Brun-Buisson, Karadimas, & Lepage, 2003). Specificity for voluntary physician reports of HCAI and automated surveillance were both 91% (Bouam et al., 2003).

Patient rectal temperatures are an integral component of the patient physical exam and are often interpreted as indicators of a patient's general health. VTHs that have made full transitions to using EMR systems should contain a large amount of patient rectal temperature data. Patient temperatures may be a useful indicator of infection. One human study that looked at fever and respiratory complaints in patients visiting emergency rooms for influenza surveillance found that fever was a useful surrogate marker for incident influenza-attributable morbidity (Olson et al., 2007). Increases in fever and respiratory visits corresponded in timing and magnitude with laboratory-confirmed influenza (Olson et al., 2007).

1.3 Conclusions

This review shows that the burden of MRSP via canine carriers to veterinary teaching hospitals may vary be geographic location. Further, risk factors for MRSP colonization among different patient populations within a hospital are poorly understood. HCAI surveillance within VTHs are also lacking. The EMR is a relatively new technology within the veterinary field and provide infection control professionals with

access to a large number of patient data. Use of the EMR system within VTHs may provide novel techniques into HCAI surveillance and allow for improved detection of HCAI as well as an estimate for baseline rates of HCAI.

2 Prevalence and characterization of canine Methicillin-Resistant *Staphylococcus pseudintermedius* in a veterinary teaching hospital

2.1 Summary

Background: *Staphylococcus pseudintermedius* is a commensal organism in dogs and an opportunistic pathogen. The emergence of methicillin-resistant *S. pseudintermedius* (MRSP) strains is of significant concern. The prevalence of MRSP in dogs with varying risk factors for infection, as well as serial isolation, has not been extensively described.

Hypothesis/Objective: To determine the prevalence and persistence of MRSP colonization in populations of dogs with different risk factors for infection seen at the Colorado State University Veterinary Teaching Hospital (CSU-VTH).

Animals: Two hundred and forty-three dogs presented to the CSU-VTH.

Methods: Swabs were obtained from colonization sites at enrollment and at a follow-up appointment whenever possible, owners completed a standardized questionnaire, and the medical record was examined. Enriched cultures were performed to detect MRSP.

Results: The overall prevalence of MRSP colonization at enrollment (9/243) was 4% and at follow-up (7/155) was 5%. Dermatology patients had a significantly higher prevalence of colonization with MRSP compared to other groups. Colonization persistence in paired samples was seen in Dermatology patients only. Colonization was not associated with hospitalization or recent antimicrobial use.

Conclusions and Clinical Importance: Prevalence of MRSP colonization and persistence was highest in Dermatology patients. The overall prevalence of MRSP

colonization in dogs was low and similar to previous reports. Hospitalization and recent antimicrobial use were not found to be risk factors for MRSP colonization.

2.2 Introduction

Staphylococcus pseudintermedius is a commensal bacterium of dogs in the *Staphylococcus intermedius* group that can be an opportunistic pathogen (Harvey & Noble, 1998). It is the most commonly isolated bacterium from lesions of skin and ear infections (Bloom, 2014; Zur, Gurevich, & Elad, 2016) and surgical site infections in dogs (Turk, Singh, & Weese, 2015). However, *S. pseudintermedius* can be isolated frequently from healthy dogs as well, at rates ranging from 46-92%, depending upon the sampling site and method of isolation employed (Bannoehr & Guardabassi, 2012). Common canine carriage sites of *S. pseudintermedius* include the anal region, rostral nares, and oral cavity (Devriese & De Pelsmaecker, 1987). It is thought that resident bacteria from these and other carriage sites are the pathogen source in dogs in which opportunistic infections occur (Pinchbeck et al., 2006).

The development of antimicrobial resistance in bacteria is a significant concern, both from an animal welfare and public health standpoint (Pomba et al., 2016). One of the mediators of methicillin-resistance in staphylococci is the gene *mecA*, which codes for PBP2a, an altered penicillin-binding protein (PBP) inducing resistance to all beta-lactam drugs (van Duijkeren et al., 2011). The *mecA* gene is located on the staphylococcal chromosomal cassette (*SCCmec*), a mobile genetic element that is transmissible among staphylococcal species and was first discovered in *S. aureus* (Descloux, Rossano, & Perreten, 2008; Katayama, Ito, & Hiramatsu, 2000). Because of this cassette's mobility, it is not surprising that methicillin resistance mediated by *mecA*

has also emerged in *S. pseudintermedius*, appearing to be increasing in frequency since 2006 (Weese & van Duijkeren, 2010).

Recent hospitalization and antimicrobial use have been reported to be risk factors for MRSP colonization and/or infection in dogs (Huerta et al., 2011; Nienhoff et al., 2011; Weese, Faires, Frank, Reynolds, & Battisti, 2012). Contamination or colonization of clinic personnel and equipment as well as cross-infection of patients within a veterinary clinic have been demonstrated (Nazarali et al., 2015; van Duijkeren et al., 2008; Zubeir et al., 2007), underscoring the potential importance of *S. pseudintermedius* as a cause of hospital associated infections in dogs requiring vigilance in veterinary care settings. While clinical human infections with MRSP appear to be rare, its importance as a potential zoonosis also deserves appropriate recognition of transmission risks (Somayaji et al., 2016).

Colonization rates of methicillin-resistant *S. pseudintermedius* (MRSP) in healthy dogs are low (Bean & Wigmore, 2016; Beck et al., 2012; Griffeth et al., 2008; Hanselman et al., 2008; Vengust et al., 2006), but 34-66% of dogs with pyoderma and/or otitis are reported to be MRSP infected (Beck et al., 2012; Kawakami et al., 2010; Siak et al., 2014; Weese et al., 2012). A search of medical records for canine dermatology patients cared for at Colorado State University Veterinary Teaching Hospital (CSU-VTH) in 2014-2015 using search terms of pyoderma, otitis, *Staphylococcus*, antimicrobial resistance (AMR), methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus pseudintermedius* identified a cumulative incidence of documented MRSP in only 2% of dermatology patients (37/1,917). While this suggests that there may be a relatively low risk of transmission of MRSP at the CSU-

VTH,dogs can be colonized with MRSP without developing apparent infections. As such, this study was designed to evaluate the risk of colonization and persistence of carriage of MRSP in dogs that were presented for 3 different types of care at the CSU-VTH.

2.3 Materials and Methods

2.3.1 Study overview

A longitudinal study was conducted to estimate rates of colonization in dogs belonging to three different risk groups: those admitted to the Community Practice, Dermatology and Surgical Oncology services at the Colorado State University Veterinary Teaching Hospital (CSU-VTH). Signalment and history was collected using a standardized questionnaire, and dogs were sampled on two occasions to identify colonization with MRSP. Relationships between potential risk factors and the likeilihood of colonization were assessed using logistic regression. The methods used in this study were reviewed and approved by the Institutional Animal Care and Use Committee at Colorado State University (approval number 14-5079A).

2.3.2 Study population

The Community Practice, Surgical Oncology, and Dermatology Services were selected to represent groups of dogs predicted to have, respectively, low, moderate, and high risks for exposure, colonization, and infection with MRSP. Each service enrolled eligible dogs based on convenience sampling during the study period. Dogs were eligible for the study if they presented to 1 of the 3 selected services during the period from October, 2014 through June, 2015. Owner consent was obtained, and owners agreed to a follow-up sampling.

2.3.2.1. Community Practice

Dogs enrolled through Community Practice were predicted to have a low risk of active infection or colonization. Patients were eligible for inclusion in the study if the patient was presented for vaccination or another type of wellness appointment and had no history of receiving systemic antibiotics or visiting a veterinary hospital in the last 6 months. Owners who enrolled their dogs through Community Practice were given a financial incentive to return for follow-up sampling within 2 to 4 weeks.

2.3.2.2. Surgical Oncology

Patients enrolled through Surgical Oncology received planned surgery as part of the therapy for their cancer-related illness and stayed overnight (≥ 12 hours) at the CSU-VTH. They were considered to be at moderate risk for acquiring an infection during hospitalization, given they were undergoing invasive procedures and exposures to multiple hospital areas and departments during their treatment and potentially receiving antimicrobials. Follow-up samples for patients enrolled through Surgical Oncology occurred one hour prior to discharge, i.e. both admission and follow-up samples occurred during the same hospital stay.

2.3.2.3. Dermatology

Patients from the Dermatology service were considered to have a high risk of colonization and active infection because *S. pseudintermedius* is recognized as an important pathogen in dermatological disease in dogs. Since these patients were being seen in a tertiary teaching hospital and their disease was likely chronic, it was also thought probable that they would have recently received antimicrobial drugs. Dogs presenting to the Dermatology service were eligible for inclusion into the study if the

patient was presenting for first time or recheck appointment regardless of antimicrobial history or history of MRSP pyoderma. Clients were instructed to return with their dogs in 2 to 4 weeks for a follow-up sample.

2.3.3 Sample collection

Patients enrolled in the study were sampled for MRSP colonization twice: once at enrollment and once at follow-up.

Each patient was sampled at the nares, oral cavity, and anus using a different culturette swab for each site. Sampling was performed by veterinary personnel working in the participating services, who were trained in order to standardize collection. Additionally, all services were provided with written instructions regarding inclusion criteria and sampling technique. Clean nitrile exam gloves were worn when sampling. For sampling of the nares, culturette swabs were placed just inside the nares and gently rotated. If the nares were too small to insert a swab, the nasal planum was swabbed instead. For sampling of the oral cavity, culturette swabs were placed in the left and right maxillary and mandibular commissures at the junction of the gingiva and labial mucosa. For sampling of the anus, the anal ring was swabbed circumferentially with a culturette swab. Once sampling was complete, each swab was placed in commercial sample transport tubes containing Amies media, and the 3 tubes were placed into a plastic bag for transport to the laboratory. Random numbers were generated and used to label samples to mask patient identification and medical histories were not available in order to blind laboratory personnel.

A questionnaire was designed prior to the study to uniformly collect information regarding each patient. The questionnaire was administered each time samples were

collected. History pertaining to antimicrobial treatments (topical or oral) within the prior 12 months, methicillin-resistant *Staphylococcus* infection history within the prior 12 months and surgery or penetrating wound history within the prior 12 months were actively and uniformly obtained from the client as well as from the medical records from the CSU-VTH and referring veterinarian. Antimicrobial history between sampling times was obtained at follow-up sampling, allowing for a prospective gathering of data.

2.3.4 Laboratory methods

Samples for each patient were pooled and placed in 10% salt-meat enrichment broth (HiMedia) (Chapman, 1945; Fairbrother & Southall, 1950; Maitland & Martyn, 1948) and incubated at 37°C for 18 hours. Samples were then placed on a screening agar containing oxacillin (2 μg/ml) and incubated at 37°C for 18-24 hours. Three suspected staphylococcal colonies were selected from each plate, and streaked for isolation onto a blood agar plate and incubated at 37°C for 18-24 hours. Suspect colonies were Gram-stained and tested for catalase reaction. Identification of presumed MRSP colonies was confirmed using PCR to identify the *nuc* gene for *S. pseudintermedius* (Sasaki et al., 2007b, 2010) and also by matrix-assisted laser desorption/ionization time-of-flight spectrometry (MALDI-TOF).

2.3.5 Data analysis

Information regarding patient signalment, history, and laboratory testing results were entered in a computer spreadsheet. Data were analyzed descriptively to summarize the prevalence of recovery of MRSP. Proportions from paired samples were compared using McNemar's test, and proportions for independent samples were compared using the chi-square test. Width adjusted 95% confidence intervals (95%CI)

for binomial proportions were calculated, adding 2 successes and 2 failures to actual counts (Agresti & Coull, 1998).

2.4 Results

A total of 243 patients were enrolled in the study (Table 1); 60 dogs were enrolled through the Community Practice service, 71 dogs were enrolled through the Dermatology service and 112 dogs were enrolled through the Surgical Oncology service. Patients enrolled through the Community Practice service were widely variable in age (Table 1), whereas a majority of patients enrolled through the Surgical Oncology service were > 7 years old, and a majority of patients enrolled through the Dermatology service, were > 2 years old.

Dermatology was the only service with a majority of enrolled patients having received prior or current systemic or topical antimicrobial treatment within the previous 12 months (72%; 51/71) compared to the Community Practice (5%; 3/60) or Surgical Oncology (37%; 41/112) services. The proportion of patients with surgery or wounds within the previous 12 months was 8% (5/60) for Community Practice patients, 20% (14/71) for Dermatology patients and 34% (38/112) for Surgical Oncology patients. Four of the patients presented to Dermatology (4/71; 5%) and 1 of the patients presented to Surgical Oncology (1/112; 0.9%), for a total of 5/243 (2%), had been diagnosed with MRSP in the previous 12 months (Table 1).

The proportion of MRSP colonization was 4% (9/243; 95% CI, 2% – 7%) at enrollment and 5% (7/156; 95% CI, 2% – 9%) at follow-up (Table 1). Dermatology had the greatest proportion of patients, at 8 %, (6/71; 4% - 17%), that tested positive for MRSP at colonization sites (Fisher's P-value < 0.05). No patients enrolled through the

Community Practice service (0/60) were culture-positive for MRSP at colonization sites at the time of admission, and 3% (3/112) of patients enrolled through the Surgical Oncology service were positive (Table 2). History of prior surgery or penetrating wound, antimicrobial drug treatment, or prior MRSP infection was not associated with the likelihood of being culture positive at the time of admission ($P > 0.05$).

Paired samples (i.e., at enrollment and follow-up) were collected from 64% (155/243) of enrolled patients. Among patients that had both paired samples, 94% (145/155; 95% CI, 89% – 96%) cultured negative at both time points, 5% (7/155; 95% CI, 2% – 9%) were cultured positive at 1 time point (either at enrollment or follow-up) and 2% (3/155; 95% CI, 0% – 6%) cultured positive at both time points. For patients that cultured positive at enrollment only, 1 patient (33%; 1/3; 95% CI, 0% - 4%) had a surgical procedure or penetrating wound within the prior 12 months to enrollment and only 1 patient (33%; 1/3; 95% CI, 0% - 4%) received antimicrobials within the 12 months prior to enrollment. None of these patients were diagnosed with MRSP within the previous 12 months. For patients that cultured positive only at follow-up, 1 (25%; 1/4; 95% CI, 0% - 4%) patient underwent surgery or had a penetrating wound within the 12 months prior to enrollment, 1 (25%; 1/4; 95% CI, 0% - 4%) patient had been treated with antimicrobials within the prior 12 months to enrollment, and 2 (50%; 2/4; 95% CI, 0% - 5%) patients had received antimicrobials between enrollment and follow-up. None of these patients had a history of MRSP within the prior 12 months. All 3 patients that cultured positive at both enrollment and follow-up were Dermatology patients and had received antimicrobials within the 12 months prior to enrollment; 1 (33%; 1/3; 95% CI, 0% - 13%) patient had received antimicrobials between enrollment and follow-up. None

of these patients had a history of MRSP infections or surgery or penetrating wounds within the 12 months prior to enrollment.

Among patients with paired samples, there was no difference in the proportion that were culture-positive at admission compared to those that were culture-positive at follow-up (McNemar's *P*-value = 1.0). The proportion of study subjects from which paired samples were collected was notably higher for the Surgical Oncology patients (79%; 88/112; 95% CI, 70% – 85%) in comparison to the Dermatology patients (58%; 41/71; 95% CI, 46% - 69%) and the Community Practice patients (45%; 27/60; 95% CI, 33% – 58%).

MRSA was isolated from colonization sites from 4 patients on the first sampling; 3 were enrolled through Dermatology and 1 through Surgical Oncology. All of these patients had a history of antimicrobial use in the past 12 months but had not been previously diagnosed with resistant staphylococci. One of the Dermatology patients was co-colonized with MRSP. This patient also had a history of surgery or wound in the last 12 months. MRSA was isolated from one Community Practice patient on the follow-up sample; this patient was also co-colonized with MRSP at this time and had not been colonized with either MRSP or MRSA on the enrollment sample. Since this patient was a Community Practice patient, it did not have hospitalization or antimicrobial use risk factors.

2.5 Discussion

Results of this study suggest that the burden of MRSP colonization in canine patients at the CSU-VTH was, regardless of the predicted risk of the population, relatively low (Table 2), similar to previous reports of MRSP colonization in the United

States (Detwiler et al., 2013; Hanselman et al., 2008). This lower burden of colonization is consistent with the inference obtained from evaluating documented diagnosis of MRSP infections among dermatology patients treated at the CSU-VTH prior to this study (data not shown). While the goal of this study was to characterize MRSP colonization, culture methods used in this study also allowed detection of MRSA, and the prevalence of colonization with this zoonotic pathogen was also very limited.

While all clients agreed to return for follow-up sampling at the time they enrolled their dogs, and despite attempts to contact all participating clients, follow-up sampling was less complete than anticipated. Not surprisingly, follow-up sampling was most complete for Surgical Oncology patients where both samples were obtained within the same hospital stay. The services utilized a convenience sampling strategy rather than random sampling, which could have created an enrollment bias; however,enrolling personnel were unaware of MRSP colonization status at time of enrollment suggesting that this bias was unlikely to affect results. As predicted, this study suggests that healthy patients (represented by those enrolled through the Community Practice service) were less likely to carry MRSP. In addition, Surgical Oncology patients, despite their increased exposure to multiple areas of the hospital environment during their hospitalization, did not have a higher risk of acquisition of MRSP compared to the other populations and also did not exhibit persistence of colonization. Because of the high number of dogs that were Surgical Oncology patients for which paired samples were obtained, it would seem likely that acquisition of MRSP between enrollment and discharge would have been detected.

Although prevalence was lower than in some recent reports, this study supports the impression that patients with dermatological disease may be at higher risk of MRSP colonization (Beck et al., 2012; Kania et al., 2004). Dermatology patients had a significantly higher proportion of MRSP colonization for both enrollment samples and follow-up samples (Table 2) compared to the other populations. Based on paired samples collected, colonization persistence among patients also only occurred among those enrolled by the Dermatology service (Appendix 2). History of MRSP infection did not preclude enrollment, but this was not associated with colonization during this study. However, since Dermatology patients tended to be more likely to have colonization that persisted for at least 2 to 4 weeks compared to the other populations, this suggested that colonization tends to be more transient in non-dermatological patients. These results are in contrast to the findings of Windahl et al. (2012), who reported that the overall median length of MRSP carriage in dogs with a history of clinical MRSP infection was 11 months and the duration of carriage was not affected by the presence of wounds or dermatological disease.

Association of recent antimicrobial treatment with MRSP colonization and infection has been mixed in previous studies (Beck et al., 2012; Weese et al., 2012). This study did not find an association between previous antimicrobial use and MRSP colonization. This study also did not find an association between hospitalization in the Surgical Oncology patients and MRSP colonization, while previous studies have found an association between hospitalization and MRSP colonization (Nienhoff et al., 2011). It is possible that the low overall prevalence of MRSP colonization in canine patients admitted to the CSU-VTH makes it less likely for dogs to nosocomially acquire MRSP in

this particular veterinary care setting. The possibility of false negatives obtained in the culture process for the colonization samples should also be considered; however, the cultures of the lesions in the dermatological patients were performed in the clinical laboratory serving the CSU-VTH and demonstrated a similar low prevalence.

In humans, colonization by MRSA is a known risk factor for subsequent MRSA infection and associated sequelae (Huang & Platt, 2003). It stands to reason that MRSP colonization in dogs is a likely risk factor for subsequent MRSP infection. In fact, such an association has been shown for pre-operative MRSP-colonized dogs receiving tibial plateau leveling osteotomies (TPLO) surgeries and post-operative surgical site infection by MRSP (Nazarali et al., 2015). Based on this information and our study results, dermatologic patients should be potentially considered to be at higher risk of complications associated with MRSP infection sequelae when undergoing surgical procedures such as TPLO due to their relatively high rate of more persistent colonization. In addition, these patients should be considered to be at a relatively higher risk of being a reservoir of MRSP for transmission to in-contact animals and people and contamination of the environment.

2.6 Tables

Table 1 - Demographics of enrolled patients

Characteristics		Total (n = 243)		Community Practice (n = 60)		Dermatology (n = 71)		Surgical Oncology (n = 112)	
		Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI	Number (%)	95% CI
Age	< 2 years	32 (13)	(9, 18)	24 (40)	(29, 53)	6 (8)	(4, 17)	2 (2)	(0, 6)
	2 - 7 years	65 (27)	(22, 33)	18 (30)	(20, 43)	31 (44)	(33, 55)	16 (14)	(9, 22)
	> 7 years	146 (60)	(54, 66)	18 (30)	(20, 43)	34 (48)	(37, 59)	94 (84)	(76, 90)
Sex	Intact female	8 (3)	(2, 6)	4 (7)	(3, 16)	1 (1)	(0, 8)	3 (3)	(1, 8)
	Spayed female	97 (40)	(34, 46)	23 (38)	(27, 51)	32 (45)	(34, 57)	42 (38)	(29, 47)
	Intact male	11 (5)	(3, 8)	8 (13)	(7, 24)	1 (1)	(0, 8)	2 (2)	(0, 6)
	Castrated male	127 (52)	(46, 58)	25 (42)	(30, 54)	37 (52)	(41, 63)	65 (58)	(49, 67)
AMD[1]	Yes	95 (39)	(33, 45)	3 (5)	(2, 14)	51 (72)	(60, 81)	41 (37)	(28, 46)
	No	148 (61)	(55, 67)	57 (95)	(86, 98)	20 (28)	(19, 40)	71 (63)	(54, 72)
MRSP Infection[2]	Yes	5 (2)	(1, 5)	0	(0, 6)	4 (6)	(2, 14)	1 (1)	(0, 5)
	No	232 (95)	(92, 97)	60 (100)	(94, 100)	66 (93)	(85, 97)	106 (95)	(89, 98)
	Unknown	6 (2)	(1, 5)	0	(0, 6)	1 (1)	(0, 8)	5 (4)	(2, 10)
Surgery/Wound[3]	Yes	57 (23)	(19, 29)	5 (8)	(4, 18)	14 (20)	(12, 30)	38 (34)	(26, 43)
	No	186 (77)	(71, 81)	55 (92)	(82, 96)	57 (80)	(70, 88)	74 (66)	(57, 74)

AMD = antimicrobial drug; MRSP = methicillin-resistant *Staphylococcus*; CI = confidence interval

[1]Patients that received antimicrobial treatment within 12 months prior to enrollment.

[2]Patients that had a methicillin-resistant *Staphylococcus* infection within 12 months prior to enrollment

[3]Patients that had surgery or penetrating wound with 12 months prior to enrollment.

Table 2 - Proportion of MRSP positive samples at enrollment and follow-up

	Enrollment Samples			Follow-up Samples		
Study Group	**n**	**MRSP Positive (%)**	**95% CI (%)**	**n**	**MRSP Positive (%)**	**95% CI (%)**
Community Practice	60	0	(0, 6)	27	1 (4)	(1, 18)
Dermatology	71	6 (8)	(4, 17)	41	4 (10)	(4, 23)
Surgical Oncology	112	3 (3)	(1, 8)	87	2 (2)	(1, 8)
Total	243	9 (4)	(2, 7)	155	7 (5)	(2, 9)

MRSP = Methicillin-resistant *Staphylococcus pseudintermedius*; CI = Confidence interval

3 Fevers detected in canine patients after admission to a veterinary teaching hospital using electronic medical record data

3.1 Summary

Background: The ability to identify healthcare-associated infections (HCAI) in veterinary hospitals is frequently hampered by limited surveillance capability. Rectal temperatures are commonly recorded in electronic medical record (EMR) databases for all patients. Since post-admission fever may be an indication of HCAI, electronic records of rectal temperatures may assist in HCAI surveillance.

Hypothesis/Objective: To estimate the incidence of post-admission fevers in hospitalized canine patients at the Colorado State University Veterinary Teaching Hospital (CSU-VTH) and associations with type of patient care and duration of hospitalization.

Study Population: Six thousand four hundred and sixty-nine canine patients hospitalized between January 1, 2012 and June 30, 2015 at the CSU-VTH.

Methods: Retrospective study. Patient data were extracted from the EMR database, summarized, and analyzed to assess associations between fever after admission and patient variables.

Results: The estimated cumulative incidence of fevers after admission was 9%. There were positive associations between the development of post-admission fever and complicated case management requiring multiple services (OR = 1.3; 95% CI = 0.9 – 1.9) and hospitalization >2 days (OR = 2.4; 95%; CI = 2.0 – 2.9).

Conclusions and Clinical Importance: Rectal temperatures in EMR databases may provide useful information for HCAI surveillance.

3.2 Introduction

Control of healthcare-associated infections (HCAI) is critically important to the delivery of the highest quality care in veterinary hospitals (Morley, 2013; Morley et al., 2013). The adverse impacts of HCAI on human and veterinary healthcare are well known (Calfee, 2012; Klevens, 2007; Morley, P.S. 2013) as well as the beneficial effect of surveillance in reducing their incidence (Benedict, Morley, & Metre, 2008; Pearson, 2009). However, implementation of HCAI surveillance programs in veterinary hospitals has frequently been a challenge for several reasons. There is limited information available regarding risk factors for healthcare-associated infections (HCAI) in veterinary medicine (Benedict et al., 2008; Burgess & Morley, 2015; Morley, 2013; Ruple-Czerniak et al., 2013). Without such information, it is difficult to logically target appropriate surveillance efforts. In a patient population of various species with different susceptibilities to numerous potential pathogens, it is difficult to select which specific HCAI should be monitored. Additionally, the veterinary profession has an incomplete understanding of acceptable rates of HCAIs, frequently because hospitals do not perform comprehensive surveillance to establish baseline rates.

Syndromic surveillance, or the measurement of non-specific indicators of disease such as fever of undetermined origin, diarrhea and/or vomiting, or intravenous catheter site inflammation, is a system for monitoring the health of a population that can be used to estimate rates of HCAI (Ruple-Czerniak et al., 2013). Rather than targeting a specific pathogen requiring laboratory confirmation, syndromic surveillance allows the “casting

of a wide net" to identify patients manifesting any clinical signs that could be indicative of an HCAI. The increasing availability and use of electronic medical record (EMR) systems has the potential to facilitate the implementation of syndromic surveillance programs for HCAIs by bypassing the manual extraction of patient parameters from handwritten medical records. The Colorado State University Veterinary Teaching Hospital (CSU-VTH) has been utilizing an EMR to record patient data, including rectal temperatures, since 2010.

The purpose of this study was to determine the cumulative incidence of post-admission fevers in hospitalized canine patients at the CSU-VTH and assess whether the occurrence of a post-admission fever was associated with type of patient care or duration of hospitalization. It was hypothesized that dogs with more severe disease, complex case management, and longer duration of hospitalization would be at higher risk of developing a fever of unknown origin after admission to the hospital.

3.3 Materials and methods

3.3.1 Study Overview

A retrospective longitudinal study was used to estimate the frequency that fevers were detected after admission among dogs hospitalized at the CSU-VTH. Patient data were obtained from an EMR system that was custom designed for use at this hospital for admissions occurring between January 1, 2012, and June 30, 2015. Visits were classified by the service providing care as a proxy for type of illness. Data were summarized, and logistic regression was used to investigate associations between the outcome of interest (fever after arrival) and two exposure variables of interest (type of patient care, and duration of hospitalization categorized as ≤2 days or <2 days).

3.3.2 EMR Description

The EMR system used during the study period was a customized computer system designed for use at the CSU-VTH (VetPoint©, College of Veterinary Medicine & Biomedical Sciences, Colorado State University). Patient information was entered into standardized web-based forms by care providers, and data were stored in relational databases on computers located at Colorado State University. Each patient was assigned a unique identifying number within the medical records system ("case number"), and each patient visit was also assigned a unique identifying number ("invoice number") which was linked to charges recorded within the CSU-VTH accounting system. Rectal temperatures were recorded along with other physical examination (PE) findings on a standardized PE form. Charges for services and materials that were used in the care of patients were recorded within the accounting system by the different hospital services (cost-centers) within the CSU-VTH (e.g. Internal Medicine, Surgery, Oncology, Emergency and Critical Care (ECC) services (including both Urgent Care and Critical Care), Anesthesiology, Cardiology and Cardiovascular Surgery, Community Practice, Dentistry and Oral Surgery, Dermatology, Ophthalmology, Radiation Therapy, Sports Medicine, Diagnostic Imaging, Bacteriology, Clinical Pathology, etc.). The link between charges invoiced by the different service centers and the unique invoice numbers were used to classify patients with regard to the type of care that they received.

Ideally, for use in a computerized surveillance system, temperatures would have been recorded in a standard fashion, in a single field. However, in actual practice, temperatures are measured and recorded in a variety of places in the medical records.

While specific fields for recording rectal temperatures were only contained within the physical examination (PE) forms, rectal temperatures were sometimes also recorded in other comment or free-text fields which were not searchable in a systematic fashion. The PE forms were required to be associated with a subjective-objective-assessment-plan (SOAP) form, and there was only a single PE form available per SOAP form. In addition to rectal temperatures, other data that could be entered into the PE forms, e.g. attitude, capillary refill, hydration status, were not available for analysis. While multiple SOAP forms could be completed for patients on each hospitalization day, it was very infrequent that multiple SOAP form were opened on any given day to capture patient information. As such, there was typically only a single rectal temperature recorded per patient per day.

3.3.3 Inclusion criteria and case definition

Medical record databases were searched to identify all dogs that were admitted to the CSU-VTH between January 1, 2012 and June 30, 2015, were hospitalized for ≥ 1 night, documented as being afebrile (≤102.5°F or ≤39.2°C) at admission, and had rectal temperatures recorded ≥ 1 additional time during the same hospitalization period (i.e., the rectal temperatures must have been recorded at least twice during hospitalization). Patients that subsequently developed a fever (>102.5°F or >39.2°C) after admission were identified as having the outcome of interest.

3.3.4 Type of patient care and duration of hospitalization

Visits were classified by the service providing care as a proxy for type of illness, disease severity, complexity of case management (i.e. number of involved personnel), and likelihood of invasive procedures. Patients were divided into 7 different categories:

Medicine, Oncology, Surgery, Medicine and Emergency and Critical Care (ECC), Oncology and ECC, Surgery and ECC, and Other. Patients who were seen by ECC likely had more severe disease and exposure to additional personnel than patients not seen by ECC. Patients were classified in the "Other" category if they were cared for by ECC in combination with not just one, but at least two of the Oncology, Surgery, and Medicine Services and potentially additional specialty services as well, indicating that these patients had the most complex disease.

Patients that were cared for by Cardiology and Cardiovascular Surgery and Neurology service centers were classified as Internal Medicine cases for the purposes of analysis in this study. Patient visits in which the associated care centers only included diagnostic services (e.g. Radiology, Bacteriology, Clinical Pathology) with no additional involvement by at least one Primary, Specialty, Outpatient or ECC service, were excluded.

Duration of hospitalization was determined using financial databases and client charges for hospitalization.

3.3.5 Analysis

Extracted data were summarized in computer databases, and analyzed to characterize the risk for fever occurrence after admission. Additionally, analyses were conducted to compare the risk of fever after admission in different patient groups, and to evaluate whether fever occurrence was associated with duration of hospitalization. The case type categories were used to create mutually exclusive classification variables that were used in multivariable logistic regression models (Table 3). Patient demographic information was analyzed descriptively, and the cumulative incidence of fevers that

were recognized after admission was calculated. Repeated measures multivariable logistic regression was used to investigate a priori hypothesis that occurrence of fevers were associated with duration of hospitalization and the type of care that patients received (alpha = 0.05) (R, R Core Team 2013). For the purpose of this analysis, duration of hospitalization was classified dichotomously (≤2 days, or >2 days). Odds ratios (OR), confidence intervals (CI) and p-values were calculated using the results of the multivariable logistic regression models.

3.4 Results

The initial dataset extracted from the EMR contained 84,608 unique patient visits for dogs. After excluding visits where patients were not hospitalized at the VTH, 11,345 (13%) unique visits remained. Visits where the patient was not seen by a primary care service were further excluded, leaving 11,251 unique visits eligible for inclusion into the study. Finally, after exclusion of visits with <2 rectal temperature records in the EMR or visits where the temperature taken at admission was febrile were excluded, 6,469 (8%) unique visits were included in the study. Fevers that developed after admission (with afebrile temperatures at admission) were reported for 9% (588/6,469) of patient visits during the study period.

Of these 6,469 patients, 297 (5%) were intact females, 2,835 (44%) were spayed females, 438 (7%) were intact males, and 2,895 (45%) were neutered males (Table 1). Medicine patients comprised 4% (225/6,469), 20% (1,226/6,469) were Medicine cases with ECC involvement, 8% (516/6,469) were Surgery cases, 16% (1,064/6,469) were Surgery cases with ECC involvement, 5% (346/6,469) were Oncology cases, 8% (519/6,469) were Oncology cases with ECC involvement, and 40% (2,573/6,469) were

cases classified as Other. The length of stay for 79% (5,079 /6,469) of patient visits was ≤ 2 days. The 5 most commonly enrolled breeds were mixed breeds (27%; 1,778 /6,469), Labrador Retrievers (10%; 633/6,469), Golden Retrievers 4%; 278/6,469), Chihuahuas (3%; 217/6,469) and Staffordshire terriers (2%; 159/6,469) (Table 1). Other breeds that made up the top 70% of enrolled dogs included dachshunds, German Shepherds, boxers, Australian shepherds, beagles, huskies, border collies, shih tzus, beagles, Yorkshire terriers, Australian cattle dogs, English bulldogs, Jack Russell terriers, miniature schnauzers, and Rottweilers. The breeds of the remaining dogs made up 31% (1,945/6,469) of the enrolled patient population.

Controlling for the duration of hospitalization, there were significant differences in the risk of developing fevers after admission among patients cared for by different services (*P*-value < 0.001, Table 3). Patients in the "Other" category (with the most complex case management) had the highest risk of developing a fever of unknown origin. (OR = 1.31, CI = 0.93 – 1.85). Cases seen by Medicine alone had the lowest risk of fever (OR = 0.37, CI = 0.17-0.80) (Table 3).

Controlling for differences in services managing the cases, duration of hospitalization was also associated with the odds of developing fevers after admission. Patients hospitalized for > 2 days had over twice the odds of developing fevers after admission compared to those hospitalized for 1-2 days (OR 2.4; 95%CI=2.0-2.9; *P*-value < 0.001).

3.5 Discussion

This study demonstrated that canine patients with critical illness and complex case management that were hospitalized for greater than 2 days had an increased risk

of developing fever of unknown origin. Fever of unknown origin has been previously associated with HCAI in canine patients in critical care units of small animal hospitals (Ruple-Czerniak et al., 2013). The positive association of fever with duration of hospitalization is consistent with previous studies that showed similar associations between increased length of stay and HCAI acquisition (Eugster, Schawalder, Gaschen, & Boerlin, 2004; Smarick et al., 2004). Patients that have longer hospital stays are likely to have more severe illness, but it also creates opportunities for increased exposure to infectious agents within the hospital environment. Case complexity, i.e., the involvement of more than one service in the care of the patient, increases the exposure of the patient to numerous personnel and areas of the hospital, potentially increasing exposure to nosocomial pathogens. Therefore, it stands to reason that case complexity would increase risk for the development of HCAI.

This study also shows that the EMR could potentially help identify risk of HCAI due to other patient populations. While the current study focuses on hospitalized patients, the EMR reveals that the vast majority of patients that visit the VTH are not hospitalized (87%; 73,263/84,608). While the risk of HCAI acquisition to non-hospitalized patients is likely lower than that of patients who are hospitalized, non-hospitalized patients may pose an infectious risk to other patients. EMR data can also be used to understand the infectious risk from patients febrile at admission. Of the visits where the patient was hospitalized under the care of a primary service, 27% (3,052/11,251) of these patients were febrile upon admission. While these visits were not the focus of this study and were ultimately excluded, these patients could be a source of infection to other patients in the hospital.

This study did not specifically examine the association between fevers after admission and HCAIs. This association was difficult to examine because there is currently no method of indicating HCAI occurrence in VTH patients in the EMR. A fever identified after admission may be a part of the presenting patient's disease process and not necessarily due to HCAI. Another study limitation is that, while multiple temperatures are often collected per patient visit per day, typically only one temperature per day was entered into the EMR. Rectal temperatures are subject to variation throughout the day. It is possible that, with only one temperature per day per patient visit available in the EMR, the number of fevers after admission may be underestimated.

Anecdotally, the greatest hindrance to consistent patient data entry was the complexity of the patient data entry process of the EMR. While ease of data entry was not evaluated in this study, it is reasonable that less frequent recordings of patient data will occur if the entry process is complicated. Patient data such as rectal temperatures, where variation throughout the day is to be expected, requires frequent collection and entry into the EMR. In contrast, other syndromes used in surveillance for HCAI, such as IV catheter site inflammation, urinary tract inflammation, acute respiratory disorders, GI disorders or surgical site inflammation could be entered once a day without the anticipation of loss of sensitivity (Ruple-Czerniak et al., 2013).

This study demonstrates the potential use of the EMR in a veterinary teaching hospital for retrospective syndromic surveillance in hospitalized patients to identify HCAI. Further work to support the correlation of HCAI with fever of unknown origin and other syndromes will be helpful to validate this approach. In addition, the exploration of methods to increase ease of data entry into the EMR and add "check-box" areas for

syndromic surveillance will be useful for these types of studies. This study also identified the risk factors of duration of hospitalization and complex case management with the development of fever, a potential indicator of HCAI.

3.6 Tables

Table 3 - Patient demographics for study subjects (n = 6,469)

Characteristics		Total (n = 6469) (%)	Internal Medicine (n = 225) (%)	Internal Medicine + ECC (n = 1226) (%)	Surgery (n = 516) (%)	Surgery + ECC (n = 1064) (%)	Oncology (n = 346) (%)	Oncology + ECC (n = 519) (%)	Other (n = 2573) (%)
Sex	Intact female	297 (5)	8 (4)	46 (4)	35 (7)	65 (6)	10 (3)	5 (1)	128 (5)
	Spayed female	2835 (44)	106 (47)	571 (47)	239 (46)	430 (40)	153 (44)	228 (44)	1108 (43)
	Intact male	438 (7)	21 (9)	90 (7)	35 (7)	100 (9)	18 (5)	24 (5)	150 (6)
	Neutered male	2895 (45)	90 (40)	518 (42)	206 (40)	468 (44)	165 (48)	262 (50)	1186 (46)
	Undetermined	4 (0)	0 (0)	1 (0)	1 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Length of stay	≤ 2 days	5079 (79)	188 (84)	754 (62)	492 (95)	723 (68)	279 (81)	375 (72)	2268 (88)
	> 2 days	1390 (21)	37 (16)	472 (38)	24 (5)	341 (32)	67 (19)	144 (28)	305 (12)
Breed	Mix	1778 (27)	60 (27)	263 (21)	137 (27)	194 (18)	92 (27)	117 (23)	915 (36)
	Labrador	633 (10)	20 (9)	90 (7)	73 (14)	118 (11)	56 (16)	73 (14)	203 (8)
	Golden retriever	278 (4)	8 (4)	36 (3)	29 (6)	64 (6)	37 (11)	46 (9)	58 (2)
	Chihuahua	217 (3)	8 (4)	21 (2)	5 (1)	16 (2)	1 (0)	2 (0)	164 (6)
	Staffordshire	159 (2)	3 (1)	16 (1)	9 (2)	14 (1)	4 (1)	5 (1)	108 (4)
	Dachshund	150 (2)	14 (6)	49 (4)	0 (0)	49 (5)	0 (0)	5 (1)	33 (1)
	German Shepherd	145 (2)	2 (1)	30 (2)	17 (3)	29 (3)	5 (1)	12 (2)	50 (2)
	Boxer	132 (2)	7 (3)	19 (2)	7 (1)	12 (1)	7 (2)	20 (4)	60 (2)
	Australian shepherd	114 (2)	1 (0)	17 (1)	9 (2)	18 (2)	9 (3)	6 (1)	54 (2)
	Husky	103 (2)	3 (1)	13 (1)	11 (2)	21 (2)	8 (2)	8 (2)	39 (2)
	Border collie	102 (2)	1 (0)	24 (2)	6 (1)	14 (1)	2 (1)	4 (1)	51 (2)
	Shih tzu	102 (2)	3 (1)	28 (2)	5 (1)	20 (2)	1 (0)	6 (1)	39 (2)
	Beagle	100 (2)	3 (1)	18 (1)	6 (1)	16 (2)	3 (1)	15 (3)	39 (2)
	Yorkie	99 (2)	1 (0)	23 (2)	9 (2)	25 (2)	0 (0)	2 (0)	39 (2)
	Australian cattle dog	87 (1)	0 (0)	14 (1)	4 (1)	14 (1)	1 (0)	6 (1)	48 (2)
	English bulldog	86 (1)	0 (0)	16 (1)	3 (1)	33 (3)	3 (1)	11 (2)	20 (1)
	Jack Russell terrier	82 (1)	4 (2)	13 (1)	3 (1)	14 (1)	3 (1)	2 (0)	43 (2)
	Miniature Schnauzer	82 (1)	2 (1)	24 (2)	4 (1)	14 (1)	1 (0)	6 (1)	31 (1)
	Rotweiler	75 (1)	3 (1)	19 (2)	11 (2)	9 (1)	5 (1)	11 (2)	17 (1)
	Other	1945 (31)	82 (45)	493 (41)	168 (35)	370 (37)	108 (31)	162 (31)	562 (22)

Table 4 – Visits categorized by case type and ECC involvement

Services Providing Care	Counts
Medicine	225
Medicine + critical care	1226
Oncology	346
Oncology + critical care	519
Surgery	516
Surgery + critical care	1064
Any other service combinations seen	2573
Total	6469

Table 5 - Results of multivariable analysis with occurrence of fever after admission among canine visits to the VTH against case type and length of stay by patient in hospital

Variables	Category	Total	OR	95% CI	p-value
Case Type	Medicine	225	0.37	0.17 - 0.80	
	Medicine + critical care	1226	0.94	0.65 - 1.37	
	Oncology	346	0.35	0.18 - 0.67	
	Oncology + critical care	519	0.69	0.43 - 1.10	< 0.001
	Surgery + critical care	1064	0.72	0.48 - 1.07	
	Other	2573	1.31	0.93 - 1.85	
	Surgery	516	Ref.		
Length of Stay	> 2 days	1390	2.39	1.99 - 2.88	< 0.001
	≤ 2 days	5079	Ref.		

4 Conclusions

This study provides a baseline estimate of the prevalence of canine MRSP colonization upon admission to the CSU-VTH (4%). This estimate falls within the range of previous reports about MRSP colonization. This study also shows that the greatest prevalence of MRSP colonization is among patients presenting to the VTH for skin disease, compared to surgical oncology or community practice patients. This group was also the only group to demonstrate colonization persistence. In this study, no healthy patients presented with a positive MRSP colonization status. Cancer patients receiving surgical procedures had a prevalence of MRSP colonization between healthy patients and patients presenting for skin disease, suggesting that cancer patients receiving surgical procedures may be more likely to present as MRSP carriers, but less likely than patients presenting for skin disease.

This study also shows that fevers after admission are associated with known risk factors for HCAIs and may be a useful measure in a syndromic approach to HCAI surveillance. Cases with the most complex management had an increased odds of having a fever after admission. Also, visits with a longer duration of stay in the hospital had an increased odds of having a fever after admission.

5 References

Allaker, R. P., Lloyd, D. H., & Bailey, R. M. (1992). Population sizes and frequency of staphylococci at mucocutaneous sites on healthy dogs. *Veterinary Record*, *130*(14), 303–304.

Allaker, R. P., Lloyd, D. H., & Simpson, A. I. (1992). Occurrence of Staphylococcus intermedius on the hair and skin of normal dogs. *Research in Veterinary Science*, *52*(2), 174–176. https://doi.org/10.1016/0034-5288(92)90006-N

Atalay, B., Ergin, F., Cekinmez, M., Caner, H., & Altinors, N. (2005). Brain abscess caused by Staphylococcus intermedius. *Acta Neurochirurgica*, *147*(3), 347–348.

Baciewicz AM, Self TH, & Bekemeyer WB. (1987). Update on rifampin drug interactions. *Archives of Internal Medicine*, *147*(3), 565–568. https://doi.org/10.1001/archinte.1987.00370030169033

Bajwa, J., Charach, M., & Duclos, D. (2013). Adverse effects of rifampicin in dogs and serum alanine aminotransferase monitoring recommendations based on a retrospective study of 344 dogs. *Veterinary Dermatology*, *24*(6), 570–e136. https://doi.org/10.1111/vde.12083

Bannoehr, J., & Guardabassi, L. (2012). Staphylococcus pseudintermedius in the dog: taxonomy, diagnostics, ecology, epidemiology and pathogenicity. *Veterinary Dermatology*, *23*(4), 253–e52.

Barber, M. (1947). Staphylococcal Infection due to Penicillin-resistant Strains. *British Medical Journal*, *2*(4534), 863–865.

Bean, D., & Wigmore, S. (2016). Carriage rate and antibiotic susceptibility of coagulase-positive staphylococci isolated from healthy dogs in Victoria, Australia. *Australian Veterinary Journal*, *94*(12), 456–460. https://doi.org/10.1111/avj.12528

Beck, K. M., Waisglass, S. E., Dick, H. L. N., & Weese, J. S. (2012). Prevalence of meticillin-resistant Staphylococcus pseudintermedius (MRSP) from skin and carriage sites of dogs after treatment of their meticillin-resistant or meticillin-sensitive staphylococcal pyoderma. *Veterinary Dermatology*, *23*(4), 369–e67. https://doi.org/10.1111/j.1365-3164.2012.01035.x

Bemis, D. A., Jones, R. D., Frank, L. A., & Kania, S. A. (2009). Evaluation of Susceptibility Test Breakpoints Used to Predict mecA-Mediated Resistance in Staphylococcus Pseudintevmedius Isolated from Dogs. *Journal of Veterinary Diagnostic Investigation*, *21*(1), 53–58. https://doi.org/10.1177/104063870902100108

Benedict, K. M., Morley, P. S., & Metre, D. C. V. (2008). Characteristics of biosecurity and infection control programs at veterinary teaching hospitals. *Journal of the American Veterinary Medical Association*, *233*(5), 767–773. https://doi.org/10.2460/javma.233.5.767

Berger-Bächi, B., & Rohrer, S. (2002). Factors influencing methicillin resistance in staphylococci. *Archives of Microbiology*, *178*(3), 165–171. https://doi.org/10.1007/s00203-002-0436-0

Bloom, P., & Rosser, E. (2001). Efficacy of once-daily clindamycin hydrochloride in the treatment of superficial bacterial pyoderma in dogs. *Journal of the American*

Animal Hospital Association, *37*(6), 537–542. https://doi.org/10.5326/15473317-37-6-537

Bond, R., & Loeffler, A. (2012). What's happened to Staphylococcus intermedius? Taxonomic revision and emergence of multi-drug resistance. *Journal of Small Animal Practice*, *53*(3), 147–154. https://doi.org/10.1111/j.1748-5827.2011.01165.x

Borio, S., Colombo, S., La Rosa, G., De Lucia, M., Damborg, P., & Guardabassi, L. (2015). Effectiveness of a combined (4% chlorhexidine digluconate shampoo and solution) protocol in MRS and non-MRS canine superficial pyoderma: a randomized, blinded, antibiotic-controlled study. *Veterinary Dermatology*, *26*(5), 339–e72. https://doi.org/10.1111/vde.12233

Bouam, S., Girou, E., Brun‐Buisson, C., Karadimas, H., & Lepage, E. (2003). An Intranet‐Based Automated System for the Surveillance of Nosocomial Infections: Prospective Validation Compared With Physicianschlorh‐Reports. *Infection Control and Hospital Epidemiology*, *24*(1), 51–55. https://doi.org/10.1086/502115

Bryan, J., Frank, L. A., Rohrbach, B. W., Burgette, L. J., Cain, C. L., & Bemis, D. A. (2012). Treatment outcome of dogs with meticillin-resistant and meticillin-susceptible Staphylococcus pseudintermedius pyoderma. *Veterinary Dermatology*, *23*(4), 361–e65. https://doi.org/10.1111/j.1365-3164.2012.01034.x

Burgess, B. A., & Morley, P. S. (2015). Veterinary Hospital Surveillance Systems. *Veterinary Clinics of North America: Small Animal Practice*, *45*(2), 235–242. https://doi.org/10.1016/j.cvsm.2014.11.002

Calfee, D. P. (2012). Crisis in Hospital-Acquired, Healthcare-Associated Infections. *Annual Review of Medicine*, *63*(1), 359–371. https://doi.org/10.1146/annurev-med-081210-144458

Campanile, F., Bongiorno, D., Borbone, S., Venditti, M., Giannella, M., Franchi, C., & Stefani, S. (2007). Characterization of a Variant of the SCCmec Element in a Bloodstream Isolate of Staphylococcus intermedius. *Microbial Drug Resistance*, *13*(1), 7–10. https://doi.org/10.1089/mdr.2006.9991

Carrico, R., & Ramírez, J. (2007). A process for analysis of sentinel events due to health care–associated infection. *American Journal of Infection Control*, *35*(8), 501–507. https://doi.org/10.1016/j.ajic.2006.12.008

Castor, M. L., Wooley, R. E., Shotts, E. B., Brown, J., & Payeur, J. B. (1989). Characteristics of Salmonella isolated from an outbreak of equine salmonellosis in a veterinary teaching hospital. *Journal of Equine Veterinary Science*, *9*(5), 236–241. https://doi.org/10.1016/S0737-0806(89)80078-4

Chalfine, A., Cauet, D., Lin, W. C., Gonot, J., Calvo-Verjat, N., Dazza, F., Billuart, O., Kitzis, M. D., Bleriot, J. P., Pibarot, M. L., Carlet, J. (2006). Highly Sensitive and Efficient Computer‐Assisted System for Routine Surveillance for Surgical Site Infection. *Infection Control and Hospital Epidemiology*, *27*(8), 794–801. https://doi.org/10.1086/506393

Chapman, G. H. (1945). The Significance of Sodium Chloride in Studies of Staphylococci. *Journal of Bacteriology*, *50*(2), 201–203.

Cherry, B., Burns, A., Johnson, G. S., Pfeiffer, H., Dumas, N., Barrett, D., McDonough, P., Eidson, M. (2004). Salmonella Typhimurium Outbreak Associated with

Veterinary Clinic. *Emerging Infectious Diseases*, *10*(12), 2249–2251. https://doi.org/10.3201/eid1012.040714

Chiller, K., Selkin, B. A., & Murakawa, G. J. (2001). Skin Microflora and Bacterial Infections of the Skin. *Journal of Investigative Dermatology Symposium Proceedings*, *6*(3), 170–174. https://doi.org/10.1046/j.0022-202x.2001.00043.x

Cox, H. U., Hoskins, J. D., Newman, S. S., Foil, C. S., Turnwald, G. H., & Roy, A. F. (1988). Temporal study of staphylococcal species on healthy dogs. *American Journal of Veterinary Research (USA)*. Retrieved from http://agris.fao.org/agris-search/search.do?recordID=US8852886

Dallap Schaer, B. L., Aceto, H., & Rankin, S. C. (2010). Outbreak of Salmonellosis Caused by Salmonella enterica Serovar Newport MDR-AmpC in a Large Animal Veterinary Teaching Hospital. *Journal of Veterinary Internal Medicine*, *24*(5), 1138–1146. https://doi.org/10.1111/j.1939-1676.2010.0546.x

Descloux, S., Rossano, A., & Perreten, V. (2008). Characterization of New Staphylococcal Cassette Chromosome mec (SCCmec) and Topoisomerase Genes in Fluoroquinolone- and Methicillin-Resistant Staphylococcus pseudintermedius. *Journal of Clinical Microbiology*, *46*(5), 1818–1823. https://doi.org/10.1128/JCM.02255-07

Detwiler, A., Bloom, P., Petersen, A., & Rosser, E. J. (2013). Multi-drug and methicillin resistance of staphylococci from canine patients at a veterinary teaching hospital (2006–2011). *Veterinary Quarterly*, *33*(2), 60–67. https://doi.org/10.1080/01652176.2013.799792

Devriese, L. A., & De Pelsmaecker, K. (1987). The anal region as a main carrier site of Staphylococcus intermedius and Streptococcus canis in dogs. *Veterinary Record*, *121*(13), 302–303. https://doi.org/10.1136/vr.121.13.302

Devriese, L. A., Hajek, V., Oeding, P., Meyer, S. A., & Schleifer, K. H. (1978). Staphylococcus hyicus (Sompolinsky 1953) comb. nov. and Staphylococcus hyicus subsp. chromogenes subsp. nov. *International Journal of Systematic and Evolutionary Microbiology*, *28*(4), 482–490. https://doi.org/10.1099/00207713-28-4-482

Devriese, L. A., Hermans, K., Baele, M., & Haesebrouck, F. (2009). Staphylococcus pseudintermedius versus Staphylococcus intermedius. *Veterinary Microbiology*, *133*(1–2), 206–207. https://doi.org/10.1016/j.vetmic.2008.06.002

Devriese, L. A., Vancanneyt, M., Baele, M., Vaneechoutte, M., De Graef, E., Snauwaert, C., Cleenwerck, I., Dawyndt, P., Swings, J., Decostere, A., Haesebrouck, F. (2005). Staphylococcus pseudintermedius sp. nov., a coagulase-positive species from animals. *International Journal of Systematic and Evolutionary Microbiology*, *55*(4), 1569–1573. https://doi.org/10.1099/ijs.0.63413-0

Dorea, F. C., Sanchez, J., & Revie, C. W. (2011). Veterinary syndromic surveillance: Current initiatives and potential for development. *Preventive Veterinary Medicine*, *101*(1–2), 1–17. https://doi.org/10.1016/j.prevetmed.2011.05.004

Epstein, C. R., Yam, W. C., Peiris, J. S. M., & Epstein, R. J. (2009). Methicillin-resistant commensal staphylococci in healthy dogs as a potential zoonotic reservoir for community-acquired antibiotic resistance. *Infection, Genetics and Evolution*, *9*(2), 283–285. https://doi.org/10.1016/j.meegid.2008.11.003

Eugster, S., Schawalder, P., Gaschen, F., & Boerlin, P. (2004). A Prospective Study of Postoperative Surgical Site Infections in Dogs and Cats. *Veterinary Surgery*, *33*(5), 542–550. https://doi.org/10.1111/j.1532-950X.2004.04076.x

Evans, R. S., Abouzelof, R. H., Taylor, C. W., Anderson, V., Sumner, S., Soutter, S., Kleckner, R., Lloyd, J. F. (2009). Computer Surveillance of Hospital-Acquired Infections: A 25 year Update. *AMIA Annual Symposium Proceedings*, *2009*, 178–182.

Fairbrother, R. W., & Southall, J. E. (1950). The Isolation of Staphylococcus pyogenes from Faeces. *Monthly Bulletin of the Ministry of Health and the Emergency Public Health Laboratory Service*, *9*, 170–72.

Fazakerley, J., Nuttall, T., Sales, D., Schmidt, V., Carter, S. D., Hart, C. A., & McEwan, N. A. (2009). Staphylococcal colonization of mucosal and lesional skin sites in atopic and healthy dogs. *Veterinary Dermatology*, *20*(3), 179–184. https://doi.org/10.1111/j.1365-3164.2009.00745.x

Fazakerley, J., Williams, N., Carter, S., McEwan, N., & Nuttall, T. (2010). Heterogeneity of Staphylococcus pseudintermedius isolates from atopic and healthy dogs. *Veterinary Dermatology*, *21*(6), 578–585. https://doi.org/10.1111/j.1365-3164.2010.00894.x

Foster, G., Ross, H. M., Hutson, R. A., & Collins, M. D. (1997). Staphylococcus lutrae sp. nov., a New Coagulase-Positive Species Isolated from Otters. *International Journal of Systematic and Evolutionary Microbiology*, *47*(3), 724–726. https://doi.org/10.1099/00207713-47-3-724

Frank, L. A. (1990). Clinical pharmacology of rifampin. *Journal of the American Veterinary Medical Association*, *197*(1), 114–117.

Frank, L. A., Kania, S. A., Kirzeder, E. M., Eberlein, L. C., & Bemis, D. A. (2009). Risk of colonization or gene transfer to owners of dogs with meticillin-resistant Staphylococcus pseudintermedius. *Veterinary Dermatology*, *20*(5-6), 496–501. https://doi.org/10.1111/j.1365-3164.2009.00826.x

Frank, L. A., & Loeffler, A. (2012). Meticillin-resistant Staphylococcus pseudintermedius: clinical challenge and treatment options. *Veterinary Dermatology*, *23*(4), 283–e56. https://doi.org/10.1111/j.1365-3164.2012.01047.x

Fredricks, D. N. (2001). Microbial Ecology of Human Skin in Health and Disease. *Journal of Investigative Dermatology Symposium Proceedings*, *6*(3), 167–169. https://doi.org/10.1046/j.0022-202x.2001.00039.x

Ganiere, J., Medaille, C., & Mangion, C. (2005). Antimicrobial Drug Susceptibility of Staphylococcus intermedius Clinical Isolates from Canine Pyoderma. *Journal of Veterinary Medicine, Series B*, *52*(1), 25–31. https://doi.org/10.1111/j.1439-0450.2004.00816.x

Gerstadt, K., Daly, J. S., Mitchell, M., Wessolossky, M., & Cheeseman, S. H. (1999). Methicillin-resistant Staphylococcus intermedius pneumonia following coronary artery bypass grafting. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, *29*(1), 218–219. https://doi.org/10.1086/520168

Gingrich, E. N., Kurt, T., Hyatt, D. R., Lappin, M. R., & Ruch-Gallie, R. (2011). Prevalence of methicillin-resistant staphylococci in northern Colorado shelter

animals. *Journal of Veterinary Diagnostic Investigation*, *23*(5), 947–950. https://doi.org/10.1177/1040638711407301

Goehring, L. S., Landolt, G. A., & Morley, P. S. (2010). Detection and Management of an Outbreak of Equine Herpesvirus Type 1 Infection and Associated Neurological Disease in a Veterinary Teaching Hospital. *Journal of Veterinary Internal Medicine*, *24*(5), 1176–1183. https://doi.org/10.1111/j.1939-1676.2010.0558.x

Gold, R. M., Cohen, N. D., & Lawhon, S. D. (2014). Amikacin Resistance in Staphylococcus pseudintermedius Isolated from Dogs. *Journal of Clinical Microbiology*, *52*(10), 3641–3646. https://doi.org/10.1128/JCM.01253-14

Greene, C. E. (2013). *Infectious Diseases of the Dog and Cat*. Elsevier Health Sciences.

Greene, C. E., Hartmann, K., & Calpin, J. (2006). Antimicrobial drug formulary. *Infectious Diseases of the Dog and Cat. 3rd Ed. St. Louis, Mo: Saunders Elsevier*, 1200–1203.

Griffeth, G. C., Morris, D. O., Abraham, J. L., Shofer, F. S., & Rankin, S. C. (2008). Screening for skin carriage of methicillin-resistant coagulase-positive staphylococci and Staphylococcus schleiferi in dogs with healthy and inflamed skin. *Veterinary Dermatology*, *19*(3), 142–149. https://doi.org/10.1111/j.1365-3164.2008.00663.x

Guardabassi, L., Loeber, M. E., & Jacobson, A. (2004). Transmission of multiple antimicrobial-resistant Staphylococcus intermedius between dogs affected by deep pyoderma and their owners. *Veterinary Microbiology*, *98*(1), 23–27. https://doi.org/10.1016/j.vetmic.2003.09.021

Guardabassi, L., Schwarz, S., & Lloyd, D. H. (2004). Pet animals as reservoirs of antimicrobial-resistant bacteria Review. *Journal of Antimicrobial Chemotherapy*, *54*(2), 321–332. https://doi.org/10.1093/jac/dkh332

Hajek, V. (1976). Staphylococcus intermedius, a new species isolated from animals. *International Journal of Systematic and Evolutionary Microbiology*, *26*(4), 401–408.

Hanselman, B. A., Kruth, S. A., Rousseau, J., & Weese, J. S. (2009). Coagulase positive staphylococcal colonization of humans and their household pets. *The Canadian Veterinary Journal*, *50*(9), 954–958.

Hanselman, B. A., Kruth, S., & Weese, J. S. (2008). Methicillin-resistant staphylococcal colonization in dogs entering a veterinary teaching hospital. *Veterinary Microbiology*, *126*(1–3), 277–281. https://doi.org/10.1016/j.vetmic.2007.06.015

Hartman, B. J., & Tomasz, A. (1984). Low-affinity penicillin-binding protein associated with beta-lactam resistance in Staphylococcus aureus. *Journal of Bacteriology*, *158*(2), 513–516.

Hartmann, F. A., Callan, R. J., McGuirk, S. M., & West, S. E. (1996). Control of an outbreak of salmonellosis caused by drug-resistant Salmonella anatum in horses at a veterinary hospital and measures to prevent future infections. *Journal of the American Veterinary Medical Association*, *209*(3), 629–631.

Hartmann, F. A., White, D. G., West, S. E. H., Walker, R. D., & DeBoer, D. J. (2005). Molecular characterization of Staphylococcus intermedius carriage by healthy dogs and comparison of antimicrobial susceptibility patterns to isolates from dogs

with pyoderma. *Veterinary Microbiology*, *108*(1–2), 119–131. https://doi.org/10.1016/j.vetmic.2005.03.006

Harvey, R.G., & Noble, W.C., (1998). Aspects of nasal, oropharyngeal and anal carriage of Staphylococcus pseudintermedius in normal dogs and dogs with pyoderma. *Veterinary Dermatology*, *9*(2), 99–104. https://doi.org/10.1046/j.1365-3164.1998.00093.x

Henning, K. J. (2004). What is Syndromic Surveillance? *Morbidity and Mortality Weekly Report*, *53*, 7–11.

Hillier, A., Lloyd, D. H., Weese, J. S., Blondeau, J. M., Boothe, D., Breitschwerdt, E., Guardabassi, L., Papich, M. G., Rankin, S., Turnidge, J. D., Sykes, J. E. (2014). Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Veterinary Dermatology*, *25*(3), 163–e43. https://doi.org/10.1111/vde.12118

Huang, S. S., & Platt, R. (2003). Risk of Methicillin-Resistant Staphylococcus aureus Infection after Previous Infection or Colonization. *Clinical Infectious Diseases*, *36*(3), 281–285. https://doi.org/10.1086/345955

Huerta, B., Maldonado, A., Ginel, P. J., Tarradas, C., Gómez-Gascón, L., Astorga, R. J., & Luque, I. (2011). Risk factors associated with the antimicrobial resistance of staphylococci in canine pyoderma. *Veterinary Microbiology*, *150*(3–4), 302–308. https://doi.org/10.1016/j.vetmic.2011.02.002

Igimi, S., Takahashi, E., & Mitsuoka, T. (1990). Staphylococcus schleiferi subsp. coagulans subsp. nov., isolated from the external auditory meatus of dogs with

external ear otitis. *International Journal of Systematic Bacteriology*, *40*(4), 409–411. https://doi.org/10.1099/00207713-40-4-409

Jones, R. D., Kania, S. A., Rohrbach, B. W., Frank, L. A., & Bemis, D. A. (2007). Prevalence of oxacillin- and multidrug-resistant staphylococci in clinical samples from dogs: 1,772 samples (2001–2005). *Journal of the American Veterinary Medical Association*, *230*(2), 221–227. https://doi.org/10.2460/javma.230.2.221

Kadlec, K., Duijkeren, E. van, Wagenaar, J. A., & Schwarz, S. (2011). Molecular basis of rifampicin resistance in methicillin-resistant Staphylococcus pseudintermedius isolates from dogs. *Journal of Antimicrobial Chemotherapy*, dkr118. https://doi.org/10.1093/jac/dkr118

Kalra, L., Camacho, F., Whitener, C. J., Du, P., Miller, M., Zalonis, C., & Julian, K. G. (2013). Risk of methicillin-resistant Staphylococcus aureus surgical site infection in patients with nasal MRSA colonization. *American Journal of Infection Control*, *41*(12), 1253–1257. https://doi.org/10.1016/j.ajic.2013.05.021

Kania, S. A., Williamson, N. L., Frank, L. A., Wilkes, R. P., Jones, R. D., & Bemis, D. A. (2004). Methicillin resistance of staphylococci isolated from the skin of dogs with pyoderma. *American Journal of Veterinary Research*, *65*(9), 1265–1268. https://doi.org/10.2460/ajvr.2004.65.1265

Katayama, Y., Ito, T., & Hiramatsu, K. (2000). A New Class of Genetic Element, Staphylococcus Cassette Chromosome mec, Encodes Methicillin Resistance in Staphylococcus aureus. *Antimicrobial Agents and Chemotherapy*, *44*(6), 1549–1555. https://doi.org/10.1128/AAC.44.6.1549-1555.2000

Kawakami, T., Shibata, S., Murayama, N., Nagata, M., Nishifuji, K., Iwasaki, T., & Fukata, T. (2010). Antimicrobial Susceptibility and Methicillin Resistance in *Staphylococcus pseudintermedius* and *Staphylococcus schleiferi* subsp. *coagulans* Isolated from Dogs with Pyoderma in Japan. *Journal of Veterinary Medical Science*, *72*(12), 1615–1619. https://doi.org/10.1292/jvms.10-0172

Kelesidis, T., & Tsiodras, S. (2010). Staphylococcus intermedius is not only a zoonotic pathogen, but may also cause skin abscesses in humans after exposure to saliva. *International Journal of Infectious Diseases*, *14*(10), e838–e841. https://doi.org/10.1016/j.ijid.2010.02.2249

Kempker, R., Mangalat, D., Kongphet-Tran, T. M., & Eaton, M. (2009). Beware of the Pet Dog: A Case of Staphylococcus intermedius Infection. *Journal of the Medical Sciences*, *338*(5), 425–427. https://doi.org/10.1097/MAJ.0b013e3181b0baa9

Kikuchi, K., Karasawa, T., Piao, C., Itoda, I., Hidai, H., Yamaura, H., Totsuka, K., Morikawa, T., Takayama, M. (2004). Molecular confirmation of transmission route of Staphylococcus intermedius. *Journal of Infection and Chemotherapy*, *10*(1), 46–48. https://doi.org/10.1007/s10156-003-0281-3

Klevens, R. M., Edwards, J. R., Richards, C. L., Horan, T. C., Gaynes, R. P., Pollock, D. A., & Cardo, D. M. (2007). Estimating Health Care-Associated Infections and Deaths in U.S. Hospitals, 2002. *Public Health Reports (1974-)*, *122*(2), 160–166.

Konkle, D. M., Nelson, K. M., & Lunn, D. P. (1997). Nosocomial Transmission of Cryptosporidium in a Veterinary Hospital. *Journal of Veterinary Internal Medicine*, *11*(6), 340–343. https://doi.org/10.1111/j.1939-1676.1997.tb00477.x

Kwon, N. H., Park, K. T., Moon, J. S., Jung, W. K., Kim, S. H., Kim, J. M., Hong, S. K., Koo, H. C., Joo, Y. S., Park, Y. H. (2005). Staphylococcal cassette chromosome mec (SCCmec) characterization and molecular analysis for methicillin-resistant Staphylococcus aureus and novel SCCmec subtype IVg isolated from bovine milk in Korea. *Journal of Antimicrobial Chemotherapy*, *56*(4), 624–632. https://doi.org/10.1093/jac/dki306

Laarhoven, L. M., de Heus, P., van Luijn, J., Duim, B., Wagenaar, J. A., & van Duijkeren, E. (2011). Longitudinal Study on Methicillin-Resistant Staphylococcus pseudintermedius in Households. *PLoS ONE*, *6*(11). https://doi.org/10.1371/journal.pone.0027788

Littlewood, D., Lakhani, K. H., Paterson, S., Wood, J. L. N., & Chanter, N. (1999). Clindamycin hydrochloride and clavulanate-amoxycillin in the treatment of canine superficial pyoderma. *Veterinary Record*, *144*(24), 662–665. https://doi.org/10.1136/vr.144.24.662

Loeffler, A., Baines, S. J., Toleman, M. S., Felmingham, D., Milsom, S. K., Edwards, E. A., & Lloyd, D. H. (2008). In vitro activity of fusidic acid and mupirocin against coagulase-positive staphylococci from pets. *Journal of Antimicrobial Chemotherapy*, *62*(6), 1301–1304. https://doi.org/10.1093/jac/dkn398

Loeffler, A., Cobb, M. A., & Bond, R. (2011). Comparison of a chlorhexidine and a benzoyl peroxide shampoo as sole treatment in canine superficial pyoderma. *Veterinary Record*, *169*(10), 249–249. https://doi.org/10.1136/vr.d4400

Loeffler, A., Linek, M., Moodley, A., Guardabassi, L., Sung, J. M. L., Winkler, M., Weiss, R., Lloyd, D. H. (2007). First report of multiresistant, mecA-positive

Staphylococcus intermedius in Europe: 12 cases from a veterinary dermatology referral clinic in Germany. *Veterinary Dermatology*, *18*(6), 412–421. https://doi.org/10.1111/j.1365-3164.2007.00635.x

Loeffler, A., Pfeiffer, D. U., Lloyd, D. H., Smith, H., Soares-Magalhaes, R., & Lindsay, J. A. (2010). Meticillin-resistant Staphylococcus aureus carriage in UK veterinary staff and owners of infected pets: new risk groups. *Journal of Hospital Infection*, *74*(3), 282–288. https://doi.org/10.1016/j.jhin.2009.09.020

Madewell, B. R., Tang, Y. J., Jang, S., Madigan, J. E., Hirsh, D. C., Gumerlock, P. H., & Silva, J. (1995). Apparent Outbreaks of Clostridium Difficile-Associated Diarrhea in Horses in a Veterinary Medical Teaching Hospital. *Journal of Veterinary Diagnostic Investigation*, *7*(3), 343–346. https://doi.org/10.1177/104063879500700308

Maitland, H. B., & Martyn, G. (1948). A selective medium for isolating staphylococcus based on the differential inhibiting effect of increased concentrations of sodium chloride. *The Journal of Pathology and Bacteriology*, *60*(4), 553–561. https://doi.org/10.1002/path.1700600403

Medleau, L., Long, R. E., Brown, J., & Miller, W. H. (1986). Frequency and antimicrobial susceptibility of Staphylococcus species isolated from canine pyodermas. *American Journal of Veterinary Research*, *47*(2), 229–231.

Morgan, D. J., Lomotan, L. L., Agnes, K., McGrail, L., & Roghmann, M. (2010). Characteristics of Healthcare‐Associated Infections Contributing to Unexpected In‐Hospital Deaths. *Infection Control and Hospital Epidemiology*, *31*(8), 864–866. https://doi.org/10.1086/655018

Morley, P. S. (2013). Evidence-Based Infection Control In Clinical Practice: If You Buy Clothes for the Emperor, Will He Wear Them? *Journal of Veterinary Internal Medicine*, *27*(3), 430–438. https://doi.org/10.1111/jvim.12060

Morley, P. S., Anderson, M. E. C., Burgess, B. A., Aceto, H., Bender, J. B., Clark, C., Daniels, J. B., Davis, M. A., Hinchcliff, K. W., Johnson, J. R., McClure, J., Perkins, G. A., Pusterla, N., Traub-Dargatz, J. L., Weese, J. S., Whittem, T. L. (2013). Report of the third Havemeyer workshop on infection control in equine populations. *Equine Veterinary Journal*, *45*(2), 131–136. https://doi.org/10.1111/evj.12000

Morris, D. O., Boston, R. C., O'Shea, K., & Rankin, S. C. (2010). The prevalence of carriage of meticillin-resistant staphylococci by veterinary dermatology practice staff and their respective pets. *Veterinary Dermatology*, *21*(4), 400–407. https://doi.org/10.1111/j.1365-3164.2010.00866.x

Murphy, K. M. (2008). The use of linezolid to treat methicillin-resistant staphylococcal infections in dogs and cats. *Vet. Dermatol*, *19*, 110.

Nazarali, A., Singh, A., Moens, N. M. M., Gatineau, M., Sereda, C., Fowler, D., Kim, S., Kisiel, A., Reynolds, D., Ringwood, B., Bruce, C., Gibson, T., Rousseau, J., Weese, J. S. (2015). Association between methicillin-resistant Staphylococcus pseudintermedius carriage and the development of surgical site infections following tibial plateau leveling osteotomy in dogs. *Journal of the American Veterinary Medical Association*, *247*(8), 909–916. https://doi.org/10.2460/javma.247.8.909

Nienhoff, U., Kadlec, K., Chaberny, I. F., Verspohl, J., Gerlach, G.-F., Kreienbrock, L., Schwartz, S., Simon, D., Nolte, I. (2011). Methicillin-resistant Staphylococcus pseudintermedius among dogs admitted to a small animal hospital. *Veterinary Microbiology*, *150*(1–2), 191–197. https://doi.org/10.1016/j.vetmic.2010.12.018

Noli, C., & Morris, D. (2011). Guidelines on the use of systemic aminoglycosides in veterinary dermatology. *Veterinary Dermatology*, *22*(4), 379–380. https://doi.org/10.1111/j.1365-3164.2011.00991.x

Olson, D. R., Heffernan, R. T., Paladini, M., Konty, K., Weiss, D., & Mostashari, F. (2007). Monitoring the Impact of Influenza by Age: Emergency Department Fever and Respiratory Complaint Surveillance in New York City. *PLOS Med*, *4*(8), e247. https://doi.org/10.1371/journal.pmed.0040247

Pai, M. P., Momary, K. M., & Rodvold, K. A. (2006). Antibiotic Drug Interactions. *Medical Clinics*, *90*(6), 1223–1255. https://doi.org/10.1016/j.mcna.2006.06.008

Paul Bloom. (2014). Canine superficial bacterial folliculitis: Current understanding of its etiology, diagnosis and treatment. *The Veterinary Journal*, *199*(2), 217–222. https://doi.org/10.1016/j.tvjl.2013.11.014

Paul, N. C., Moodley, A., Ghibaudo, G., & Guardabassi, L. (2011). Carriage of Methicillin-Resistant Staphylococcus pseudintermedius in Small Animal Veterinarians: Indirect Evidence of Zoonotic Transmission. *Zoonoses and Public Health*, *58*(8), 533–539. https://doi.org/10.1111/j.1863-2378.2011.01398.x

Pearson, A. (2009). Historical and changing epidemiology of healthcare-associated infections. *Journal of Hospital Infection*, *73*(4), 296–304. https://doi.org/10.1016/j.jhin.2009.08.016

Perreten, V., Kadlec, K., Schwarz, S., Andersson, U. G., Finn, M., Greko, C., Moodley, A., Kania, S., Frank, L., Bemis, D., Franco, A., Iurescia, M., Battisti, A., Duim, B., Wagenaar, J. A., van Duijkeren, E., Weese, J. S., Fitzgerald, J. R., Rossano, A., Guardabassi, L. (2010). Clonal spread of methicillin-resistant Staphylococcus pseudintermedius in Europe and North America: an international multicentre study. *Journal of Antimicrobial Chemotherapy*, *65*(6), 1145–1154. https://doi.org/10.1093/jac/dkq078

Pinchbeck, L. R., Cole, L. K., Hillier, A., Kowalski, J. J., Rajala-Schultz, P. J., Bannerman, T. L., & York, S. (2006). Genotypic relatedness of staphylococcal strains isolated from pustules and carriage sites in dogs with superficial bacterial folliculitis. *American Journal of Veterinary Research*, *67*(8), 1337–1346. https://doi.org/10.2460/ajvr.67.8.1337

Pollari, F. L., Bonnett, B. N., Allen, D. G., Bamsey, S. C., & Martin, S. W. (1996). Quality of computerized medical record abstract data at a veterinary teaching hospital. *Preventive Veterinary Medicine*, *27*(3), 141–154. https://doi.org/10.1016/0167-5877(95)01004-1

Pomba, C., Rantala, M., Greko, C., Baptiste, K. E., Catry, B., van Duijkeren, E., Mateus, A., Moreno, M., Pyorala, S., Ruzauskas, M., Sanders, P., Teale, C., Threlfall, E. J., Kunsagi, Z., Torren-Edo, J., Jukes, H., Törneke, K. (2016). Public health risk of antimicrobial resistance transfer from companion animals. *Journal of Antimicrobial Chemotherapy*, dkw481. https://doi.org/10.1093/jac/dkw481

Riegel, P., Jesel-Morel, L., Laventie, B., Boisset, S., Vandenesch, F., & Prévost, G. (2011). Coagulase-positive Staphylococcus pseudintermedius from animals

causing human endocarditis. *International Journal of Medical Microbiology*, *301*(3), 237–239. https://doi.org/10.1016/j.ijmm.2010.09.001

Rubin, J. E., & Chirino-Trejo, M. (2011). Prevalence, Sites of Colonization, and Antimicrobial Resistance Among Staphylococcus Pseudintermedius Isolated from Healthy Dogs in Saskatoon, Canada. *Journal of Veterinary Diagnostic Investigation*, *23*(2), 351–354. https://doi.org/10.1177/104063871102300227

Ruple-Czerniak, A., Aceto, H. W., Bender, J. B., Paradis, M. R., Shaw, S. P., Van Metre, D. C., Weese, J. S., Wilson, D. A., Wilson, J. H., Morley, P. S. (2013). Using Syndromic Surveillance to Estimate Baseline Rates for Healthcare-Associated Infections in Critical Care Units of Small Animal Referral Hospitals. *Journal of Veterinary Internal Medicine*, *27*(6), 1392–1399. https://doi.org/10.1111/jvim.12190

Sasaki, A., Shimizu, A., Kawano, J., Wakita, Y., Hayashi, T., & Ootsuki, S. (2005). Characteristics of *Staphylococcus intermedius* Isolates from Diseased and Healthy Dogs. *Journal of Veterinary Medical Science*, *67*(1), 103–106. https://doi.org/10.1292/jvms.67.103

Sasaki, T., Kikuchi, K., Tanaka, Y., Takahashi, N., Kamata, S., & Hiramatsu, K. (2007a). Methicillin-Resistant Staphylococcus pseudintermedius in a Veterinary Teaching Hospital. *Journal of Clinical Microbiology*, *45*(4), 1118–1125. https://doi.org/10.1128/JCM.02193-06

Sasaki, T., Kikuchi, K., Tanaka, Y., Takahashi, N., Kamata, S., & Hiramatsu, K. (2007b). Reclassification of Phenotypically Identified Staphylococcus intermedius Strains.

Journal of Clinical Microbiology, *45*(9), 2770–2778. https://doi.org/10.1128/JCM.00360-07

Sasaki, T., Tsubakishita, S., Tanaka, Y., Sakusabe, A., Ohtsuka, M., Hirotaki, S., Kawakami, T., Fukata, T., Hiramatsu, K. (2010). Multiplex-PCR Method for Species Identification of Coagulase-Positive Staphylococci. *Journal of Clinical Microbiology*, *48*(3), 765–769. https://doi.org/10.1128/JCM.01232-09

Schott II, H. C., Ewart, S. L., Walker, R. D., Dwyer, R. M., Dietrich, S., Eberhart, S. W., Kusey, J., Stick, J., Derksen, F. J. (2001). An outbreak of salmonellosis among horses at a veterinary teaching hospital. *Journal of the American Veterinary Medical Association*, *218*(7), 1152–1159. https://doi.org/10.2460/javma.2001.218.1152

Schwartz, B. S., Graber, C. J., Diep, B. A., Basuino, L., Perdreau-Remington, F., & Chambers, H. F. (2009). Doxycycline, Not Minocycline, Induces Its Own Resistance in Multidrug-Resistant, Community-Associated Methicillin-Resistant Staphylococcus aureus Clone USA300. *Clinical Infectious Diseases*, *48*(10), 1483–1484. https://doi.org/10.1086/598510

Scott, D. W., Beningo, K. E., Miller, W. H., & Rothstein, E. (1998). Efficacy of clindamycin hydrochloride capsules for the treatment of deep pyoderma due to Staphylococcus intermedius infection in dogs. *The Canadian Veterinary Journal*, *39*(12), 753–756.

Scott, R. D. (2009). *The direct medical costs of healthcare-associated infections in US hospitals and the benefits of prevention*. Division of Healthcare Quality Promotion

National Center for Preparedness, Detection, and Control of Infectious Diseases, Centers for Disease Control and Prevention.

Seguin, J. C., Walker, R. D., Caron, J. P., Kloos, W. E., George, C. G., Hollis, R. J., Jones, R. N., Pfaller, M. A. (1999). Methicillin-Resistant Staphylococcus aureus Outbreak in a Veterinary Teaching Hospital: Potential Human-to-Animal Transmission. *Journal of Clinical Microbiology*, *37*(5), 1459–1463.

Siak, M., Burrows, A. K., Coombs, G. W., Khazandi, M., Abraham, S., Norris, J. M., Weese, J. S., Trott, D. J. (2014). Characterization of meticillin-resistant and meticillin-susceptible isolates of Staphylococcus pseudintermedius from cases of canine pyoderma in Australia. *Journal of Medical Microbiology*, *63*(9), 1228–1233. https://doi.org/10.1099/jmm.0.076117-0

Smarick, S. D., Haskins, S. C., Aldrich, J., Foley, J. E., Kass, P. H., Fudge, M., & Ling, G. V. (2004). Incidence of catheter-associated urinary tract infection among dogs in a small animal intensive care unit. *Journal of the American Veterinary Medical Association*, *224*(12), 1936–1940. https://doi.org/10.2460/javma.2004.224.1936

Somayaji, R., Priyantha, M. a. R., Rubin, J. E., & Church, D. (2016). Human infections due to Staphylococcus pseudintermedius, an emerging zoonosis of canine origin: report of 24 cases. *Diagnostic Microbiology and Infectious Disease*. https://doi.org/10.1016/j.diagmicrobio.2016.05.008

Starlander, G., Börjesson, S., Grönlund-Andersson, U., Tellgren-Roth, C., & Melhus, Å. (2014). Cluster of Infections Caused by Methicillin-Resistant Staphylococcus pseudintermedius in Humans in a Tertiary Hospital. *Journal of Clinical Microbiology*, *52*(8), 3118–3120. https://doi.org/10.1128/JCM.00703-14

Stegmann, R., Burnens, A., Maranta, C. A., & Perreten, V. (2010). Human infection associated with methicillin-resistant Staphylococcus pseudintermedius ST71. *Journal of Antimicrobial Chemotherapy*, dkq241. https://doi.org/10.1093/jac/dkq241

Steneroden, K. K., Van Metre, D. C., Jackson, C., & Morley, P. S. (2010). Detection and Control of a Nosocomial Outbreak Caused by Salmonella Newport at a Large Animal Hospital. *Journal of Veterinary Internal Medicine*, *24*(3), 606–616. https://doi.org/10.1111/j.1939-1676.2010.0484.x

Talan, D. A., Goldstein, E., Staatz, D., & Overturf, G. D. (1989). Staphylococcus intermedius: Clinical presentation of a new human dog bite pathogen. *Annals of Emergency Medicine*, *18*(4), 410–413. https://doi.org/10.1016/S0196-0644(89)80582-7

Tillotson, K., Savage, C. J., Salman, M. D., Gentry-Weeks, C. R., Rice, D., Fedorka-Cray, P. J., Hendrickson, D. A., Jones R. L., Nelson, W., Traub-Dargatz, J. L. (1997). Outbreak of Salmonella infantis infection in a large animal veterinary teaching hospital. *Journal of the American Veterinary Medical Association*, *211*(12), 1554–1557.

Trzcinski, K., Cooper, B. S., Hryniewicz, W., & Dowson, C. G. (2000). Expression of resistance to tetracyclines in strains of methicillin-resistant Staphylococcus aureus. *Journal of Antimicrobial Chemotherapy*, *45*(6), 763–770. https://doi.org/10.1093/jac/45.6.763

Turk, R., Singh, A., & Weese, J. S. (2015). Prospective Surgical Site Infection Surveillance in Dogs. *Veterinary Surgery*, *44*(1), 2–8. https://doi.org/10.1111/j.1532-950X.2014.12267.x

Umscheid, C. A., Mitchell, M. D., Doshi, J. A., Agarwal, R., Williams, K., & Brennan, P. J. (2011). Estimating the Proportion of Healthcare-Associated Infections That Are Reasonably Preventable and the Related Mortality and Costs. *Infection Control & Hospital Epidemiology*, *32*(02), 101–114. https://doi.org/10.1086/657912

Vandenesch, F., Célard, M., Arpin, D., Bes, M., Greenland, T., & Etienne, J. (1995). Catheter-related bacteremia associated with coagulase-positive Staphylococcus intermedius. *Journal of Clinical Microbiology*, *33*(9), 2508–2510.

van Duijkeren, E., Box, A. T. A., Heck, M. E. O. C., Wannet, W. J. B., & Fluit, A. C. (2004). Methicillin-resistant staphylococci isolated from animals. *Veterinary Microbiology*, *103*(1–2), 91–97. https://doi.org/10.1016/j.vetmic.2004.07.014

van Duijkeren, E., Houwers, D. J., Schoormans, A., Broekhuizen-Stins, M. J., Ikawaty, R., Fluit, A. C., & Wagenaar, J. A. (2008). Transmission of methicillin-resistant Staphylococcus intermedius between humans and animals. *Veterinary Microbiology*, *128*(1–2), 213–215. https://doi.org/10.1016/j.vetmic.2007.11.016

van Duijkeren, E., Catry, B., Greko, C., Moreno, M. A., Pomba, M. C., Pyörälä, S., Ruzauskas, M., Sanders, P., Threlfall, E. J., Torren-Edo, J., Torneke, K., S. A. G. on A. (2011). Review on methicillin-resistant Staphylococcus pseudintermedius. *Journal of Antimicrobial Chemotherapy*, *66*(12), 2705–2714. https://doi.org/10.1093/jac/dkr367

van Duijkeren, E., Kamphuis, M., van der Mije, I. C., Laarhoven, L. M., Duim, B., Wagenaar, J. A., & Houwers, D. J. (2011). Transmission of methicillin-resistant Staphylococcus pseudintermedius between infected dogs and cats and contact pets, humans and the environment in households and veterinary clinics. *Veterinary Microbiology*, *150*(3–4), 338–343. https://doi.org/10.1016/j.vetmic.2011.02.012

Varaldo, P. E., Kilpper-Balz, R., Biavasco, F., Satta, G., & Schleifer, K. H. (1988). Staphylococcus delphini sp. nov., a Coagulase-Positive Species Isolated from Dolphins. *International Journal of Systematic and Evolutionary Microbiology*, *38*(4), 436–439. https://doi.org/10.1099/00207713-38-4-436

Venezia, R. A., Domaracki, B. E., Evans, A. M., Preston, K. E., & Graffunder, E. M. (2001). Selection of high-level oxacillin resistance in heteroresistant Staphylococcus aureus by fluoroquinolone exposure. *Journal of Antimicrobial Chemotherapy*, *48*(3), 375–381. https://doi.org/10.1093/jac/48.3.375

Vengust, M., Anderson, M. E. E., Rousseau, J., & Weese, J. S. (2006). Methicillin-resistant staphylococcal colonization in clinically normal dogs and horses in the community. *Letters in Applied Microbiology*, *43*(6), 602–606. https://doi.org/10.1111/j.1472-765X.2006.02018.x

Ward, M. P., Brady, T. H., Couëtil, L. L., Liljebjelke, K., Maurer, J. J., & Wu, C. C. (2005). Investigation and control of an outbreak of salmonellosis caused by multidrug-resistant Salmonella typhimurium in a population of hospitalized horses. *Veterinary Microbiology*, *107*(3–4), 233–240. https://doi.org/10.1016/j.vetmic.2005.01.019

Weber, S. G., Gold, H. S., Hooper, D. C., Karchmer, A. W., & Carmeli, Y. (2003). Fluoroquinolones and the Risk for Methicillin-resistant *Staphylococcus aureus* in Hospitalized Patients1. *Emerging Infectious Diseases*, *9*(11), 1415–1422. https://doi.org/10.3201/eid0911.030284

Weese, J. S., & Armstrong, J. (2003). Outbreak of Clostridium difficile-Associated Disease in a Small Animal Veterinary Teaching Hospital. *Journal of Veterinary Internal Medicine*, *17*(6), 813–816. https://doi.org/10.1111/j.1939-1676.2003.tb02519.x

Weese, J. S., Caldwell, F., Willey, B. M., Kreiswirth, B. N., McGeer, A., Rousseau, J., & Low, D. E. (2006). An outbreak of methicillin-resistant Staphylococcus aureus skin infections resulting from horse to human transmission in a veterinary hospital. *Veterinary Microbiology*, *114*(1–2), 160–164. https://doi.org/10.1016/j.vetmic.2005.11.054

Weese, J. S., Faires, M. C., Frank, L. A., Reynolds, L. M., & Battisti, A. (2012). Factors associated with methicillin-resistant versus methicillin-susceptible Staphylococcus pseudintermedius infection in dogs. *Journal of the American Veterinary Medical Association*, *240*(12), 1450–1455. https://doi.org/10.2460/javma.240.12.1450

Weese, J. S., & van Duijkeren, E. (2010). Methicillin-resistant Staphylococcus aureus and Staphylococcus pseudintermedius in veterinary medicine. *Veterinary Microbiology*, *140*(3–4), 418–429. https://doi.org/10.1016/j.vetmic.2009.01.039

Werckenthin, C., Cardoso, M., Martel, J. L., & Schwarz, S. (2001). Antimicrobial resistance in staphylococci from animals with particular reference to bovine

Staphylococcus aureus, porcine Staphylococcus hyicus, and canine Staphylococcus intermedius. *Veterinary Research*, *32*(3-4), 22. https://doi.org/10.1051/vetres:2001129

Werner, A. H., & Russell, A. D. (1999). Mupirocin, fusidic acid and bacitracin: activity, action and clinical uses of three topical antibiotics. *Veterinary Dermatology*, *10*(3), 225–240. https://doi.org/10.1046/j.1365-3164.1999.00185.x

Windahl, U., Reimegård, E., Holst, B. S., Egenvall, A., Fernström, L., Fredriksson, M., Trowald-Wigh, G., Andersson, U. G. (2012). Carriage of methicillin-resistant Staphylococcus pseudintermedius in dogs--a longitudinal study. *BMC Veterinary Research*, *8*, 34. https://doi.org/10.1186/1746-6148-8-34

Wright, M. (2008). Automated surveillance and infection control: Toward a better tomorrow. *American Journal of Infection Control*, *36*(3, Supplement), S1–S6. https://doi.org/10.1016/j.ajic.2007.09.003

Wright, M., Fisher, A., John, M., Reynolds, K., Peterson, L. R., & Robicsek, A. (2009). The electronic medical record as a tool for infection surveillance: Successful automation of device-days. *American Journal of Infection Control*, *37*(5), 364–370. https://doi.org/10.1016/j.ajic.2008.11.003

Yahav, I., & Shmueli, G. (2007). Algorithm Combination for Improved Performance in Biosurveillance Systems. In D. Zeng, I. Gotham, K. Komatsu, C. Lynch, M. Thurmond, D. Madigan, … H. Chen (Eds.), *Intelligence and Security Informatics: Biosurveillance* (pp. 91–102). Springer Berlin Heidelberg. Retrieved from http://link.springer.com/chapter/10.1007/978-3-540-72608-1_9

Zubeir, I. E. M. E., Kanbar, T., Alber, J., Lämmler, C., Akineden, Ö., Weiss, R., & Zschöck, M. (2007). Phenotypic and genotypic characteristics of methicillin/oxacillin-resistant Staphylococcus intermedius isolated from clinical specimens during routine veterinary microbiological examinations. *Veterinary Microbiology*, *121*(1–2), 170–176. https://doi.org/10.1016/j.vetmic.2006.11.014

Zur, G., Gurevich, B., & Elad, D. (2016). Prior antimicrobial use as a risk factor for resistance in selected Staphylococcus pseudintermedius isolates from the skin and ears of dogs. *Veterinary Dermatology*, *27*(6), 468–e125. https://doi.org/10.1111/vde.12382

6 Appendix

Table 6: MRSP prevalence at carriage sites at enrollment

Community Practice (n = 60)								
Intake	MRSP history[1]		Surgery/wound history[2]		AMD history[3]		Total	
	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	0	(0, 6)	5 (8)	(4, 18)	3 (5)	(2, 14)	60 (100)	(94, 100)
+	0	(0, 6)	0	(0, 6)	0	(0, 6)	0	(0, 6)
Dermatology (n = 71)								
Intake	MRSP history[1]		Surgery/wound history[2]		AMD history[3]		Total	
	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	4 (6)	(2, 14)	12 (17)	(10, 27)	47 (66)	(55, 76)	65 (92)	(83, 96)
+	0	(0, 5)	2 (3)	(1, 10)	4 (6)	(2, 14)	6 (8)	(4, 17)
Surgical Oncology (n = 112)								
Intake	MRSP history[1]		Surgery/wound history[2]		AMD history[3]		Total	
	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	0	(0, 3)	36 (32)	(24, 41)	39 (35)	(27, 44)	109 (97)	(92, 99)
+	1 (1)	(0, 5)	2 (2)	(0, 6)	2 (2)	(0, 6)	3 (3)	(1, 8)

MRSP = Methicillin-resistant *Staphylococcus pseudintermedius;* AMD = Antimicrobial drug history; CI = Confidence interval

[1]Patients that had a MRSP infection within 12 months prior to enrollment

[2]Patients that had surgery or wound within 12 months prior to enrollment

[3]Patients that received antimicrobial treatment within 12 months prior to enrollment

Table 7: MRSP recovery among patients with paired sampling (n = 155)

Intake	Follow-up	MRSP history[1]		Surgery/wound history[2]		AMD prior to enrollment[3]		AMD between sampling4		Total (%)	
		Number (%)	95% CI	Number (%)	95% CI	Number (%)	95% CI	Number (%)	95% CI	Number (%)	95% CI
-	-	2 (1)	(0, 5)	34 (22)	(16, 29)	57 (37)	(30, 45)	98 (63)	(55, 70)	145 (94)	(89, 96)
-	+	0	(0, 2)	1 (1)	(0, 4)	1 (1)	(0, 4)	2 (1)	(0, 5)	4 (3)	(1, 6)
+	-	0	(0, 2)	1 (1)	(0, 4)	1 (1)	(0, 4)	3 (2)	(0, 6)	3 (2)	(0, 6)
+	+	0	(0, 2)	0	(0, 2)	3 (2)	(0, 6)	1 (1)	(0, 4)	3 (2)	(0, 6)
Community Practice (n =27)											
Intake	Follow-up	MRSP history[1]		Surgery/wound history[2]		AMD prior to enrollment[3]		AMD between sampling4		Total (%)	
		Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	-	0	(0, 12)	1 (4)	(1, 18)	1 (4)	(1, 18)	0	(0, 12)	26 (96)	(82, 99)
-	+	0	(0, 12)	0	(0, 12)	0	(0, 12)	0	(0, 12)	1 (4)	(1, 18)
+	-	0	(0, 12)	0	(0, 12)	0	(0, 12)	0	(0, 12)	0 (0)	(0, 12)
+	+	0	(0, 12)	0	(0, 12)	0	(0, 12)	0	(0, 12)	0 (0)	(0, 12)
Dermatology (n = 41)											
Intake	Follow-up	MRSP history[1]		Surgery/wound history[2]		AMD prior to enrollment[3]		AMD between sampling4		Total (%)	
		Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	-	2 (5)	(1, 16)	6 (15)	(7, 28)	25 (61)	(46, 74)	27 (66)	(51, 78)	35 (85)	(72, 93)
-	+	0	(0, 9)	0	(0, 9)	1 (2)	(0, 13)	0	(0, 9)	1 (2)	(0, 13)
+	-	0	(0, 9)	0	(0, 9)	1 (2)	(0, 13)	2 (5)	(1, 16)	2 (5)	(1, 16)
+	+	0	(0, 9)	0	(0, 9)	3 (7)	(3, 19)	1 (2)	(0, 13)	3 (7)	(3, 19)
Surgical Oncology (n = 87)											
Intake	Follow-up	MRSP history[1]		Surgery/wound history[2]		AMD prior to enrollment[3]		AMD between sampling4		Total (%)	
		Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)	Number (%)	95% CI (%)
-	-	0	(0, 4)	27 (31)	(22, 41)	31 (36)	(26, 46)	71 (82)	(72, 88)	84 (97)	(90, 99)
-	+	0	(0, 4)	1 (1)	(0, 6)	0	(0, 4)	2 (2)	(1, 8)	2 (2)	(1, 8)
+	-	0	(0, 4)	1 (1)	(0, 6)	0	(0, 4)	1 (1)	(0, 6)	1 (1)	(0, 6)
+	+	0	(0, 4)	0	(0, 4)	0	(0, 4)	0	(0, 4)	0 (0)	(0, 4)

MRSP = Methicillin-resistant Staphylococcus pseudintermedius; AMD = Antimicrobial drug, CI = Confidence interval
[1]Patients that had MRSP infection within the12 months prior to enrollment
[2]Patients that had surgery or penetrating wound within the 12 months prior to enrollment
[3]Patients that received antimicrobial treatment within 12 months prior to enrollment
[4]Patients that received antimicrobial treatment between sampling times