



Antimicrobial use and resistance in companion animals

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JAC

Pet animals as reservoirs of antimicrobial-resistant bacteria

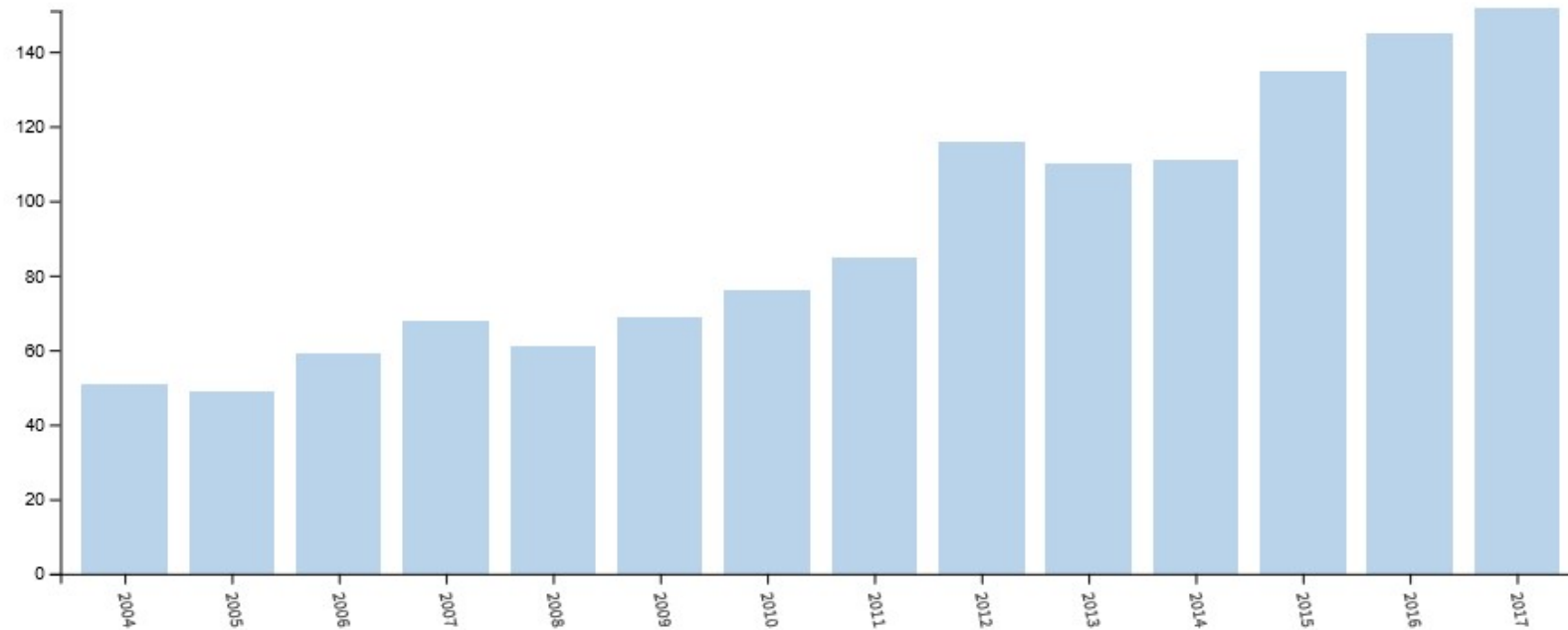
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Pet animal numbers have substantially increased in modern society and attention is increasingly devoted to pet welfare. Because of these changes, antimicrobial agents are frequently used in small animal veterinary practice, often including antimicrobial preparations used in human medicine, with heavy use of broad-spectrum agents such as aminopenicillins plus clavulanic acid, cephalosporins and fluoroquinolones. Several longitudinal studies conducted at veterinary hospitals have indicated that resistance to various antimicrobial agents has emerged amongst pet animal isolates of *Staphylococcus intermedius*, *Escherichia coli* and other bacteria, including species with a potential for zoonotic transmission and resistance phenotypes of clinical interest, such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci and multidrug-resistant *Salmonella* Typhimurium DT104. Based on a review of the current literature, the role of pets in the dissemination of antimicrobial resistance has been given little attention when compared with that of food animals. A marked contrast is evident between the current policies on antimicrobial usage in food and companion animals. Apart from a few countries where limited data on antimicrobial usage and occurrence of resistance in bacteria from pet animals are provided, national surveillance programmes only focus on food animals. However, data on pet animals are clearly needed for guiding antimicrobial use policy in small animal veterinary practice as well as for assessing the risk of transmission of antimicrobial resistance to humans.

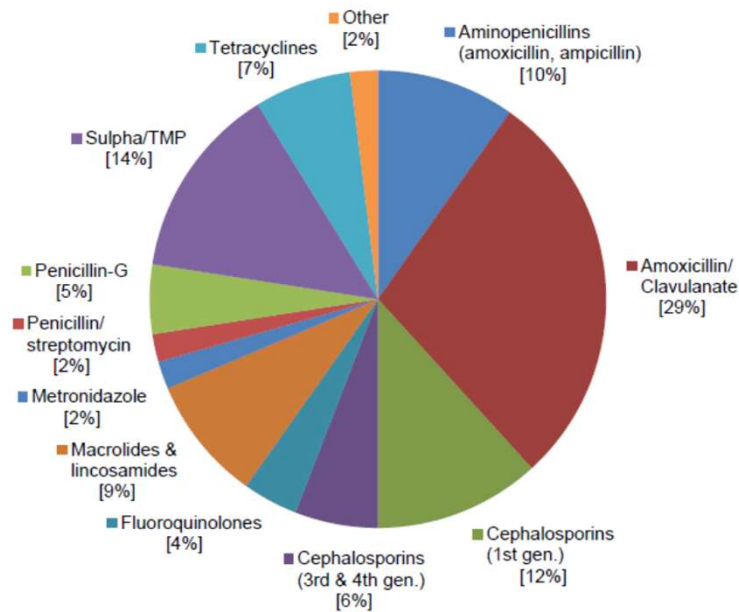
Publications on AMR in dogs and cats, 2004-2017

Web of Science, accessed on 1st June 2018



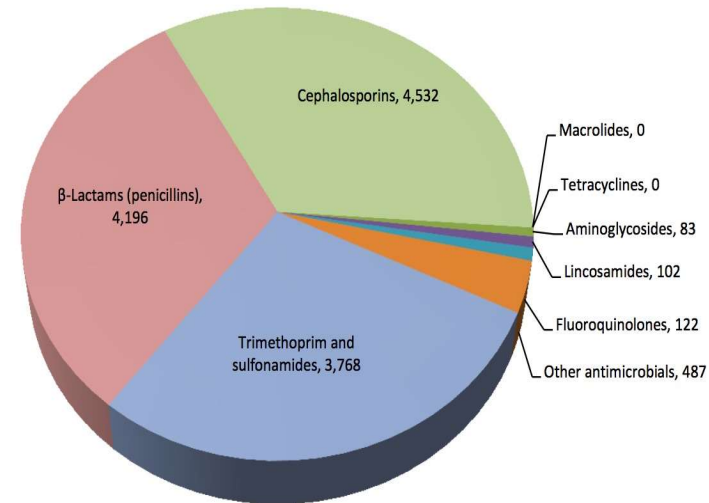
Antimicrobials used in small animals

Data from Denmark in 2011
Danish antibiotic use guidelines



Data from Canada in 2014
CCDR 2016 vol 42

Figure 54. Relative quantities of antimicrobial classes distributed for use in companion animals (percentages based on kg active ingredient), 2016.



2/3 of all antimicrobials used are β-lactams

AMR in food animals vs companion animals



Common types of infections caused by MDR bacteria in companion animals

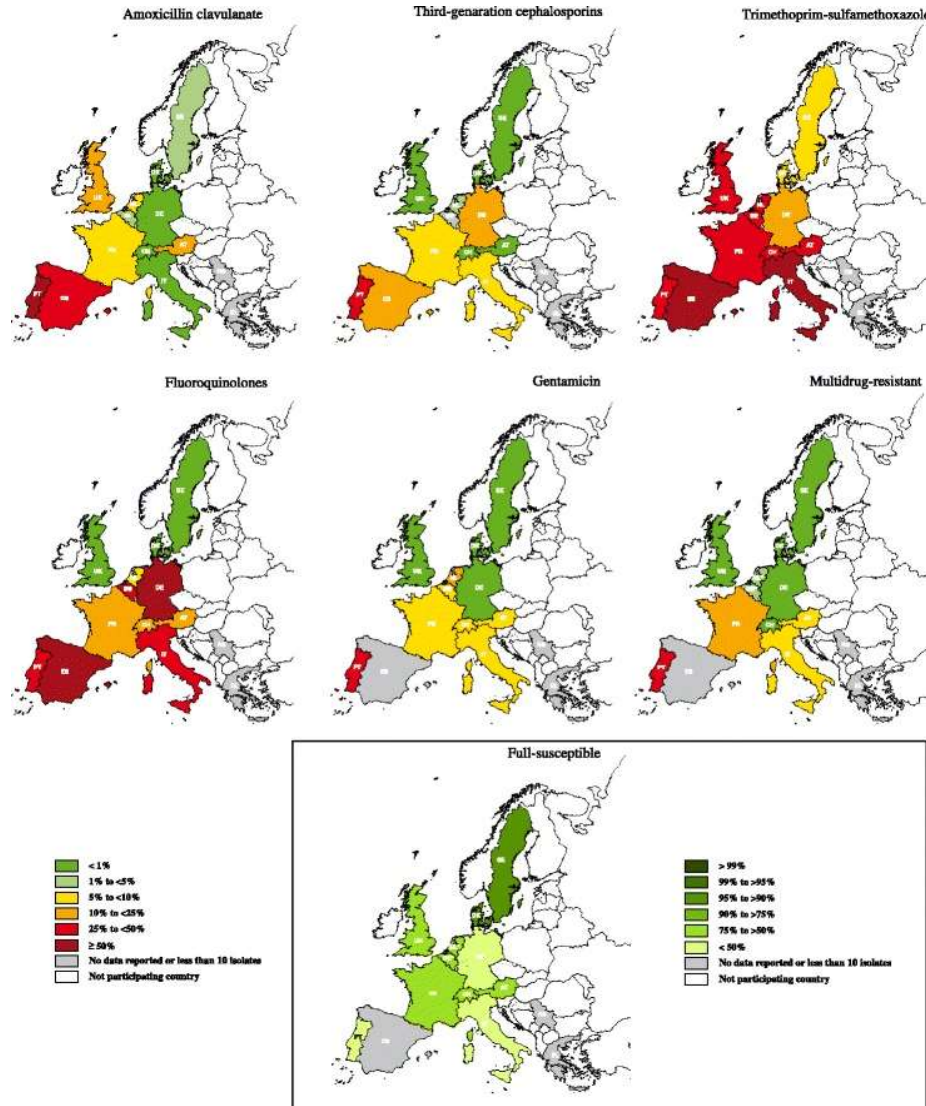
ESBL-producing E. coli	MRSA/MRSP
Urinary tract infections	Skin infections
Pyometra	Otitis
Peritonitis	Surgical site infections
Wound infections	Urinary tract infections

All these MDR bacteria are resistant to β -lactams



AMR in UTI *E. coli* from dogs and cats in Europe

Marques et al. BMV Vet Res 2017



- Southern countries generally presented higher levels of antimicrobial resistance compared to Northern countries
- Temporal increases in the prevalence of AMR were observed within countries during the study period (2008-2013)

AMR in *E. coli* from dogs and cats in DK (2011-2014)

Damborg DVT 2015

	Hunde		Katte	
	2013 (n=535)	2014 (n=781)	2013 (n=103)	2014 (n=147)
Antibiotika				
Amikacin	0.2	0.3	1.0	0.7
Amoxicillin/klavulansyre	3.2	5.4	4.9	6.1
Ampicillin	23.9	25.9	28.2	34.0
1. gen. cephalosporin ^a	4.5	7.0	4.9	8.8
3. gen. cefalosporin ^b	1.7	3.8	4.9	6.1
Enrofloxacin	2.1	2.7	1.0	0.7
Gentamicin	0.4	1.0	2.9	0.7
Imipenem	0	0	0	0
Kloramfenikol	3.9	3.5	1.9	3.4
Marbofloxacin	2.1	2.6	1.0	1.4
Sulfonamid/trimethoprim	6.7	11.5	5.8	4.1
Tetracyklin ^c	8.0	10.1	8.7	6.1

AMR in *S. pseudintermedius* from dogs and cats in DK (2013-2014) Damborg DVT 2015

Antibiotika	2013 (n=794)	2014 (n=744)
Amikacin	0.5	1.4
Amoxicillin/klavulansyre	5.0	3.2
1. gen. cephalosporin ^a	3.4	4.1
Clindamycin	22.8	21.5
Enrofloxacin	2.9	1.9
Erythromycin	23.9	24.9
Gentamicin	2.4	2.4
Kloramfenikol	13.9	14.4
Marbofloxacin	3.3	2.3
Oxacillin	4.7	3.0
Penicillin	73.7	72.6
Sulfonamid/trimethoprim	5.2	5.1
Tetracyklin ^b	30.7	32.3

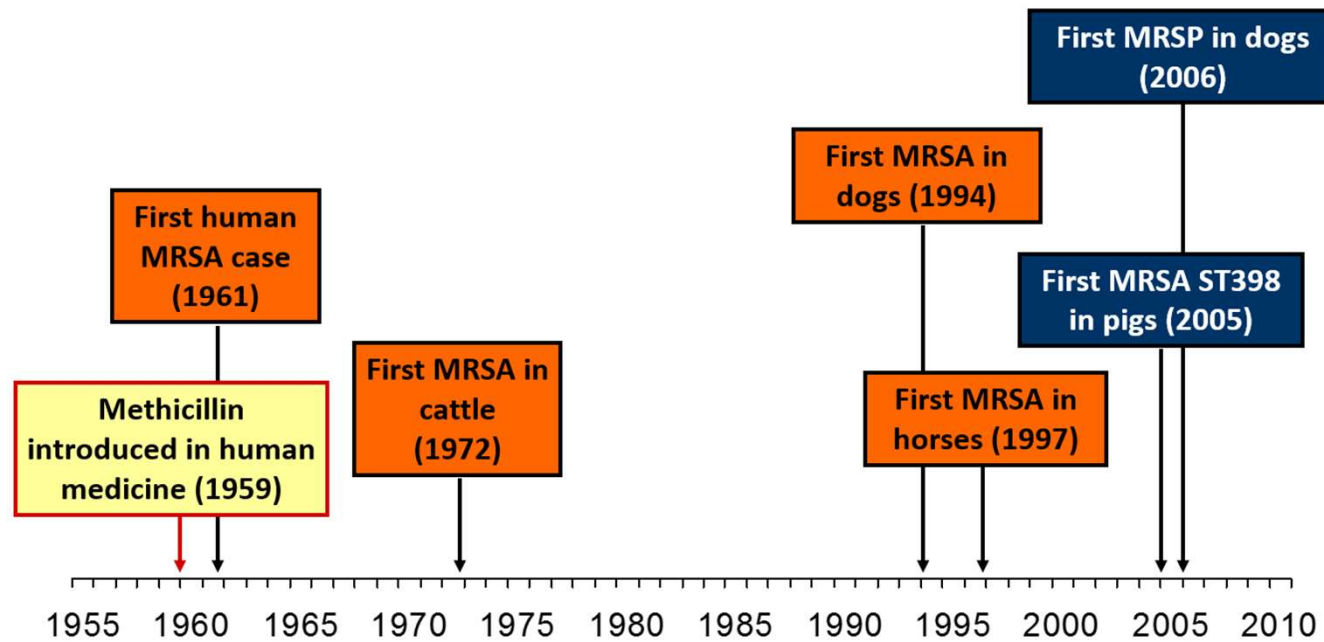
Methicillin-resistant *S. pseudintermedius* (MRSP)

- *S. pseudintermedius* is a natural commensal of dog and other members of Canidae
- MRSP originated from dogs but can infect other hosts, especially cats and to a lesser extent horses and humans
- It is widespread globally with varying prevalence among clinical isolates (from 3% in Scandinavian countries to over 50% in certain referral hospitals in the US)
- It spreads by clonal dissemination and the first clone that emerged in Europe is **clonal complex (CC) 71**



MRSP

History of methicillin resistance in pathogenic staphylococci isolated from animals



Frequency of MRSP in veterinary hospitals

Prevalence of hospital contamination

Author	Year	No.	Country	Prevalence
<i>Murphy et al.</i>	2010	101	Canada	7%
<i>vanDuijkeren et al.</i>	2011	854	Netherlands	10%



Distribution of infections

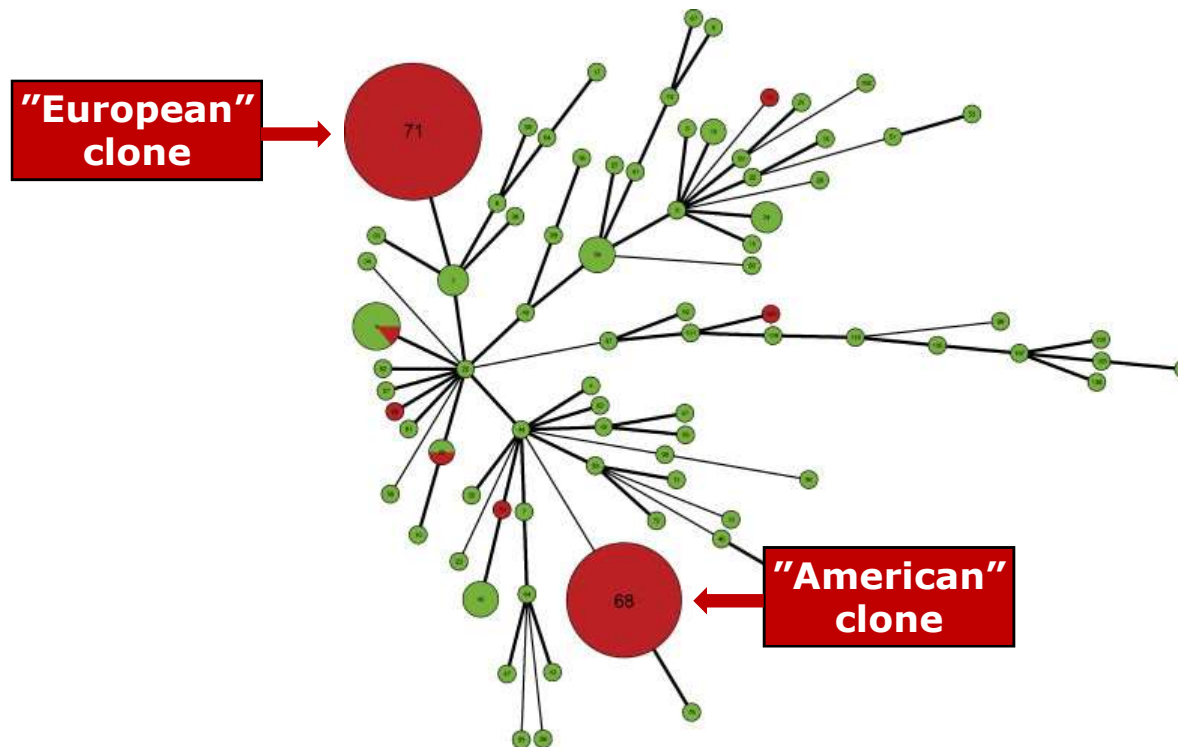
Author	Year	No. dogs	Country	Pyoderma Otitis	Wound Postsurgical	UTI	Other
<i>Morris et al.</i>	2006	78	US	66%	N.D.	9%	25%
<i>Perreten et al.</i>	2009	78	Worldwide	42%	35%	8%	15%
<i>Ruscher et al.</i>	2009	146	EU countries	29%	45%	12%	13%
<i>SVARM</i>	2011	219	Sweden	27%	40%	N.D	23%

Risk factors for MRSP colonization/infection

- **Previous hospitalization and antimicrobial therapy**
(Nienhoff et al. Vet. Microbiol. 2011; Lehner et al. Vet. Microbiol. 2014; Weese et al. J. Am. Vet. Med. Assoc. 2012)
- **Contact with MRSP patients** (Laarhoven et al. 2011)
- Prolonged carriage is associated with antimicrobial treatment for 3 weeks or longer using a drug to which the strain is resistant (Windahl et al. BMC Vet. Res. 2012)

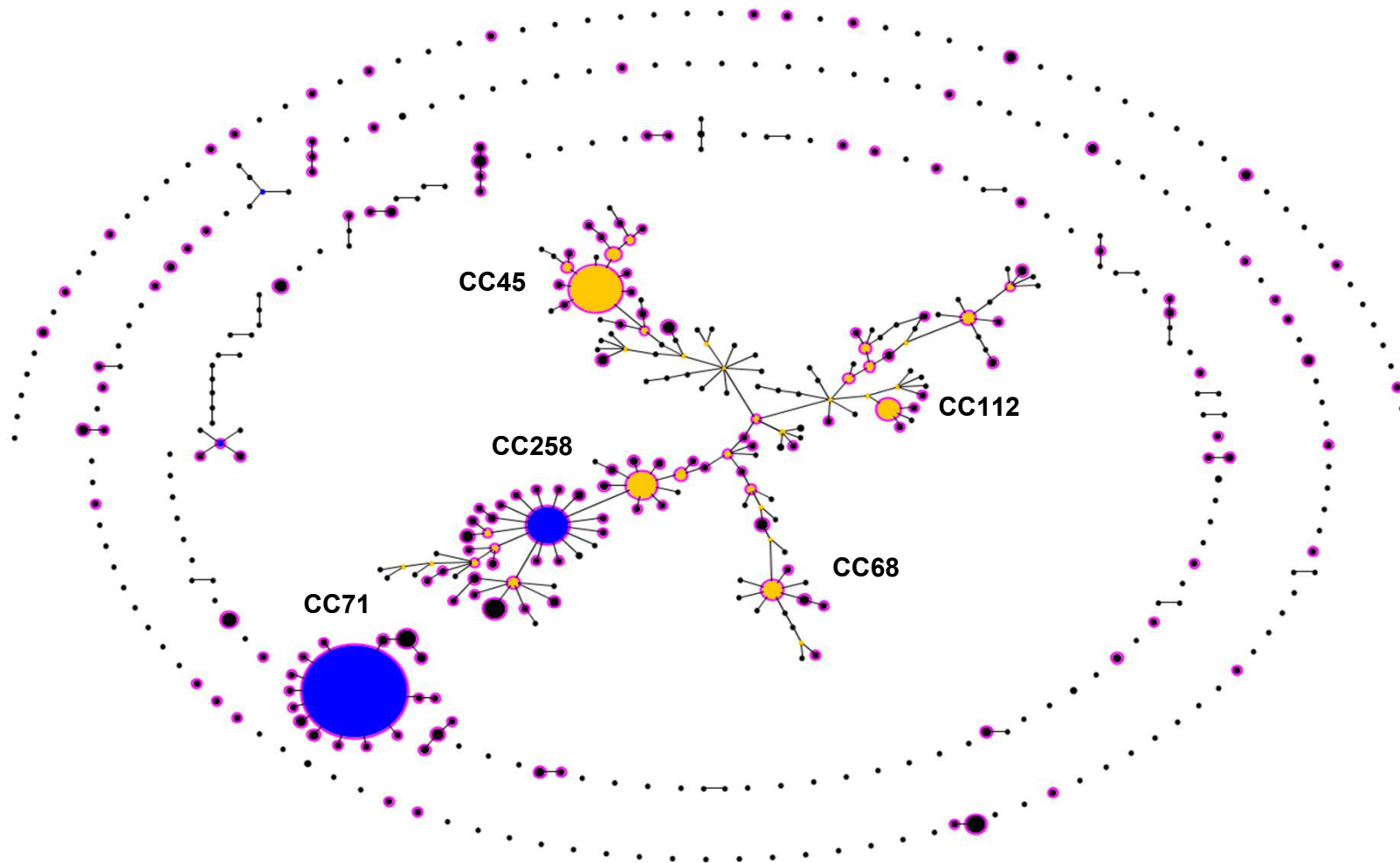
MRSP population structure

Ruscher et al. *Vet Microbiol* 2009



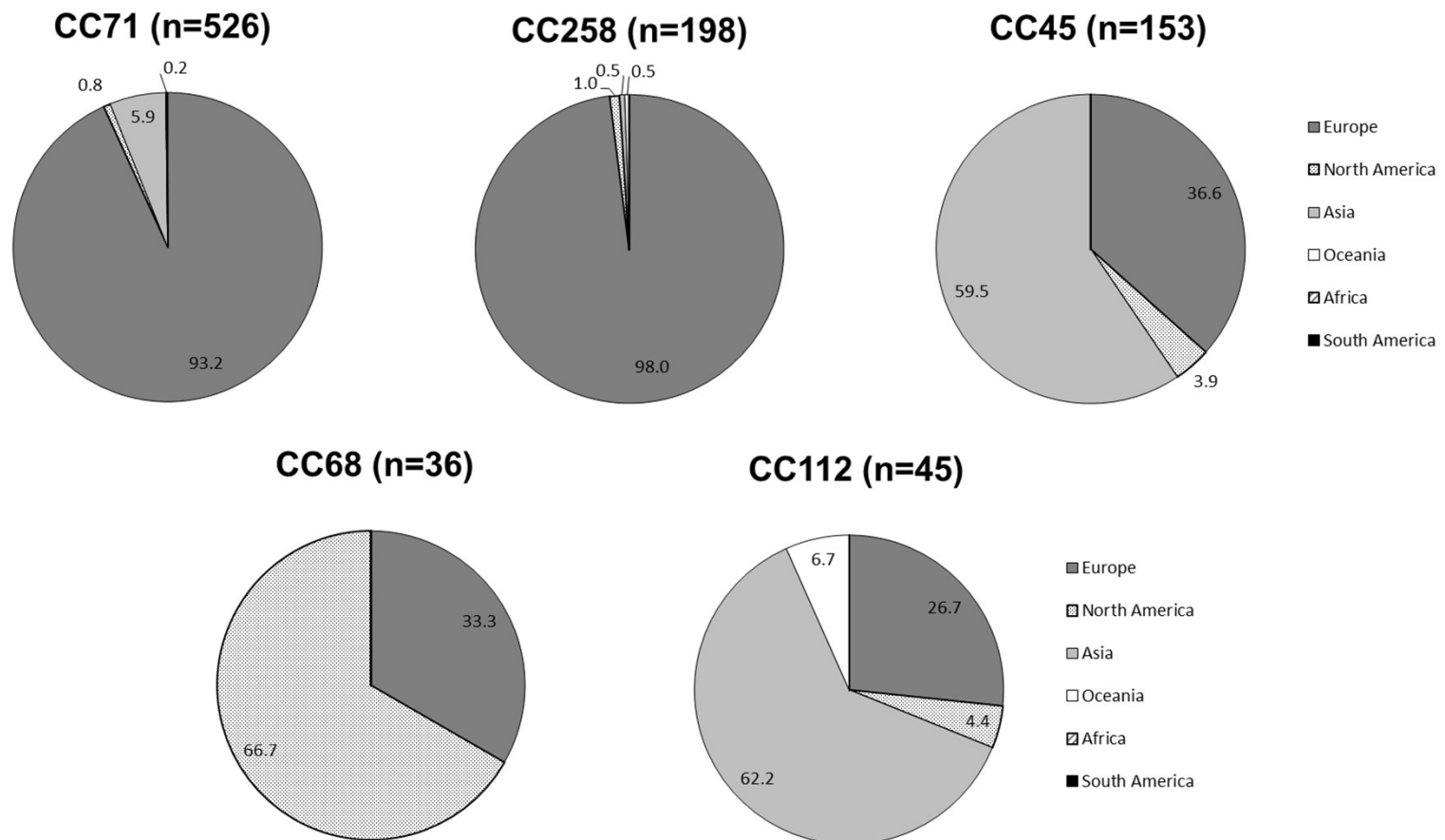
MRSP population structure

Dos Santos et al. *Front. Microbiol.* 2016



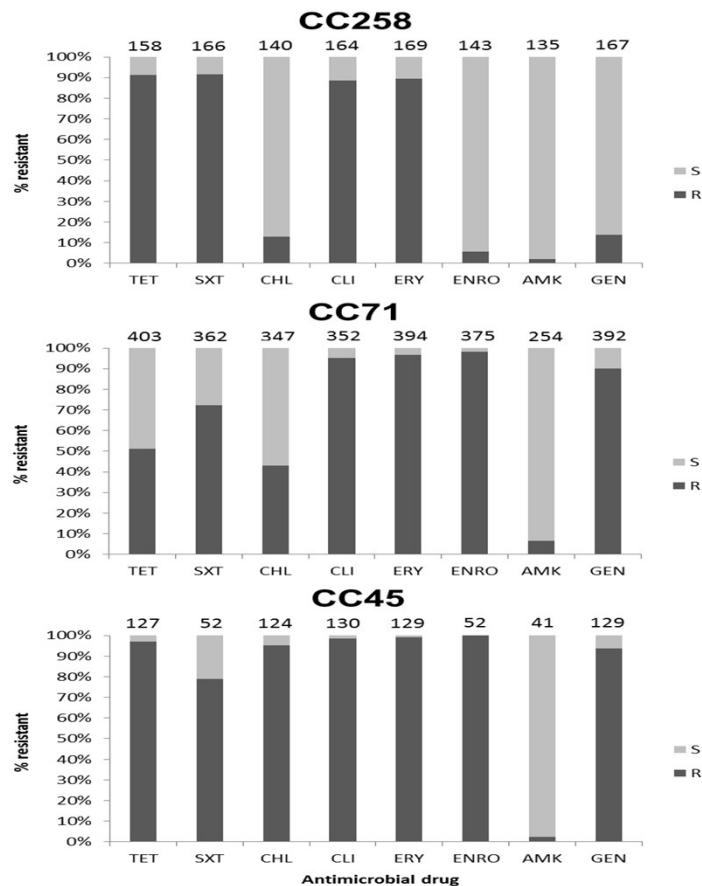
Geographical distribution of MRSP clonal complexes (CC)

Dos Santos et al. *Front. Microbiol.* 2016



AMR patterns of MRSP CCs

Dos Santos et al. *Front. Microbiol.* 2016



- > CC258 (new European clone) is generally (>90%) susceptible to enrofloxacin, chloramphenicol and gentamicin
- > CC71 (traditional European clone) has variable (30-60%) susceptibility rates to tetracyclines, chloramphenicol and sulfa/TMP
- > CC45 (Asian clone) is resistant to all antibiotics except amikacin

MRSP ST71 is truly MDR (ST68 too...)

	No. isolates	Clinda	FQs	S-TMP	Tet	Gen
Resistance profiles of MRSP ST71						
<i>Ruscher et al. 2009</i>	76	99%	99%	100%	90%	99%
<i>Perreten et al. 2009</i>	76	97%	100%	100%	68%	70%
<i>Chrobak et al. 2011</i>	23	96%	96%	N.D.	N.D.	96%
Resistance profiles of methicillin-susceptible isolates						
<i>Pedersen et al. 2007</i>	201	27%	1%	3%	24%	N.D.
<i>Bemis et al. 2009</i>	204	12%	4%	20%	33%	5%
<i>Chrobak et al. 2011</i>	56	27%	2%	N.D.	N.D.	10%
<i>Rubin et al. 2011</i>	60	13%	0%	5%	34%	0%



Antimicrobial choice is difficult since MRSP strains may be resistant to all antibiotics licensed for veterinary use

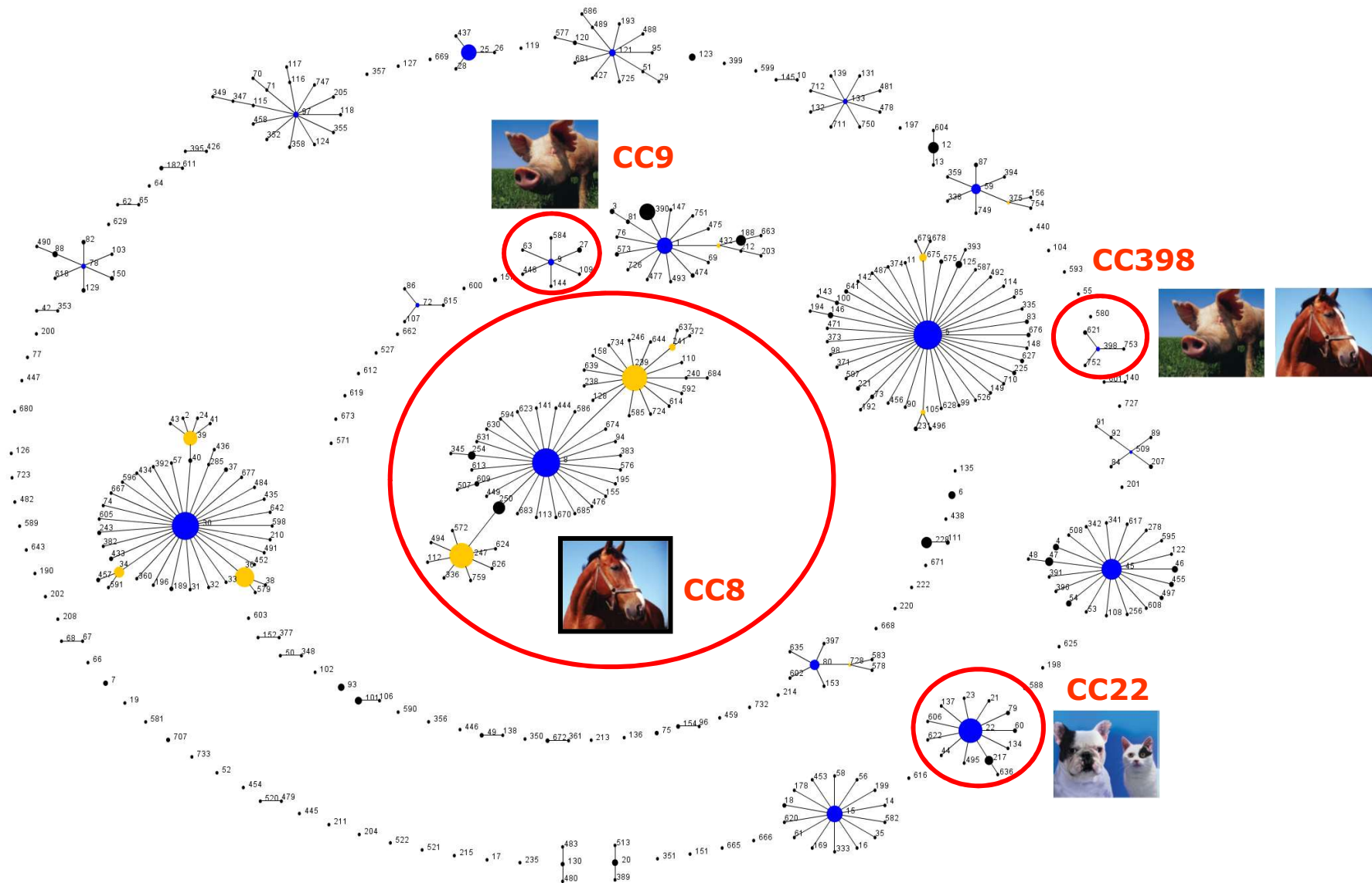
MRSP in humans

- Human infections are rare, generally due to transmission from the household pet
- The prevalence of human carriage is higher among dog owners and veterinary staff

Author	Year	No.	Country	Population	%
<i>Hanselman et al.</i>	2009	242	Canada	Dog owners	1%
<i>Morris et al.</i>	2010	171	US	Small animal veterinarians	5%
<i>vanDuijkeren et al.</i>	2011	45	Netherlands	MRSP contact owners	4%
<i>Poul et al.</i>	2011	128	Italy	Small animal dermatologists	4%
<i>Boost et al.</i>	2011	150	Hong Kong	Veterinary personnel	1%

Veterinarians may act as vectors for animal infection

MRSA population structure based on Multilocus Sequence Typing (MLST)



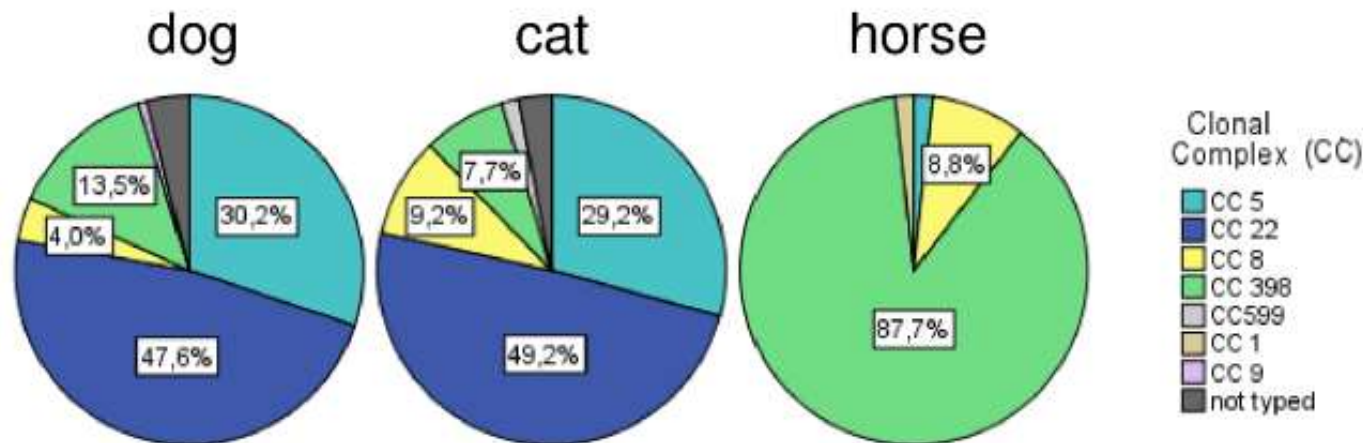
MRSA CC398 in companion animals

Data from Germany 2010-2012 (Vinvze et al. Plos One 2014)

Table 1. *S. aureus* proportion in wound samples from companion animals.

	total	%	dog	%	cat	%	horse	%
wound swabs	5,229	100	3,479	66.5	1,146	21.9	604	11.6
<i>S. aureus</i>	479	100	201	5.8	140	12.2	138	22.8
MSSA	231	48.2	75	2.2	75	6.5	81	13.4
MRSA	248	51.8	126	3.6	65	5.7	57	9.4

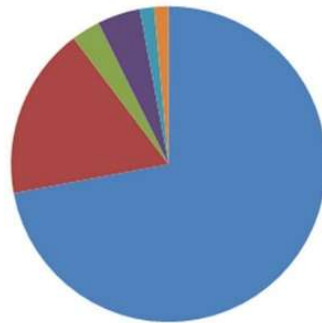
strain origin



Distribution of MRSA clones in France, 2010-2015

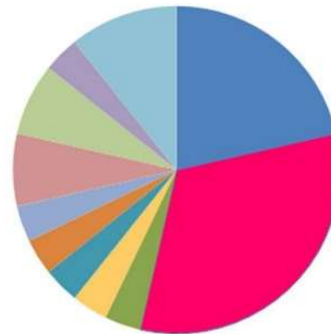
Haenni et al. *Front. Microbiol.* 2017

Horses, n=68



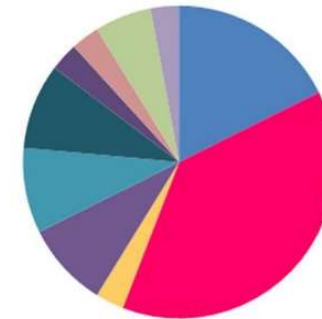
- CC398-IV (72.1%)
- CC8-IV, USA500 (17.6%)
- CC8-IV, EMRSA-14 (2.9%)
- CC130-XI (4.4%)
- CC8-atypical, Hannover clone (1.5%)
- CC49-XI (1.5%)

Dogs, n=28



- CC398-IV (21.4%)
- CC8-IV, Lyon Clone (32.1%)
- CC8-IV, EMRSA-14 (3.6%)
- CC22-IV, Barnim clone (3.6%)
- CC45-IV, Barnim clone (3.6%)
- CC1-IV/SCCFus (3.6%)
- CC8-IV+ccrA4B4, EMRSA-12/13 (3.6%)
- CC8-IV, Paediatric clone (7.1%)
- CC5-II (7.1%)
- CC59-V (3.6%)
- unassigned (10.7%)

Cats, n=34



- CC398-IV (17.6%)
- CC8-IV, Lyon clone (38.2%)
- CC22-IV, Barnim clone (2.9%)
- CC5-IV, Paediatric clone (8.8%)
- CC5-II (8.8%)
- CC398-V, Dutch LA-MRSA (8.8%)
- CC130-XI (2.9%)
- CC5-I, Geraldine clone (2.9%)
- CC5-VI, New Paediatric clone (5.9%)
- CC8-IV, Lyon clone variant sea-neg (2.9%)

Risk factors for ESBL colonization in dogs

- **COLONIZATION IN THE COMMUNITY**

- **Hospitalization** for >7 days and treatment with fluoroquinolones (Gibson et al. Epidemiol. Infect. 2011a)
- Dogs with a history of **antimicrobial therapy** in the past year and dogs from shelters or breeders (Belas et al. Vet. Rec. 2014)
- Dogs from **family households with human carriers** (Ljungquist et al. Infect. Ecol. Epidemiol. 2016)

- **COLONIZATION AFTER HOSPITAL ADMISSION**

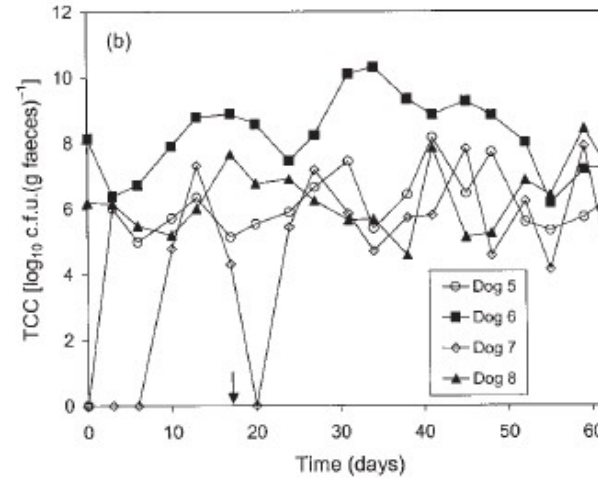
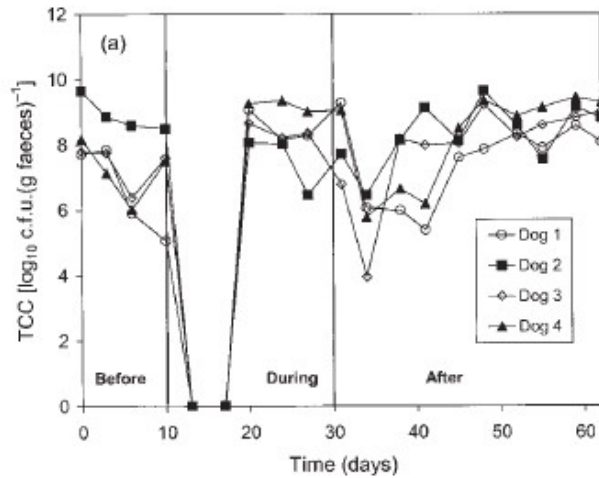
- **Hospitalization** for >6 days, treatment with **cephalosporins prior to admission**, treatment with **cephalosporins or metronidazole during hospitalization** (Gibson et al. Epidemiol. Infect. 2011b)

Effects of enrofloxacin on colonization with multidrug-resistant *E. coli* in dogs

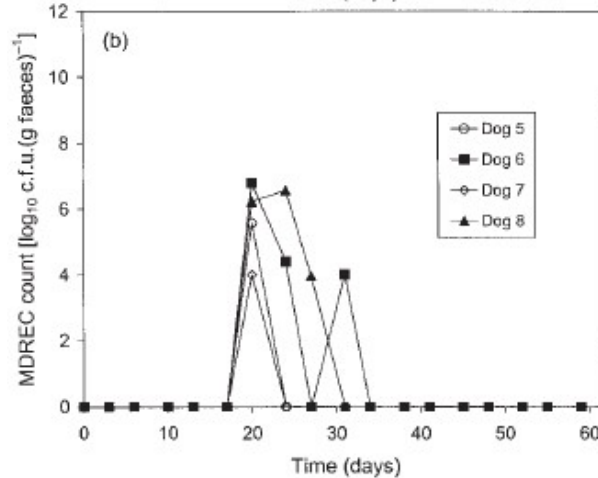
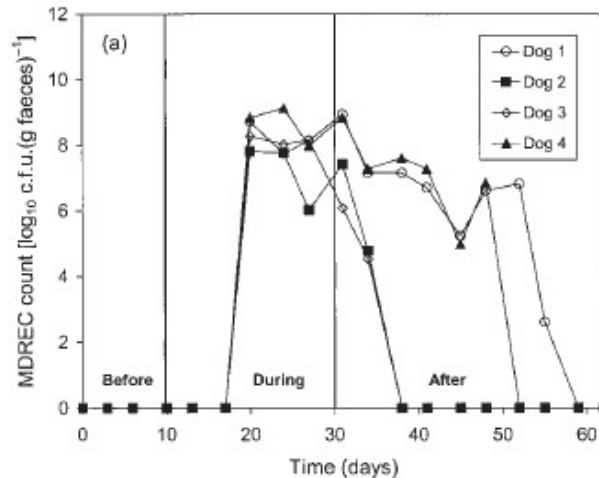
Trott et al. J. Med. Microbiol. 2004

Group A: enrofloxacin + MDR *E.*

Group B: only MDR *E. coli* (no enrofloxacin)



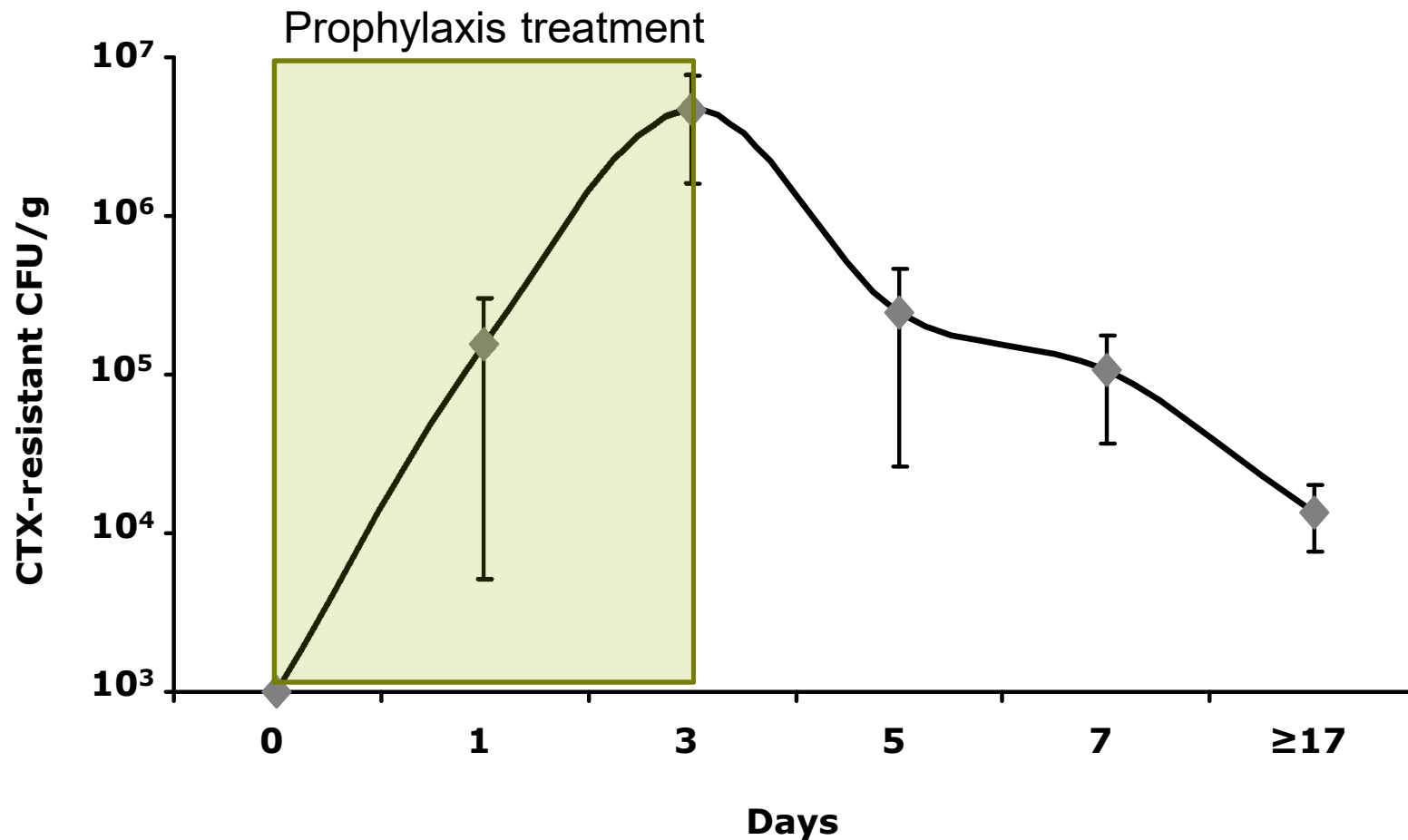
Total coliform counts



MDR *E. coli* counts

The effects of cephalosporin prophylaxis on shedding of ESBL *E. coli* in horses

Damborg et al. Vet. Microbiol. 2012



Take home messages

Antimicrobial use

- The most widely used antimicrobials are beta-lactams, especially amoxicillin-clavulanic acid and cefalexin
- Use of CIAs (i.e. ceftiofur and fluroquinolones) is generally more common than in food animals

AMR

- AMR poses serious risks to the health of companion animals because resistant bacteria are truly MDR and the therapeutic options are limited compared to human medicine
- Zoonotic risks are limited to animal owners and veterinary staff, which may serve as vectors for pet-to-pet transmission
- The level of AMR in Denmark and other Scandinavian countries are significantly lower than in the rest of the world, probably as a consequence of prudent antimicrobial use