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European multicenter study on antimicrobial resistance in bacteria isolated from companion animal urinary tract infections

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Abstract

Background: There is a growing concern regarding the increase of antimicrobial resistant bacteria in companion animals. Yet, there are no studies comparing the resistance levels of these organisms in European countries. The aim of this study was to investigate geographical and temporal trends of antimicrobial resistant bacteria causing urinary tract infection (UTI) in companion animals in Europe. The antimicrobial susceptibility of 22 256 bacteria isolated from dogs and cats with UTI was determined. Samples were collected between 2008 and 2013 from 16 laboratories of 14 European countries. The prevalence of antimicrobial resistance of the most common bacteria was determined for each country individually in the years 2012–2013 and temporal trends of bacteria resistance were established by logistic regression.

Results: The aetiology of uropathogenic bacteria differed between dogs and cats. For all bacterial species, Southern countries generally presented higher levels of antimicrobial resistance compared to Northern countries. Multidrug-resistant *Escherichia coli* were found to be more prevalent in Southern countries. During the study period, the level of fluoroquinolone-resistant *E. coli* isolated in Belgium, Denmark, France and the Netherlands decreased significantly. A temporal increase in resistance to amoxicillin-clavulanate and gentamicin was observed among *E. coli* isolates from the Netherlands and Switzerland, respectively. Other country-specific temporal increases were observed for fluoroquinolone-resistant *Proteus* spp. isolated from companion animals from Belgium.

Conclusions: This work brings new insights into the current status of antimicrobial resistance in bacteria isolated from companion animals with UTI in Europe and reinforces the need for strategies aiming to reduce resistance.

Keywords: Antimicrobial resistance, Temporal trends, MRSA, MRSP, Dog, Cat

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Background

Bacterial urinary tract infections (UTI) are frequently diagnosed in dogs and are considered rare in cats [1, 2]. Lately, increased frequencies of UTI in cats have been reported in some European countries [3–5] in particularly when concurrent diseases are present [6].

*Escherichia coli* is the most frequent isolated bacteria causing UTI in dogs and cats. Several studies show frequencies greater than 30 % [7–9]. Other commonly isolated bacteria genera include *Staphylococcus* spp., *Enterococcus* spp., *Proteus* spp. and *Klebsiella* spp. [7–10].

Previous studies in the United Kingdom and in Missouri-Columbia (USA) analysing the temporal trends of antimicrobial resistance in small collections of bacterial isolates from companion animal infections point to a significant increase in antimicrobial resistance [11, 12]. Furthermore, the emergence of multidrug-resistant bacteria (isolates resistant to three or more antimicrobial categories) in companion animals is an increasing concern [11, 13–15]. This creates new therapeutic challenges in veterinary medicine and is also a public health issue, since these pathogens may be zoonotic [16] and companion animals may play a role in the spread of resistant bacteria due to their close contact to humans [14, 17].

Antimicrobial resistance may vary according to the geographic location [9, 18]. Data on antimicrobial resistance in bacteria isolated from companion animals with UTI in Europe are not easily comparable due to differences in study design, such as variations in host species, inclusion criteria and/or time period. Thus, it is difficult to get a European overview of antimicrobial resistance as seen in human medicine surveillance programmes such as the European Antimicrobial Resistance Surveillance Network [18].

Antimicrobial therapy in UTI should ideally rely on susceptibility testing of the isolated bacteria [19]. Yet, antimicrobials are frequently administered empirically based on the presence of compatible clinical signs, urine cytological findings and in the absence of urine culture and are required to alleviate UTI symptoms while waiting for antimicrobial susceptibility testing results [19]. Besides the pharmacokinetic-pharmacodynamic properties, the empiric antimicrobial selection should consider the most likely causative agent as well as its regional susceptibility patterns [8]. Moreover, according to the World Organisation for Animal Health [20], veterinarians should adopt strategies aimed at the reduction of antimicrobial resistance. Therefore, current information on the aetiology and antimicrobial resistance focused on UTI is of crucial importance.

Under the umbrella of the European Society of Veterinary Nephrology and Urology, a multicenter retrospective study was launched in November 2013 with the goal of getting antimicrobial resistance data on bacteria isolated from companion animal with UTI across Europe. A Urinary Tract Infection Resistance – Veterinary Network (UTIR-VNet) was constituted with this purpose in mind. Partial results were presented at the annual Society meeting included in the 25th congress of the European College of Veterinary Internal Medicine, 4–6 September 2014, Mainz, Germany. The aim of this study was to determine the frequency of uropathogens in dogs and cats with urinary tract infection in Europe and to characterise the frequency and temporal trends of antimicrobial resistance over a period of six years. We hereby present a complete report and discussion of this study.

Methods

Participating countries

Between January and September 2014, 16 veterinary microbiology laboratories from 14 European countries (Austria, Belgium, Denmark, France, Germany, Greece, Italy, the Netherlands, Portugal, Serbia, Spain, Sweden, Switzerland, United Kingdom), were invited to participate in this study (Fig. 1). Laboratories were requested to send available retrospective data on animal species, age and gender, bacterial identification and antimicrobial susceptibility testing conducted in bacteria obtained from dogs and cats with UTI between 2008 and 2013. Samples were obtained with owners consent as part of the routine care of canine and feline UTI.

Bacterial Isolates

The bacteria identification varied between laboratories. Most laboratories used standard phenotypic tests, including API, while others used techniques such as PCR and MALDI-TOF. This discrepancy was particularly evident for staphylococci, which were classified to either the species or genus level depending on the laboratory.

Susceptibility testing

The following antimicrobials were included: amoxicillin-clavulanate (AMC), ampicillin (AMP), cefotaxime (CTX), cefovecin (CVN), cefoxitin (FOX), ceftazidime (CAZ), cefpodoxime (CPD), cefotifur (EFT), ciprofloxacin (CIP), enrofloxacin (ENR), gentamicin (CN), marbofloxacin (MAR), oxacillin (OX), penicillin (P) and trimethoprim/sulbactam (XST).

The retrospective nature of the study forced us to include two in vitro antimicrobial susceptibility testing methods. Laboratories from Austria, France, Germany, Greece, Italy, the Netherlands, Portugal, Serbia, Spain, United Kingdom, used standard disc diffusion method according to Clinical Laboratory Standards Institute (CLSI) guidelines [21], whereas Sweden (VetMIC, SVA, Uppsala, Sweden), Denmark and United Kingdom (COM-PAN1F Sensititre panels, Thermo Fisher), Switzerland and
Belgium (VITEK 2, BioMérieux) used broth microdilution method.

Human CLSI breakpoints [22] were used for interpretation of minimal inhibitory concentration and disk diffusion results for CAZ (30 μg), CTX (30 μg), and CIP (5 μg), whereas veterinary CLSI breakpoints [23] were used for AMC (30 μg), AMP (30 μg), CN (10 μg), CPD (10 μg), ENR (5 μg), FOX (30 μg), MAR (5 μg), OX (1 μg), P (10U), and SXT (25 μg). Clinical breakpoints from the Société Française de Microbiology [24] were used for EFT (30 μg). Results for CVN (30 μg) were interpreted according to the manufacturer guidelines. As seen in the human European Antimicrobial Resistance Surveillance Network (EARS-Net) report [18], when data on minimal inhibitory concentrations or inhibition zone diameter were not available, the laboratories’ own interpretations (susceptible, intermediate and resistant) were accepted. This was the case for Spain, Serbia, and Germany that used contemporary CLSI guidelines, for the United Kingdom that used the breakpoints from the British Society of Antimicrobial Chemotherapy [25] and for the Netherlands and Switzerland (2008–2010) that used breakpoints recommended by the Dutch Committee on Guidelines for Susceptibility testing [26].
Data analysis and statistical methods

Statistical analysis was performed using the SAS statistical software package for Windows, version 9.3, (SAS Institute Inc, Cary, North Carolina, USA).

The Fisher exact test was used to compare pathogen frequencies by species or gender of the host, by simple/multiple infection and by country. An alpha value of 0.05 was used.

Isolates were considered fully resistant when found to be resistant according to the clinical breakpoint applied. An isolate was considered susceptible when found to be susceptible or intermediate according to the clinical breakpoint applied. The antimicrobials included in this study are known to be highly concentrated in the urine so their report as susceptible may be appropriated for isolates categorized as intermediate [19].

Regarding third generation cephalosporins (3GC), laboratories tested different 3GC resistance surrogates. Therefore, to evaluate the antimicrobial resistance to 3GC, an isolate was considered as 3GC resistant when it was resistant to at least one of the five 3GC tested (CTX, CAZ, CVN, EFT or CPD). The same rational was applied to evaluate resistance to fluoroquinolones (FLU), namely using ENR, CIP or MAR as a marker of resistance. Methicillin-resistance in staphylococci was determined according to CLSI guidelines [23] using cefoxitin or oxacillin to evaluate resistance depending on the bacterial species considered. Yet, Germany and Spain did not test staphylococci against oxacillin and thus did not report methicillin-resistance. France did not test staphylococci against oxacillin and thus did not report methicillin-resistance regarding Staphylococcus pseudintermedius (MRSP). The Netherlands did not have data on staphylococci susceptibility to OX or FOX but instead reported data on the detection of the mecA gene by PCR. The frequency of methicillin-resistance did not include staphylococci only identified to the genus level.

Enterobacteriaceae were considered multidrug-resistant (MDR) when fully resistant to three or more categories of antimicrobials, namely AMC, 3GC, SXT, CN and/or FLU. Unlike the MDR definition proposed by other authors [27], intermediate isolates from this study were considered as susceptible. This difference was applied because we are considering drugs that can be highly concentrated in urine. Furthermore, this approach will reduce any overestimation of MDR frequency due to the use of different breakpoint guidelines. Full-susceptibility (FullS) was defined as an isolate being susceptible for all the above-mentioned categories of antimicrobials. Since Belgium had no data available on 3GC and the Netherlands had little data on CN, MDR and FullS percentages do not include resistance to 3GC for Belgium and resistance to CN for the Netherlands.

As a rule, statistical analysis was only done when at least ten isolates for a specific organism-antimicrobial agent combination were reported for a given country. All frequencies are presented with a confidence interval of 95 % (95 % CI). Maps of European resistance distribution were drawn considering the percentage of fully resistant isolates to the considered antimicrobial agent, over the years 2012–2013. A scale of colours was applied composed of six resistance intervals after the example of EARS-Net surveillance program reports [18].

Statistical analysis of temporal trends of antimicrobial resistance for a specific organism-antimicrobial agent combination were determined within each country. Temporal trends were only determined for countries reporting data on at least three consecutive years and ten isolates per year. A SAS LOGISTIC regression, with the year as a continuous variable and an alpha value of 0.05 was conducted. Temporal trends of resistance were mainly determined for E. coli since this was the most represented bacterial species. Yet, temporal trends of AMC, FLU and SXT in Proteus spp. were also determined for Belgium, France, the Netherlands and Sweden.

Results

Overall, data on 22,256 uropathogenic bacteria were obtained from 15,097 dog and 5963 cat positive urine cultures. Table 1 summarises the numbers of bacterial isolates obtained by year and country.

| Country | Year | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | Total |
|---------|------|------|------|------|------|------|------|------|
| AT      |      | -    | -    | -    | 144  | 185  |      | 329  |
| BE      |      | -    | -    | 547  | 578  | 623  | 739  | 2487 |
| DK      | 29   | 30   | 53   | 116  | 153  | 205  | 587  |
| FR      |      | -    | -    | 620  | 733  | 780  | 995  | 3128 |
| DE      |      | -    | 64   | 93   | 140  | 161  | 146  | 604  |
| EL      | 24   | 29   | 13   | 11   | 32   | 43   | 152  |
| IT      |      | 36   | 29   | 36   | 77   | 65   | 243  |
| NL      | 480  | 867  | 958  | 1132 | 1195 | 1307 | 5939 |
| PT      | 77   | 54   | 57   | 34   | 32   | 45   | 299  |
| RS      | 17   | 19   | 10   | 2    | 3    | 3    | 54   |
| ES      | 14   | 23   | 27   | 40   | 47   | 79   | 230  |
| SE      | 730  | 924  | 1071 | 1202 | 1355 | 1647 | 6929 |
| CH      | 109  | 120  | 112  | 125  | 114  | 174  | 754  |
| UK      | 31   | 44   | 81   | 117  | 126  | 122  | 521  |
| Total   | 1511 | 2210 | 3671 | 4267 | 4842 | 5755 | 22256 |

*AT, Austria; BE, Belgium; DK, Denmark; FR, France; DE, Germany; EL, Greece; IT, Italy; NL, the Netherlands; PT, Portugal; RS, Serbia; ES, Spain; SE, Sweden; CH, Switzerland; UK, United Kingdom.
mean ages, namely 8.77 years (SD ± 4.04, 9.00 median, 6.00 IQR, range 0.1–20) and 8.82 years (SD ± 5.03, 8.50 median, 8.1 IQR, range 0.2–22) respectively. Gender was only specified in 3885 records where 61.41 % (95 % CI 59.69–63.12 %, n = 1900/3094) of dogs and 48.29 % (95 % CI 44.81–51.78 %, n = 382/791) of cats were females.

Among all urine cultures, 94.64 % (95 % CI 94.33–94.94 %, n = 19932/21060) resulted in the growth of bacterial pure cultures, with no significant difference between cats and dogs (P = 0.1856). Both in dogs and cats, *E. coli* was the most frequently identified bacteria and accounted for 59.45 % (95 % CI 58.80–60.09 %, n = 13231/22256) of all isolates. The frequency of the remaining bacterial species differed significantly between dogs and cats (Table 2). *Enterococcus* spp. and *Staphylococcus* spp. frequencies were higher in cats, whereas *Proteus* spp. and *Klebsiella* spp. were more prevalent in dogs.

Considering the years 2012–2013, the major differences in *E. coli* (Table 3, Fig. 2) and *Proteus* spp. (Table 4, Fig. 3) antimicrobial resistance frequencies were seen between Northern (Denmark and Sweden) and Southern (Italy, Greece, Portugal and Spain) countries.

The lowest frequencies of AMC resistance in *E. coli* were detected in isolates from Denmark (2.88 %) and Belgium (4.29 %). *E. coli* from Portugal (48.15 %) had a significantly higher AMC resistance frequency (P < 0.05) when compared with all countries except for Spain, Italy and Greece (Table 3). Less than 15 % of *Proteus* spp. were resistant to AMC in all countries with exception of Portugal (50 %) and Spain (26.67 %) (Table 4).

*E. coli* resistance to 3GC had a similar distribution to what was seen for AMC (Fig. 2). The highest 3GC resistance frequencies were found in Southern countries, namely Portugal (31.25 %), Italy (24.64 %) and Spain (21.15 %) (Table 3). *Proteus* spp. 3GC resistance was lower than 5 % in Austria, Denmark, Sweden, Switzerland, United Kingdom and the Netherlands, whereas Portugal (33.33 %) and Spain (15.38 %) were the countries with the highest resistance levels (Table 4).

SXT resistance in Southern countries was higher than 25 and 45 % for *E. coli* and *Proteus* spp., respectively (Tables 3 and 4; Figs. 2 and 3). Sweden and Denmark had the lowest SXT resistance values (lower than 9 %). The remaining included countries had frequencies ranging between 10.21–21.13 % and 20–37.93 % in *E. coli* and *Proteus* spp., respectively (Tables 3 and 4).

*E. coli* FLU resistance was higher in the Southern countries and ranged from 29.03 % in Portugal to 31.88 % in Italy (Table 3). Concerning *Proteus* spp., Spain and Germany had around 50 % FLU resistance, followed by Italy and Portugal with around 40 % (Table 4). Sweden, Denmark, Belgium and the Netherlands had less than 10 % FLU resistant *E. coli*. Denmark, Sweden, United Kingdom and the Netherlands had less than 10 % FLU resistant *Proteus* spp. (Figs. 2 and 3).

### Table 2 Uropathogenic bacteria aetiology, single versus mixed infections and cat versus dog as host species

| Organism         | Overall | Single organism | Mixed infections | P     | Dogs | Cats |
|------------------|---------|-----------------|------------------|-------|------|------|
|                  | n       | (95 % CI)       | n                | (95 % CI) | n   | (95 % CI) | P     | n       | (95 % CI) |
| *Enterobacter*   | 308     | (1.23–1.54)     | 244              | (1.07–1.38) | 64  | (2.09–3.42) | <0.0001 | 194     | 1.21 (1.04–1.38) | 1.81 (1.48–2.14) | 0.0008 |
| *Enterococcus*   | 1506    | (6.44–7.10)     | 1129             | (5.34–5.99)  | 377 | (14.72–17.72) | <0.0001 | 745     | 4.66 (4.34–4.99) | 761 (11.31–12.92) | <0.0001 |
| *Escherichia coli* | 13231  | (58.80–60.09)   | 12417            | (61.62–62.97) | 814 | (33.09–36.97) | <0.0001 | 9506    | 59.51 (58.75–60.27) | 3725 (58.08–60.51) | 0.7832 |
| *Klebsiella*     | 478     | (1.96–2.34)     | 400              | (1.81–2.20)  | 78  | (2.62–4.09)  | <0.0001 | 385     | 2.41 (2.17–2.65) | 93 (1.18–1.78) | <0.0001 |
| *Proteus*        | 1992    | (8.85–9.33)     | 1770             | (8.49–9.28)  | 222 | (8.36–10.75) | 0.2824 | 1869    | 11.70 (1.20–1.22) | 123 (1.62–2.30) | <0.0001 |
| *Pseudomonas*    | 389     | (1.58–1.92)     | 315              | (1.41–1.75)  | 74  | (2.47–3.90)  | <0.0001 | 293     | 1.83 (1.63–2.04) | 96 (1.22–1.83) | 0.1249 |
| *Staphylococcus* | 2893    | (12.56–13.44)   | 2519             | (12.18–13.10) | 374 | (14.60–17.59) | <0.0001 | 1836    | 11.49 (11.00–11.99) | 1057 (15.90–17.75) | <0.0001 |
| *Streptococcus*  | 802     | (3.36–3.85)     | 586              | (2.71–3.17)  | 216 | (8.11–10.47) | <0.0001 | 675     | 4.23 (3.91–4.54) | 127 (1.67–2.37) | <0.0001 |
| Other            | 657     | (2.73–3.17)     | 552              | (2.54–3.00)  | 105 | (3.67–5.36)  | -     | 471     | 2.95 (2.69–3.32) | 186 (2.54–3.38) | -     |

*95 % CI, 95 % Confidence interval
n – Total number of isolates
P – P value obtained by Fisher exact test when comparing single versus mixed infections and cat versus dog as host. Statistically significant values are highlighted in bold
Table 3 Percentage of resistance in Escherichia coli by antimicrobial and country in 2012–2013

| Country | AMC | 3GC | FLU | CN | SXT | Combined resistance |
|---------|-----|-----|-----|----|-----|---------------------|
| AT      | 142 | 1408 | (8.36–19.81) | 11.97 | 5.63 | (1.84–9.43) |
|         |     | (142) | [a, b] | [a, b] | [a, b] | [a, b] |
| BE      | 840 | 4.29 | (2.92–5.66) | 769 | 167 | (0.80–2.53) |
|         |     | (0.0) | [c] | [c] | [c] | [c] |
| DK      | 206 | 2.88 | (0.61–5.16) | 208 | 192 | (0.06–3.79) |
|         |     | (9.81) | [a, c] | [a, c] | [a, c] | [a, c] |
| FR      | 954 | 12.79 | (10.67–15.91) | 948 | 3.6 | (2.22–4.51) |
|         |     | (10.83) | [a, d] | [a, d] | [a, d] | [a, d] |
| DE      | 153 | 11.76 | (6.66–16.87) | 153 | 1.96 | (0.00–4.16) |
|         |     | (6.71) | [a, d] | [a, d] | [a, d] | [a, d] |
| EL      | 31  | 25.81 | (10.40–41.21) | 30  | 36.2 | (16.33–52.90) |
|         |     | (7R/25) | [e, f] | [e, f] | [e, f] | [e, f] |
| IT      | 69  | 26.09 | (15.73–36.45) | 69  | 14.49 | (6.19–22.80) |
|         |     | (14.47) | [e] | [e] | [e] | [e] |
| NL      | 1461| 10.81 | (9.22–12.41) | 1457 | 3.70 | (0.00–7.82) |
|         |     | (2.76) | [a, c] | [a, c] | [a, c] | [a, c] |
| PT      | 27  | 48.15 | (29.30–66.99) | 31  | 10.00 | (0.00–20.74) |
|         |     | (15.19) | [e] | [e] | [e] | [e] |
| RS      | 3   | 28/15 | - | 3  | 0R/35 | - |
|         |     | 2R/15 | - | 3  | 0R/35 | - |
| ES      | 60  | 31.67 | (19.90–43.44) | 61  | 15.22 | (4.94–25.60) |
|         |     | (10.05) | [e] | [e] | [e] | [e] |
| SE      | 2091| 6.98 | (5.89–8.07) | 2091 | 0.19 | (0.00–0.38) |
|         |     | (0.61) | [f] | [f] | [f] | [f] |
| CH      | 133 | 10.53 | (5.31–15.74) | 132  | 6.2 | (2.52–11.12) |
|         |     | (3.59) | [a, c] | [a, c] | [a, c] | [a, c] |
| UK      | 143 | 21.68 | (14.92–28.43) | 143 | 6.52 | (1.48–11.57) |
|         |     | (14.31) | [b, f] | [b, f] | [b, f] | [b, f] |

AMC amoxicillin clavulanate, 3GC third generation cephalosporins, FLU fluoroquinolones, CN gentamicin, SXT trimethoprim/sulfamethoxazole, MDR multidrug-resistant, Full-S fully-susceptible

Overall, E. coli CN resistance was lower than 16 % (Table 3). Regarding resistance to CN in Proteus spp. the same resistance frequency occurred with the exception of Portugal where a higher resistance frequency was recorded (33.33 %) (Table 4).
Fig. 2 Percentage (%) of *Escherichia coli* antimicrobial resistance by antimicrobial and country in the years 2012–2013. Countries: AT- Austria; BE- Belgium; DK- Denmark; FR- France; DE- Germany; EL- Greece; IT- Italy; NL- the Netherlands; PT- Portugal; RS- Serbia; ES- Spain; SE- Sweden; CH- Switzerland; UK- United Kingdom. Multidrug-resistance considering combined resistance to three or more of the following antimicrobial categories: AMC, 3GC, FLU, CN and SXT. Full-susceptibility (FullS) was defined as an isolate being susceptible for all the above-mentioned categories of antimicrobials. Regarding multidrug-resistance and full-susceptibility frequencies, countries marked by asterisk: 3GC was not included for Belgium and CN for the Netherlands. Thus, these frequencies may be underestimated when compared with the remaining countries.
Table 4  Percentage of resistance in Proteus spp. by antimicrobial and country in 2012-2013

| Country  | AMC | 3GC | FLU | CN | SXT | Combined resistance |
|----------|-----|-----|-----|----|-----|---------------------|
|          | n   | % R (95% CI) | n   | % R (95% CI) | n   | % R (95% CI) | n   | % MDR (95% CI) | % FullS (95% CI) |
| AT       | 29  | 10.34 (0.00-21.43) | 29  | 0.00 (0.00-13.00) | 29  | 6.90 (0.00-17.27) | 29  | 6.90 (0.00-16.12) | 55.17 (37.07-73.27) |
| BE       | 143 | 2.10 (0.00-4.45) | 135 | 28.15 (20.56-37.53) | 155 | 9.68 (5.02-14.33) | 154 | 35.06 (27.53-42.60) | 57.60 (48.94-66.26) |
| DK       | 31  | 0.00 (0.00-1.00) | 31  | 0.00 (0.00-1.00) | 31  | 0.00 (0.00-1.00) | 31  | 6.45 (0.00-15.10) | 92.55 (44.41-84.90) |
| FR       | 215 | 3.77 (3.93-10.95) | 211 | 6.64 (3.28-9.90) | 212 | 17.92 (12.76-23.09) | 214 | 9.81 (5.83-13.80) | 66.67 (60.20-73.14) |
| DE       | 10  | 0.00 (0.00-5.00) | 10  | 10.00 (0.00-25.92) | 10  | 0.00 (0.00-1.00) | 10  | 0.00 (0.00-4.79) | 50.00 (19.01-80.99) |
| EL       | 8   | 1R/75 | 0   | 0.00 (0.00-1.00) | 8   | 4R/4S | 0   | 0.00 (0.00-1.00) | 4R/3R |
| IT       | 12  | 0.00 (0.00-1.00) | 12  | 6.33 (0.00-23.97) | 12  | 3.33 (0.00-14.37) | 12  | 6.33 (0.00-23.97) | 16.67 (0.00-37.75) |
| NL       | 261 | 6.13 (3.22-9.04) | 244 | 2.87 (0.77-4.96) | 260 | 8.58 (5.39-12.30) | 260 | 11.97 (7.20-17.08) | 69.96 (64.19-75.72) |
| PT       | 14  | 50.00 (23.81-76.19) | 15  | 33.33 (9.48-57.19) | 15  | 40.00 (15.21-64.79) | 15  | 33.33 (9.48-57.19) | 35.71 (10.61-60.81) |
| RS       | 1   | 0R/15 | 1   | 1R/05 | 1   | 0R/15 | 1   | 0R/15 | 0   | - | - |
| ES       | 15  | 26.67 (4.29-49.05) | 13  | 15.38 (0.00-35.00) | 15  | 9.00 (28.09-78.58) | 15  | 9.00 (28.09-78.58) | 14.47 |
| SE       | 170 | 2.35 (0.07-4.63) | 169 | 0.00 (0.00-1.00) | 170 | 5.90 (0.00-1.74) | 170 | 7.06 (3.21-10.91) | 91.12 (86.84-95.41) |
| CH       | 17  | 0.00 (0.00-1.00) | 17  | 0.00 (0.00-1.00) | 17  | 0.00 (0.00-1.00) | 17  | 0.00 (0.00-1.00) | 64.71 (41.99-87.42) |
| UK       | 16  | 12.50 (0.00-28.70) | 16  | 0.00 (0.00-1.00) | 16  | 0.00 (0.00-1.00) | 15  | 33.33 (9.48-57.19) | 70.00 (41.60-98.40) |

AMC: amoxicillin clavulanate, 3GC: third generation cephalosporins, FLU: fluoroquinolones, CN: gentamicin, SXT: trimethoprim/sulfamethoxazole, MDR: multidrug-resistant, FullS: fully-susceptible.

*Countries: AT: Austria; BE: Belgium; DK: Denmark; FR: France; DE: Germany; EL: Greece; IT: Italy; NL: the Netherlands; PT: Portugal; RS: Serbia; ES: Spain; SE: Sweden; CH: Switzerland; UK: United Kingdom.

95% CI. 95% confidence interval.

Stat. Dif.: statistically significant differences. Countries with no statistical difference are marked with the same letter. Countries were compared by Fisher exact test with an alpha value of 0.05. Countries with less than ten tested isolates were not compared. Regarding MDR and FullS, only countries tested for all the considered antimicrobials were compared.

n: Total number of Proteus spp. tested for the considered antimicrobial category.

MDR and FullS percentages do not include resistance to 3GC for Belgium and resistance to CN for the Netherlands.

**Proteus** spp. (16.67%). Most of the remaining countries had MDR levels lower than 10%, with the exception of MDR **E. coli** from United Kingdom (15.56%) and France (11%). The highest **E. coli** and **Proteus** spp. FullS frequencies were found in Denmark and Sweden (Tables 3 and 4).

Due to the limited number of **Staphylococcus** spp. isolates available, the percentage of resistance to antimicrobials was determined on fewer countries for this group of bacteria (Tables 5 and 6). In most countries, **Staphylococcus pseudintermedius** was the most frequently
Fig. 3 Percentage (%) of Proteus spp. antimicrobial resistance by antimicrobial and country in the years 2012–2013. Countries: AT- Austria; BE- Belgium; DK- Denmark; FR- France; DE- Germany; EL- Greece; IT- Italy; NL- the Netherlands; PT- Portugal; RS- Serbia; ES- Spain; SE- Sweden; CH- Switzerland; UK- United Kingdom. Multidrug resistance considering combined resistance to three or more of the following antimicrobial categories: AMC, 3GC, FLU, CN and SXT. Full-susceptibility was defined as an isolate being susceptible for all the above-mentioned categories of antimicrobials. Regarding multidrug-resistance and full-susceptibility frequencies, countries marked by asterisk: 3GC was not included for Belgium and CN for the Netherlands. Thus, these frequencies may be underestimated when compared with the remaining countries.
isolated followed by coagulase negative staphylococci (CoNS) (Table 5). In general, the overall antimicrobial resistance levels in Southern countries were higher than in Northern countries (Fig. 4) as seen in Gram-negative bacteria (Figs. 2 and 3).

Besides the limited number of staphylococci, methicillin-resistance results were also limited due to the identification only to genus level or lack of testing the appropriate antimicrobial surrogate. Denmark and Sweden showed the lowest S. pseudintermedius methicillin-resistant (MRSP) (0 and 1.15 %, respectively). The remaining countries had MRSP frequencies higher than 8 %, attaining 50 % in Italy. Methicillin-resistance was also high in CoNS (Table 5).

Staphylococci SXT resistance ranged from 2.77 to 63.16 % and showed similar geographical distribution to Gram-negative bacteria (Fig. 4). Among the participating countries, Staphylococci FLU resistance frequencies were higher in Italy (42.11 %) and again lower in Sweden (1.54 %) and Denmark (1.96 %), with the remaining countries varying between 6.59 and 26.92 % (Table 6). Italy, Austria, Germany and Switzerland CN resistant staphylococci frequencies ranged between 26.32 and 9.76 % while the remaining countries had less than 6 %.

Regarding resistance temporal trends, most countries had no significant changes in E. coli resistance over the

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### Table 5 Staphylococcus spp. and methicillin-resistance by country in 2012–2013

| Country | Staphylococci species by country | Methicillin-resistance within each group |
|---------|---------------------------------|----------------------------------------|
|         | N | SA (% (95 % CI)b) | SP (% (95 % CI)b) | CoPS (% (95 % CI)b) | CoNS (% (95 % CI)b) | SPP (% (95 % CI)b) | MRSA n tested | MRSP n tested | MRCoNS n tested |
| AT      | 78 | 7.69 | 19.23 | 6.41 | 56.41 | 10.26 | 5 | 1R/45 | 15 | 33.33 |
|         |    | (1.78–13.61) | (10.48–27.98) | (0.97–11.85) | (45.41–67.41) | (3.52–16.99) |    | (9.48–57.19) |    | (14.50–41.31) |
| BE      | 122 | 14.75 | 52.46 | 0 | 32.79 | 0 | 18 | 5.56 | 64 | 12.50 |
|         |    | (8.46–21.05) | (43.60–61.32) |    | (24.46–41.12) |    |    | (0–16.14) |    | (4.40–20.60) |
| DK      | 52 | 1.92 | 53.85 | 1.92 | 28.85 | 13.46 | 1 | 15 | 27 | 0 |
|         |    | (0.56–6) | (40.30–67.40) | (0.56–6) | (16.53–41.16) | (4.18–22.74) |    |    |    |    |
| FR      | 242 | 8.26 | 72.73 | 0 | 19.01 | 0 | 20 | 40.0 | 0 | - |
|         |    | (4.80–11.73) | (67.12–78.34) |    | (14.06–23.95) |    |    | (18.53–61.47) |    | (6.44–28.34) |
| DE      | 64 | 4.69 | 0 | 0 | 39.06 | 6.25 | 0 | 0 | 0 | - |
|         |    | (0.98–7) |    |    | (37.75–62.25) |    |    |    |    |    |
| EL      | 10 | 1.00 | 0 | 0 | 90 |    | - | - | 1 | R |
|         |    | (0–28.59) |    |    | (71.41–100) |    |    |    |    |    |
| IT      | 19 | 0.94 | 47.95 | 0 | 47.12 | 0 | - | - | 18 | 50.0 |
|         |    | (84.70–12) | (42.82–53.07) |    | (42.0–52.24) |    |    | (26.90–73.10) |    |    |
| NL      | 365 | 4.93 | 47.95 | 0 | 47.12 | 0 | 0 | - | 174 | 10.92 |
|         |    | (1.12–27.1) | (42.82–53.07) |    | (42.0–52.24) |    |    | (6.29–15.55) |    | (0–1.72) |
| PT      | 7 | 1SA | 4SP | 0CoPS | 0CoNS | 2SPP | 1 | 1R | 4 | 2R/25 |
|         |    |    |    |    |    |    |    |    |    |    |
| RS      | 0 | - | - | - | - | - | - | - | - | - |
| ES      | 13 | 0 | 15.38 | 46.15 | 38.46 | - | - | - | - | - |
|         |    | (0–35.0) | (19.05–73.25) | (12.02–64.91) |    |    |    |    |    |    |
| SE      | 325 | 8.62 | 53.54 | 2.46 | 32.31 | 3.08 | 28 | 0 | 174 | 1.15 |
|         |    | (5.56–11.67) | (48.12–58.96) | (0.78–4.15) | (27.22–37.39) | (1.20–4.95) |    | (0–27.3) |    | (0.69–8.84) |
| CH      | 46 | 4.35 | 52.17 | 4.35 | 34.78 | 4.35 | 2 | 0R/25 | 20 | 10.00 |
|         |    | (0–10.24) | (37.74–66.61) | (0–10.24) | (21.02–48.55) | (0–10.24) |    | (0–23.15) |    | (42.81–90.52) |
| UK      | 32 | 12.50 | 53.13 | 6.25 | 18.75 | 9.38 | 3 | 1R/25 | 12 | 8.33 |
|         |    | (1.04–23.96) | (35.84–70.41) | (1.04–23.96) | (5.23–32.27) | (0–19.47) |    | (0–23.97) |    |    |

Staphylococci identification varied according to the country. Some countries identified staphylococci to species level, others to genus level and others included data on the coagulase test. Thus, the staphylococci results were grouped as follows: 1. *Staphylococcus aureus* (SA): 2. *Staphylococcus pseudintermedius* (SP): 3. coagulase positive staphylococci (CoPS): 4. coagulase negative staphylococci (CoNS) and 5. other staphylococci (SPP). Group 2 includes staphylococci identified only as CoPS or staphylococci species known to be coagulase positive other than SA and SP. Group 3 includes staphylococci identified only as CoNS or staphylococci species known to be coagulase negative. Group 4 includes staphylococci identified as *Staphylococcus aureus*, *MRSA* methicillin-resistant *Staphylococcus aureus*, *MRSP* methicillin-resistant *Staphylococcus pseudintermedius*, *MRCoNS* methicillin-resistant coagulase negative staphylococci

*Countries: AT, Austria; BE, Belgium; DK, Denmark; FR, France; DE, Germany; EL, Greece; IT, Italy; NL, the Netherlands; PT, Portugal; RS, Serbia; ES, Spain; SE, Sweden; CH, Switzerland; UK, United Kingdom

95 % CI 95 % Confidence interval

N. Total number of staphylococci tested for methicillin-resistance within each group.
time periods considered (Table 7). Belgium showed a significant decrease in *E. coli* resistance to all antimicrobials and an increase in full susceptible isolates. Denmark (AMC, FLU, SXT), France (3GC, FLU), the Netherlands (3GC, FLU, SXT, MDR) and Sweden (CN, MDR) had also significant decreases in *E. coli* resistance over time (Table 7). However, the Netherlands (AMC) and Switzerland (CN) had a significant increase in *E. coli* resistance (Table 7). A rising trend was also detected in *Proteus* spp. FLU resistance from Belgium (Table 8).

Table 6 Percentage of resistance in *Staphylococcus* spp. by antimicrobial and country in 2012–2013

| Countrya | FLU | CN | SXT |
|----------|-----|----|-----|
| n        | % R (95 % CI)b | n | % R (95 % CI)b | n | % R (95 % CI)b |
|          | [Stat. Dif.]
| AT       | 78  | 26.92 (17.08–36.77) | 78  | 19.23 (10.48–27.98) | 78  | 20.51 (11.55–29.47) |
|          |     | [a, b]                |     | [a]                 |     | [a, b]               |
| BE       | 116 | 7.76 (2.89–12.63)    | 107 | 3.74 (0.14–7.33)   | 122 | 13.11 (7.12–19.10)  |
|          |     | [c, d]                |     | [b]                 |     | [a, b, c]            |
| DK       | 51  | 1.96 (0.00–5.77)     | 51  | 3.92 (0.00–9.25)   | 51  | 0                    |
| FR       | 238 | 23.53 (18.14–28.92)  | 237 | 5.06 (2.27–7.85)   | 242 | 11.57 (7.54–15.60)  |
|          |     | [a, g]                |     | [b]                 |     | [a, c]               |
| DE       | 55  | 18.18 (7.99–28.38)   | 55  | 10.91 (2.67–19.15) | 55  | 23.64 (12.41–34.86) |
|          |     | [a, d, g]             |     | [a, b]              |     | [b]                  |
| EL       | 10  | 20.00 (0.00–44.79)   | 0   | -                   | 9   | 1R/85                |
|          |     | [a, d, e, g]          |     |                     |     |                      |
| IT       | 19  | 42.11 (19.90–64.31)  | 19  | 26.32 (6.52–46.12) | 19  | 63.16 (41.47–84.85) |
|          |     | [a, i]                |     | [a]                 |     | [e]                  |
| NL       | 364 | 6.59 (4.04–9.14)     | 9   | 1R/85               | 365 | 11.51 (8.23–14.78)  |
|          |     | [c, i]                |     |                     |     | [c]                  |
| PT       | 6   | 3R/3S                 | 7   | 2R/5S               | 7   | 1R/65                |
|          |     | -                     |     | -                   |     | -                    |
| RS       | 0   | -                     | 0   | -                   | 0   | -                    |
|          |     | -                     |     |                     |     |                      |
| ES       | 13  | 15.38 (0.00–35.00)   | 8   | 0R/85               | 11  | 18.18 (0.00–40.97)  |
|          |     | [a, d, e, h, l]       |     | -                   |     | [a, b, c]            |
| SE       | 325 | 1.54 (0.20–2.88)     | 325 | 0                   | 325 | 2.77 (0.99–4.55)    |
|          |     | [f]                   |     |                     |     | [d]                  |
| CH       | 41  | 24.39 (11.25–37.54)  | 41  | 9.76 (0.067–18.84) | 41  | 19.51 (7.38–31.64)  |
|          |     | [a, b]                |     | [a, b]              |     | [a, b, c]            |
| UK       | 31  | 12.90 (11.10–24.70)  | 22  | 4.55 (0.00–13.25)  | 30  | 16.67 (3.33–30.00)  |
|          |     | [b, c, e, g]          |     | [a, b, c]           |     | [a, b, c]            |

FLU fluoroquinolones, CN gentamicin, SXT trimethoprim/sulfamethoxazole

*aCountries: AT, Austria; BE, Belgium; DK, Denmark; FR, France; DE, Germany; EL, Greece; IT, Italy; NL, the Netherlands; PT, Portugal; RS, Serbia; ES, Spain; SE, Sweden; CH, Switzerland; UK, United Kingdom*

b95 % CI, 95 % Confidence interval
cStat. Dif., Statistical significant differences. Countries with no statistical difference are marked with the same letter. Countries were compared by fisher exact test with an alpha value of 0.05. Countries with less than ten tested isolates were not compared
dn, Total number of *Staphylococcus* spp. tested for the considered antimicrobial category
Discussion

Published data on antimicrobial resistance in bacteria isolated from companion animal UTIs over Europe is scarce [19] and the comparison between studies is impaired by the use of different inclusion criteria and different time periods. Moreover, UTI resistance frequencies are usually reported together with susceptibility data from other sites of infection [11, 28], combining different bacteria genera [8, 9] and several countries [29, 30]. These facts impair the establishment of a global epidemiological overview of UTI bacteria resistance in Europe. This is the first large study to analyse antimicrobial susceptibility data of canine and feline isolates from several European countries allowing an epidemiological overview of UTI resistance trends in Europe.

In accordance to previous studies [7–9, 31, 32], *E. coli* was the most frequently isolated bacteria in dogs and cats. *Enterococcus* presented a significantly higher frequency in cats and *Proteus* spp. in dogs. While not compared in previous studies, this difference could be expected based on some published data focused on cats [7, 9] and dogs [32] separately.

One of the most important findings from this study was the overall higher resistance frequencies found in the Southern countries (Italy, Greece, Portugal and Spain) when compared with the Northern countries (Denmark and Sweden). The lower frequency of antimicrobial resistance in Northern countries, such as Sweden, is likely a consequence of the tight regulations and surveillance on antimicrobial prescribing and resistance in companion animals. In light of the present results, such strategies could be useful in aiming the reduction of antimicrobial resistance in the Southern countries.

Resistance to Beta-Lactams

*Amoxicillin-clavulanate*

Considering that AMC is one of the most used antimicrobials in animals, the levels of resistance detected in this study are worrisome, especially in the Southern countries. Previous published reports showed different frequencies of AMC resistance in *E. coli* and in *Proteus* spp. that are likely due to the fact they report to different time frames and inclusion criteria [10, 32–37]. In the absence of clinical data it is not possible to know if this resistance relates to uncomplicated or complicated UTI [19]. Thus, these results need to be further investigated in order to establish whether AMC is a suitable empiric therapeutic choice for companion animals UTI in Southern Europe.

*Third generation cephalosporins*

Southern countries had also higher levels of resistance to 3GCs. Although Greece was not included due to limited data, considering that seven out of the nine tested isolates were resistant to 3GCs, one can expect the prevalence of 3GC resistance to be high. Previous studies in Portugal found a considerable lower 3GC resistance value (1.4 %) in *E. coli* from dogs in earlier years [10]. In the present work, the lower Swedish results for 3GC resistance in *E. coli* and *Proteus* spp. are in agreement with early studies [38]. Being of critical importance to humans [39], prudent use of 3GC is of upmost importance.

*Methicillin-resistance*

The frequency of methicillin-resistant staphylococci, especially *S. pseudintermedius* and CoNS, varied considerably between countries and confirmed previous reports on a low MRSP prevalence in Scandinavia compared to elsewhere in Europe [40]. Resistance to methicillin in
coagulase-positive Staphylococcus (S. aureus and S. pseu-
dintermedius) was detected in this study and is a great
animal and public health concern [41]. Currently, the
recommended methods for the detection of methicillin-
resistance in Staphylococci are mainly phenotypic but in
some circumstances the molecular detection of the
meca A gene is clinically and epidemiologically necessary
[22, 23, 42]. This should be taken in consideration for
the harmonization of veterinary susceptibility testing in
Europe.

Resistance to fluoroquinolones
In this study, high resistance frequencies towards the
fluoroquinolones were found in E. coli, Proteus spp and
Staphylococcus spp. isolates in the southern European
countries but also in Proteus spp. from Germany,
Belgium and Switzerland and Staphylococcus spp. from
Austria, Switzerland and France. Several authors [32, 34,
43, 44] have reported lower FLU resistance frequencies
than the ones found in this study, especially regarding the
Southern countries [43, 44]. The results of high

| Table 7 | Temporal trends of antimicrobial resistance in Escherichia coli by country |
|---------|-------------------------------------------------|
| **Country** | **(Years)** | **AMC** | **3GC** | **FLU** | **CN** | **SXT** | **MDR** | **FullS** |
|          |          | **(95 % CI) c** | **(95 % CI) c** | **(95 % CI) c** | **(95 % CI) c** | **(95 % CI) c** | **(95 % CI) c** | **(95 % CI) c** |
| BE       | 2010–13 | 0.787 | 0.698 | 0.885 | 0.406 | 1.029 | 0.108 | 0.0088 |
|          |         | 0.0018 | 0.0006 | 0.3537 | 0.0314 | 0.779 | 0.0016 | <0.0001 |
| DK       | 2008–13 | 0.677 | 0.869 | 0.485 | 0.3353 | 1.185 | 0.916 | 0.0008 |
|          |         | 0.796 | 0.0926 | 0.239 | 0.274 | 0.856 | 0.917 | <0.0001 |
| FR       | 2010–13 | 0.529d | 0.822 | 0.938 | 0.900 | 1.040 | 0.380d | 1.275d |
|          |         | 1.275d | 0.958 | 0.771 | 0.673 | 1.524 | 0.528 | 0.0001 |
| DE       | 2009–13 | 0.0107 | 0.917 | 0.917 | 0.917 | 0.917 | 0.917 | 0.917 |
|          |         | 0.0016 | 0.0016 | 0.0016 | 0.0016 | 0.0016 | 0.0016 | 0.0016 |
| NL       | 2008–13 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 |
|          |         | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 |
| PT       | 2008–13 | 1.222 | 1.222 | 1.222 | 1.222 | 1.222 | 1.222 | 1.222 |
|          |         | 1.087 | 1.087 | 1.087 | 1.087 | 1.087 | 1.087 | 1.087 |
| ES       | 2010–13 | 0.570 | 0.570 | 0.570 | 0.570 | 0.570 | 0.570 | 0.570 |
|          |         | 0.810 | 0.810 | 0.810 | 0.810 | 0.810 | 0.810 | 0.810 |
| SE       | 2008–13 | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 |
|          |         | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 | 0.961 |
| CH       | 2008–13 | 1.493 | 1.493 | 1.493 | 1.493 | 1.493 | 1.493 | 1.493 |
|          |         | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 | 1.189 |
| UK       | 2008–13 | 1.306 | 1.306 | 1.306 | 1.306 | 1.306 | 1.306 | 1.306 |
|          |         | 1.355 | 1.355 | 1.355 | 1.355 | 1.355 | 1.355 | 1.355 |
| **AMC** | amoxicillin clavulanate, 3GC third generation cephalosporins, FLU fluoroquinolones, CN gentamicin, SXT trimethoprim/sulfamethoxazole, MDR multidrug-resistant, FullS fully-susceptible |
| **CI** | 95 % confidence interval |
| **Odds ratio** | ORb |

**Notes:**
- BE, Belgium; DK, Denmark; FR, France; DE, Germany; EL, Greece; IT, Italy; NL, the Netherlands; PT, Portugal; ES, Spain; SE, Sweden; CH, Switzerland; UK, United Kingdom
- *p* < 0.05
- **Bold** indicates statistically significant differences compared to 2008
resistance frequencies towards the fluoroquinolones found in this study are concerning because fluoroquinolones are considered a good first choice for pyelonephritis treatment and should otherwise be used as a second line antimicrobial [19].

**Resistance to folate inhibitors and to aminoglycosides**

In this study, resistance to SXT in Europe was high, especially in *E. coli* and *Proteus* spp. The higher SXT resistance found in *Proteus* spp., than in *E. coli* from several European countries, is consistent with other reports [34, 36, 45]. Compared with previous studies, these results show a superior SXT resistance in *E. coli* and *Proteus* spp. from Italy and Portugal [10, 43] and *Staphylococcus* spp. from Belgium [36].

Also in agreement to previous studies, gentamicin was the antimicrobial with lower resistance in *E. coli*, *Proteus* spp. and *Staphylococcus* spp. all-over Europe [32, 34, 35, 37, 38, 43, 45]. Nevertheless, the distribution seemed to follow the same pattern, with increased resistance in Southern over Northern countries.

**Multidrug-resistance**

Finally, MDR bacteria presented the worst scenario once again in *E. coli* from Southern countries and in *Proteus* spp. from Portugal. The emergence of MDR bacteria in companion animals has been previously described [46, 47] and represents a great therapeutic challenge and public health concern. However, MDR/FullS frequencies are seldom reported and published data account for different antimicrobials, thus impairing any comparisons with the present results [10, 32, 35, 38, 45].

**Trends in antimicrobial resistance**

The surveillance of antimicrobial resistance is an important tool to guide the implementation of antimicrobial stewardship strategies. In this study, most countries had no significant changes in antimicrobial resistance over the time frame considered. Nevertheless, decreasing trends in antimicrobial resistance were found in *E. coli*. These encouraging trends were not detected in AMC and CN resistance in *E. coli* from the Netherlands and Switzerland, respectively, where an increasing trend was observed. Although no changes over time were detected in *E. coli* resistance against AMC and 3CGs in Portugal, the considerably lower resistance frequencies previously reported in earlier years [10], point to a possible increasing trend [33]. The same may be the case for *E. coli* AMC resistance in Germany and Switzerland [34, 35].

Despite reporting clear trends such as the difference in resistance between Northern and Southern countries, data from this study should be interpreted with caution. Due to the retrospective nature of this study, data on clinical history such as the type of UTI and previous antimicrobial treatment were unavailable. Furthermore, the use of laboratory data may represent a bias towards resistance, since urine cultures from complicated cases tend to be requested more often than simple uncomplicated UTI [8, 31]. These limitations are not restricted to certain countries, and are therefore not likely to hamper comparison of data across borders.

### Table 8 Temporal trends of antimicrobial resistance in *Proteus* spp. by country

| Country (Years) | AMC OR<sup>b</sup>(95 % CI)<sup>c</sup> | FLU OR<sup>b</sup>(95 % CI)<sup>c</sup> | SXT OR<sup>b</sup>(95 % CI)<sup>c</sup> |
|----------------|------------------------------------|------------------------------------|------------------------------------|
| BE (2010–13)   | 0.627 (0.312–1.259) 0.1889          | 1.292 (1.006–1.659) 0.0450          | 0.891 (0.726–1.092) 0.2649          |
| FR (2010–13)   | 0.945 (0.625–1.431) 0.7908          | 1.004 (0.764–1.319) 0.9770          | 0.954 (0.756–1.205) 0.6944          |
| NL (2008–13)   | 1.092 (0.860–1.387) 0.4709          | 0.970 (0.829–1.135) 0.7067          | 1.010 (0.903–1.129) 0.8660          |
| SE (2008–13)   | 0.892 (0.657–1.210) 0.4620          | 0.884 (0.494–1.583) 0.6788          | 0.941 (0.759–1.165) 0.5756          |

| *AMC* amoxicillin clavulanate, *FLU* fluoroquinolones, *SXT* trimethoprim/sulfamethoxazole |
| Statistically significant trends are highlighted in bold |
| BE, Belgium; DK, Denmark; FR, France; NL, the Netherlands; SE, Sweden; CH, Switzerland |
| OR, Odds ratio |
| 95 % CI, 95 % Confidence interval |
EARS network reports of resistance on bacteria from human invasive infections [18], this limitation weakens the comparison of resistance between countries in the present and future surveillance studies. This harmonization would allow future within and between countries resistance frequencies comparisons over time and would also provide relevant information on the impact of different antimicrobial usage policies. Thus, the authors agree that the harmonization of methods and interpretative criteria in veterinary medicine should be a priority. The role of the new veterinary committee on antimicrobial susceptibility testing VetCAST [48] may be crucial in this harmonization process. Despite these limitations, the results from this study provide relevant and updated information on the current antimicrobial resistance in UTI bacteria from companion animals in Europe. Similar studies should also be conducted regarding other types of infection to improve the awareness on the European distribution of antimicrobial resistance in companion animals. Ideally, monitoring of companion animal antimicrobial resistance should be implemented in Europe, as it is the case for food producing animals. Such surveillance would provide crucial information to promote the appropriate use of antimicrobial and therefore limit the spread of resistance.

Conclusions
This work brings new insights into the current scenario of the European antimicrobial resistance bacteria isolated from companion animals with UTI. An important finding from this study was the higher frequency of resistance in Southern European countries (Italy, Greece, Spain, Portugal) when compared to Northern European countries (Denmark, Sweden). Furthermore, there is an evident need to harmonize methods and interpretative criteria in veterinary medicine. Given the limitations of retrospective studies, an European surveillance network gathering data on antimicrobial resistance is of the upmost importance to facilitate the development of national evidence-based guidelines.

Authors
CM and LTG carried out the antimicrobial susceptibility testing from the respective laboratory. CM and LTG conducted statistical analysis. CM wrote the initial draft and KB, EMB, PD, MAMD, RD, IL, DM, GO, VP, XR, JS, DT, GW, RGZ, SS, LG and CP made critical improvements for the final manuscript. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
The information supporting the conclusions of this article is included within the article.

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Availability of data and material
The information supporting the conclusions of this article is included within the article.

Authors’ contributions
CM conceived the study and its coordination. CP and CM participated in the design of the study and contacted the collaborating laboratories included. All authors were responsible for data regarding the bacteria identification and susceptibility testing from the respective laboratory. CM and LTG conducted statistical analysis. CM wrote the initial draft and KB, EMB, PD, MAMD, RD, IL, DM, GO, VP, XR, JS, DT, GW, RGZ, SS, LG and CP made critical improvements for the final manuscript. All authors read and approved the final manuscript.

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