# The impact of antimicrobial use guidelines on prescription habits in fourteen Flemish small animal practices

*De impact van advies omtrent het gebruik van antimicrobiële middelen op het voorschrijfgedrag in veertien Vlaamse praktijken voor kleine huisdieren*

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## ABSTRACT

**A prospective study was performed to explore the prescription habits in fourteen first-line, small animal practices during first consultations of cats and dogs. Consultations one month prior to the implementation of antimicrobial use guidelines and at least 20 days thereafter were examined. Differences in the proportion of consultations during which antimicrobials were prescribed, were assessed. Additionally, changes in the choice of active substance were critically evaluated against the introduced antimicrobial use guidelines. The proportion of consultations where antimicrobials were prescribed decreased in cats and dogs (both –12%) after the introduction of the antimicrobial use guidelines. There was an increase of consultations of cats (+13%) and dogs (+10%) where veterinarians handled according to those guidelines. However, an increase in the prescription of third-choice antimicrobials and highest priority critically important antimicrobials was noticed both in cats (+8% and +12%, respectively) and dogs (both +5%). This unexpected increase invites to create extra awareness amongst prescribers.**

## SAMENVATTING

Aan de hand van een prospectieve studie werd het voorschrijfgedrag met betrekking tot antimicrobiële middelen onderzocht in veertien eerstelijnspraktijken voor kleine huisdieren. Verschillen in het aantal consultaties van katten en honden waarbij antimicrobiële middelen werden voorgeschreven, werden onderzocht gedurende één maand voor en minstens twintig dagen na het invoeren van de adviezen betreffende het gebruik van antimicrobiële middelen. Daarnaast werden ook veranderingen in de keuze van actieve substanties vergeleken met de adviezen. Het aantal consultaties waarbij antimicrobiële middelen werden voorgeschreven daalde zowel bij honden als katten (−12% bij beide diersoorten) na het invoeren van de adviezen. Er was een stijging in het aantal consultaties bij katten (+13%) en honden (+10%) in de praktijken waar de dierenartsen handelden volgens de adviezen. Er werd echter ook een stijging vastgesteld in het voorschrijven van derdekeuze- en kritisch belangrijke antimicrobiële middelen bij kat (+8% en +12%, respectievelijk) en hond (beide +5%). Deze onverwachte stijging wijst erop dat het verantwoord gebruik van antimicrobiële middelen verder onder de aandacht dient te worden gebracht.

## INTRODUCTION

The use of antimicrobials in veterinary medicine may promote the selection of bacteria with acquired resistance genes in animals and humans (Dewulf et al., 2007; Magalhães et al., 2010; Burow et al., 2014; Chantziaras et al., 2014). For long, research has focused on food animals as reservoir for antimicrobial resistance (Bates et al., 1994; Robredo et al., 2000; Wooldridge, 2012), but also companion animals play

a role (Harvey et al., 1994; Guardabassi et al., 2004; Loeffler et al., 2005; Lloyd, 2007; Bramble et al., 2011). It is likely that intense contact with companion animals is a risk factor for the transfer of antimicrobial resistance between humans and animals (Guardabassi et al., 2004; Weese and van Duijkeren, 2010).

There is plenty of evidence that decreased antimicrobial use in veterinary medicine is beneficial in reducing the occurrence of antimicrobial resistance and is not necessarily associated with inferior production results. For example, the prevalence of vancomycin-resistant enterococci in food animals (Bager et al., 1999; Klare et al., 1999; Pantosti et al., 1999; Van den Bogaard et al., 2000) and humans (Klare et al., 1999) decreased after the ban of avoparcin in animal feed. In 2015, the prevalence of extended spectrum beta-lactamases/AmpC producing *E. coli* in poultry in the Netherlands decreased in comparison with previous years, possibly because of a reduced antimicrobial use (Anonymous, 2016). No negative effects in swine productivity were noticed after a substantial decrease in antimicrobial consumption (Aarestrup et al., 2010; Postma et al., 2016).

Penicillins and cephalosporins are by far the most used antimicrobial drugs in dogs and cats (Watson and Maddison, 2001; Rantala et al., 2004; Regula et al., 2009; Thomson et al., 2009; Escher et al., 2011; Mateus et al., 2011; Murphy et al., 2012; Pleydell et al., 2012). For Belgium, this was confirmed by the sixth European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report, which described that in 2014, mainly penicillins and first- and second-generation cephalosporins were used in small animals (EMA, 2016).

In human medicine, antimicrobial use guidelines have been developed and implemented as one of the strategic goals to optimize antimicrobial use (Goldmann et al., 1996), and they have shown to have a positive effect on the antimicrobial prescribing behavior (Smith et al., 2012; Lee et al., 2016). In veterinary medicine, only in a limited number of studies, the impact of antimicrobial guidelines has been investigated. In Germany, antimicrobial guidelines seems to decrease antimicrobial drug use in pigs (Ungemach et al., 2006). In a Canadian veterinary teaching hospital, the implementation of antimicrobial use guidelines resulted in a decrease in the number of prescriptions and the use of first-generation cephalosporins, fluoroquinolones, penicillins, tetracyclines and third-line drugs (carbapenems and vancomycin) (Weese, 2006). Although it was not the main focus of their study, some researchers have looked into the role of guidelines for antimicrobial use in small animals (Rantala et al., 2004; Thomson et al., 2009; Escher et al., 2011; Pleydell et al., 2012). They concluded that the compliance was moderate to good, but varied with the disease, and that the level of performing the necessary diagnostic steps could be improved.

In 2014, the Belgian centre of expertise on Antimicrobial Consumption and Resistance in Animals (AMCRA) provided antimicrobial guidelines for the practising veterinarians. Some antimicrobial drugs are classified as critically important and highest priority critically important antimicrobials based on the lists provided by the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE) (WHO, 2011; OIE, 2015). The aim of this study was to evaluate the impact of introducing these antimicrobial use guidelines on the prescription habits of veterinarians in small animal practices in Flanders. The hypotheses were that veterinarians would refrain from the prescription of antimicrobials, if not needed according to the guidelines, and that they would prescribe less critically important antimicrobials.

## MATERIALS AND METHODS

### Study design

The antimicrobial use guidelines include twenty-five clinical conditions and describe what requirements should be met for diagnosis and whether antimicrobial treatment is advised (Table 1). If antimicrobials are indicated, the guidelines list first-, second- and/or third-choice antimicrobials per condition. This classification is based on the scientific literature regarding antimicrobial susceptibility, pharmacokinetics, pharmacodynamics and clinical efficacy of the therapy for a given indication. The guidelines are available in Dutch and French at www.e-formularium.be.

For practical reasons, the veterinarians were selected in the regions of Antwerp and East-Flanders by using a website that listed all veterinarians per geographic region (VetWorks, 2011). The selected veterinarians received an email with an invitation to participate in the study, and were subsequently contacted by phone to make an appointment if they had indicated that they were willing to participate.

One of the authors paid personal visits to all participating practices. During the first visit, the consultations from at least a month prior to the visit were extracted from the practice management system. This information per consultation contained the animal species (cat/dog), condition and/or symptoms and antimicrobial treatments. Next, the antimicrobial use guidelines were explained and distributed as a pocket-size booklet (AMCRA, 2014). The veterinarians were asked to implement the guidelines as much as possible when treating cats and dogs during at least twenty working days. They were also instructed to write down in a logbook when and why they had chosen not to follow the guidelines. During the second practice visit, the consultations between the first and second practice visits were extracted from the management system. The veterinarians filled in a questionnaire regarding perceived usefulness of the antimicrobial use guidelines (e.g. user-friendliness, feasibility, structure of the book) using a five-point Likert scale (1 = totally

disagree, 2 = disagree, 3 = neutral, 4 = agree and 5 = totally agree) and the logbook information was collected.

## Definitions

The clinical conditions included in the study were listed in six groups: skin, respiratory tract, digestive tract, urogenital tract, ear and other (osteomyelitis, sepsis and antimicrobial prophylaxis) (Table 1). Five types of consultations were not withheld for further evaluation: 1) consultations that concerned other conditions than those described in the antimicrobial use guidelines, 2) when details on the animal species, condition/symptoms and/or active substance were missing, 3) consultations where multiple diagnoses were mentioned, because it was impossible to determine for which condition the antimicrobials were prescribed, 4) consultations that were re-examinations and 5) consultations for chronic pathologies.

Prescribing an off-label product was defined as prescribing an active substance not registered for cats or dogs and/or the condition.

## Statistical analysis

The first outcome of interest was whether the veterinarian had prescribed antimicrobials during a consultation, irrespective of whether or not the guidelines were followed. A second outcome of interest was

**Table 1. The conditions included in the antimicrobial use guidelines and indication for antimicrobial use according to these guidelines.**

| Condition | Antimicrobials indicated? |
|---|---|
| Pyoderma | |
| • Surface | No |
| • Superficial | Yes |
| • Deep | Yes |
| Wounds and skin abscess formation | |
| • Non-complicated | No |
| • Signs of systemic illness, infected wound, extension of the abscess to deeper tissues | Yes |
| Rhinitis/sinusitis dog | No |
| Laryngitis/tracheitis dog | |
| • Non-complicated | No |
| • Signs of systemic illness, deeper infections | Yes |
| Bronchitis/(broncho)pneumonia/canine infectious tracheobronchitis | |
| • Non-complicated | No |
| • Signs of systemic illness, deeper infections | Yes |
| Bronchitis/(broncho)pneumonia cat | |
| • Non-complicated | No |
| • Signs of systemic illness, deeper infections | Yes |
| Upper respiratory tract disease cat | |
| • Conjunctivitis | No |
| • Rhinitis | No |
| • Upper respiratory tract disease | Yes |
| Infections of the mouth cavity | No, unless abscess formation and fistulation are confirmed or in case of a secondary bacterial infection |
| Infections of the gums and parodontium | No, unless the animal is immunocompromised |
| Gastro-enteritis | No, unless the presence of blood in the vomit or stool, fever, leucocytosis/neutropenia, left shift in the blood or indications for an aspiration pneumonia |
| Hepatitis and/or cholangitis | No, unless of bacterial origin |
| Abscesses of the anal gland | No, unless abscess formation and/or fistulation |
| Lower urinary tract infection dog | Yes |
| Lower urinary tract infection cat | No, unless culture and sensitivity test confirm a bacterial origin |
| Pyelonefritis | Yes |
| Prostatitis dog | Yes |
| Balanoposthitis dog | No, unless culture results confirm a bacterial origin |
| Orchitis dog | No |
| Vaginitis | No, unless culture results confirm a bacterial origin |
| Endometritis/pyometra | Yes |
| Osteomyelitis | Yes |
| Otitis externa dog | Yes, topical only |
| Otitis externa cat | Yes, topical only |
| Sepsis | Yes |
| Antimicrobial prophylaxis | |
| • Clean surgeries | No |
| • Clean-contaminated, contaminated or dirty surgeries | Yes |

* Signs of systemic illness such as anorexia, and fever.

**Table 2. The number of consultations included in the analysis and the number of consultations where antimicrobials were prescribed before and after the introduction of the antimicrobial use guidelines per veterinary practice and animal species.**

| Veterinary practice | Cat | | | | | Dog | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Consults prescribed / Total consults | | | | | Consults prescribed / Total consults | | | | |
| Veterinary practice | Before guidelines | | After guidelines | | Evolution | Before guidelines | | After guidelines | | Evolution |
| | n | % | n | % | % | n | % | n | % | % |
| 1 | 9/10 | 90% | 7/11 | 64% | -26% | 13/15 | 87% | 11/12 | 92% | +5% |
| 2 | 33/33 | 100% | 9/9 | 100% | +0% | 78/78 | 100% | 53/53 | 100% | +0% |
| 3 | 24/49 | 49% | 41/94 | 44% | -5% | 54/99 | 55% | 77/166 | 46% | -8% |
| 4 | 5/8 | 63% | 13/13 | 100% | +38% | 23/24 | 96% | 25/25 | 100% | +4% |
| 5 | 12/13 | 92% | 5/10 | 50% | -42% | 16/17 | 94% | 17/27 | 63% | -31% |
| 6 | 5/6 | 83% | 9/9 | 100% | +17% | 20/20 | 100% | 15/15 | 100% | +0% |
| 7 | 5/5 | 100% | 1/1 | 100% | +0% | 21/21 | 100% | 20/20 | 100% | +0% |
| 8 | 10/16 | 63% | 12/15 | 80% | +18% | 12/17 | 71% | 26/31 | 84% | +13% |
| 9 | 9/9 | 100% | 8/9 | 89% | -11% | 7/8 | 88% | 7/11 | 64% | -24% |
| 10 | 9/13 | 69% | 3/10 | 30% | -39% | 2/5 | 40% | 5/8 | 63% | +23% |
| 11 | 5/8 | 63% | 29/47 | 62% | -1% | 14/19 | 74% | 76/116 | 66% | -8% |
| 12 | 8/8 | 100% | 2/2 | 100% | +0% | 6/6 | 100% | 9/9 | 100% | +0% |
| 13 | 1/5 | 20% | 3/8 | 38% | +18% | 7/10 | 70% | 7/14 | 50% | -20% |
| 14 | 7/15 | 47% | 6/9 | 67% | +20% | 4/8 | 50% | 8/15 | 53% | 3% |
| **Total** | **142/198** | **72%** | **148/247** | **(60%)** | **-12%** | **277/347** | **80%** | **356/522** | **68%** | **-12%** |

whether the veterinarian had handled according to the antimicrobial use guidelines during a consultation. Whenever antimicrobials were prescribed, the following two requirements had to be fulfilled to be in agreement with the antimicrobial use guidelines: 1) a clear indication to use antimicrobials as part of the treatment protocol was present and 2) a first- (or second-) choice antimicrobial was selected. For each outcome of interest, a generalized linear mixed model was fitted to examine the association with the introduction of the antimicrobial guidelines, the clinical condition and the self-reported frequency of working according to the guidelines (i.e. whether they indicated to work 'sometimes' or 'most of the times' according to the guidelines. A logit link function and binomial distribution were assumed. To account for clustering of consultations in veterinary practices, a random effect for veterinary practice was included. Separate models were made for cats and dogs.

To examine the strength of the association between the prescription of antimicrobials and whether antimicrobials were indicated according to the guidelines, odds ratios (OR) and Cohen's kappa coefficients were estimated with 95% confidence intervals (CI) (McHugh, 2012).

The prescription of an active antimicrobial substance was expressed as percentage compared to the total number of antibiotic prescriptions. The same accounts for the numbers of first-, second- and third-choice, off-label and highest priority critically important antimicrobials. The data on active substances, first-, second-, third-choice antimicrobials, off-label, highest priority critically important antimicrobials before and after the introduction of the antimicrobial use guidelines and the self-reported frequency of working according to the guidelines were analyzed using a Pearson $\chi^2$ test. When the number of consultations was lower than five, the Fisher's exact test was applied. All analyses were performed with SPSS 22.0 (IBM Corp, Armonk, NY) or SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The significance level was set at 5%.

## RESULTS

Of the 62 invited veterinarians, 23 expressed their willingness to participate. Six veterinarians discontinued their participation after the first visit to the practice, because they feared that it would be too much work to record all data or to consult the antimicrobial use guidelines. One veterinarian was not convinced about the purpose of the study, because in his opinion, only a limited amount of antimicrobials are generally being prescribed in small animal practices. One veterinarian only handed over data on consultations from the period before the introduction of the antimicrobial use guidelines, and one veterinarian only handed in data on consultations where antimicrobials had been prescribed. As a result, complete datasets for analysis containing 1314 consultations were available from 14 veterinary practices.

**Table 3. Overview of the number of consultations, during which antimicrobials were prescribed and whether the guidelines were followed per animal species and clinical condition, before and after the introduction of the antimicrobial guidelines.**

| Cat | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Consults prescribed / Total consults | | | | | Consults according to guidelines / Total consults | | | | |
| Clinical conditions | Before guidelines | | After guidelines | | Evolution | Before guidelines | | After guidelines | | Evolution |
| | n | % | n | % | | n | % | n | % | |
| Skin | 67/69 | 97% | 43/47 | 91% | -6% | 5/69 | 7% | 5/47 | 11% | +4% |
| Respiratory | 17/20 | 85% | 27/33 | 82% | -3% | 4/20 | 20% | 7/33 | 21% | +1% |
| Digestive | 17/30 | 57% | 33/54 | 61% | +4% | 12/30 | 40% | 23/54 | 43% | +3% |
| Urogenital | 17/23 | 74% | 25/33 | 76% | +2% | 5/23 | 22% | 10/33 | 30% | +8% |
| Ears | 3/4 | 75% | 6/7 | 86% | +11% | 1/4 | 25% | 2/7 | 29% | +4% |
| Other | 21/52 | 40% | 14/73 | 19% | -21% | 32/52 | 62% | 59/73 | 81% | +19% |
| **Dog** | | | | | | | | | | |
| | Consults prescribed / Total consults | | | | | Consults according to guidelines / Total consults | | | | |
| Clinical conditions | Before guidelines | | After guidelines | | Evolution | Before guidelines | | After guidelines | | Evolution |
| | n | % | n | % | | n | % | n | % | |
| Skin | 77/82 | 94% | 68/83 | 82% | -12% | 21/82 | 26% | 26/83 | 31% | +5% |
| Respiratory | 25/29 | 86% | 32/35 | 91% | +5% | 8/29 | 28% | 7/35 | 20% | -8% |
| Digestive | 57/83 | 69% | 107/166 | 64% | -4% | 35/83 | 42% | 76/166 | 46% | +4% |
| Urogenital | 18/21 | 86% | 26/31 | 84% | -2% | 9/21 | 43% | 16/31 | 52% | +9% |
| Ears | 33/39 | 85% | 46/54 | 85% | +0% | 20/39 | 51% | 32/54 | 59% | +6% |
| Other | 67/93 | 72% | 77/153 | 50% | -22% | 26/90 | 29% | 75/151 | 50% | +21% |

## Cats

The database contained 198 cat consultations before and 247 consultations after the introduction of antimicrobial use guidelines. Antimicrobials were prescribed in 72% (142/198) and in 60% (148/247) of the consultations before and after the introduction of antimicrobial use guidelines, respectively (Table 2). Although a decrease was noticed, the introduction of antimicrobial use guidelines did not significantly influence the proportion of consultations where antimicrobials are prescribed ($P = 0.71$). The prescription pattern varied significantly with the clinical condition ($P < 0.001$) (Table 3). As expected, antimicrobials were more likely prescribed when indicated by the guidelines, 92% (36/39) versus 67% (106/159) before (OR 6.0, 95% CI 1.8; 20.4) and 88% (38/43) versus 54% (110/204) after (OR 6.5, 95% CI 2.5; 17.2) the introduction of the guidelines (Table 4). However, it was also noticed that a very substantial amount of prescriptions were actually not indicated, 54% (106/198) before and 45% (110/247) after the introduction of the guidelines, respectively. The corresponding values for Cohen's kappa (0.13 and 0.17 before and after, respectively) indicate only a slight agreement between the prescription and the actual indication of antimicrobials (McHugh, 2012). The percentage of consultations handling according to the antimicrobial use guidelines increased from 30% to 43% after the introduction of antimicrobial use guidelines ($P = 0.24$). Handling according to the guidelines varied significantly with the clinical condition ($P < 0.001$) (Table 3).

Amoxicillin clavulanate and third-generation cefovecin (critically important) were the most commonly prescribed antimicrobials before and after the introduction of the antimicrobial use guidelines although their relative proportions changed (Table 5). There was a significant difference in the relative frequency of prescriptions before and after the guidelines for the following antimicrobials: amoxicillin clavulanate (-15%, $P < 0.001$), cefovecin (+11%, $P < 0.01$) and doxycycline (+6%, $P < 0.01$). An overall significant shift in the prescription pattern concerning first-, second- and third-choice antimicrobial as well as off-label products was noticed after the introduction of antimicrobial use guidelines ($P = 0.02$). The relative number of prescriptions of second-choice antimicrobials decreased by 16%, while the prescription of first-choice (+4%), third-choice (+8%) antimicrobials and off-label products (+3%) increased. Furthermore, the relative number of prescriptions of highest priority critically important antimicrobials increased by 12% ($P = 0.02$) after the introduction of the antimicrobial use guidelines.

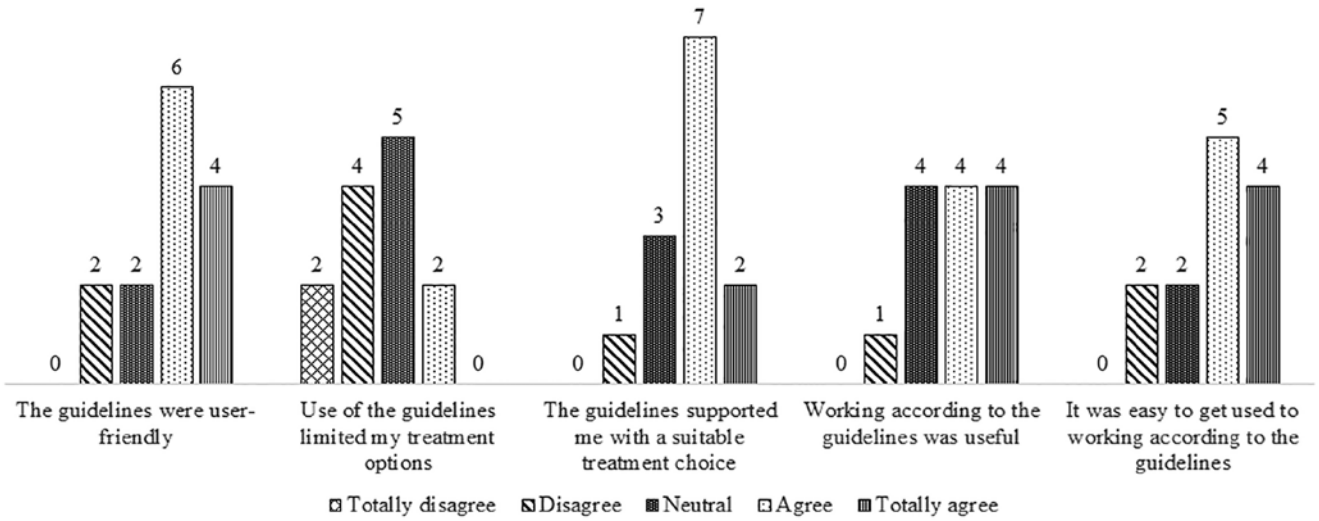


**Figure 1. Results of the questionnaire regarding perceived usefulness of the antimicrobial guidelines. A five-point Likert-scale was used: (1) strongly disagree, (2) disagree, (3) undecided, (4) agree and (5) strongly agree. Thirteen veterinarians answered all questions, one veterinarian only answered whether the guidelines were user-friendly.**

## Dogs

Antimicrobials were prescribed in 80% (277/347) before and in 68% (356/522) of the consultations after the introduction of antimicrobial use guidelines (Table 2). Similarly as for cats, this decrease was not significantly associated with the introduction of antimicrobial use guidelines (P = 0.49). The prescription pattern varied significantly with the clinical condition (P < 0.001) (Table 3). Antimicrobials are more likely prescribed when indicated by the guidelines, 88% (107/122) versus 76% (170/225) before (OR 2.3, 95% CI 1.2; 4.3) and 87% (138/159) versus 60% (218/363) after (OR 4.4, 95% CI 2.6; 7.2) the introduction of the guidelines (Table 4). Again, a considerable amount of prescriptions were actually not indicated, 49% (170/347) before and 42% (218/522) after the introduction of the guidelines, respectively. The corresponding values for Cohen's kappa (0.09 and 0.20 before and after, respectively) indicate only a slight agreement between the prescription and the actual indication of antimicrobials. The percentage of consultations handling according to the antimicrobial use guidelines increased from 35% to 45%. This increasing trend was not significantly associated with the introduction of antimicrobial use guidelines (P = 0.13), but varied significantly with the clinical condition (P < 0.001) (Table 3).

Amoxicillin clavulanate and cephalexin were the most commonly prescribed antimicrobials before and after the introduction of the guidelines. There was a significant difference in the relative frequency of pre-

**Table 4. Associations between the prescription of antimicrobials and whether the prescription was indicated according to the guidelines both before and after the introduction of the guidelines per animal species.**

| | Cat | | | | Dog | | | |
|---|---|---|---|---|---|---|---|---|
| **Before the guidelines** | n=198 | | Indicated | | n=347 | | Indicated | |
| | | | Yes | No | | | Yes | No |
| | Prescribed | Yes | 36 | 106 | Prescribed | Yes | 107 | 170 |
| | | No | 3 | 53 | | No | 15 | 55 |
| | OR: | 6.0 | 95% CI: 1.8; 20.4 | | OR: | 2.3 | 95% CI: 1.2; 4.3 | |
| | Kappa: | 0.13 | 95% CI: 0.06; 0.20 | | Kappa: | 0.09 | 95% CI: 0.03; 0.16 | |
| **After the guidelines** | n=247 | | Indicated | | n= 522 | | Indicated | |
| | | | Yes | No | | | Yes | No |
| | Prescribed | Yes | 38 | 110 | Prescribed | Yes | 138 | 218 |
| | | No | 5 | 94 | | No | 21 | 145 |
| | OR: | 6.5 | 95% CI: 2.5; 17.2 | | OR: | 4.4 | 95% CI: 2.6; 7.2 | |
| | Kappa: | 0.17 | 95% CI: 0.10; 0.25 | | Kappa: | 0.20 | 95% CI: 0.14; 0.26 | |

OR = odds ratio; CI = confidence interval

**Table 5. Active substances prescribed in cats and dogs, before and after the introduction of antimicrobial use guidelines.**

| Antimicrobial | % Cats (n) | | | % Dogs (n) | | |
|---|---|---|---|---|---|---|
| | Before | After | D | Before | After | D |
| Amoxicillin | 15% (27) | 10% (17) | -5% | 5% (16) | 9% (39) | +4%* |
| Amoxicillin clavulanate | 29% (52) | 14% (23) | -15%* | 25% (86) | 20% (84) | -5%* |
| Azithromycin | | 1% (1) | +1% | | | |
| Cephalexin | 3% (5) | 8% (13) | +5% | 21% (89) | 22% (94) | +1% |
| Cephalosporins | | | | 0.3% (1) | | |
| Cefazolin | 3% (5) | 2% (4) | -1% | 13% (44) | 9% (37) | -4%* |
| Cefoperazone | | | | | 0.2% (1) | |
| Cefovecin | 31% (55) | 42% (70) | +11%* | 3% (9) | 1% (6) | -2% |
| Chloramphenicol | 1% (2) | 1% (1) | | | | |
| Clindamycin | 2% (4) | 2% (3) | | 1% (3) | 4% (16) | +3%* |
| Difloxacin | 3% (5) | 1% (1) | -2% | | 0.2% (1) | |
| Doxycycline | | 6% (10) | +6%* | 3% (10) | 2% (9) | -1% |
| Enrofloxacin | 3% (5) | 4% (7) | +1% | 3% (12) | 7% (30) | +4%* |
| Fusidic acid/ Framycetin | | 1% (1) | +1% | 2% (6) | 2% (9) | |
| Gentamicin | 1% (1) | 1% (2) | | 3% (12) | 4% (15) | |
| Lincomycin | 1% (1) | | -1% | | 1% (3) | +1% |
| Lincomycin Spectinomycin | 2% (3) | 1% (1) | -1% | | | |
| Marbofloxacin | 1% (1) | 2% (3) | +1% | 5% (15) | 4% (15) | -1% |
| Metronidazole | | | | 4% (10) | 4% (16) | |
| Metronidazole Spiramycin | 3% (5) | 4% (6) | +1% | 5% (17) | 5% (22) | |
| Mupirocin | | | | 0.3% (1) | | |
| Neomycin | | 1% (1) | +1% | 2% (8) | 1% (5) | -1% |
| Ofloxacin | 1% (2) | 1% (2) | | | 1% (2) | |
| Orbifloxacin | | | | | 2% (8) | +2%* |
| Oxytetracyclin /Polymyxin B | 1% (1) | 1% (1) | | 1% (3) | 0.2% (1) | |
| Polymyxin B | 1% (1) | | -1% | 1% (4) | 2% (8) | +1% |
| Pradofloxacin | 1% (1) | | -1% | 0.3% (1) | | |
| Procaine Benzyl penicillin | | 1% (1) | +1% | | | |
| Procaine Benzyl penicillin/ Neomycin | 1% (1) | | -1% | | 1% (2) | +1% |
| Procaine Benzyl penicillin/ Streptomycin Nafcillin | 1% (1) | | -1% | | | |
| Tobramycin | 1% (1) | | -1% | | | |
| Trimethoprim Sulphonamides | 1% (1) | | -1% | 1% (2) | 1% (2) | |
| **Total number of prescriptions** | **180** | **168** | | **349** | **425** | |

D = difference between the percentage before and after the introduction of antimicrobial use guidelines. * Significant difference (5% significance level following $\chi^2$ test or Fisher's exact test).

scriptions before and after the guidelines for the following antimicrobials: amoxicillin (+4%, P = 0.02), amoxicillin clavulanate (−5%, P = 0.03), cefazolin (−4%, P = 0.04), clindamycin (+3%, P = 0.01), enrofloxacin (+4%, P = 0.04) and orbifloxacin (+2%, P = 0.01) (Table 5). An overall significant shift in the prescription pattern concerning first-, second- and third-choice antimicrobial as well as off-label products was noticed after the introduction of antimicrobial use guidelines (P = 0.04). The relative number of prescriptions of off-label antimicrobials decreased by 10%, while the prescription of first- (+5%), second- (+1%) and third- (+5%) choice antimicrobials increased. Furthermore, the relative number of prescriptions of highest priority critically important antimicrobials increased by 5% (P = 0.06) after the introduction of the antimicrobial use guidelines.

### Logbooks and questionnaires

Unfortunately, the logbooks were not consistently used to write down the reasons for divergence from antimicrobial use guidelines. Therefore, these data could not be used for further evaluation. Thirteen veterinarians answered all questions, while one veterinarian only answered whether the guidelines were user-friendly (Figure 1). The Likert-scale questions revealed that veterinarians were positive about the antimicrobial use guidelines: the guidelines were evaluated as user-friendly (mean score 3.9) and useful (3.8). The guidelines supported the veterinarians with a suitable treatment choice (3.8) and did not limit the treatment options of the veterinarians (2.5). The veterinarians also indicated that it was easy to get used to work according to the guidelines (3.8). Veterinarians

mentioned the format and size of the booklet with antimicrobial use guidelines and the clear grouping of the different conditions as positive features.

Nine veterinarians indicated that they were most of the time able to work according to the guidelines; five sometimes. Surprisingly, antimicrobials were more likely prescribed during consultations of veterinarians who stated to work most of the time according to the guidelines compared to veterinarians who stated to work sometimes according to the guidelines, both in cats (OR = 9.2; 95% CI 2.9; 29.6) and dogs (OR = 19.2; 95% CI = 2.9; 124.8). Furthermore, the guidelines were less likely to be followed during consultations of the 'most of the time' veterinarians compared to the 'sometimes' veterinarians, both in cats (OR = 0.26; 95% CI 0.12; 0.57) and dogs (OR = 0.47; 95% CI 0.23; 0.98). The most frequently mentioned reason to diverge from the guidelines was the use of cefovecin in cats because of the perceived difficulty to administer tablets in contrast to the user-friendly injection. Other reasons to diverge from the guidelines were practical reasons (drug not in stock), good experience with other antimicrobials for that specific condition, and declination of additional diagnostic tests by the owner, preventing to comply with the diagnostic requirements before prescribing an antimicrobial.

## DISCUSSION

After the introduction of the antimicrobial use guidelines, a decrease was observed in the percentage of consultations where antimicrobials were prescribed and more prescriptions were made according to the guidelines. Unfortunately, the observed improvements in the number of consultations without use of antimicrobials and according to the guidelines were not statistically significant when taking into account the clustering of the results within the veterinary practices. This is likely the result of the fact that the effect of the introduction of the guidelines was not consistent for the participating veterinarians, in combination with the limited sample size (14 veterinary practices) (Table 2). The increase in prescription of third-choice antimicrobials after the introduction of antimicrobial use guidelines was also an unexpected result. Nevertheless, the results of this study gave some food for thought concerning the prescription habits in small animal practices and antimicrobial use guidelines.

In this study, mainly penicillins and third- and fourth-generation cephalosporins were prescribed in cats, whereas penicillins and first- and second-generation cephalosporins were predominant in dogs. These results are comparable to previous data obtained in Belgium and the rest of Europe (Regula et al., 2009; Mateus et al., 2011; De Briyne et al., 2014) and also aligned to a certain extent with the results described in a Canadian study, conducted in 2004, in which the percentage of cases where antimicrobials were prescribed, decreased (Weese, 2006). Unlike the Canadian study, where the prescription of first-, second- as well as third-choice antimicrobials decreased, in the present study, the prescription of second-choice antimicrobials decreased significantly in cats, while the prescription of the third-choice antimicrobials increased after the introduction of antimicrobial use guidelines. However, the study designs differed considerably. In the previous study, six years before and four years after the introduction of antimicrobial use guidelines were assessed. Furthermore, it did not distinguish between cats and dogs, and the data were gathered in a small animal teaching hospital, not in individual small animal practices. It is likely that better results were obtained because of the fact that veterinarians working in a tertiary care veterinary teaching hospital might be more strict in respecting the guidelines, and it might be easier to implement guidelines in one referral practice than in multiple, first-line practices. Moreover, the longer study period in the Canadian study made it possible for the veterinarians to get familiar with these guidelines and to implement them in their routine. In the present study, the veterinarians were only briefly personally instructed on how to work with the antimicrobial use guidelines, and the study period may have been too short.

Notable was the unexpected increase of the prescription of third-choice antimicrobials in cats and dogs; in particular, the prescription of cefovecin increased substantially. Cefovecin is a broad-spectrum, third-generation cephalosporin registered for the treatment of cats and dogs and is classified among the highest priority critically important antibiotics (WHO, 2011). In cats, the antimicrobial activity following a single injection lasts up to 14 days (SPC Convenia, 2013). The parenteral administration route makes cefovecin an easy antimicrobial to administer. Previous studies have indicated that the ease of administration is the key factor explaining the popularity of this antimicrobial (De Briyne et al., 2013), as also stated by the participating veterinarians. The preference is likely also influenced by anticipated low owner compliance in administering a short-term oral antimicrobial therapy (Grave and Tanem, 1999).

The results from this study indicate that antimicrobials were prescribed far more often than indicated both before and after the implementation of the antimicrobial use guidelines, showing that there is still a large margin for the reduction of antibiotic use in small animal medicine. It has been described that small animal veterinarians mainly base their decision whether or not to prescribe antimicrobials on the observed clinical signs. Less frequently, they await the results of bacteriological culture or cytology (Hughes et al., 2012). Other factors that are taken into account are the ease of administration, financial constraints and client expectations (Hughes et al., 2012). Moreover, the veterinarians' self-reported frequency of working according to the antimicrobial use guidelines did not correspond with the measured frequencies of prescribing antimicrobials and working according to the

guidelines. This non-correspondence together with the large margin for the reduction of antimicrobial use might suggest that veterinarians are not always aware of their actual antimicrobial use and that increasing the self-consciousness in combination with measuring objectively the antimicrobial use is needed. For instance, a centralized data-collection system on antimicrobial use in small animals, existing already in several European countries for farm animals, can be useful to measure the antimicrobial use in a standardized manner, to compare the use between veterinary practices and to provide feedback to veterinary practices about their use. Antimicrobial use guidelines can, in combination with this monitoring, be a useful tool to support veterinarians towards a more responsible use of antimicrobials.

The results of this study suggest that antimicrobial use guidelines can be a supportive tool for a more responsible use of antimicrobials, which can serve as basis for further research. With a larger sample size, a more balanced design and a longer observation period, more detailed, condition-specific and clear results on the usefulness of antimicrobial guidelines may be obtained. Another step is to develop communication strategies to inform large groups of veterinarians about the need of the responsible use of antibiotics and about the benefits of using the antimicrobial use guidelines. Together with the aforementioned monitoring of antimicrobial use, all of this may help in targeted communication with and training of small animal veterinarians, aiming at a restricted and more responsible use of antibiotics.

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