Antimicrobial prescription in cats in Switzerland before and after the introduction of an online antimicrobial stewardship tool: a trend towards more prudent use

Alina Hubbuch[1,2], Kira Schmitt[2,3], Claudia Lehner[1,4], Sonja Hartnack[5], Simone Schuller[4], Gertraud Schüpbach-Regula[6], Meike Mevissen[7], Ruth Peter[1], Cedric Müntener[1], Hanspeter Naegeli[1], Barbara Willi[2]

[1]Institute of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, CH-8057 Zurich, Switzerland

[2]Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, CH-8057 Zurich, Switzerland

[3]Institute for Food Safety and Hygiene, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 272, CH-8057 Zurich, Switzerland

[4]Division of Small Animal Internal Medicine, Vetsuisse Faculty, University of Bern, Länggassstrasse 128, CH-3012 Bern, Switzerland

[5]Section of Epidemiology, Vetsuisse Faculty, University of Zurich,

Winterthurerstrasse 270, CH-8057 Zurich, Switzerland

[6]Veterinary Public Health Institute (VPHI), Vetsuisse Faculty, University of Bern, Schwarzenburgstrasse 161, CH-3097 Liebefeld, Switzerland

[7]Division of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty, University of Bern, Länggassstrasse 124, CH-3012 Bern, Switzerland

Abstract

Background: Antimicrobial stewardship activities are essential to improve prudent antimicrobial use. The aim of the present study was to evaluate changes in antimicrobial prescriptions in cats after the introduction of prudent use guidelines promoted by an online antimicrobial stewardship tool (AntibioticScout.ch) in Switzerland. Data from 792 cats presented to two university hospitals and 14 private practices in 2018 were included and compared to 776 cases from 2016. Cats were diagnosed with acute upper respiratory tract disease (aURTD), feline lower urinary tract disease (FLUTD) and abscesses. Clinical history, diagnostic work-up and antimicrobial prescriptions (class, dosage, duration) were assessed. Type and proportions [95% CI] of antimicrobial prescriptions were compared between the two evaluation periods and a generalized mixed effects model was applied to evaluate compliance with the Swiss prudent use guidelines.

Results: From 2016 to 2018, the proportion of antimicrobial prescription in all included cases decreased from 75.0% [71.8–78.0] to 66.7% [63.3–69.9]; this decrease was most pronounced for cases treated at the university hospitals (67.1% [59.5–74.0] to 49.3% [40.9–57.8]) and for cats with FLUTD (60.1% [54.6–65.4] to 48.8% [43.2–54.4]). The use of 3rd generation cephalosporins in private practices declined from 30.7% [26.5–35.1] to 22.1% [18.4–26.2], while the overall use of non-potentiated aminopenicillins increased from 19.6% [16.4–23.0] to 27.8% [24.1–31.9]. In cases where antimicrobial therapy was indicated, compliance with the guidelines did not increase (33.3% [26.6–40.6] to 33.5% [27.2–40.2], OR 1.0 [0.6–1.6]), neither at universities nor in private practices. On the other hand, antimicrobial treatment was more often withheld in cases with no indication for antimicrobial therapy (35.6% [30.1–41.4] to 54.0% [47.6–60.4], OR 2.4 [1.6–3.5]); this was found for private practices (26.7% [20.8–33.4] to 46.0% [38.4–53.7]) and for aURTD cases (35.0% [26.5–44.2] to 55.4% [44.7–65.8]).

Conclusions: Overall proportion of antimicrobial prescription, unjustified antimicrobial therapy and, in private practices, the use of 3rd generation cephalosporins decreased from 2016 to 2018 for the investigated feline diseases. However, overall compliance with the guidelines was still low and requires further efforts to foster prudent antimicrobial use in cats.

Keywords: antimicrobial stewardship program, prescription guidelines, antibiotics, prescription patterns, companion animals, HPCIA, highest priority critically important antimicrobial, One Health

Background

A One Health approach is required to combat the development and spread of antimicrobial-resistant bacteria (1, 2). Antimicrobial use is thought to be a major driving force towards antimicrobial resistance (3, 4) and over-prescription of antimicrobials seems to be common in human and veterinary medicine (5-9). The majority of the quantities of antimicrobials sold in Europe are used to treat food producing animals and the role of companion animals in this context has been neglected for a long time (10). However, highest priority critically important antimicrobials (HPCIAs) are commonly administered to companion animals (11-13). In cats, the extensive use of 3rd generation cephalosporins is regarded a critical issue, specifically the common administration of cefovecin, which is popular due to the convenient application as depot preparation (12-18). This can foster the development and spread of antimicrobial resistant microorganisms in veterinary patients, e.g. extended-spectrum beta-lactamase producing *Enterobacteriaceae* (19, 20). Numerous reports support a transmission of resistant bacteria from companion animals to humans, underlining the need to promote prudent antimicrobial use also in small animal medicine (21-27).

Antimicrobial stewardship programs aim at the preservation of the effectiveness of available antimicrobial agents and include different approaches, such as staff education, infection prevention and control, surveillance of antimicrobial resistance and health-care associated infections, the propagation of prudent antimicrobial use and restrictions for HPCIA (28, 29). A common tool to enhance prudent antimicrobial use are prescription guidelines. In veterinary medicine, various countries and organizations have developed guidelines that are adapted to national requirements or local needs (30-35). To date, only very few studies have investigated the impact of those guidelines on antimicrobial prescription in companion animals. A decrease of antimicrobial prescriptions after the introduction of prudent use guidelines has been reported in Flemish small animal practices and in a veterinary teaching hospital in Canada (9, 36). In a Europe-wide survey, veterinarians in countries with national policies for antimicrobial use, as for example Sweden, seemed to prescribe critically important antibiotics less frequently than in countries without such policies (11). In Denmark, 65% of the companion animal practitioners reported in a questionnaire-based survey that the Danish national antibiotic use guidelines had influenced their prescription habits (37).

In Switzerland, the ban of antimicrobial growth promoters in 1999 together with other regulations and activities (e.g. drug recording requirements in food-producing animals, herd

management by specialized veterinarians, disease eradication and vaccination programs) were associated with a reduction in antimicrobial use in the last years (38). Since November 2015, a national Strategy on Antimicrobial Resistance (StAR) reinforces these measures (39). Antimicrobial sale numbers in Switzerland showed a decrease of 41.1% between 2012 and 2018, while sales of antimicrobials exclusively registered for companion animals dropped by 13.4% (40). However, population-adjusted antimicrobial sales for food-producing animals are still high compared to countries such as Sweden, Norway, Finland and Iceland, which emphasizes the need for further actions (10).

In December 2016, an online antimicrobial stewardship tool (AntibioticScout.ch) was introduced to promote the Swiss guidelines on prudent antimicrobial use. This tool contains specific recommendations on antimicrobial prescription for various disease complexes (41-43). A previous study evaluated the a priory compliance with the guidelines for cats with acute upper respiratory tract disease (aURTD), feline lower urinary tract disease (FLUTD) and abscesses in Switzerland in 2016, before implementation of AntibioticScout.ch. The study reported an overall poor compliance of 17–24%, and 3rd generation cephalosporins were the second most commonly prescribed antibiotic class in these patients (44).

The present study is a follow-up investigation of the previous study (44) and examined changes in antimicrobial prescription in cats in Switzerland after launching the online antimicrobial stewardship tool AntibioticScout.ch. For this purpose, data for 2016 and 2018 from fourteen private veterinary practices and two university hospitals regarding cats with aURTD, FLUTD and abscesses were compared and prescription patterns and compliance with the guidelines evaluated.

Methods

This follow-up study evaluated diagnostic work-up and antimicrobial prescription patterns for three feline disease complexes (aURTD, FLUTD, abscesses) in patients presented between January 1st and December 31st 2018 using identical methods and data from the same fourteen veterinary practices and two university hospitals as in a previously published study (44). Briefly, the electronic records of the veterinary practices and university hospitals were searched using predefined search terms and inclusion criteria applied as described (44). In the university hospitals, all cases that matched the inclusion criteria were included, whereas in the private practices, 16 cases per indication and practice were chosen using the randomizer function of Microsoft® Excel (Microsoft Corporation, Washington, USA) to avoid overrepresentation of large practices. Cats with abscesses were only included in private practices because they are rarely presented to university hospitals (44). In two practices, only 10 and 14 cases with aURTD and 10 and 6 cases with FLUTD could be included in 2018 because of an insufficient number of patients matching the inclusion criteria. Data on medical history, clinical symptoms, diagnostic work-up and details on antimicrobial therapy and diagnosis were collected (44). HPCIAs were defined according to the World Health Organization (WHO) to include third or higher generation cephalosporins, quinolones, macrolides, ketolides, glycopeptides and polymyxins (45).

Compliance with the Swiss guidelines published in December 2016 in the online tool AntibioticScout.ch was evaluated (41-43). Details of the guidelines are displayed in Table 1. For a comparison of the two evaluation periods (2016 and 2018), data was grouped into cases in which antimicrobials were indicated (guidelines followed-/not followed) and cases in which antimicrobials were not indicated (guidelines followed-/not followed, Table 2). This allowed to account for the different proportions of cases presented with and without an indication for antimicrobial therapy in the two evaluation periods. Treatment decisions were defined as correct if in agreement with the guidelines and as incorrect if in disagreement with the guidelines.

For statistical analysis, IBM SPSS Statistics 23® (IBM, New York, USA) and the software R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria (46)) were used. A Mann-Whitney U Test was performed to compare continuous data such as age and treatment duration between the two evaluation periods. Categorical variables (university hospital versus private practice, sex, breed, pretreatment, hospitalization, diagnostic work-up, local wound

treatment, drainage, indication for antimicrobial use, antimicrobial treatment, prescribed antimicrobial classes and use of HPCIAs, serial or combination therapy) were presented as proportions with binomial 95% confidence intervals (CI), which were calculated with the command binom.test() in the package DescTools (47). A generalized mixed effects model (lme4 package (48)) was used to compare compliance with the guidelines between 2016 and 2018 and between the disease complexes (aURTD, FLUTD, abscess). The analysis was done separately for cases with and without indication for antimicrobial use (Table 2). The different hospitals and practices were used as random effects and, year and group as fixed effects. Additionally, an interaction between year and disease was tested.

Table 1: Swiss prudent use guidelines for cats with aURTD[a], FLUTD[b] and abscesses.

Indication	Comment	Antibiotic	Dosage (mg/kg)	Application frequency	Treatment duration (days)
aURTD[a]	AMU[c] is only indicated if poor general condition, fever, lethargy and/ or anorexia are present	Doxycycline	10 / 5	SID[d]/BID[e]	5−14
		Amoxicillin	15−20	BID[e]/TID[f]	5−14
FLUTD[b]	Complicated UTI[g] are defined as infections that are caused by anatomical or functional changes or disorders of the immune system	**Uncomplicated UTI[g]:**			
		Amoxicillin	11−15	BID[e]/TID[f]	5−7
		Complicated UTI[g]:			
		Amoxicillin/Clavulanic acid	12.5−20	BID[e]/TID[f]	5−28
Abscess	AMU[c] is only indicated if signs of generalization, poor general condition, severely contaminated wounds, and/ or proximity to delicate tissues (e.g., joints) are present	Amoxicillin	15−20	BID[e]	5−7
		Amoxicillin/Clavulanic acid	12.5−20	BID[e]	5−7
		Cefalexin	20−30	BID[e]/TID[f]	5−7
		Clindamycin	10−15	BID[e]	5−7
		Cefazolin	20	BID[e]	5−7

Consistent with the Swiss prudent use guidelines presented in December 2016 as previously published (44); in April 2019 the Swiss prudent use guidelines have been revised; [a]aURTD, acute upper respiratory tract disease; [b]FLUTD, feline lower urinary tract diseases; [c]AMU, antimicrobial use; [d]SID, once daily; [e]BID, twice daily; [f]TID, three times daily; [g]UTI, urinary tract infection

Table 2: Details on categorization to evaluate compliance with the Swiss prudent use guidelines.

Category[a]	Explanation
AMU[b] indicated	
Guidelines followed	Antimicrobial class, dose and treatment duration in complete agreement with the guidelines
Guidelines not followed	Antimicrobial use/non-use not in agreement with the guidelines, i.e. different dose[c] or treatment duration[d], different antimicrobial class[e] or no antibiotics prescribed despite being indicated
AMU[b] not indicated	
Guidelines followed	No antibiotics prescribed
Guidelines not followed	Unjustified prescription of antibiotics

[a]Based on the Justification Scores in Schmitt et al., 2019 (44); [b]AMU, antimicrobial use; [c]A deviation of up to 20% above or below the recommended dose was accepted; [d]A margin of one day shorter or longer was tolerated; [e]Cases were only listed once, i.e. if dose or treatment duration as well as antimicrobial class deviated from the guidelines, cases were listed in "different antimicrobial class"

Results

Case characteristics

A total of 792 cases (aURTD, n=244; FLUTD, n=324; abscesses, n=224) was included in 2018 and compared to 776 cases from 2016 (44). Case characteristics are shown in Table 3. There was no difference in the proportion of cases presented to university hospitals compared to private practices between 2016 and 2018. Moreover, the sex and breed distribution for the three disease complexes was not different between the two evaluation periods (Table 3), as well as the age distribution in cases with FLUTD and abscesses. However, cats suffering from aURTD in 2018 were significantly older compared to cats in 2016 (Additional file 1).

The proportion of cases that had been pretreated with antibiotics or that were hospitalized was not different between 2016 and 2018 for the three disease complexes (aURTD, FLUTD and abscesses, Table 3). As in 2016 (44), the proportion of cases pretreated with antibiotics or hospitalized was higher at the university hospitals compared to private practice cases in 2018 (university hospitals vs. private practices, pretreatment: 20.1% [13.9–27.6] vs. 3.9% [2.5–5.6]; hospitalization: 67.4% [59.1–74.9] vs. 10.8% [8.5–13.5]).

Diagnostic work-up

The proportion of cases with aURTD tested for feline herpesvirus-1 and feline calicivirus by PCR did not change between 2016 and 2018 (Table 3). As in 2016 (44), this diagnostic work-up was more commonly performed at the university hospitals compared to private practices in 2018 (university hospitals: 57.1% [37.2–75.5]; private practices: 1.9% [0.5–4.7]).

Urine sediment analysis or bacterial culture from an aseptically collected urine were performed in similar proportions of cases with FLUTD in 2016 and 2018 (Table 3). The proportion of cases receiving this diagnostic work-up increased in private practices from 2016 to 2018 (27.1% [21.1–33.8] to 43.8% [36.9–50.8]). Despite this increase, diagnostic work-up in cats with FLUTD was still more common at university hospitals (80.2% [71.7–87.0]) compared to private practices in 2018. Of cases with diagnostic work-up, a total of 36.9% [29.4–45.0] were diagnosed with bacteriuria in 2018, which was similar in 2016 (37.0% [29.6–44.8]).

Table 3: Characteristics of cases in 2016 and 2018 for cats with aURTD[a], FLUTD[b] and abscesses.

Parameter		aURTD[a]		FLUTD[b]		Abscesses	
		2016	2018	2016	2018	2016	2018
		% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]
Total number of cases		n = 227	n = 244	n = 333	n = 324	n = 216	n = 224
Treatment location	University hospital	18.9 [14.1-24.7]	11.5 [7.8-16.2]	39.0 [33.8-44.5]	35.8 [30.6-41.3]	0.0[d]	0.0[d]
	Private practice	81.1 [75.3-85.9]	88.5 [83.8-92.2]	61.0 [55.5-66.2]	64.2 [58.7-69.4]	100.0[d]	100.0[d]
Sex	Female	43.6 [37.1-50.3]	39.8 [33.6-46.2]	42.0 [36.7-47.5]	40.7 [35.3-46.3]	29.6 [23.6-36.2]	31.3 [25.2-37.8]
	Male	53.3 [46.6-59.9]	55.3 [48.9-61.7]	57.4 [51.8-62.7]	57.1 [51.5-62.6]	68.5 [61.9-74.7]	65.6 [59.0-71.8]
	Unknown	3.1 [1.2-6.3]	4.9 [2.6-8.4]	0.6 [0.1-2.2]	2.2 [0.9-4.4]	1.9 [0.5-4.7]	3.1 [1.3-6.3]
Breed	Purebred	19.4 [14.5-25.1]	20.9 [16.0-26.5]	20.7 [16.5-25.5]	21.6 [17.2-26.5]	6.5 [3.6-10.6]	7.6 [4.5-11.9]
	Mixed breed	75.8 [69.7-81.2]	75.0 [69.1-80.3]	74.2 [69.1-78.8]	73.5 [68.3-78.2]	88.0 [82.9-92.0]	87.5 [82.4-91.5]
	Unknown	4.8 [2.4-8.5]	4.1 [2.0-7.4]	5.1 [3.0-8.0]	4.9 [2.8-7.9]	5.6 [2.9-9.5]	4.9 [2.5-8.6]
Pretreatment	Yes[e]	9.3 [5.8-13.8]	8.2 [5.1-12.4]	8.1 [5.4-11.6]	8.6 [5.8-12.2]	3.2 [1.3-6.6]	2.7 [1.0-5.7]
	Unknown	2.6 [1.0-5.7]	2.0 [0.7-4.7]	2.4 [1.0-4.7]	1.2 [0.3-3.1]	0.9 [0.1-3.3]	0.4 [0.0-2.5]
Hospitalization	Yes[e]	15.9 [11.4-21.3]	10.7 [7.1-15.2]	36.0 [30.9-41.4]	36.7 [31.5-42.2]	6.0 [3.2-10.1]	9.8 [6.3-14.5]
Indication for AMU[f]	Yes	28.2 [22.4-34.5]	32.0 [26.2-38.2]	17.1 [13.2-21.6]	17.0 [13.1-21.5]	30.1 [24.1-36.7]	36.6 [30.3-43.3]
	No	**52.9 [46.1-59.5]**	**37.7 [31.6-44.1]**	31.8 [26.9-37.1]	33.6 [28.5-39.1]	30.6 [24.5-37.2]	21.0 [15.8-26.9]
	Unknown	18.9 [14.1-24.7]	30.3 [24.6-36.5]	51.1 [45.5-56.5]	49.4 [43.8-55.0]	39.4 [32.8-46.2]	42.4 [35.9-49.2]
Diagnostic work-up[g]	Yes[e]	11.9 [8.0-16.8]	8.2 [5.1-12.4]	52.3 [46.7-57.7]	56.8 [51.2-62.3]	NA[h]	NA[h]
Local wound treatment	Yes[e]	NA[h]	NA[h]	NA[h]	NA[h]	72.2 [65.7-78.1]	81.3 [75.5-86.1]
	Unknown	NA[h]	NA[h]	NA[h]	NA[h]	5.6 [2.9-9.5]	5.8 [3.1-9.7]
Drainage	Yes[e]	NA[h]	NA[h]	NA[h]	NA[h]	15.3 [10.8-20.8]	21.4 [16.2-27.4]

Non-overlapping 95% confidence intervals are shown in bold; Data from cases from 2016 has been published previously (44); [a]aURTD, acute upper respiratory tract disease; [b]FLUTD, feline lower urinary tract disease; [c]CI, 95% confidence interval; [d]Cases with abscesses were only recruited in private practices (see materials and methods); [e]Values for the category "no" (reference group) are not shown; [f]AMU, antimicrobial use; [g]PCR for feline herpesvirus-1 and feline calicivirus in cases with aURTD; sediment analysis or culture of aseptically collected urine in cases with FLUTD; [h]NA, not applicable

Antimicrobial prescriptions in 2016 and 2018 for all cases

Proportions of prescribed antimicrobial classes in 2016 and 2018 are shown in Figure 1. Details on antimicrobial prescriptions in 2016 and 2018 for all cases, and separated for university hospitals and private practices, are shown in Additional file 2.

From 2016 to 2018, the overall proportion of antimicrobial prescriptions decreased (2016: 75.0% [71.8–78.0]; 2018: 66.7% [63.3–69.9]); this decline was observed at the university hospitals (2016: 67.1% [59.5–74.0]; 2018: 49.3% [40.9–57.8]), but not in private practices (2016: 77.3% [73.7–80.6]; 2018: 70.5% [66.8–74.0]). In 2018, antimicrobial treatment was more commonly performed in private practices compared to university hospitals. Overall use of HPCIAs did not change from 2016 to 2018 (2016: 33.0% [29.2–37.0]; 2018: 28.8% [25.0–32.9]), neither at the university hospitals (2016: 12.9% [7.4–20.4]; 2018: 12.7% [6.0–22.7]) nor in private practices (2016: 38.0% [33.6–42.6]; 2018: 31.3% [27.1–35.8]). The use of 3rd generation cephalosporins, however, decreased in private practices (2016: 30.7% [26.5–35.1]; 2018: 22.1% [18.4–26.2]) and the overall use of non-potentiated aminopenicillins increased (Figure 1). Combination or serial therapy occurred more commonly in 2018 (2016: 17.0% [14.0–20.3]; 2018: 27.7% [23.9–31.7]).

Antimicrobial prescriptions in 2016 and 2018 for cats with aURTD, FLUTD and abscesses

Details of antimicrobial prescriptions in cats with aURTD, FLUTD and abscesses are given in Table 4. From 2016 to 2018, the proportion of antimicrobial treatments in cats with aURTD did not change, but more cases received serial/combination therapy in 2018 (Table 4). Treatment duration in cats with aURTD was similar in 2016 (median duration (range) = 12 (4–37) days) compared to 2018 (median duration (range) = 10 (1–21) days).

In 2018, less cases with FLUTD were treated with antimicrobials compared to 2016 (Table 4), and treatment duration decreased from a median duration (range) of 13 (1–56) days to 9.5 (1–42) days ($p = 0.006$). The proportions of antimicrobial classes used in cats with FLUTD did not change (Table 4).

In cats with abscesses, the proportion of antimicrobial prescriptions was very high in 2018 and did not change compared to 2016. The antimicrobial classes that were prescribed were similar in both evaluation periods (Table 4) and treatment duration did not change between 2016 and 2018 (2016: median duration (range) = 9 (1–28) days; 2018: median duration (range) = 9 (2–28) days).

Figure 1: Comparison of antimicrobial classes prescribed in 2016 and 2018.

Proportions of prescribed antimicrobial classes (dots) per total number of cases with antimicrobial treatment in 2016 (n = 582) and 2018 (n = 528) and corresponding 95% confidence intervals (lines). *Others (antimicrobial classes used in ≤2% of prescriptions) included amphenicoles, lincosamides, macrolides, penicillins, nitroimidazoles. Gen., generation; pot., potentiated.

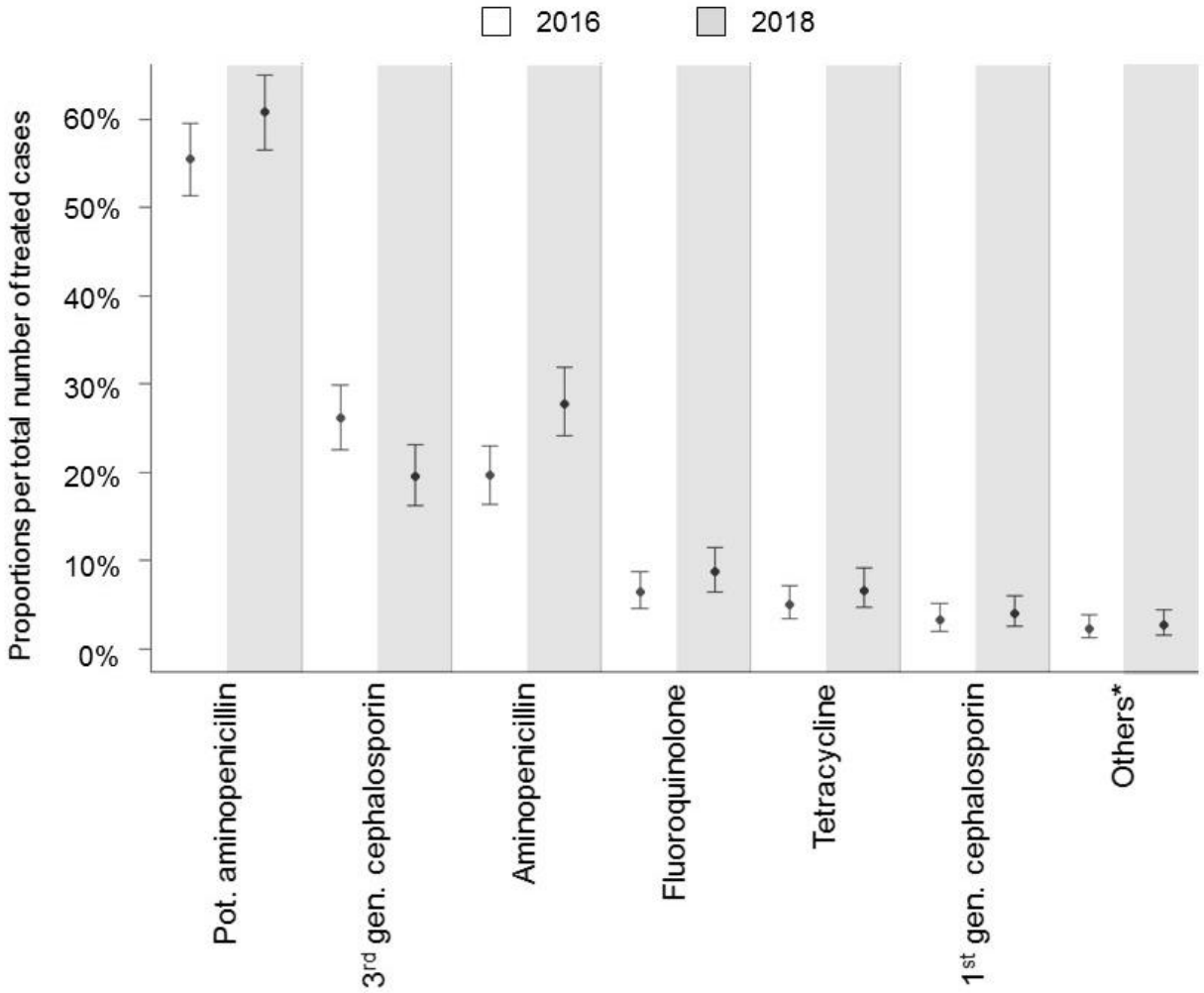

Table 4: Antimicrobial prescriptions in 2016 and 2018 for cases with aURTD[a], FLUTD[b] and abscesses.

Parameter		aURTD[a]		FLUTD[b]		Abscesses	
		2016	**2018**	**2016**	**2018**	**2016**	**2018**
		% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]
Total number of cases		n = 227	n = 244	n = 333	n = 324	n = 216	n = 224
Antimicrobial treatment	Yes[d]	77.1 [71.1-82.4]	67.6 [61.4-73.5]	**60.1 [54.6-65.4]**	**48.8 [43.2-54.4]**	95.8 [92.2-98.1]	91.5 [87.1-94.8]
Details of antimicrobial treatment		n = 175	n = 165	n = 200	n = 158	n = 207	n = 205
Pot. aminopenicillin		40.0 [32.7-47.7]	49.1 [41.2-57.0]	60.5 [53.4-67.3]	69.6 [61.8-76.7]	63.8 [56.8-70.3]	63.4 [56.4-70.0]
3rd generation cephalosporin		28.0 [21.5-35.3]	23.6 [17.4-30.9]	25.5 [19.6-32.1]	13.9 [8.9-20.3]	25.1 [19.4-31.6]	20.5 [15.2-26.7]
Aminopenicillin		23.4 [17.4-30.4]	29.1 [22.3-36.7]	11.5 [7.4-16.8]	20.9 [14.8-28.1]	24.2 [18.5-30.6]	32.2 [25.9-39.1]
Fluoroquinolone		4.0 [1.6-8.1]	8.5 [4.7-13.8]	12.5 [8.3-17.9]	15.8 [10.5-22.5]	2.4 [0.8-5.5]	3.4 [1.4-6.9]
Tetracycline		16.0 [10.9-22.3]	20.6 [14.7-27.6]	0.5 [0.0-2.8]	0.0 [0.0-2.3]	0.0 [0.0-1.8]	0.5 [0.0-2.7]
1st generation cephalosporin		0.6 [0.0-3.1]	0.0 [0.0-2.2]	3.0 [1.1-6.4]	1.3 [0.2-4.5]	5.8 [3.0-9.9]	9.3 [5.7-14.1]
Others[e]		4.0 [1.6-8.1]	3.6 [1.3-7.7]	0.5 [0.0-2.8]	0.0 [0.0-2.3]	2.4 [0.8-5.5]	3.9 [1.7-7.5]
HPCIAs[f]	Yes[d]	33.7 [26.8-41.2]	33.9 [26.8-41.7]	38.0 [31.2-45.1]	29.7 [22.7-37.5]	27.5 [21.6-34.2]	23.9 [18.2-30.3]
Serial/combination therapy	Yes[d]	**14.3 [9.5-20.4]**	**30.3 [23.4-37.9]**	13.0 [8.7-18.5]	19.6 [13.7-26.7]	23.2 [17.6-29.5]	31.7 [25.4-38.6]

Non-overlapping 95% confidence intervals are shown in bold; Data from cases from 2016 has been published previously (44); [a]aURTD, acute upper respiratory tract disease; [b]FLUTD, feline lower urinary tract disease; [c]CI, 95% confidence interval; [d]Values for the category "no" (reference group) are not shown; [e]Others (antimicrobial classes used in ≤2% of prescriptions) included amphenicoles, lincosamides, macrolides, penicillins, nitroimidazoles; [f]HPCIAs, highest priority critically important antimicrobials

Compliance with the Swiss prudent use guidelines

Details on compliance with the Swiss prudent use guidelines promoted by AntibioticScout.ch for the three disease complexes are shown in Table 5. Details for all cases and separated for the university hospitals and private practices are given in Additional file 3.

Overall, the proportion of correct treatment decisions in cases in which antimicrobials were indicated did not increase from 2016 to 2018 (2016: 33.3% [26.6–40.6]; 2018: 33.5% [27.2–40.2]), neither at the university hospitals (2016: 26.8% [16.9–38.6]; 2018: 42.2% [27.7–57.8]) nor in private practices (2016: 37.4% [28.5–46.9]; 2018: 31.2% [24.3–38.7]).

When cases without indication for antimicrobial treatment were analyzed, more correct treatment decisions were made in 2018 compared to 2016 (2016: 35.6% [30.1–41.4]; 2018: 54.0% [47.6–60.4]), i.e. the proportion of unjustified antimicrobial therapies declined. This decline was found in cases in private practices (2016: 26.7% [20.8–33.4]; 2018: 46.0% [38.4–53.7]), but not at the university hospitals (2016: 55.6% [44.7–66.0]; 2018: 73.0% [61.4–82.6]).

When compliance with consensus guidelines was analyzed for cats with aURTD, a similar trend was seen. The proportion of correct treatment decisions in cases in which antimicrobials were indicated did not increase, but compliance increased in cases without an indication for antimicrobial treatment (Table 5). Compliance with the treatment recommendations was generally low, mostly due to the use of potentiated aminopenicillins instead of the recommended non-potentiated aminopenicillins or doxycycline (Table 5). In cases with FLUTD or abscesses, the proportion of correct treatment decisions did not change between 2016 and 2018, neither in cases with or without indication for antimicrobial treatment. Treatment duration and prescription of an antibiotic class not recommended by the guidelines, especially the use of potentiated instead of non-potentiated aminopenicillins, was common in cats with FLUTD (Table 5). In cats with abscesses, unnecessary treatments and treatments exceeding the recommended duration were common (Table 5).

Generalized mixed effects model

A generalized mixed effects model was calculated for cases with and without an indication for antibiotic treatment (Table 5) to assess compliance of prescription with the AntibioticScout.ch guidelines. In cases with an indication for antimicrobial treatment, correct treatment decisions were not more likely in 2018 compared to 2016 (OR 1.0 [0.6–1.6). In these cases, cats with

FLUTD or abscesses were more often treated according to the guidelines than cats with aURTD, independently of the evaluation period (FLUTD: OR 5.1 [2.6–10.0]; abscess: OR 5.4 [2.9–10.0]). In cases without indication for antimicrobial treatment, correct treatment decisions were more common in 2018 than 2016 (OR 2.4 [1.6–3.5]). In these cases, correct treatment decisions were significantly less likely in cats with abscesses compared to cats with aURTD (OR 0.1 [0.0–0.2]). There was no significant interaction between year and disease complex.

Table 5: Compliance with the guidelines in 2016 and 2018 for cases with aURTD[a], FLUTD[b] and abscesses.

Category	aURTD[a]		FLUTD[b]		Abscesses	
	2016	2018	2016	2018	2016	2018
	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]	% [CI][c]
AMU[d] indicated	n = 64	n = 78	n = 57	n = 55	n = 65	n = 82
Guidelines followed	10.9 [4.5-21.2]	16.7 [9.2-26.8]	38.6 [26.0-52.4]	45.5 [32.0-59.4]	50.8 [38.1-63.4]	41.5 [30.7-52.9]
Guidelines not followed	89.1 [78.8-95.5]	83.3 [73.2-90.8]	61.4 [47.6-74.0]	54.5 [40.6-68.0]	49.2 [36.6-61.9]	58.5 [47.1-69.3]
a. Different dose/duration	6.3 [1.7-15.2]	2.6 [0.3-9.0]	1.8 [0.0-9.4]	5.5 [1.1-15.1]	24.6 [14.8-36.9]	34.1 [24.0-45.4]
b. Different antimicrobial class	75.0 [62.6-85.0]	67.9 [56.4-78.1]	54.4 [40.7-67.6]	38.2 [25.4-52.3]	21.5 [12.3-33.5]	22.0 [13.6-32.5]
c. Unjustified non-use	7.8 [2.6-17.3]	12.8 [6.3-22.3]	5.3 [1.1-14.6]	10.9 [4.1-22.2]	3.1 [0.4-10.7]	2.4 [0.3-8.5]
AMU[d] not indicated	n = 120	n = 92	n = 106	n = 109	n = 66	n = 47
Guidelines followed	**35.0 [26.5-44.2]**	**55.4 [44.7-65.8]**	55.7 [45.7-65.3]	67.9 [58.3-76.5]	4.5 [0.9-12.7]	19.1 [9.1-33.3]
Guidelines not followed	**65.0 [55.8-73.5]**	**44.6 [34.2-55.3]**	44.3 [34.7-54.3]	32.1 [23.5-41.7]	95.5 [87.3-99.1]	80.9 [66.7-90.9]
Treatment duration[e]	n = 140	n = 127	n = 178	n = 134	n = 153	n = 164
Guidelines followed	89.3 [82.9-93.9]	88.2 [81.3-93.2]	44.4 [37.0-52.0]	54.5 [45.7-63.1]	39.2 [31.4-47.4]	39.6 [32.1-47.6]
Guidelines not followed	10.7 [6.1-17.1]	11.8 [6.8-18.7]	55.6 [48.0-63.0]	45.5 [36.9-54.3]	60.8 [52.6-68.6]	60.4 [52.4-67.9]
a. Too long	10.7 [6.1-17.1]	10.2 [5.6-16.9]	50.6 [43.0-58.1]	38.8 [30.5-47.6]	57.5 [49.3-65.5]	56.1 [48.1-63.8]
b. Too short	0.0 [0.0-2.6]	1.6 [0.2-5.6]	5.1 [2.3-9.4]	6.7 [3.1-12.4]	3.3 [1.1-7.5]	4.3 [1.7-8.6]

Non-overlapping 95% confidence intervals are shown in bold; Data from cases from 2016 has been published previously (44); [a]aURTD, acute upper respiratory tract disease; [b]FLUTD, feline lower urinary tract disease; [c]CI, 95% confidence interval; [d]AMU, antimicrobial use; [e]Treatment duration is unknown or not applicable for numbers not listed

Discussion

The results of this study indicate an overall trend towards a more prudent antimicrobial prescribing practice in cats in Switzerland after the introduction of an online antimicrobial stewardship tool (AntibioticScout.ch) in December 2016. Between 2016 and 2018, overall proportion of antimicrobial use in cats with aURTD, FLUTD and abscesses declined, as well as prescriptions of 3rd generation cephalosporins in private practices. Furthermore, antimicrobials were more commonly withheld in cases where antimicrobial treatment was not recommended by the guidelines. This decrease of antimicrobial use is also supported by the total sale statistics of antimicrobials registered for companion animals in Switzerland, which showed a decline of 4.9% during the same period (40). Other studies also reported a reduction of antimicrobial prescriptions in both human and small animal medicine after the implementation of antimicrobial stewardship programs, underlining that these activities could have an impact towards more prudent treatment strategies (9, 36, 49-52).

The reduction in the use of 3rd generation cephalosporins from 30.7% to 22.1% in the private practices in 2018 is encouraging. The overall proportion of treatments with HPCIAs, however, did not decrease, which is possibly due to a slight increase in the use of fluoroquinolones in 2018. Furthermore, the proportion of cases receiving HPCIAs was still very high, especially in private practices (31.3%). HPCIAs are not recommended for any of the investigated diseases and should only be used based on antimicrobial susceptibility testing. A significant decrease in the use of 3rd generation cephalosporins in the university hospitals was not found (7.8% to 2.8%). However, this antibiotic class was already infrequently used in 2016.

Despite an overall decline in antimicrobial prescriptions, over-prescription was still common in 2018, especially in cats with abscesses. A total of 91.5% of the cats with abscesses in 2018 received antimicrobial therapy, compared to 67.6% of cases with aURTD and 48.8% of cats with FLUTD. This is striking because various studies from human medicine indicate that cure rates in uncomplicated skin abscesses are not influenced by antibiotic use as long as appropriate local wound therapy is applied (53-55). Interestingly, 81.3% of the cats with abscesses in 2018 received a local wound treatment and 21.4% a drainage. This highlights that antimicrobials, although not indicated, are often prescribed in addition to local wound therapy in cats with abscesses.

Potentiated aminopenicillins were still by far the most commonly applied antimicrobials in 2018. The use of potentiated aminopenicillins instead of non-potentiated aminopenicillins was also a common reason for lack of compliance with the guidelines in cats with aURTD and FLUTD. It should be mentioned that, in 2018, no oral preparations of non-potentiated aminopenicillins for cats were on the market in Switzerland, which likely dissuaded veterinarians from following the guidelines in cases of uncomplicated urinary tract infections. In cases with aURTD, doxycycline is also listed as a first-line treatment. However, doxycycline was rarely prescribed despite its activity against *Chlamydia* sp. infection, possibly due to the potential risk of esophageal strictures in cats (56).

Nevertheless, the use of non-potentiated aminopenicillins which are recommended as first-line treatment option for all three disease complexes increased from 2016 to 2018 (41). A comparably high percentage of non-potentiated aminopenicillins was prescribed in private practices in 2018. Preparations authorized for subcutaneous application accounted for most of these treatment. After discharge, the veterinarians had to switch to oral preparations of potentiated aminopenicillins. Because this was classified as serial therapy in the study, the increase in serial/combination therapy in 2018, especially evident in private practices and in cases with aURTD, should therefore be interpreted with caution.

For the evaluation of compliance with the guidelines, the cases were separated into those with and without indication for antimicrobial treatment. Cases with insufficient data for classification were excluded from the analysis. Therefore, almost 50% of the cases obtained from private practices were not suitable for assessment, mainly because of a lack of diagnostic work-up in cats with FLUTD or because the clinical symptoms in cats with aURTD and abscesses were not recorded. In the cases with an indication for antimicrobial treatment, the proportion of correct treatment decisions did not increase. As described before, the unjustified use of potentiated instead of non-potentiated aminopenicillins was a common reason for non-compliance. Difficulties to orally administer medications to cats could be another reason, favoring the use of 3rd generation cephalosporins, which can be injected as depot preparation (Convenia®, Zoetis, Delémont, CH) (57). Moreover, treatment duration was frequently in disagreement with the guidelines, especially in cases with abscesses. Antibiotics were often prescribed for a longer duration than recommended.

In cases where antimicrobial treatment was not indicated, proportion of correct treatment decisions increased from 35.6% to 54.0%, meaning that unjustified antimicrobial use declined

for the investigated disease complexes. A study analyzing antimicrobial treatments of cats presented to Flemish small animal practices also noted a decrease of unjustified antimicrobial use, as well as an increase of compliance with the guidelines after their introduction (9). In a study in human medicine, it was shown that the time period under investigation after implementation of guidelines has a great impact on the result: whereas 100% of the urinary tract infections were treated as recommended right after the introduction of the guidelines, only 39% of prescriptions followed the guidelines after one year (58). In our study, prescriptions were assessed in 2016 and 2018 over a one year period, which should provide a representative figure of the prescription habits. The veterinarians in the Flemish study, however, were actively instructed to follow the guidelines and the follow-up period was not clearly specified (9).

There were several differences in the antimicrobial prescription habits between the university hospitals and private practices. Firstly, as in 2016, HPCIAs were less commonly used at the university hospitals than in private practices (44). Secondly, proportion of cases treated with antimicrobials was lower at the university hospitals compared to private practices and the decrease in antimicrobial prescriptions was more pronounced. Thirdly, antimicrobials were more commonly withheld at the universities in cases where antimicrobial treatment was not indicated. Fourth, diagnostic work-up was more commonly performed at the universities, as already reported in 2016 (44). These findings indicate a trend towards a more restrictive use of antimicrobials at the university hospitals, which is important, as they could serve as role models for veterinary students and referring veterinarians. Despite this, overall compliance with the national guidelines did not improve at the university hospitals from 2016 to 2018.

In private practices, urine sediment analysis or bacterial culture from an aseptically collected urine was more commonly performed in 2018, which could have contributed to the reduction of antimicrobial prescriptions in cases with FLUTD. Bacterial culture of urine should be further promoted, since it could prevent unnecessary antibiotic administrations. Bacterial cystitis is considered to be rare in cats, with reported prevalences of 3–15% in cats presented with FLUTD (59-62). Bacterial cystitis was much more common in cats with FLUTD in this study. This was also the case when diagnoses based on urine sediment analysis were excluded and only cases with a positive bacterial culture result were considered (31.0% in 2016, 33.3% in 2018). Our results are however in agreement with a study in cats in Norway that also reported bacteriuria in 33% of cats presented with FLUTD (63).

This report has some limitations. The true impact of the online antimicrobial stewardship tool on the antimicrobial prescribing of Swiss veterinarians cannot be unequivocally assessed, as different actions were implemented in Switzerland as part of the national StAR program to combat antimicrobial resistance starting in November 2015. These actions, together with a generally increased awareness of the importance of prudent antimicrobial use among veterinarians could have contributed to the prescription changes observed in this study. However, AntibioticScout.ch provides a user friendly decision support tool informing veterinary practitioners in a most direct and effective way. Second, the investigated practices only represent a small proportion of practices in Switzerland and their participation was on a voluntary basis, which could have favored the inclusion of practices with more interest in prudent antimicrobial use. Third, the limited information in the patient records especially in private practices impeded the evaluation of compliance with the guidelines. Fourth, data were analyzed by different observers in 2016 and 2018; because judgement of prudent antimicrobial use leaves some margin of interpretation, this could have had an influence on the results of the study.

Conclusions

A trend towards a more prudent antimicrobial use in cats with aURTD, FLUTD and abscesses was found in Switzerland in 2018, after the implementation of the online antimicrobial stewardship tool AntibioticScout.ch. The overall antimicrobial use, the prescription of 3rd generation cephalosporins in private practices and unjustified antimicrobial use decreased from 2016 to 2018 for the investigated disease complexes. Nevertheless, over-prescription of antimicrobials and use of HPCIA was still common and overall compliance with the guidelines still poor. Antimicrobial stewardship activities should therefore be further promoted, and the availability of first-line antimicrobials with a convenient application in cats should be advanced.

List of abbreviations

aURTD: acute upper respiratory tract disease

FLUTD: feline lower urinary tract disease

CI: confidence interval

OR: odds ratio
HPCIA: highest priority critically important antimicrobial
StAR: Strategy on Antimicrobial Resistance
vs.: versus
PCR: polymerase chain reaction
WHO: World Health Organization
AMU: antimicrobial use
NA: not applicable
SID: once daily
BID: twice daily
TID: three times daily
UTI: urinary tract infection

Declarations

Ethics approval and consent to participate: All data collected in this study were generated as part of the diagnostic work-up and treatment of the patients. Permissions were obtained to access the data. Formal ethical approval was not required due to the retrospective nature of the study.

Consent for publication: Not applicable

Availability of data and material: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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

Funding: This research was supported by the Swiss National Science Foundation (NRP72 grant 407240_167054). The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' contributions: HN, BW and SS conceived the study. BW, SS and RP were responsible for the coordination of the study. AH, CL and KS were responsible for data collection, and SH and GS were responsible for the statistical analyses. BW and AH drafted the manuscript. BW, MM, HN, SS, CM, SH, GS, KS and CL edited the manuscript. All authors read and approved the final manuscript.

Acknowledgements: We are thankful for the participation of all private practices and clinics. This study was the doctoral thesis of A. Hubbuch.

References

1. Weese JS, Giguère S, Guardabassi L, Morley PS, Papich M, Ricciuto DR, et al. ACVIM consensus statement on therapeutic antimicrobial use in animals and antimicrobial resistance. J Vet Intern Med. 2015;29(2):487-98.
2. McEwen SA, Collignon PJ. Antimicrobial Resistance: a One Health Perspective. Microbiol Spectr. 2018;6(2).
3. Holmes AH, Moore LSP, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. The Lancet. 2016;387(10014):176-87.
4. Butaye P, van Duijkeren E, Prescott JF, Schwarz S. Antimicrobial resistance in bacteria from animals and the environment. Vet Microbiol. 2014;171(3-4):269-72.
5. Cusini A, Rampini SK, Bansal V, Ledergerber B, Kuster SP, Ruef C, et al. Different patterns of inappropriate antimicrobial use in surgical and medical units at a tertiary care hospital in Switzerland: a prevalence survey. PLoS One. 2010;5(11):e14011.
6. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM, Jr., et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. JAMA. 2016;315(17):1864-73.
7. Glinz D, Leon Reyes S, Saccilotto R, Widmer AF, Zeller A, Bucher HC, et al. Quality of antibiotic prescribing of Swiss primary care physicians with high prescription rates: a nationwide survey. J Antimicrob Chemother. 2017;72(11):3205-12.
8. Van Cleven A, Sarrazin S, de Rooster H, Paepe D, Van der Meeren S, Dewulf J. Antimicrobial prescribing behaviour in dogs and cats by Belgian veterinarians. Vet Rec. 2018;182(11):324.
9. Sarrazin S, Vandael F, Van Cleven A, De Graef E, De Rooster H, Dewulf J. The impact of antimicrobial use guidelines on prescription habits in fourteen Flemish small animal practices. Vlaams Diergeneeskundig Tijdschrift. 2017;86(3):173-82.
10. European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption. Sales of veterinary antimicrobial agents in 30 European countries in 2016. 2018. https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-30-european-countries-2016-trends-2010-2016-eighth-esvac_en.pdf. Accessed 19 Jun 2019.
11. De Briyne N, Atkinson J, Pokludová L, Borriello SP. Antibiotics used most commonly to treat animals in Europe. Vet Rec. 2014;175(13):325.

12. Buckland EL, O'Neill D, Summers J, Mateus A, Church D, Redmond L, et al. Characterisation of antimicrobial usage in cats and dogs attending UK primary care companion animal veterinary practices. Vet Rec. 2016;179(19):489.
13. Murphy CP, Reid-Smith RJ, Boerlin P, Weese JS, Prescott JF, Janecko N, et al. Out-patient antimicrobial drug use in dogs and cats for new disease events from community companion animal practices in Ontario. Can Vet J. 2012;53(3):291-8.
14. Hardefeldt LY, Holloway S, Trott DJ, Shipstone M, Barrs VR, Malik R, et al. Antimicrobial Prescribing in Dogs and Cats in Australia: Results of the Australasian Infectious Disease Advisory Panel Survey. J Vet Intern Med. 2017;31(4):1100-7.
15. Hardefeldt LY, Selinger J, Stevenson MA, Gilkerson JR, Crabb H, Billman-Jacobe H, et al. Population wide assessment of antimicrobial use in dogs and cats using a novel data source - A cohort study using pet insurance data. Vet Microbiol. 2018;225:34-9.
16. Hopman NEM, Hulscher MEJL, Graveland H, Speksnijder DC, Wagenaar JA, Broens EM. Factors influencing antimicrobial prescribing by Dutch companion animal veterinarians: A qualitative study. Prev Vet Med. 2018;158:106-13.
17. Mateus AL, Brodbelt DC, Barber N, Stärk KD. Qualitative study of factors associated with antimicrobial usage in seven small animal veterinary practices in the UK. Prev Vet Med. 2014;117(1):68-78.
18. Singleton DA, Sánchez-Vizcaíno F, Dawson S, Jones PH, Noble PJM, Pinchbeck GL, et al. Patterns of antimicrobial agent prescription in a sentinel population of canine and feline veterinary practices in the United Kingdom. Vet J. 2017;224:18-24.
19. Paterson DL. Resistance in gram-negative bacteria: enterobacteriaceae. Am J Med. 2006;119(6 Suppl 1):S20-8; discussion S62-70.
20. Zogg AL, Simmen S, Zurfluh K, Stephan R, Schmitt SN, Nüesch-Inderbinen M. High Prevalence of Extended-Spectrum beta-Lactamase Producing Enterobacteriaceae Among Clinical Isolates From Cats and Dogs Admitted to a Veterinary Hospital in Switzerland. Front Vet Sci. 2018;5:62.
21. Guardabassi L, Loeber ME, Jacobson A. Transmission of multiple antimicrobial-resistant Staphylococcus intermedius between dogs affected by deep pyoderma and their owners. Vet Microbiol. 2004;98(1):23-7.
22. Prescott JF, Boerlin P. Antimicrobial use in companion animals and Good Stewardship Practice. Vet Rec. 2016;179(19):486-8.

23. Grönlund Andersson U, Wallensten A, Haeggman S, Greko C, Hedin G, Hökeberg I, et al. Outbreaks of methicillin-resistant Staphylococcus aureus among staff and dogs in Swedish small animal hospitals. Scand J Infect Dis. 2014;46(4):310-4.
24. Guardabassi L, Larsen J, Weese JS, Butaye P, Battisti A, Kluytmans J, et al. Public health impact and antimicrobial selection of meticillin-resistant staphylococci in animals. J Glob Antimicrob Resist. 2013;1(2):55-62.
25. Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial-resistant bacteria. J Antimicrob Chemother. 2004;54(2):321-32.
26. Paul NC, Moodley A, Ghibaudo G, Guardabassi L. Carriage of methicillin-resistant Staphylococcus pseudintermedius in small animal veterinarians: indirect evidence of zoonotic transmission. Zoonoses Public Health. 2011;58(8):533-9.
27. Zhang XF, Doi Y, Huang X, Li HY, Zhong LL, Zeng KJ, et al. Possible Transmission of mcr-1–Harboring Escherichia coli between Companion Animals and Human. Emerg Infect Dis. 2016;22(9):1679-81.
28. Guardabassi L, Prescott JF. Antimicrobial stewardship in small animal veterinary practice: from theory to practice. Vet Clin North Am Small Anim Pract. 2015;45(2):361-76, vii.
29. Lloyd DH, Page SW. Antimicrobial Stewardship in Veterinary Medicine. Microbiol Spectr. 2018;6(3).
30. British Small Animal Veterinary Association (BSAVA), Small Animal Medicine Society (SAMSoc). Guide to Responsible Use of Antibacterials: PROTECT ME. 2018. https://www.bsavalibrary.com/content/book/10.22233/9781910443644#chapters. Accessed 18 Jun 2019.
31. Swedish Veterinary Association. Guidelines for the clinical use of antibiotics in the treatment of dogs and cats. 2009. https://svf.se/media/ahwpbt52/policy-ab-english-10b.pdf. Accessed 18 Jun 2019.
32. Holloway S, Trott D, Shipstone M, Barrs V, Malik R, Burrows M. AIDAP Antibiotic prescribing detailed guildelines. West Ryde NSW: Zoetis; 2013.
33. Federation of European Companion Animal Veterinary Associations (FECAVA). FECAVA Recommendations for Appropriate Antimicrobial Therapy. 2018. https://www.fecava.org/wp-content/uploads/2019/03/FECAVA_ABtherapy_2018_LR1.pdf. Accessed 17 Oct 2019.
34. Guidelines for the prudent use of antmicrobials in veterinary medicine. Official Journal of the European Union. 2015:C 299/7.

35. Jessen L, Damborg P, Spohr A, Goericke-Pesch S, Langhorn R, Houser G, et al. Antibiotic Use Guidelines for Companion Animal Practice (2 nd edition). Frederiksberg: Companion Animal Group, Danish Veterinary Association; 2018.
36. Weese JS. Investigation of antimicrobial use and the impact of antimicrobial use guidelines in a small animal veterinary teaching hospital: 1995–2004. J Am Vet Med Assoc. 2006;228(4):553-8.
37. Jessen LR, Sørensen TM, Lilja ZL, Kristensen M, Hald T, Damborg P. Cross-sectional survey on the use and impact of the Danish national antibiotic use guidelines for companion animal practice. Acta Vet Scand. 2017;59(1):81.
38. Gesellschaft Schweizer Tierärztinnen und Tierärzte (GST). GST-Positionspapier zu Antibiotika-Resistenzen. 2015. https://www.gstsvs.ch/fileadmin/media/pdf/Positionspapiere/GST_Positionspapier_AB-Resistenzen_2015.pdf. Accessed 22 Jul 2019.
39. Schweizerische Eidgenossenschaft. Strategie Antibiotikaresistenzen (StAR). https://www.star.admin.ch/star/de/home.html. Accessed 14 Oct 2019.
40. Bundesamt für Lebensmittelsicherheit und Veterinärwesen (BLV). ARCH-Vet - Bericht über den Vertrieb von Antibiotika und Antibiotikaresistenzen in der Veterinärmedizin in der Schweiz 2018. https://www.blv.admin.ch/blv/de/home/tiere/tierarzneimittel/antibiotika/vertrieb.html. Accessed 30 Jul 2019.
41. Institute of Veterinary Pharmacology and Toxicology. AntibioticScout.ch. 2019. https://www.vetpharm.uzh.ch/php/abscout.php. Accessed 27 Sep 2019.
42. Peter R, Müntener C, Demuth D, Heim D, Mevissen M, Schüpbach-Regula G, et al. [AntibioticScout: Online tool for antimicrobial stewardship in veterinary medicine]. Schweiz Arch Tierheilkd. 2016;158(12):805-10.
43. Peter R, Demuth D, Müntener C, Lampart M, Heim D, Mevissen M, et al. [AntibioticScout.ch: A decision supporting tool for antimicrobial stewardship: application to companion animal medicine]. Schweiz Arch Tierheilkd. 2017;159(10):525-33.
44. Schmitt K, Lehner C, Schuller S, Schüpbach-Regula G, Mevissen M, Peter R, et al. Antimicrobial use for selected diseases in cats in Switzerland. BMC Vet Res. 2019;15(1):94.
45. World Health Organisation (WHO). Critically Important Antimicrobials for Human Medicine, 6th Revision. 2019. https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/. Accessed 21 Jun 2019.

46. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; 2019.
47. Signorell A, et mult. al. DescTools: Tools for descriptive statistics. R package version 0.99.28. ed2019.
48. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software. 2015;67(1).
49. Kaki R, Elligsen M, Walker S, Simor A, Palmay L, Daneman N. Impact of antimicrobial stewardship in critical care: a systematic review. J Antimicrob Chemother. 2011;66(6):1223-30.
50. Ranji SR, Steinman MA, Shojania KG, Gonzales R. Interventions to Reduce Unnecessary Antibiotic Prescribing : A Systematic Review and Quantitative Analysis. Med Care. 2008;46(8):847-62.
51. Roque F, Herdeiro MT, Soares S, Teixeira Rodriques A, Breitenfeld L, Figueiras A. Educational interventions to improve prescription and dispensing of antibiotics: a systematic review. BMC Public Health. 2014;14:1276.
52. Vodicka TA, Thompson M, Lucas P, Heneghan C, Blair PS, Buckley DI, et al. Reducing antibiotic prescribing for children with respiratory tract infections in primary care: a systematic review. Br J Gen Pract. 2013;63(612):e445-54.
53. Ju NR, Koyfman A. Do oral antibiotics after incision and drainage of simple abscesses improve cure rates? Ann Emerg Med. 2015;65(1):112-3.
54. Rajendran PM, Young D, Maurer T, Chambers H, Perdreau-Remington F, Ro P, et al. Randomized, double-blind, placebo-controlled trial of cephalexin for treatment of uncomplicated skin abscesses in a population at risk for community-acquired methicillin-resistant Staphylococcus aureus infection. Antimicrob Agents Chemother. 2007;51(11):4044-8.
55. Hankin A, Everet WW. Are Antibiotics Necessary After Incision and Drainage of a Cutaneous Abscess? Ann Emerg Med. 2007;50(1):49-51.
56. Lappin MR, Blondeau J, Boothe D, Breitschwerdt EB, Guardabassi L, Lloyd DH, et al. Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. J Vet Intern Med. 2017;31(2):279-94.
57. De Briyne N, Atkinson J, Pokludová L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. Vet Rec. 2013;173(19):475.

58. Deuster S, Roten I, Muehlebach S. Implementation of treatment guidelines to support judicious use of antibiotic therapy. J Clin Pharm Ther. 2010;35(1):71-8.
59. Gerber B, Boretti FS, Kley S, Laluha P, Müller C, Sieber N, et al. Evaluation of clinical signs and causes of lower urinary tract disease in European cats. J Small Anim Pract. 2005;46(12):571-7.
60. Sævik BK, Trangerud C, Ottesen N, Sørum H, Eggertsdóttir AV. Causes of lower urinary tract disease in Norwegian cats. J Feline Med Surg. 2011;13(6):410-7.
61. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. J Am Vet Med Assoc. 2001;218(9):1429-35.
62. Weese JS, Blondeau J, Boothe D, Guardabassi LG, Gumley N, Papich M, et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. Vet J. 2019;247:8-25.
63. Eggertsdóttir AV, Lund HS, Krontveit R, Sørum H. Bacteriuria in cats with feline lower urinary tract disease: a clinical study of 134 cases in Norway. J Feline Med Surg. 2007;9(6):458-65.

Additional files

Additional file 1: Age distribution in 2016 and 2018 for cats with aURTD[a], FLUTD[b] and abscesses.

Parameter	aURTD[a]			FLUTD[b]			Abscesses		
	2016	**2018**		**2016**	**2018**		**2016**	**2018**	
	Median (range)	Median (range)	*p*-value	Median (range)	Median (range)	*p*-value	Median (range)	Median (range)	*p*-value
Number of cases	n = 219	n = 234		n = 328	n = 315		n = 209	n = 217	
Age[c] (years)	3 (0.04-19)	6 (0.08-21)	0.002	8 (0.17-21)	8 (0.25-22)	0.899	7 (0.50-18)	7 (0.03-20)	0.772

Data from cases from 2016 has been published previously (44); [a]aURTD, acute upper respiratory tract disease; [b]FLUTD, feline lower urinary tract disease; [c]Age is unknown for numbers not listed

Additional file 2: Antimicrobial prescriptions in 2016 and 2018 and separated for university hospitals and private practices.

Parameter		Total		University hospitals		Private practices	
		2016	**2018**	**2016**	**2018**	**2016**	**2018**
		% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]
Total number of cases		n = 776	n = 792	n = 173	n = 144	n = 603	n = 648
Antimicrobial treatment	Yes[b]	**75.0 [71.8-78.0]**	**66.7 [63.3-69.9]**	**67.1 [59.5-74.0]**	**49.3 [40.9-57.8]**	77.3 [73.7-80.6]	70.5 [66.8-74.0]
Details of antimicrobial treatment		n = 582	n = 528	n = 116	n = 71	n = 466	n = 457
Pot. aminopenicillin		55.5 [51.4-59.6]	60.8 [56.5-65.0]	85.3 [77.6-91.2]	84.5 [74.0-92.0]	48.1 [43.4-52.7]	57.1 [52.4-61.7]
3rd generation cephalosporin		26.1 [22.6-29.9]	19.5 [16.2-23.1]	7.8 [3.6-14.2]	2.8 [0.3-9.8]	**30.7 [26.5-35.1]**	**22.1 [18.4-26.2]**
Aminopenicillin		**19.6 [16.4-23.0]**	**27.8 [24.1-31.9]**	1.7 [0.2-6.1]	5.6 [1.6-13.8]	24.0 [20.2-28.2]	31.3 [27.1-35.8]
Fluoroquinolone		6.4 [4.5-8.7]	8.7 [6.4-11.4]	5.2 [1.9-10.9]	8.5 [3.2-17.5]	6.7 [4.6-9.3]	8.8 [6.3-11.7]
Tetracycline		5.0 [3.4-7.1]	6.6 [4.7-9.1]	2.6 [0.5-7.4]	4.2 [0.9-11.9]	5.6 [3.7-8.1]	7.0 [4.8-9.7]
1st generation cephalosporin		3.3 [2.0-5.1]	4.0 [2.5-6.0]	4.3 [1.4-9.8]	2.8 [0.3-9.8]	3.0 [1.7-5.0]	4.2 [2.5-6.4]
Others[c]		2.2 [1.2-3.8]	2.7 [1.5-4.4]	0.9 [0.0-4.7]	2.8 [0.3-9.8]	2.6 [1.3-4.5]	2.6 [1.4-4.5]
HPCIAs[d]	Yes[b]	33.0 [29.2-37.0]	28.8 [25.0-32.9]	12.9 [7.4-20.4]	12.7 [6.0-22.7]	38.0 [33.6-42.6]	31.3 [27.1-35.8]
Serial/combination therapy	Yes[b]	**17.0 [14.0-20.3]**	**27.7 [23.9-31.7]**	8.6 [4.2-15.3]	11.3 [5.0-21.0]	**19.1 [15.6-23.0]**	**30.2 [26.0-34.6]**

Non-overlapping 95% confidence intervals are shown in bold; Data from cases from 2016 has been published previously (44); [a]CI, 95% confidence interval; [b]Values for the category "no" (reference group) are not shown; [c]Others (antimicrobial classes used in ≤2% of prescriptions) included amphenicoles, lincosamides, macrolides, penicillins, nitroimidazoles; [d]HPCIAs, highest priority critically important antimicrobials

Additional file 3: Compliance with guidelines in 2016 and 2018 and separated for university hospitals and private practices.

Category	Total		University hospital		Private practices	
	2016	**2018**	**2016**	**2018**	**2016**	**2018**
	% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]	% [CI][a]
AMU[b] indicated	n = 186	n = 215	n = 71	n = 45	n = 115	n = 170
Guidelines followed	33.3 [26.6-40.6]	33.5 [27.2-40.2]	26.8 [16.9-38.6]	42.2 [27.7-57.8]	37.4 [28.5-46.9]	31.2 [24.3-38.7]
Guidelines not followed	66.7 [59.4-73.4]	66.5 [59.8-72.8]	73.2 [61.4-83.1]	57.8 [42.2-72.3]	62.6 [53.1-71.5]	68.8 [61.3-75.7]
a. Different dose/duration	11.3 [7.1-16.7]	15.3 [10.8-20.9]	2.8 [0.3-9.8]	8.9 [2.5-21.2]	16.5 [10.3-24.6]	17.1 [11.7-23.6]
b. Different antimicrobial class	50.0 [42.6-57.4]	42.8 [36.1-49.7]	**67.6 [55.5-78.2]**	**33.3 [20.0-49.0]**	39.1 [30.2-48.7]	45.3 [37.7-53.1]
c. Unjustified non-use	5.4 [2.6-9.7]	8.4 [5.0-12.9]	2.8 [0.3-9.8]	15.6 [6.5-29.5]	7.0 [3.1-13.2]	6.5 [3.3-11.3]
AMU[b] not indicated	n = 292	n = 248	n = 90	n = 74	n = 202	n = 174
Guidelines followed	**35.6 [30.1-41.4]**	**54.0 [47.6-60.4]**	55.6 [44.7-66.0]	73.0 [61.4-82.6]	**26.7 [20.8-33.4]**	**46.0 [38.4-53.7]**
Guidelines not followed	**64.4 [58.6-69.9]**	**46.0 [39.6-52.4]**	44.4 [34.0-55.3]	27.0 [17.4-38.6]	**73.3 [66.6-79.2]**	**54.0 [46.3-61.6]**
Treatment duration[c]	n = 471	n = 425	n = 109	n = 65	n = 362	n = 360
Guidelines followed	56.1 [51.4-60.6]	58.8 [54.0-63.5]	61.5 [51.7-70.6]	67.7 [54.9-78.8]	54.4 [49.1-59.6]	57.2 [51.9-62.4]
Guidelines not followed	43.9 [39.4-48.6]	41.2 [36.5-46.0]	38.5 [29.4-48.3]	32.3 [21.2-45.1]	45.6 [40.4-50.9]	42.8 [37.6-48.1]
a. Too long	41.0 [36.5-45.6]	36.9 [32.3-41.7]	36.7 [27.7-46.5]	18.5 [9.9-30.0]	42.3 [37.1-47.5]	40.3 [35.2-45.5]
b. Too short	3.0 [1.6-4.9]	4.2 [2.5-6.6]	**1.8 [0.2-6.5]**	**13.8 [6.5-24.7]**	3.3 [1.7-5.7]	2.5 [1.1-4.7]

Non-overlapping 95% confidence intervals are shown in bold; Data from cases from 2016 has been published previously (44); [a]CI, 95% confidence intervall; [b]AMU, antimicrobial use; [c]Treatment duration is unknown or not applicable for numbers not listed