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Valentina Foglia Manzillo , Maria Francesca Peruzy , Manuela Gizzarelli , Berardino Izzo , Paolo Sarnelli , Antonio Carrella , Giuseppina Vinciguerra , Claudia Chirollo , Nour el Houda Ben-Fayala , Ines Balestrino * , Gaetano Oliva

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Simple Summary: Companion animals are increasingly being recognized as important contributors to the spreading of antimicrobial resistant bacteria. The present work aimed to measure the antimicrobial drug prescribing in dogs and cats in the Campania region, Italy by analyzing the Veterinary Electronic Prescriptions (VEPs) between 2019 and 2020. The overall percentage of antibiotics prescribed in dog was 65.03 % and in cat 31.35 %. In dogs the 90.48 % of VEPs prescribed for systemic treatment included an antimicrobial Critically Important or Highly Important or Important for human medicine The main prescribed antimicrobials were the metronidazole-spiramycin (29.71%), amoxicillin-clavulanic (19.58%), enrofloxacin and cephalexin in dogs (16.52 %) and enrofloxacin (22.64%) and amoxicillin-clavulanic acid (21.37 %) in cats. Based on the results the wide use of broad-spectrum or second-line antibiotics is emerged together with the use of the critically important antimicrobials for human medicine.

Abstract: Companion animals are increasingly being recognized as important contributors to the spreading of antimicrobial resistant bacteria. The present work aimed to measure the antimicrobial drug prescribing in dogs and cats in the Campania region, Italy by analyzing the Veterinary Electronic Prescriptions (VEPs) between 2019 and 2020. The medical records associated with antimicrobial drug prescription were collected considering the drug delivery (systemic or local) and the rationale for the treatment chosen. In the period under investigation, 166879 drugs were prescribed of which 129116 (73.37 %) were antimicrobial. A total of 83965 (65.03 %) antibiotics were prescribed to dogs, 40477 (31.35 %) to cats, and 4674 (3.62 %) to other companion animals. In dogs the 90.48 % of VEPs prescribed for systemic treatment included an antimicrobial Critically Important or Highly Important or Important for human medicine (WHO, 2018). The most widely commonly prescribed class were fluoroquinolones. The main prescribed antimicrobials were the metronidazole-spiramycin (29.71%), amoxicillin-clavulanic (19.58%), enrofloxacin and cephalexin in dogs (16.52 %) and enrofloxacin (22.64%) and amoxicillin-clavulanic acid (21.37 %) in cats. Based on the results the wide use of broad-spectrum or second-line antibiotics is emerged together with the use of the critically important antimicrobials for human medicine.

Keywords: antimicrobials; companion animals; veterinary electronic prescription; antimicrobial resistance

1. Introduction

In the last years, Antimicrobial Resistance (AR), meaning "*the inability or reduced ability of an antimicrobial agent to inhibit the growth of a bacterium*" [1] represents one of the most important human- and animal health-threatening issues worldwide. After the discovery of penicillin in the 1940s more

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than 150 antibiotics have been developed and for most of them, resistance has been reported [2]. Therefore, drug resistance is a serious public health concern that threatens to undermine decades of medical progress because, in the last years, the discovery of novel antibiotics for humans and animals has slowed while antibiotic use to treat bacterial infection has increased. Moreover, bacteria can exhibit resistance to more than one antibiotic (multidrug-resistant bacteria) causing infection with more serious health impact [3].

The overuse and misuse of antibiotics in humans and food-producing animals are considered the main reasons for the worldwide increase in antibiotic resistance in bacteria [4]. Food-producing animals play an important role in the transmission of antibiotic-resistant bacteria (ARB) to humans and therefore the surveillance of antimicrobial use (AMU) in most countries has been focused on them while little emphasis has been laid on AMU surveillance in pet animals [5]. Companion animals are increasingly being recognized as important contributors to the spreading of resistant bacteria [6] and therefore with the recent EU Reg. 2019/6 on veterinary medicinal products, they have been included in the surveillance. However, in Europe, the surveillance intended specifically for companion animals will be applied only at the beginning of January 2029 [7].

The presence of resistant bacteria in pets may be due to the close relationship with humans which may lead to a bacterial exchange between them or to the excessive or unnecessary use of antibiotics to treat infectious diseases or even, non-infectious conditions (EMA Committee for Medicinal Products for Veterinary Use -CVMP -, 2018). Veterinarians, like other physicians, through correct and not excessive antibiotic prescription, play a pivotal role in the fight against antibiotic resistance [6]. Veterinarians should prescribe antibiotic therapy only to treat infectious diseases and should choose the antibiotic considering the target species and the pathology [2]. However, off-label use of antimicrobials in dogs and cats, including antimicrobial drugs for humans, is a common practice although there is still little scientific evidence supporting it [8]. Of particular concern is the prescription and the use of critically important antimicrobials (fluoroquinolones, third-generation cephalosporins, aminoglycosides, and carbapenems) in companion animals which may represent a significant risk for human health [5]. The continuous collection and analysis of data on the use of antimicrobials are essential to identify and implement interventions to prevent antimicrobial resistance in human and animal health [5]. To date, few data on antimicrobial use in dogs and cats are available [9]. Smaller-scale studies described patterns of antibiotic use based on data extracted from the clinical or prescribing records of veterinary hospitals and clinics [10]. These methods produce local insights into antibiotic practices but the use of teaching hospitals, in some cases, limits the generalizability of their findings.

With the 2017 European Law it has been introduced the electronic prescriptions for veterinary drugs and medicated feeding stuffs to control the distribution and administration of veterinary medicine along with the monitoring of the antimicrobial resistance in bacteria. In Italy, the national information system for the management of the electronic prescription of veterinary medicine has been developed by the general direction of animal health and veterinary medicine (AHVM) of the Italian Ministry of Health in collaboration with Experimental Zooprophylactic Institute of Abruzzo and Molise. The system is part of the broader simplification and digitalization project of the Italian government, *the 2015-2017 Simplification Agenda*, which, for the topics related to veterinary health and food safety, provides for the introduction of innovative solutions to facilitate both the National Health Service and the citizens in the fulfillment of regulatory obligations through the so-called "dematerialization". Veterinary Electronic Prescription (VEP), mandatory in Italy from 16 April 2019, represents an important modification of the previous operating model (paper-based) for the management and traceability of veterinary medicines (Legislative Decree No. 193/06 implementing an EU Directive of 2004).

The present work aimed to measure the antimicrobial drug prescribing in veterinary practice in dogs and cats in the Campania region, southern Italy by analyzing the VEPs between April 2019 to December 2020 considering the drug delivery (systemic or local) and the rationale for the treatment chosen.

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2. Materials and Methods

In this retrospective study, VEPs were collected from "VET INFO," an internet portal of the Ministry of Health, in which each veterinarian through a personal account profile enters data and issues the recipe (www.vetinfo.sanita.it). The system is divided into different types of prescriptions: companion animals including horses (not destinated to human consumption), food-producing animals, and veterinary drugs from farm-held stock supply or veterinary stock medicines.

Only records of dogs and cats associated with antimicrobial drug prescriptions in the Campania region, southern Italy, between 16 April 2019 to 31 December 2020 were included in the analysis.

The medical record of each dog and cat associated with antimicrobial drug prescription were collected considering the drug delivery (systemic or local) and the rationale for the treatment chosen: skin, respiratory, gastrointestinal, genitourinary, mammary, metabolic, cardiovascular, neurological, oncological, orthopedic, parasitic, ear and eye diseases, sepsis and general surgery. Data that did not belong to these categories were classified as "other."

The collected data were initially recorded using spreadsheet software (Microsoft® Excel® 2018) and differences in the frequency of antibiotics prescriptions were assessed using the chi-square test. A probability value of less than 0.05 ($p < 0.05$) was defined as statistically significant.

3. Results

In the period under investigation a total of 166879 drugs were prescribed through the VEPs to companion animals of which 129116 (73.37 %) were antimicrobial. A total of 83965 (65.03 %) antibiotics were prescribed to dogs, 40477 (31.35 %) to cats, and 4674 (3.62 %) to other companion animals not included in the present analysis.

3.1. Antimicrobial Agents in Canine Specie

In dogs, 62941 (74.96 %) and 21024 (25.04 %) antibiotics prescriptions and a total of 25 and 20 different molecules or combinations were prescribed for systemic and local therapy, respectively (Table 1 and 2).

Table 1. Antibiotics prescribed in dogs for systemic therapy to treat the following diseases: skin (SK), respiratory (RES), gastrointestinal (GI), genitourinary (GU), ophthalmology (OPH), orthopedic (ORT), mammary (MAM), sepsis (SEP), general surgery (SUR), metabolic (MET), cardiovascular (CAR), neurological (NEU), oncological (ONC) and parasitic (PAR). Data that did not belonged to these categories were classified as "other.".

Antibiotics	Rationale for the treatment chosen															
	SK	RES	GI	GU	OPH	ORT	MAM	SEP	SUR	MET	CAR	NEU	ONC	PAR	other	Tot.
Amikacin*								1				1			7	9
Amoxicillin*	9	5	2	5		3	1	4		1					68	98
Amoxicillin-Clavulanic acid*	1834	815	352	556	57	179	107	181	15	55	13	49	37	6	8068	12324
Ampicillin*															9	9
Benzylpenicillin*	1							1								2
Benzylpenicillin-Dihydrostreptomycin*	38	20	8	8		3	5	16	1	2		1		1	95	198
Cefadroxil**	714	166	31	95	12	76	30	45	1	9		35	11	1	1387	2613
Cefalexin**	1482	213	90	149	16	265	32	82	11	10	2	105	6	7	3961	6431
Cefovecin**	3		1												8	12
Chlortetracycline**	6		16		1			1		1				86	104	215
Clindamycin**	231	24	37	17	5	220	4	80		8		111	7	5	1011	1760
Doxiciclin	188	697	106	80	159	84	3	351		114	5	31	9	157	3260	5244
Enrofloxacin*	1004	571	188	1866	26	104	36	175	2	59	9	37	23	16	6283	10399
Formosulfathiazole **	5						1								2	8
Gentamicin*	1		1					1		1					6	10
Kanamycin*-Isopropamide iodide			71							1					91	163
Lincomycin** - Spectinomycin***	1			6		1		3				3			28	42

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Marbofloxacin*	325	105	35	416	31	45	9	48	1	6		48	4		1769	2842
Metronidazole***	3		104					1		2			1	11	209	331
Metronidazole***-spiramycin*	1421	247	5128	179	16	104	65	388	17	108	14	8	13	169	10822	18699
Oxytetraciclin	1	4		3				6		2				1	39	56
Pradofloxacin*	262	55	6	48	2	11	1	13				7	1		364	770
Sulphadiazine/sulphadimethoxaxole-Trimetoprim															2	2
Sulfametopyrazine	2	4	166			1				2				159	354	688
Tylosin*		2	1												13	16
Tot.	7531	2928	6343	3428	325	1096	294	1397	48	381	43	436	112	619	37960	62941

Antimicrobial classified by WHO (2018) as Critically Important*, Highly Important** and Important ***for human medicine.

Table 2. Antibiotics prescribed in dogs for local therapy to treat skin, ear, and eye disease.

Antibiotics	**Rationale for the treatment chosen**			
	skin disease	**ear disease**	**eye disease**	**Tot.**
Betamethasone/Clotrimazole/Gentamicin		1182		1182
Cloramphenicol/Betamethasone			8	8
Clostebol/Paromomycin/Prednisolone	114			114
diethanolamine fusidate/framycetin sulphate/nystatin/prednisolone		218		218
Econazole/Flumetasone/Gentamicin/Tetracaine	104	237		341
Enrofloxacin/Silver Sulfadiazine		797		797
Fluocinolone/Neomycin			175	175
Fusidic acid			16	16
Fusidic acid/Betamethasone	288			288
Gentamicin			39	39
Hydrocortisone aceponate / Miconazole nitrate / Gentamicin sulphate		4263		4263
Marbofloxacin/Clotrimazole/Dexamethasone		2058		2058
Marbofloxacin/Gentamicin sulfate/Ketoconazole/Prednisolone		810		810
Marbofloxacin/Ketokonazole/Prednisolone	11			11
Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate	1321	2107		3428
Orbifloxacin / Posaconazole / Mometasone fuorate		1322		1322
Rifaximin/ Colistin/ Miconazole/ carbarele/ triamcinolone		1230		1230
Terbinafine/Florfenicol/Betamethasone		3460		3460
Thiabendazole/Neomycin/Dexamethasone		633		633
Tobramycin			631	631
Tot.	1838	18317	869	21024

For systemic therapy, 31505 (50.05 %) VEPs contained one single-active compound and within them the most widely prescribed antimicrobial class was fluoroquinolones (44.47 %), while 31436 (49.95 %) combined two molecules (Table 3).

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Table 3. Antibiotics classes prescribed for systemic therapy in dogs and cats. VEP contained two active compounds belonging to two classes were denoted as "antimicrobial association".

Antimicrobial Classes	Prescriptions in Dogs (N.)	Prescriptions in Cats (N.)	Total (N.)
Aminoglycosides	19	4	23
b-Lactams	9165	4160	13325
Fluoroquinolones	14011	12419	26430
Lincosamides	1760	1225	2985
Macrolide	16	1	17
Nitroimidazoles	331	64	395
Sulfonamides	688	1258	1946
Tetracyclines	5515	5556	11071
Antimicrobial Associations	31436	12957	44393

A total of 56951 VEPs (90.48 %) included a antimicrobial classified by WHO (2018) either as Critically Important or Highly Important or Important for human medicine (Table 1).

In general, the most commonly prescribed drug was the Metronidazole-Spiramycine (n= 18699, 29.71 %) ($p < 0.05$) followed by Amoxicillin-Clavulanic acid (n = 12324, 19.58 %), Enrofloxacin (n = 10399, 16.52 %) ($p < 0.05$) and Cephalexin (n = 6431, 10.22 %) (Table 1).

Skin (n = 7531, 11.97 %) and gastrointestinal disease (n = 6343, 10.08 %) were the most frequent reason for the antimicrobial therapeutic prescription ($p < 0.05$). For skin diseases, the most common drugs prescribed were Amoxicillin-Clavulanic acid (n = 1834, 24.35 %) ($p < 0.05$), Cephalexin (n = 1482, 19.68 %) ($p < 0.05$), Metronidazole-Spiramycine (n= 1421, 18.88 %) ($p < 0.05$) and Enrofloxacin (n= 1004, 13.33 %) ($p < 0.05$). For gastrointestinal disease, Metronidazole-Spiramycine (n = 5128, 80.85 %) ($p < 0.05$) was the most used (Table 1).

Metronidazole-Spiramycine was also commonly prescribed for sepsis (n= 388, 27.77 %) ($p> 0.05$), surgery (n= 17, 35.42 %) ($p > 0.05$), cardiovascular disease (n= 14, 32.56 %) ($p> 0.05$) and parasitic diseases (n= 169, 27.30 %) ($p > 0.05$) (Table 1).

Amoxicillin-Clavulanic acid was commonly prescribed to treat respiratory diseases (n= 815, 27.83 %) ($p < 0.05$), mammary diseases (n= 107, 36.39 %) ($p < 0.05$), and oncological diseases (n= 37, 33.04 %) ($p < 0.05$). Doxycycline was commonly prescribed for ophthalmology disease (n= 159, 48.92 %) ($p < 0.05$), and metabolic disease (n= 114, 29.92 %) ($p > 0.05$).

Enrofloxacin (n= 1866, 54.43 %) for genitourinary diseases ($p < 0.05$), Cephalexin (n= 265, 24.18 %) for orthopedic disorders ($p < 0.05$), and Clindamycin (n= 111, 25.46 %) and Cephalexin (n= 105, 24.08 %) for neurological diseases ($p > 0.05$) (Table 1).

For the local therapy, the combination of Hydrocortisone aceponate / Miconazole nitrate / Gentamicin sulphate was the most prescribed (n = 4263, 20.28 %) ($p < 0.05$) followed by Terbinafine/Florfenicol/Betamethasone (n = 3460, 16.46 %) and Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate (n = 3428, 16.31 %) (Table 2).

Ear diseases (n = 18317, 87.12 %) was the most frequent reason for antimicrobial therapeutic prescription ($p < 0.05$), and Hydrocortisone aceponate / Miconazole nitrate / Gentamicin sulphate was the most prescribed (n = 4263, 23.27 %) ($p < 0.05$), followed by Terbinafine/Florfenicol/Betamethasone (n = 3460, 18.89 %). While Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate (n = 1321, 71.87 %) ($p < 0.05$) and Tobramycin (n = 631, 72.61 %) ($p < 0.05$) were the most frequently prescribed for skin and eye disease, respectively (Table 2).

3.3. Antimicrobial Agents in Feline Specie

In cats, 37644 (93.00 %) and 2833 (7.00 %) antibiotics prescriptions and a total of 23 and 19 different molecules or combinations were prescribed for systemic and local therapy, respectively (Table 4 and 5).

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Table 4. Antibiotics prescribed in dogs for systemic therapy to treat the following diseases: skin (SK), respiratory (RES), gastrointestinal (GI), genitourinary (GU), ophthalmology (OPH), orthopedic (ORT), mammary (MAM), sepsis (SEP), general surgery (SUR), metabolic (MET), cardiovascular (CAR), neurological (NEU), oncological (ONC) and parasitic (PAR). Data that did not belonged to these categories were classified as "other.".

Antibiotics	Rationale for the treatment chosen															
	SK	RES	GI	GU	OPH	ORT	MAM	SEP	SUR	MET	CAR	NEU	ONC	PAR	other	Tot.
Amikacin*			1												1	2
Amoxicillin*	73	71	20	17	4	5	4	3		4		4	14	7	290	516
Amoxicillin-clavulanic acid*	996	1158	234	508	55	107	21	188	5	34	1	7	18	9	4703	8044
Benzylpenicillin-Dihydrostreptomycin	*	9	2	2	1			5							39	60
Cefadroxil**	235	106	16	58	2	9	5	17	2	9	1	1	1	3	462	927
Cefalexin**	454	287	37	95	10	58	10	50	1	8		5	2	3	1669	2689
Cefovecin**	2	1	1					1					1		21	27
Ceftiofur**															1	1
Chlortetracycline**	1	3	25											134	124	287
Clindamycin**	133	44	19	5	6	84		58		7		53	5	10	801	1225
Doxiciclin	90	1376	105	102	96	17	4	247		95	6	8	4	52	3049	5251
Enrofloxacin*	747	825	203	1832	23	75	11	161	6	32	1	12	1	9	4925	8863
Formosulfathiazole **	3														3	6
Gentamicin*															2	2
Kanamycin*-Isopropamide iodide			95							1				1	88	185
Lincomycin** - Spectinomycin***				5				1								6
Marbofloxacin*	115	104	39	303	14	16	1	19		8		5	1		961	1586
Metronidazole***	1	1	18				1			1					42	64
Metronidazole***-Spiramycin*	233	108	1356	24	8	29	14	109	2	34		3	5	70	2661	4656
Oxytetraciclin		1						2							15	18
Pradofloxacin*	213	398	44	220	18	38		67		3		1	1	2	965	1970
Sulfametopyrazine	2	52	342	3	1			1						297	560	1258
Tylosin*															1	1
Tot.	3300	4544	2557	3174	238	438	71	929	16	236	9	99	53	597	21383	37644

Antimicrobial classified by WHO (2018) as Critically Important*, Highly Important** and Important ***for human medicine.

Table 5. Antibiotics prescribed in cats for local therapy to treat skin, ear, and eye disease.

Antibiotics	Rationale for the treatment chosen			
	skin disease	ear disease	eye disease	Tot.
Betamethasone/Clotrimazole/Gentamicin		46		46
Clostebol/Paromomycin/Prednisolone	9			9
diethanolamine fusidate/framycetin sulphate/nystatin/prednisolone		33		33
Econazole/Flumetasone/Gentamicin/Tetracaine	24	42		66
Enrofloxacin/Silver Sulfadiazine		53		53
Fluocinolone/Neomycin			58	58
Fusidic acid			3	3
Fusidic acid/Betamethasone	27			27
Gentamicin			19	19
Hydrocortisone aceponate / Miconazole nitrate / Gentamicin sulphate		65		65
Marbofloxacin/Clotrimazole/Dexamethasone		56		56
Marbofloxacin/Gentamicin sulfate/Ketoconazole/Prednisolone		16		16
Marbofloxacin/Ketokonazole/Prednisolone	2			2
Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate	290	791		1081
Orbifloxacin / Posaconazole / Mometasone fuorate		25		25
Rifaximin/ Colistin/ Miconazole/ carbarele/ triamcinolone		171		171

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Terbinafine/Florfenicol/Betamethasone		40		40
Thiabendazole/Neomycin/Dexamethasone	402	337		739
Tobramycin			324	324
Tot.	754	1675	404	2833

For systemic therapy, 24687 (65.58 %) VEPs contained one single-active compound and within them the most widely prescribed antimicrobial class was fluoroquinolones (50.31 %), while 12957 (34.42 %) combined two molecules (Table 3).

In general, the most frequent antibiotics prescribed for systemic therapy were Enrofloxacin (n = 8863, 23.54 %) and Amoxicillin-Clavulanic acid (n = 8044, 21.37 %) ($p < 0.05$) (Table 4).

A total of 26270 VEPs (69.78 %) included a antimicrobial classified by WHO (2018) either as Critically Important or Highly Important or Important for human medicine (Table 4).

Respiratory disease (n = 4544, 12.07 %) followed by skin disease (n = 3300, 8.77 %) was the most common reason for drug prescriptions. Doxycycline (n = 1376, 30.28 %) and Amoxicillin-Clavulanic acid (n = 1158, 25.48 %) were the most prescribed drugs for respiratory diseases ($p < 0.05$) while Amoxicillin-Clavulanic acid (n = 996, 30.18 %) and Enrofloxacin (n = 747, 22.64 %) for skin disease ($p < 0.05$) (Table 4).

Metronidazole-Spiramycin (n = 1356, 53.03 %) ($p < 0.05$), Enrofloxacin (n = 1832, 57.72 %) ($p < 0.05$), Clindamycin (n = 53, 53.54 %) ($p < 0.05$), and Sulfametopyrazine (n = 297, 49.75 %) ($p < 0.05$) were commonly prescribed respectively for gastrointestinal, genitourinary, neurology and parasitic disease (Table 4).

Doxycycline was commonly prescribed for ophthalmology (n = 96, 40.34 %) ($p < 0.05$), metabolic (n = 95, 40.25 %) ($p < 0.05$), sepsis (n = 247, 26.59 %) ($p < 0.05$) and cardiovascular (n = 6, 66.67 %) ($p > 0.05$) diseases (Table 4).

Amoxicillin-Clavulanic acid (n = 107, 24.43 %) and Clindamycin (n = 84, 19.18 %) ($p < 0.05$) were the molecules most prescribed for orthopedic disorder, Amoxicillin-Clavulanic acid (n = 21, 29.58 %) and Metronidazole-Spiramycin (n = 14, 19.72 %) for mammary diseases ($p > 0.05$), Enrofloxacin (n = 6, 37.5 %) and Amoxicillin-Clavulanic acid (n = 5, 31.25 %) for general surgery ($p > 0.05$) and Amoxicillin-Clavulanic acid (n = 18, 33.96 %) and Amoxicillin (n = 14, 26.42 %) for oncological diseases ($p < 0.05$).

For the local therapy, the combination of Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate (n = 1081, 38.16 %) diseases ($p < 0.05$) and Thiabendazole/Neomycin/Dexamethasone (n = 739, 26.09 %) diseases ($p < 0.05$) were the most prescribed (Table 5).

Ear Disease was the most common reason for the antimicrobial therapeutic prescription (n = 1675, 59.12 %) diseases ($p < 0.05$) and Miconazole nitrate/Polymyxin B sulfate/Prednisolone acetate (n = 791, 47.22 %) ($p < 0.05$) was the most prescribed (Table 5).

Thiabendazole/Neomycin/Dexamethasone (n = 402, 53.32 %) ($p < 0.05$) and Tobramycin (n = 324, 80.20 %) ($p < 0.05$) were commonly prescribed for skin and eye disease, respectively (Table 5).

4. Discussion

In the present study a total of 129116 antibiotic were prescribed to companion animals between 2019 and 2020 in Campania Region. Over the two-year period, the percentage of antimicrobials prescribed out of the total drugs prescribed (73.73 %) was higher than those recorded at the University Veterinary Teaching Hospital (OVUD) in our previous research (41.6 %,) [10], then those recorded previously in another Italian study conducted at the hospital of the university of Pisa (30.6 %,) [11] and then those reported by Schnepf et al. [7] at a veterinary teaching hospital in Germany (17.83 %). Although it is speculative, based on the results of the present work the trend of prescribing antimicrobials is likely higher in the private veterinary practice. Indeed, in contrast with the studies of Chirollo et al. [10], Escher et al. [11], and Schnepf et al. [7] in which only animals referred to the hospitals were included in the analysis, in the present work VEPs of all practitioners working in Campania region were recorded providing a broader picture of antimicrobial prescription practices in companion animals.

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A higher number of antimicrobial prescriptions was found in dogs (n = 83965, 65.03 %) compared with cats (n = 40477, 31.35 %). This result is in contrast with those reported by Escher et al.[11] in which a significant higher percentage of antimicrobial prescriptions was recorded for cats (cats: 44.00% *vs* dogs: 27.3 %) and Murphy et al. [12] and Buckland et al. [13] in which studies a similar percentage of antimicrobial prescription was overserved between dogs and cats.

In general, most of VEPs contained one single-active compound and within them the most widely commonly prescribed class both in dogs and in cats were Fluoroquinolones (dogs = 44.47 %; cats = 50.31 %). The use of fluoroquinolones in dogs and cats that should be limited only to a second-line therapy was much more common in the present study than in any other study available in the literature therapy [10, 12, 14].

Furthermore, our study demonstrated that there was a widespread use of antimicrobial classified by WHO (2018) as critically important for human health (Tables 1 and 5). Unfortunately, the prescription of these antibiotics is common in the small veterinary practice [15]. This critical behavior is of particular concern for the risk of the emergence and transmission bacteria resistant to antimicrobials that are considered of a greatest importance for human medicine.

In general, the most prescribed drugs were the Metronidazole-Spiramycin, Amoxicillin-Clavulanic, Enrofloxacin and Cephalexin in dogs and Enrofloxacin and Amoxicillin-Clavulanic acid in cats. Results of the present work are in line with those reported in our previous research [10] in which, Cefalexin (18 %), Amoxicillin/Clavulanate (18 %) and Metronidazole-Spiramycine (10 %), resulted commonly prescribed in dog [10]. However, in this previous study the association of Cephalexin and Clindamycin that it was never recorded in the present work, was also highly prescribed (17 %). Concerning cats, Amoxicillin-Clavulanic acid (41%) and Enrofloxacin (17 %) were highly recorded as well in the research of Chirollo et al. [10]. Results of the present work are in contrast to those reported by Mouiche et al. [5] in Cameroon in which the most commonly used antimicrobials in dogs and cats were Sulfamethoxypyridazine-Trimethoprim, Benzylpenicillin-Streptomycin, and Marbofloxacin. Moreover, the third-generation cephalosporin Cefovecin, widely used in UK and Belgium in cats was not commonly prescribed in the present work [13, 14, 16].

In addition, it turned out that Metronidazole was used in combination with Spiramycin; antimicrobial association (such as Metronidazole-Spiramycin) are used in specific cases to obtain a synergistic effect, to allow lower doses of either active ingredient or to avoid the emergence of resistance [17]. In the present research it was the most frequent antibiotic prescribed in dogs for gastrointestinal, sepsis, cardiovascular and parasitic disease and for general surgery and in cats for gastrointestinal disease. Results are of particular concern since Metronidazole alone or in combination with Spiramycin may produce severe side effects in cats and dogs and therefore, prudent use is essential [7].

Potentiated penicillins (Amoxicillin-Clavulanic acid) and first-generation cephalosporins (such as Cephalexin) are used in veterinary medicine as first-line therapy. In the present research, Amoxicillin-Clavulanic acid was the most frequent antibiotic prescribed in dogs for skin, respiratory, mammary and oncological diseases and in cats for skin, mammary and oncological diseases and for orthopedic disorders. Amoxicillin-Clavulanic acid was also the most commonly used potentiated agent for both species (dogs: 44.68 %; cats: 28.97 %) in UK [13]. It is abroad spectrum and not expensive antimicrobial, and it is often used for suspected infection without culture and antibiogram. Cephalexin, commonly prescribed here during orthopedic disorders in dogs is generally used as relatively narrow-spectrum antimicrobial under current guidelines [10]. However, in the study of Chirollo et al. [10] in orthopedic diseases the association of Cefalexin and Clindamycin was preferred.

Interesting, the use Enrofloxacin that should be used in dogs and cats as second-line therapy was much more common in our research than in any other study available in the literature [5, 9, 13]. As reported by Lhermie et al. [15] Fluoroquinolones are used to treat urinary tract infections. Indeed, in the present study the Fluoroquinolones Enrofloxacin was commonly used for genitourinary diseases both in dogs and cats.

Skin diseases was one of the most common reasons for antimicrobial treatment in both dogs and cats. These results are in line with those reported by Mouiche et al. (2021). In the present work

Amoxicillin-Clavulanic acid was the most prescribed antimicrobial. Concerning cats, results are in line with those reported by Murphy et al. [12]. Whilst they are in contrast with those reported for dogs by Escher et al. [11] and Murphy et al. [12] in which the most common antibiotics prescribed in case of skin diseases were Cephalosporins. Skin disease are among the most common reason for consultation in small-animal practice and the use of topical medication instead of systemic medication should increase [18].

Even if the national guidelines promote topical rather than systemic antimicrobial use where appropriate, in the present study, a preferential use of a systemic therapy emerged. In general, the use of systemic treatments increases the exposure of the gut microbial population to antimicrobial and therefore increase the risk of the occurrence of antibiotic resistant bacteria [18].

Ear diseases were instead the most commonly reason for local antimicrobial therapeutic prescriptions in both dogs and cats. Different bacteria, such as *Pseudomonas, Proteus, Enterococcus, Streptococcus,* and *Corynebacterium* can cause ear infections. Acute and uncomplicated otitis externa can often be treated successfully with antibiotic and typically local therapy is preferred [19].

5. Conclusions

In conclusion, the main antimicrobials that were prescribed between the years 2019-2020 in Campania region were the Metronidazole-Spiramycin, Amoxicillin-Clavulanic, Enrofloxacin and Cephalexin in dogs and Enrofloxacin and Amoxicillin-Clavulanic acid in cats. Based on results the widely use of broad-spectrum or second line antibiotics is emerged. Focus should be on performing the proper diagnostic steps and the treatment of suspected infection without culture and antibiogram should be avoided along with the use of the critically important antimicrobials for human medicine. Moreover, further efforts must be made to decrease the overall use of systemic antibiotics in companion animals.

This evidence could be used by governing bodies to develop actions for a more stringent controls on the use of antimicrobials in veterinary practice.

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