



## OPEN ACCESS

## EDITED BY

Benito Soto-Blanco,  
Federal University of Minas Gerais, Brazil

## REVIEWED BY

Clara Marín,  
Universidad CEU Cardenal Herrera, Spain  
Irene Bueno,  
University of Bristol, United Kingdom

## \*CORRESPONDENCE

Ana M. Sahagún  
✉ amsahp@unileon.es  
Cristina López  
✉ clopcd@unileon.es

RECEIVED 27 October 2023

ACCEPTED 12 December 2023

PUBLISHED 08 January 2024

## CITATION

Romero B, Susperregui J, Sahagún AM, Fernández N, López C, de la Puente R, Altónaga JR and Díez R (2024) Drug prescription pattern in exotic pet and wildlife animal practice: a retrospective study in a Spanish veterinary teaching hospital from 2018 to 2022.

*Front. Vet. Sci.* 10:1328698.

doi: 10.3389/fvets.2023.1328698

## COPYRIGHT

© 2024 Romero, Susperregui, Sahagún, Fernández, López, de la Puente, Altónaga and Díez. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

# Drug prescription pattern in exotic pet and wildlife animal practice: a retrospective study in a Spanish veterinary teaching hospital from 2018 to 2022

Beatriz Romero<sup>1</sup>, Julen Susperregui<sup>2</sup>, Ana M. Sahagún<sup>1\*</sup>,  
Nélida Fernández<sup>1</sup>, Cristina López<sup>1\*</sup>, Raúl de la Puente<sup>1</sup>,  
José R. Altónaga<sup>3</sup> and Raquel Díez<sup>1</sup>

<sup>1</sup>Department of Biomedical Sciences, Veterinary Faculty, Institute of Biomedicine (IBIOMED), University of León, León, Spain, <sup>2</sup>Applied Mathematics, Department of Mathematics, University of León, León, Spain, <sup>3</sup>Department of Veterinary Medicine, Surgery and Anatomy, Director of the Veterinary Teaching Hospital of the University of León (HVULE), University of León, León, Spain

Exotic companion animals have had an important role in our society since ancient times. Preserving animal health is necessary to do a responsible use of veterinary medicines. This study aimed to describe the prescription patterns of drugs in exotic pets and wildlife animals attending the Veterinary Teaching Hospital of the University of León (HVULE). A retrospective study was carried out between 2018 and 2022. Birds were the largest group of exotic animals attending the HVULE. Visits were related to emergency reasons and for musculoskeletal disorders. One-third of the animals were eventually euthanised. Regarding pharmacological treatments, the most frequently active ingredients used were pentobarbital, isoflurane, meloxicam, and within antibiotics, marbofloxacin (category B in the classification of European Medicines Agency).

## KEYWORDS

antibiotic, prescription pattern, exotic animal, veterinary teaching hospital, wildlife animal

## 1 Introduction

The adjective *exotic* is a term with several definitions, all equally valid to define an *exotic animal*. However, there are other expressions more commonly used, such as non-traditional or non-domestic animals (1). The American Veterinary Medical Association (AVMA) considers *exotic companion animals* as all species that coexist with humans, both domestic and non-domestic, representing hundreds of animal species of reptiles, amphibians, birds and mammals, the Pisces group, and the phylum *Arthropoda* (2). In Spain, Royal Decree 630/2013, which regulates the Spanish catalog of invasive exotic species, defines an *exotic pet animal* as “an animal of non-native wildlife that is individually dependent on humans, lives with them and has assumed the habit of captivity” (3).

Although according to the AVMA, dogs and cats are by far the largest companion animal population in the United States, between 2017 and 2018, the ownership of other types of pets, such as fish, ferrets, rabbits, hamsters, guinea pigs, turtles, snakes, and lizards, has increased significantly (4). In Europe, the number of ornamental birds is estimated to be approximately

50 million, whereas ornamental fish are approximately 300 million, small mammals 27 million, and reptiles 8 million (5). In Spain, according to data from 2021, there are more than 29 million pets, including nearly 8 million fish, 5 million birds, 1.5 million reptiles, and 1.5 million small mammals (6). However, the recent Law 7/2023 on the Protection of the Rights and Welfare of Animals may change this trend in this country, as it prohibits “the keeping, breeding, trade, sale, offer for sale, exchange or donation and import or export as pets of individuals of species not included in a positive list of pets” (7), which has not yet established.

This growing demand for exotic animals poses new challenges for veterinarians, as they are expected to effectively care for, diagnose, and treat a huge variety of animal species. Specifically, in the case of the different groups of exotic animals, both companion and wild ones, their anatomy and physiology may vary enormously, and also the way in which disorders manifest themselves. This makes the selection and prescription of medicines for these patients a complex process, as pharmacokinetic, efficacy, and safety data are often lacking in exotic animal medicine (8). In many cases, this often leads to the use of drugs in an extralabel manner (9) and, consequently, to an increased risk of adverse effects.

In addition, exotic practitioners are aware that the prevalence of daily emergency events, particularly those resulting in death, is higher among exotic animals than with other species such as dogs or cats (2). Among the reasons that may explain this fact is that most exotic species, as prey animals, tend to mask their diseases. Furthermore, the interaction time of owners with these animals may not be as long as with a dog or cat. Moreover, the behavioral patterns indicative of pain or disease in these animal species are not well known, which may lead to treatment failure to provide help to the animal when it is essential (2).

Among global health problems, zoonosis and antimicrobial resistance best illustrate the *One Health* concept (10). This approach is a global strategy that recognizes the interdependence among human, animal, and environmental health (11, 12), and they should be considered as a whole (13), as animal health is fundamental to ensuring public health, food security and supply, the economy, and preservation of animal species (14). Moreover, these species may be a major source of zoonoses, especially in young children and immunocompromised people (15). As for antimicrobial resistance, several studies have pointed out that antimicrobials are not often used in companion animals according to European recommendations (16–21), thus favoring the development of resistance (22, 23). Recently, increasing attention has been paid to the role of companion animals as potential reservoirs of resistant and multi-resistant pathogens for humans (24–27) as we live in close contact with them (24–26). However, in exotic animal medicine little or no information is available on antimicrobial resistance. A study carried out in wildlife rescue centers revealed that birds may be housed for long periods of time and receive antimicrobial treatments, which could potentially lead to the acquisition and subsequent colonization by antimicrobial-resistant bacteria (28).

In veterinary medicine, drugs are available to preserve animal health provided they are used responsibly (14). Rational use of medicines is based on using the right drug, at the right dose and at the right cost, as described by World Health Organization (WHO) (29). In humans, the assessment of drug utilization patterns with WHO indicators is increasingly necessary to promote rational use of

medicines (30, 31). In veterinary practice, these indicators are not still defined, although antimicrobials are the drugs for which most progress has been made. In the European Union (EU), Regulation 2019/6 states that within 8 years from 28 January 2022, data on antimicrobial medicinal products should be collected from animals other than food-producing ones not later than in 2029 (32). More recently, Spanish regulations have had set a deadline to start the collection of pet data on 31 January 2025 (RD 666/2023) (33). As for exotic animals, information is scarce and scattered, often only as guidelines to manage a certain animal species, disorder, or pharmacological group (9, 34, 35), or related to common practice of veterinarians with a certain type of animals (8, 36) but not about the current consumption of drugs. Therefore, this study aimed to describe the prescription patterns of medicines in exotic pets and wildlife animals attending the Veterinary Teaching Hospital of the University of León (HVULE).

## 2 Materials and methods

### 2.1 Study site

The HVULE is the Veterinary Teaching Hospital of the Faculty of Veterinary at the University of Leon (Spain). The hospital is organized into two separate clinical departments according to the target species: small animals and large ones, both with their emergency facilities. In 2023, all the teaching staff were qualified veterinarians.

### 2.2 Study design and data collection

A retrospective study was designed to evaluate the drug prescription patterns in exotic pets and wildlife patients treated at the HVULE between 1 January 2018 to 31 December 2022.

Data of all exotic pets and wildlife (birds, mammals, and reptiles, both wild and kept animals) of the 5-year period were collected through an inductive method. All data used in this study were obtained by reviewing the individual medical records stored in GestorVet (GestorVet, Las Palmas de Gran Canaria, Spain), an online management software, one of the most widely used in veterinary clinics and hospitals in Spain. For each animal, the following data were collected: history number, year of clinical record, medical check-up, species, weight, anatomical system/organ involved, if hospitalization occurred and days of hospitalization, number of treatments and if euthanasia was applied, as well as the different treatments prescribed in the HVULE, route of administration, and dosage regimen. All medications were categorized according to the WHO anatomical-therapeutic-chemical veterinary (ATCvet) classification system (37). Any combination medicine (multicomponent products) was considered as a single medicine. The European Medicines Agency (EMA) Categorization of antibiotics for use in animals was used to classify antibiotics (Category A—Avoid; Category B—Restrict; Category C—Caution; Category D—Prudence) (38). Data were exported to Microsoft Access (Microsoft Office 2019). Patients whose medical records lacked essential information, those who died before or during consultation without having received treatment and those who did not receive any treatment were excluded.

The Strengthening the Reporting of Observational Studies in Epidemiology—Veterinary Extension (STROBE-Vet) Statement was used to report data (39).

## 2.3 Calculation of the administered daily amount

The administered daily amount (in grams) was also calculated for each given drug administration. For this purpose, the following formula was used:

$$\text{Administered Daily Amount (ADA)} = \text{Amount of drug} \times \text{Proportion of active ingredient in this drug}$$

## 2.4 Calculation of the prescription diversity

Prescription diversity (PD) is defined as “the frequency and variety with which a practice prescribes pharmaceutical classes (PC) within a determined pharmaceutical family (PF)” (40). It is calculated as follows, adjusted to a 0–1 scale where 1 represents maximal diversity:

$$\text{Prescription Diversity (PD)} = 1 - \frac{\sum np(np-1)}{NP(NP-1)}$$

np is the number of prescriptions of a particular PC within a PF, and NP is the total number of prescriptions within a PF.

## 2.5 Data management and statistical analysis

Data analysis was performed with the statistical package IBM SPSS Statistics 26 (IBM Corporation, Armonk, NY, United States). Descriptive statistics (frequencies, mean, standard deviation, ranges, and percentages with 95% confidence intervals) were used to analyse the study population. Odds ratio (OR) was calculated with their respective 95% confidence intervals (95% CI). Multivariable forward-step ordinal logistic regression analysis was conducted to assess the impact of each predictor on euthanasia and antibiotic prescriptions. A *p*-value of  $\leq 0.05$  was always considered as significant.

## 3 Results

Data were available from a total of 17,483 medical records registered in GestorVet for the 5-year period studied. Of those, 1,420 (8.1%) were exotic pets and wildlife animals. After applying exclusion criteria, 503 animals were included in the study, which received 1,081 medical treatments.

Table 1 summarizes the results of some background information about the animals assessed. Birds were the most frequently treated, being 247 (57.8%) birds of prey or raptors (order *Falconiformes*, *Accipitriformes*, and *Strigiformes*) and 180 (42.2%) synanthropic

TABLE 1 Background information of the exotic pets and wildlife animals visiting the HVULE (Spain) from 2018 to 2022.

Characteristics	Frequency (%) ( <i>n</i> = 503)	95% CI
<b>Year of clinical record</b>		
2018	43 (8.5)	0.061–0.110
2019	57 (11.3)	0.086–0.141
2020	131 (26.0)	0.222–0.299
2021	145 (28.8)	0.249–0.328
2022	127 (25.2)	0.215–0.290
<b>Hospital visit</b>		
Emergency	400 (79.5)	0.760–0.830
Medical check-up	97 (19.3)	0.158–0.227
Hospital discharge	3 (0.6)	0.000–0.013
Surgery	2 (0.4)	0.000–0.009
Image diagnosis	1 (0.2)	0.000–0.006
<b>Animal class</b>		
Birds	427 (84.9)	0.818–0.880
Mammals	71 (14.1)	0.111–0.172
Reptiles	5 (1.0)	0.001–0.019

CI, Confidence interval.

birds (order *Ciconiiformes*, *Columbiformes*, and *Apodiformes*). As for mammals, 32 were rodents (45.1%), 17 lagomorphs (23.9%), 15 mustelids (21.2%), 4 hedgehogs (5.6%), and 3 other animals (4.2%). Finally, all reptiles were chelonians (5 animals, 1%). Birds were 22 times more likely to have visited the hospital for an emergency than mammals (OR = 22.1; 95% CI: 12.1–40.6). The proportion of cases evaluated increased progressively over the study period approximately 195%, despite the COVID-19 pandemic. In addition, if an animal was admitted for emergency care, it was almost 4 times more probably to be hospitalized (OR = 3.8; 95% CI: 2.3–6.1), and approximately 2 times more likely to be euthanised (OR = 1.9; 95% CI: 1.2–3.2).

Table 2 shows the clinical characteristics of the animals attending the hospital. For those who were hospitalized, the length of stay was  $4.56 \pm 6.96$  days (range 1–71, median 2.0), and the mean administered treatments were  $2.15 \pm 1.02$  (range 1–7, median 2.0). Birds were again 3.4 times more probably to be hospitalized than mammals (OR = 3.4; 95% CI: 1.7–5.9) and 8.4 times more likely to be euthanised (OR = 8.4; 95% CI: 3.3–21.3). However, all animals undergoing surgery were mammals.

Table 3 displays the multivariate analysis carried out to identify those variables associated with euthanasia in exotic animals. Non-hospitalized, birds, emergency visits, and the existence of musculoskeletal disorders had a significant impact on euthanasia. In addition, there was a significant year-on-year increase of 2.1 (CI: 1.1–3.8; *p* = 0.019).

With respect to the treatments followed (*n* = 1,081), 1,069 (98.9%) were medications included in the ATCvet classification. Table 4 lists these treatments according to the first level of this classification, showing that nearly half of them belonged to group QN (Nervous system). When the fourth level was considered, the most commonly chemical/therapeutic subgroup was QB05BB (solutions affecting the

TABLE 2 Clinical characteristics of the exotic pets and wildlife animals visiting the HVULE (Spain) from 2018 to 2022.

Clinical characteristics	Frequency (%) (n = 503)	95% CI
<b>Anatomical system/organ affected</b>		
Musculoskeletal	297 (59.0)	0.547–0.633
Digestive	112 (22.3)	0.186–0.259
Sense organs	22 (4.4)	0.026–0.062
Respiratory	18 (3.6)	0.020–0.052
Nervous	13 (2.6)	0.012–0.040
Genitourinary	8 (1.6)	0.005–0.027
Infectious	7 (1.4)	0.004–0.024
Cardiovascular	2 (0.4)	0.000–0.009
Others*	24 (4.8)	0.029–0.066
<b>Euthanasia</b>		
No	332 (66.0)	0.619–0.701
Yes	171 (34.0)	0.299–0.381
<b>Hospitalization</b>		
No	247 (49.1)	0.447–0.535
Yes	256 (50.9)	0.465–0.553
<b>Hospitalization days (n = 256)</b>		
1–3	157 (61.3)	0.270–0.351
4–8	70 (27.3)	0.109–0.169
≥9	29 (11.3)	0.037–0.078
<b>Surgery</b>		
No	496 (98.6)	0.976–0.996
Yes	7 (1.4)	0.004–0.024
<b>Number of treatments</b>		
1	120 (23.9)	0.201–0.276
2	251 (49.9)	0.455–0.543
3	101 (20.1)	0.166–0.236
≥4	31 (6.1)	0.041–0.083

CI, Confidence interval. \* Others include those animals electrocuted or poisoned.

TABLE 3 Multivariate ordinal logistic regression analysis of factors relevant to being euthanised.

Variables	OR (95% CI)	p-value
Hospital visit (emergency)	4.615 (1.005–21.199)	0.049
Animal class (birds)	6.811 (1.108–41.871)	0.038
System affected (musculoskeletal)	31.72 (4.184–240.4)	0.001
Hospitalization	2510.2 (206.4–30529.9)	<0.001
Year	2.078 (1.126–3.838)	0.019

CI, Confidence interval; OR, Odds ratio.

electrolyte balance), which was used in 188 animals, followed by halogenated hydrocarbons (QN01AB,  $n = 186$ ), oxicams (QM01AC,  $n = 173$ ), and barbiturates (QN51AA) for animal euthanasia ( $n = 171$ ). Specifically for each drug (fifth-level code), pentobarbital was administered to 187 animals (171 for animal euthanasia and 16 for

sedation) followed by isoflurane ( $n = 184$ ), meloxicam ( $n = 173$ ), and electrolyte solutions ( $n = 153$ ). It should be highlighted that 171 animals were euthanised with drugs from group QN (Nervous system). The HVULE protocol for birds consisted of inhaled isoflurane (5%) and intracardiac pentobarbital (0.1 g/kg). For mammals, intramuscular dexmedetomidine (0.04 mg/kg) or acepromazine (0.1 mg/kg), intravenous propofol (3 mg/kg) and intravenous pentobarbital (2 mg/kg) were used with the same purpose.

In group QN (Nervous system), subgroup analgesics (QN02) were also used ( $n = 111$ ; 22.3%). In this case, all were opioids (QN02A), with a PD of 0.67. Parenteral buprenorphine (45.9%) was the main opioid employed (76.5% in birds and 23.5% in mammals), followed by tramadol (27.9%), butorphanol (22.5%), and methadone (3.6%). Butorphanol and methadone were only administered parenterally to birds and mammals, respectively, whereas tramadol was administered to both birds (90.3%) and mammals (9.7%) by parenteral (77.4%) or oral (22.6%) routes.

All prescriptions of the group QM (Musculoskeletal system) were non-steroidal anti-inflammatory drugs (NSAID), specifically meloxicam ( $n = 173$ ) and robenacoxib ( $n = 3$ ), with a PD for NSAID very small (0.03). Meloxicam was more commonly administered parenterally (79.2%) than orally (20.8%) and more frequently used in birds (85.5%) than mammals (14.5%). As for robenacoxib, this drug was administered only in mammals and by the parenteral route.

Group QJ01 *Antibacterials for systemic use* were used only in 12.5% of treatments, with a PD of 0.58. The most prescribed therapeutic subgroup was QJ01M *Quinolone and quinoxaline antibacterials* (Table 5), with marbofloxacin as the most used compound, followed by metronidazole.

According to the EMA Categorization of antibiotics for prudent and responsible use in animals (38), only 1 (0.7%) of the active ingredients administered were classified as Avoid; 103 (72.0%) as Restrict; 9 (6.3%) as Caution; and 30 (21.0%) as Prudence. Most antibiotics ( $n = 90$ ; 62.9%) were administered as parenteral treatments, followed by oral ( $n = 43$ ; 30.1%) and local treatments ( $n = 10$ ; 7.0%). The PD for all antibiotics was 0.63. Figure 1 shows the antibiotic prescriptions according to the EMA categorization and year of study. Altogether, 2.7 grams of antibacterials for systemic use was documented for exotic animals over the 5-year period (Table 6), with clear differences between birds and mammals. The quinolone and quinoxaline subgroup was the most prescribed one in both animal classes.

Table 7 summarizes the results of the multivariate analysis, identifying those variables associated with antibiotic prescription patterns in exotic animals. The need for hospitalization, being a mammal, non-emergency visits, and any condition different from digestive or musculoskeletal disorders had a significant impact on antibiotic prescription.

Furthermore, when comparing treatments with and without antibiotics, the likelihood of an antibiotic being administered parenterally was 1.8 times higher (OR = 1.8; 95% CI: 0.9–3.7;  $p = 0.119$ ) than topically. The same happened for the oral route, which was 5.2 times higher (OR = 5.2; 95% CI: 2.4–11.5;  $p < 0.001$ ) to be used than the topical one. Finally, if only the two main routes of administration were considered (oral and parenteral), antibiotics were 2.9 times more likely to be administered by the oral route than parenterally (OR = 2.9; 95% CI: 1.9–4.6;  $p < 0.001$ ).

TABLE 4 Anatomical groups (first-level ATCvet) prescribed among exotic animals.

ATCvet anatomical group	Frequency (%) ( <i>n</i> = 1,069)	95% CI
Group QA Alimentary tract and metabolism	10 (0.9)	0.004–0.015
Group QB Blood and blood-forming organs	196 (18.4)	0.160–0.207
Group QC Cardiovascular system	2 (0.2)	0.000–0.004
Group QD Dermatologicals	8 (0.7)	0.002–0.013
Group QG Genito urinary system and sex hormones	2 (0.2)	0.000–0.004
Group QH Systemic hormonal preparations, excluding sex hormones and insulins	13 (1.2)	0.006–0.019
Group QJ Antiinfectives for systemic use	133 (12.5)	0.105–0.144
Group QM Musculoskeletal system	176 (16.5)	0.142–0.187
Group QN Nervous system	497 (46.5)	0.435–0.495
Group QP Antiparasitic products, insecticides, and repellents	17 (1.6)	0.008–0.023
Group QS Sensory organs	4 (0.4)	0.000–0.007
<b>ATC anatomical group</b>		
Group S Sensory organs	11 (1.0)	0.004–0.016

CI, Confidence interval.

TABLE 5 J01 therapeutic subgroups (third-level group ATCvet) prescribed among exotic animals.

ATCvet therapeutic subgroup J01	Frequency (%) ( <i>n</i> = 133)	95% CI
Subgroup Q01C Beta-lactam antibacterials, penicillins	3 (2.3)	0.000–0.048
Subgroup Q01D Other beta-lactam antibacterials	4 (3.0)	0.001–0.059
Subgroup Q01E Sulfonamides and trimethoprim	13 (9.8)	0.047–0.148
Subgroup Q01F Macrolides, lincosamides and streptogramins	3 (2.3)	0.000–0.048
Subgroup Q01M Quinolone and quinoloxaline antibacterials	94 (70.7)	0.638–0.791
Subgroup Q01X Other antibacterials	16 (12.0)	0.065–0.176

CI, Confidence interval.

## 4 Discussion

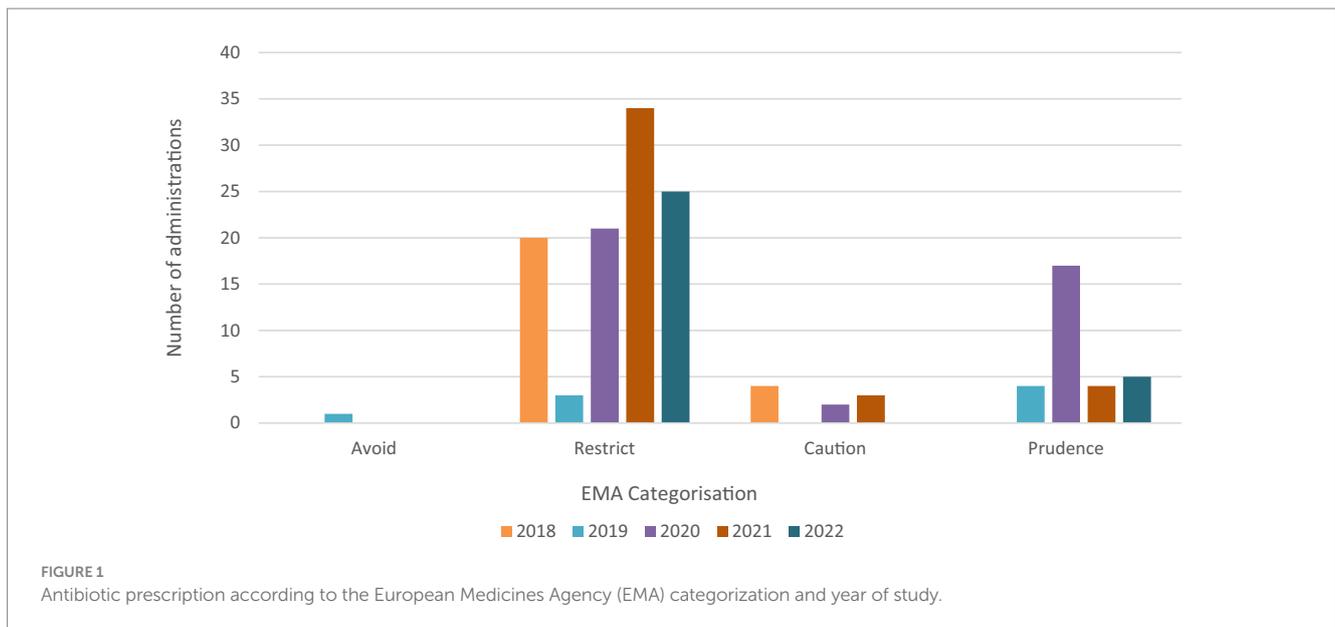
To our knowledge, this is the first study which describes the pattern prescription in exotic pets and wildlife animals in a Veterinary Teaching Hospital over a long period of study. Most of the studies found in the literature are surveys (36, 41), and others are focussed on all types of pets (dogs, cats, and exotics) (40, 42).

As shown before, birds were the largest group of exotic animals attending the hospital over the study period. In Europe, 15.7% of pets are birds; 9.5%, small mammals; and 3.7%, reptiles. Italy, Turkey, and Spain have the largest populations of ornamental birds; Russia, Germany, and France of small mammals and France and Spain of reptiles (5). In Spanish households, the dog is the preferred pet (21.9%) followed by the cat (8.2%). However, the presence of other pets, mainly birds and fish, has increased considerably in the last years (43). In addition, according to a survey conducted at the University of Dublin with exotic pet veterinarians, birds occupied the largest number of their visits (96.4%), followed by small mammals (89.3%) and reptiles (78.6%) (44). Dogs and cats visited the veterinary at least once a year (45, 46). In contrast, only 50% of exotic pet owners said that they have visited a veterinary clinic in 2019 (47).

We have observed that birds went to the hospital for an emergency much more than small mammals. According to veterinary professionals, the percentage of emergencies seen daily is much higher in exotic animals than in dogs and cats (2). Several reasons may explain these differences. In this sense, these species may mask their

illness until it is well advanced, and probably owners do not spend as much time observing their pets. In addition, they have specific environmental requirements, and their behavioral patterns of pain or illness are not still well understood (2).

Related to hospitalization, it should be taken into account that exotic animals usually visit the veterinarian when pathologies are much more advanced than in other domestic animals. This may be related to the lack of experience with these species, the equipment, or diagnostic tests specifically addressed to other animal species. In addition, the economic constraints of owners (44) for treatment or the lack of authorized medicines for these animals should be considered. In these situations, with very advanced pathological disorders and unfavorable prognosis, euthanasia must be done to reduce the animal's suffering (48). It is important to perform this procedure using techniques that minimize stress (48). For this purpose, in 2013 the AVMA published guidelines for the euthanasia of exotic species (48). Acceptable methods of euthanasia include intravenous administration if performed without causing fear or distress. They recommend intramuscular deep sedation or prior anesthesia in these species, as carried out in the HVULE. Some drugs included in the AVMA guideline are xylazine, opioid analgesics, dexmedetomidine (used for small mammals in the HVULE), alfaxalone, or midazolam, among others (48). Once the animal is unconscious, euthanasia solutions are administered intravenously (route of administration used in small mammals in the HVULE), intraosseous, intracardiac, or intrathoracic (the latter two used in birds in this hospital) (48). Euthanasia rates



were relatively higher (34.0%) compared to companion animals, such as dogs (1%), cats (2%), or rabbits (4%) (43), but more similar to values observed in backyard poultry (29.9%) (49). These authors related their euthanasia rates to the increased severity of the disorders in these animals (49).

Regarding pharmacological treatments, the most frequent group used was QN, with pentobarbital and isoflurane as the most often prescribed active ingredients, as one-third of the animals assessed in this study were euthanased. Opioids were also used quite frequently. Veterinarians prescribe and administer an important amount of opioid analgesics to treat pain in animals (50). Butorphanol is a synthetic opioid indicated for the treatment of acute pain in birds and small mammals (51, 52), recommended in birds as preoperative and postoperative analgesic medication (51–56), and for mild pain and short-term analgesia in small mammals (57, 58). As for buprenorphine, it is commonly administered in veterinary medicine for analgesia and sedation, although little information is available on its use in exotic animals. It is not recommended for pain control in reptiles, but used in birds, whereas in small mammals there is more research providing evidence of its analgesic and sedative effects (59).

The second most used group was QB (blood and blood-forming organs), in certain solutions affecting the electrolyte balance, which is in accordance with the fact that half of our patients were hospitalized and received fluid therapy. Fluid administration is essential to treat many medical conditions or provide support therapy to patients. Regarding routes of administration, subcutaneous fluids are a valid treatment of choice for hypovolemic avian and reptile patients. In particular, electrolyte solutions are an option for the majority of exotic animal fluid treatment needs (60).

Within the QM group, meloxicam was used quite often as a high number of patients had musculoskeletal disorders. This drug is commonly prescribed off-label for pain and inflammation in many exotic and zoo animals, including reptiles and birds (61). Nowadays, it is the current drug of choice due to its widespread use and low incidence of reported toxicity in exotic animal practices. In a study in which this drug was administered to over 700 captive birds (60 different species) in zoos, no mortality was observed (62). In addition, several studies reported no significant renal, gastrointestinal, or haemostatic

adverse events at the doses evaluated (63–66). Vultures are more sensitive to the renal adverse effects of several NSAIDs, except for meloxicam (67). The preference for this NSAID is also reflected in the low PD of our veterinary hospital for the population assessed.

Inappropriate use of antimicrobials is a potential threat to public health (34). Multidrug-resistant bacteria have been reported in several exotic animal species, such as methicillin-resistant staphylococci in rabbits and birds, extended-spectrum  $\beta$ -lactamase-producing enterobacteria in turtles and wild birds, or resistant *Escherichia coli* in wild birds (28, 68–72). Specifically in the Iberian Peninsula, *Pseudomonas* spp. showed the highest levels of resistance among birds, mammals, and reptiles, and multidrug resistance was also significant in *Enterobacterales* (73). In 2015, WHO adopted a global action plan to address antimicrobial resistance and proposed to ban the prophylactic use of antimicrobials in healthy animals (74). To this end, the EU has significantly restricted the prophylactic use of antimicrobials (32). Moreover, since 2014, the EMA has categorized antibiotics for veterinary use taking into account the public health risk of their use in animals due to the potential development of resistance, as well as the need for their use (38).

For those antibiotics belonging to category B (Restrict), we found that marbofloxacin was the most widely used in the HVULE. Fluoroquinolones are frequently used in birds, mainly due to their wide safety margin. However, injectable solutions are highly irritant and may cause tissue necrosis (75). In addition, some studies have recognized that fluoroquinolones have detrimental effects on reproduction in scavenging birds (76). In general, these antibiotics that reduce hatchability and total egg hatch, and cause joint deformities in chicks, increased embryonic heart rate and biochemical signs of stress (77). Since the 1980s, the livestock industry has been using fluoroquinolones as antimicrobials in food-producing animals (78, 79). A 1998–2001 survey of UK veterinarians on dermatological treatments showed that the most commonly used antibiotics in dogs, cats, and exotic animals were cefalexin, amoxicillin, and enrofloxacin (41). In another study carried out in the UK in 2016, fluoroquinolones were the most usually prescribed antibiotic group (49%) in rabbits and third-generation cephalosporins (36%) in cats and amoxicillin with clavulanic acid (29%) in dogs (40). In Germany, amoxicillin with

**TABLE 6** Amount of QJ01 Antibacterials for systemic use; QM01A Antiinflammatory and antirheumatic products, non-steroids, and QN02A Opioids prescribed in exotic animals.

	Birds amount in grams	Mammals amount in grams	Total amounts in grams (%)
<b>QJ01 Antibacterials for systemic use</b>			
Subgroup Q01C Beta-lactam antibacterials, penicillins			0.0936 (3.5)
Amoxicillin	–	0.0089	0.0089 (0.3)
Amoxicillin and beta-lactamase inhibitor	–	0.0029	0.0029 (0.1)
Piperacillin and beta-lactamase inhibitor	–	–	0.0820 (3.0)*
Subgroup Q01D Other beta-lactam antibacterials			0.1368 (5.0)
Cefovecin	–	0.1398	0.1368 (5.0)
Subgroup Q01E Sulfonamides and trimethoprim			0.3505 (12.9)
Trimethoprim	–	0.1054	0.1054 (3.9)
Sulfamethoxazole and trimethoprim	0.1980	0.0472	0.2452 (9.0)
Subgroup Q01F Macrolides, lincosamides, and streptogramins			0.0606 (2.2)
Tilmicosin	–	0.0145	0.0145 (0.5)
Clindamycin	0.0461	–	0.0461 (1.7)
Subgroup Q01M Quinolone and quinoxaline antibacterials			1.4679 (54.2)
Enrofloxacin	–	0.1169	0.1169 (4.3)
Marbofloxacin	1.2361	0.1147	1.3509 (49.8)
Subgroup Q01X Other antibacterials			0.6007 (22.2)
Metronidazole	0.4296	0.1711	0.6007 (22.2)
Total	1.9098	0.7181	2.7100 (100)
<b>QM01A Antiinflammatory and antirheumatic products, non-steroids</b>			
Meloxicam	0.1092	0.0081	0.1173 (96.6)
Celecoxib	–	0.0041	0.0041 (3.4)
Total	0.1092	0.0122	0.1214 (100)
<b>QN02A Opioids</b>			
Buprenorphine	0.4298	0.0188	0.4486 (61.5)
Tramadol	0.2535	0.0206	0.2741 (37.5)
Methadone	–	0.0052	0.0052 (0.7)
Butorphanol	0.0021	–	0.0021 (0.3)
Total	0.6854	0.0446	0.7300 (100)

\* Prescribed to a chelonian.

**TABLE 7** Multivariate ordinal logistic regression analysis of factors relevant to the antibiotic prescription pattern.

Variables	OR (95% CI)	p-value
Hospital visit (no emergency)	2.190 (1.469–3.261)	<0.001
Animal class (mammals)	2.075 (1.385–3.109)	<0.001
Organ affected (Others vs. musculoskeletal)	2.081 (1.379–3.135)	<0.001
Organ affected (Others vs. digestive)	2.452 (1.462–4.115)	0.001
Hospitalization	2.477 (1.642–3.732)	<0.001
Year	1.121 (0.969–1.310)	0.121

CI, Confidence interval; OR, Odds ratio.

clavulanic acid was the most prescribed drug in dogs (47.89%) and cats (48.15%) in 2017–18 (42). In contrast, in backyard poultry, the most prescribed antibiotic was enrofloxacin (40.6%), followed by tylosin (19.5%) and amoxicillin with clavulanic acid (12.1%).

Furthermore, 92.4% of those antibiotics prescribed for chickens were for systemic administration (oral or injectable) and only 5.2% for topical administration (49). Another survey among Swiss veterinarians on antibiotics usage in exotic pets showed that fluoroquinolones were the most commonly prescribed drugs in rabbits (82%), rodents (86%), birds (83%), and reptiles (97%) (36).

We have observed that antibiotics from category A (Avoid), which should be given to companion animals under exceptional circumstances, were used only once at the HVULE, whereas those belonging to category B (Restrict), whose use should be restricted in animals due to their critical importance in human medicine, were prescribed in the hospital quite frequently. However, antibiotics belonging to category C (Caution), which should be used only when there are no effective category D (Prudence) antimicrobials, are minimal. Finally, although category D is the first group of choice, their use is not very high in our study. The prescription of antimicrobials classified in EMA categories A and B should be based on antimicrobial susceptibility testing whenever possible

(38). Some countries, such as the Netherlands (80), Belgium (81), and Denmark (82), have national legislation that requires susceptibility testing to verify that no other antibiotics in categories C or D are clinically effective before an antimicrobial belonging to fluoroquinolones or third-/fourth-generation cephalosporins can be prescribed, and it is also the case in Spain (33).

As for the PD of antibiotics, our value was 0.63, which is much lower than those reported in 2016 for dogs (0.83) and cats (0.75), and very similar to that determined for rabbits (0.64) in the UK (40). In 2018, the prevalence of PD data increased in Germany for dogs and cats to 0.93 and 0.88, respectively (42). Our data may reflect that evidence-based guidelines for the treatment of infections, including antimicrobial stewardship, are not yet available for exotic animals. In the absence of appropriate veterinary medicines, common practice is based on personal experience of successful strategies implemented by individual veterinarians. As a result, off-label use of critical antimicrobials such as fluoroquinolones, aminopenicillins, third-generation cephalosporins, or macrolides is frequent in exotic pets, which underscores the need for guidance for prudent antibiotic use. The positive influence of these recommendations has already been demonstrated in dogs and cats (34).

Potential limitations of this study include the representativeness of the sample, and results may not be generalisable to other clinics or veterinary hospitals. Although significant efforts were made to identify animal species, demographic characteristics, clinical signs, and pharmaceutical prescriptions using manual and semi-automated methodologies, unclear or missing descriptions may have been overlooked by the authors. Additionally, the COVID-19 pandemic occurred during the period of study and may have had an impact on hospital visits. However, despite these limitations, our findings may help raise further discussions on the prudent use of several pharmacological groups in these types of animals, which are becoming more and more popular among the population.

This is the first study that describes the actual consumption of drugs in exotic pets and wild animals at a Veterinary Teaching Hospital. We have observed that the number of exotic animals increased over time, and they were mainly birds who went to the hospital for an emergency related to the QM group, and one-third were euthanised. As for medicines, almost half belonged to the QN group, with pentobarbital as the most used drug, followed by isoflurane and meloxicam. Regarding antibiotics, marbofloxacin (Category B—Restrict) was the most prescribed one.

Our study provides an insight into the prescription patterns in exotic animals. The findings of the study provide sufficient data to veterinary policymakers and education aimed at improving drug use practices in general and antimicrobial use, in particular in the profession.

## References

- Mitchell M, Tully T. History of exotic pets In: *Manual of exotic Pet practice*. St Louis: Elsevier Inc. (2009). 1–3.
- Brown SA, Nye RR. Essentials of the exotic Pet practice. *J Exot Pet Med.* (2006) 15:225–33. doi: 10.1053/j.jepm.2006.06.009
- Boletín Oficial del Estado. Real Decreto 630/2013, de 2 de agosto, por el que se regula el Catálogo español de especies exóticas invasoras. *España* (2013). Available at: <https://www.boe.es/buscar/act.php?id=BOE-A-2013-8565> (Accessed October 2, 2023).
- American Veterinary Medical Association. U.S. pet ownership statistics. (2019) Available at: <https://www.avma.org/resources-tools/reports-statistics/us-pet-ownership-statistics> (Accessed October 12, 2023).
- FEDIAF European Pet Food. Report the European Pet Food industry 2019. (2020). Available at: <https://www.fecava.org/news-and-events/news/fediaf-european-facts-figures-2019/> (Accessed October 12, 2023).
- Asociación Nacional de Fabricantes de Alimentos para Animales de Compañía. (2021). Available at: <https://www.anfaac.org/inicio/> (Accessed October 12, 2023).

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

Data used in this study are based on those generated for accounting and documentation purposes. Our research does not involve any regulated animals, and no scientific procedures of any kind were performed on animals. For this reason, formal approval by an ethics committee was not necessary under the provisions of the Spanish regulations.

## Author contributions

BR: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. JS: Formal Analysis, Writing – review & editing. AS: Data curation, Writing – review & editing. NF: Data curation, Writing – review & editing. CL: Project administration, Writing – review & editing. RP: Resources, Writing – review & editing. JA: Writing – review & editing. RD: Conceptualization, Methodology, Project administration, Writing – review & editing.

## Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

7. Boletín Oficial del Estado. Ley 7/2023, de 28 de marzo, de protección de los derechos y el bienestar de los animales. *España* (2023). Available at: <https://www.boe.es/buscar/doc.php?id=BOE-A-2023-7936> (Accessed October 6, 2023).
8. Di Girolamo N, Caron M, Brandao J, Reynders RM. Most veterinarians treating exotic animals use formularies to select drug dosages without consistently checking their sources. *J Am Vet Med Assoc.* (2022) 260:1–11. doi: 10.2460/javma.21.03.0116
9. Powers LV, Davidson G. Compounding and Extralabel use of drugs in exotic animal medicine. *Vet Clin North Am Exot Anim Pract.* (2018) 21:195–214. doi: 10.1016/j.cvx.2018.01.005
10. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: one health approach. *Vet World.* (2022) 15:743–9. doi: 10.14202/vetworld.2022.743-749
11. Kaplan B, Kahn LH, Monath TP. The brewing storm. *Vet Ital.* (2009) 45:9–18.
12. One Health Initiative. One health initiative will unite human and veterinary medicine. (2023). Available at: <https://onehealthinitiative.com/> (Accessed October 12, 2023).
13. Souza MJ. One health: Zoonoses in the exotic animal practice. *Vet Clin North Am Exot Anim Pract.* (2011) 14:421–6. doi: 10.1016/j.cvx.2011.05.007
14. Consejo General de Colegios Farmacéuticos. One Health: los medicamentos veterinarios. (2022). Available at: <https://www.farmaceticos.com/wp-content/uploads/2022/07/Punto-Farmacologico-162-Medicamentos-veterinarios.pdf> (Accessed September 26, 2023).
15. Chomel BB. Diseases transmitted by less common house pets. *Microbiol Spectr.* (2015) 3:10L5-0012-2015. doi: 10.1128/microbiolspec.iol5-0012-2015
16. Escher M, Vanni M, Intorre L, Caprioli A, Tognetti R, Scavia G. Use of antimicrobials in companion animal practice: a retrospective study in a veterinary teaching hospital in Italy. *J Antimicrob Chemother.* (2011) 66:920–7. doi: 10.1093/jac/dkq543
17. 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 Diergeneesk Tijdschr.* (2017) 86:173–82. doi: 10.21825/vdt.v86i3.16287
18. Mateus A, Brodbelt DC, Barber N, Stärk KDC. Antimicrobial usage in dogs and cats in first opinion veterinary practices in the UK. *J Small Anim Pract.* (2011) 52:515–21. doi: 10.1111/j.1748-5827.2011.01098.x
19. Singleton DA, Sánchez-Vizcaino 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. doi: 10.1016/j.tvjl.2017.03.010
20. Hopman NEM, Van Dijk MAM, Broens EM, Wagenaar JA, Heederik DJJ, Van Geijlswijk IM. Quantifying antimicrobial use in Dutch companion animals. *Front Vet Sci.* (2019) 6:158. doi: 10.3389/fvets.2019.00158
21. De Graef E, Decostere A, Devriese L, Haesebrouck F. Antibiotic resistance among fecal Indicator Bacteria from healthy individually owned and kennel dogs. *Microb Drug Resist.* (2004) 10:65–9. doi: 10.1089/107662904323047826
22. Rhys-Davies L, Ogden J. Vets' and Pet owners' views about antibiotics for companion animals and the use of phages as an alternative. *Front Vet Sci.* (2020) 7:513770. doi: 10.3389/fvets.2020.513770
23. Tompson AC, Mateus ALP, Brodbelt DC, Chandler CIR. Understanding antibiotic use in companion animals: a literature review identifying avenues for future efforts. *Front Vet Sci.* (2021) 8:719547. doi: 10.3389/fvets.2021.719547
24. Lloyd DH. Reservoirs of antimicrobial resistance in pet animals. *Clin Infect Dis.* (2007) 45:S148–52. doi: 10.1086/519254
25. Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial-resistant bacteria. *J Antimicrob Chemother.* (2004) 54:321–32. doi: 10.1093/jac/dkh332
26. Scott WJ. Antimicrobial resistance in companion animals. *Anim Health Res Rev.* (2008) 9:169–76. doi: 10.1017/S1466252308001485
27. Prescott J. Antimicrobial use in food and companion animals. *Anim Health Res Rev.* (2008) 9:127–33. doi: 10.1017/S1466252308001473
28. Prandi I, Bellato A, Nebbia P, Stella MC, Ala U, von Degerfeld MM, et al. Antibiotic resistant *Escherichia coli* in wild birds hospitalised in a wildlife rescue Centre. *Comp Immunol Microbiol Infect Dis.* (2023) 93:101945. doi: 10.1016/j.cimid.2023.101945
29. World Health Organization. *The rational use of drugs and WHO.* Nairobi: Dev Dialogue (1985). p. 1–4. Available at: <https://pubmed.ncbi.nlm.nih.gov/12341043/> (Accessed November 28, 2023).
30. World Health Organization. How to investigate drug use in health facilities: selected drug use indicators. (1993). Available at: [https://iris.who.int/bitstream/handle/10665/60519/WHO\\_DAP\\_93.1.pdf?sequence=1](https://iris.who.int/bitstream/handle/10665/60519/WHO_DAP_93.1.pdf?sequence=1) (Accessed September 1, 2023).
31. Laing RO, Hogerzeil HV, Ross-Degnan D. Ten recommendations to improve use of medicines in developing countries. *Health Policy Plan.* (2001) 16:13–20. doi: 10.1093/heapol/16.1.13
32. Europea Unión. Reglamento (UE) 2019/6 del Parlamento Europeo y del Consejo, de 11 de diciembre de 2018, sobre medicamentos veterinarios y por el que se deroga la Directiva 2001/82/CE. (2019). Available at: <https://www.boe.es/buscar/doc.php?id=DOUE-L-2019-80010> (Accessed September 7, 2023).
33. Boletín Oficial del Estado. Real Decreto 666/2023, de 18 de julio, por el que se regula la distribución, prescripción, dispensación y uso de medicamentos veterinarios. *España* (2023). Available at: <https://www.boe.es/buscar/doc.php?id=BOE-A-2023-16727> (Accessed July 14, 2023).
34. Broens EM, Van Geijlswijk IM. Prudent use of antimicrobials in exotic animal medicine. *Vet Clin North Am Exot Anim Pract.* (2018) 21:341–53. doi: 10.1016/j.cvx.2018.01.014
35. Zehnder A, Graham J, Antonissen G. Update on Cancer treatment in exotics. *Vet Clin North Am Exot Anim Pract.* (2018) 21:465–509. doi: 10.1016/j.cvx.2018.01.012
36. Hösli M, Overesch G, Willi B, Heim D, Hatt J-M. Survey on the use of antibiotics in exotic pets among Swiss veterinarians [article in German]. *Schweiz Arch Tierheilkd.* (2021) 163:227–37. doi: 10.48350/163644
37. World Health Organization Collaborating Centre for Drug Statistics Methodology. Guidelines for ATCvet classification 2023. (2023). Available at: [https://www.whocc.no/filearchive/publications/2023\\_atcvet\\_guidelines\\_web.pdf](https://www.whocc.no/filearchive/publications/2023_atcvet_guidelines_web.pdf) (Accessed November 27, 2023).
38. European Medicines Agency. Categorisation of antibiotics in the European Union. (2019). Available at: <https://www.ema.europa.eu/en/news/categorisation-antibiotics-used-animals-promotes-responsible-use-protect-public-animal-health> (Accessed July 6, 2023).
39. O'Connor AM, Sargeant JM, Dohoo IR, Erb HN, Cevallos M, Egger M, et al. Explanation and elaboration document for the STROBE-vet statement: strengthening the reporting of observational studies in epidemiology-veterinary extension. *J Vet Intern Med.* (2016) 30:1896–928. doi: 10.1111/jvim.14592
40. Singleton DA, Sánchez-Vizcaino F, Arsevska E, Dawson S, Jones PH, Noble PJM, et al. New approaches to pharmacovigilance for monitoring prescription frequency, diversity, and co-prescription in a large sentinel network of companion animal veterinary practices in the United Kingdom, 2014–2016. *Prev Vet Med.* (2018) 159:153–61. doi: 10.1016/j.prevetmed.2018.09.004
41. Hill PB, Lo A, Eden CAN, Huntley S, Morey V, Ramsey S, et al. Survey of the prevalence, diagnosis and treatment of dermatological conditions in small animals in general practice. *Vet Record.* (2006) 158:533–9. doi: 10.1136/vr.158.16.533
42. Schnepf A, Kramer S, Wagels R, Volk HA, Krienbrock L. Evaluation of antimicrobial usage in dogs and cats at a veterinary teaching Hospital in Germany in 2017 and 2018. *Front Vet Sci.* (2021) 8:689018. doi: 10.3389/fvets.2021.689018
43. de Agricultura Ministerio, Pesca, y Alimentación. Análisis y caracterización del sector de los animales de compañía-Informe de resultados. (2015). Available at: [https://www.mapa.gob.es/es/ganaderia/temas/produccion-y-mercados-ganaderos/20160222\\_informestudioparapublicar\\_tcm30-104720.pdf](https://www.mapa.gob.es/es/ganaderia/temas/produccion-y-mercados-ganaderos/20160222_informestudioparapublicar_tcm30-104720.pdf) (Accessed July 24, 2023).
44. Goins M, Hanlon AJ. Exotic pets in Ireland: 2. Provision of veterinary services and perspectives of veterinary professionals' on responsible ownership. *Ir Vet J.* (2021) 74:13. doi: 10.1186/s13620-021-00191-5
45. Day MJ, Horzinek MC, Schultz RD, Squires RA. WSAVA guidelines for the vaccination of dogs and cats. *J Small Anim Pract.* (2016) 57:E1–E45. doi: 10.1111/jsap.2.12431
46. Anvik JO. Acetaminophen Toxicosis in a cat. *Can Vet J.* (1984) 25:445–7.
47. Goins M, Hanlon AJ. Exotic pets in Ireland: 1. Prevalence of ownership and access to veterinary services. *Ir Vet J.* (2021) 74:14. doi: 10.1186/s13620-021-00190-6
48. American Veterinary Medical Association. AVMA guidelines for the euthanasia of animals. (2020). p. 1–121. Available at: <https://www.avma.org/sites/default/files/2020-02/Guidelines-on-Euthanasia-2020.pdf> (Accessed July 18, 2023).
49. Singleton DA, Ball C, Rennie C, Coxon C, Ganapathy K, Jones PH, et al. Backyard poultry cases in UK small animal practices: demographics, health conditions and pharmaceutical prescriptions. *Vet Record.* (2021) 188:e71–e282. doi: 10.1002/vetr.71
50. Clarke DL, Drobatz KJ, Korzekwa C, Nelson LS, Perrone J. Trends in opioid prescribing and dispensing by veterinarians in Pennsylvania. *JAMA Netw Open.* (2019) 2:e186950. doi: 10.1001/jamanetworkopen.2018.6950
51. Pollock C. Postoperative management of the exotic animal patient. *Vet Clin North Am Exot Anim Pract.* (2002) 5:183–212. doi: 10.1016/S1094-9194(03)00053-7
52. Hawkins MG. The use of analgesics in birds, reptiles, and small exotic mammals. *J Exot Pet Med.* (2006) 15:177–92. doi: 10.1053/j.jepm.2006.06.004
53. Sladky K, Krugner-Higby L, Meek-Walker E, Heath T. Serum concentrations and analgesic effects of liposome-encapsulated and standard butorphanol tartrate in parrots. *Am J Vet Res.* (2006) 67:775–81. doi: 10.2460/ajvr.67.5.775
54. Paul-Murphy JR, Krugner-Higby LA, Tourdot RL, Sladky KK, Klauer JM, Keuler NS, et al. Evaluation of liposome-encapsulated butorphanol tartrate for alleviation of experimentally induced arthritic pain in green-cheeked conures (*Pyrrhura molinae*). *Am J Vet Res.* (2009) 70:1211–9. doi: 10.2460/ajvr.70.10.1211
55. Riggs S, Hawkins M, Graigmill A, Kass P. Pharmacokinetics of butorphanol tartrate in red-tailed hawks (*Buteo jamaicensis*) and great horned owls (*Bubo virginianus*). *Am J Vet Res.* (2008) 69:596–603. doi: 10.2460/ajvr.69.5.596
56. Hawkins M, Sanchez-Migallon D, Beaufrère H, Lennox A, Carpenter J. Chapter 5:birds In: JW Carpenter, editor. *Exotic Anima Formulary* (2018). 167–375.
57. Sharp J, Zammitt T, Azar T, Lawson D. Recovery of male rats from major abdominal surgery after treatment with various analgesics. *Contemp Top Lab Anim Sci.* (2003) 42:22–7.

58. Garner H, Burke T, Lawhotn D, Storer J, Wssinger W. Butorphanol-mediated antinociception in mice: partial agonist effects and mu receptor involvement. *J Pharmacol Exp Ther.* (1997) 282:1253–61.
59. Rockwell K. Buprenorphine. *J Exot Pet Med.* (2019) 30:12–6. doi: 10.1053/j.jepm.2018.10.002
60. Parkinson L. Fluid therapy in exotic animal emergency and critical care. *Vet Clin North Am Exot Anim Pract.* (2023) 26:623–45. doi: 10.1016/j.cvex.2023.05.004
61. Papich MG. Papich handbook of veterinary drugs. 5 (2020). Available at: <https://www.sciencedirect.com/book/9780323709576/papich-handbook-of-veterinary-drugs> (Accessed July 13, 2023).
62. Cuthbert R, Parry-Jones J, Green RE, Pain DJ. NSAIDs and scavenging birds: potential impacts beyond Asia's critically endangered vultures. *Biol Lett.* (2006) 3:90–3. doi: 10.1098/rsbl.2006.0554
63. Desmarchelier M, Troncy E, Fitzgerald G, Lair S. Analgesic effects of meloxicam administration on postoperative orthopedic pain in domestic pigeons (*Columba livia*). *Am J Vet Res.* (2012) 73:361–7. doi: 10.2460/ajvr.73.3.361
64. Pereira M, Werther K. Evaluation of the renal effects of flunixin meglumine, ketoprofen and meloxicam in budgerigars (*Melopsittacus undulatus*). *Vet Rec.* (2007) 160:844–6. doi: 10.1136/vr.160.24.844
65. Montesinos A, Ardiaca M, Juan-Sallés C, Tesouro MA. Effects of meloxicam on hematologic and plasma biochemical analyte values and results of histologic examination of kidney biopsy specimens of African grey parrots (*Psittacus erithacus*). *J Avian Med Surg.* (2015) 29:1–8. doi: 10.1647/2013-056
66. Sinclair KM, Church ME, Farver TB, Lowenstine LJ, Owens SD, Paul-Murphy J. Effects of meloxicam on hematologic and plasma biochemical analysis variables and results of histologic examination of tissue specimens of Japanese quail (*Coturnix japonica*). *Am J Vet Res.* (2012) 73:1720–7. doi: 10.2460/ajvr.73.11.1720
67. Swarup D, Patra RC, Prakash V, Cuthbert R, Das D, Avari P, et al. Safety of meloxicam to critically endangered Gyps vultures and other scavenging birds in India. *Anim Conserv.* (2007) 10:192–8. doi: 10.1111/j.1469-1795.2006.00086.x
68. Briscoe JA, Morris DO, Rankin SC, Hendrick MJ, Rosenthal KL. Methicillin-resistant *Staphylococcus aureus*-associated dermatitis in a Congo African grey parrot (*Psittacus erithacus erithacus*). *J Avian Med Surg.* (2008) 22:336–43. doi: 10.1647/2008-014.1
69. Loncaric I, Künzel F. Sequence type 398 methicillin-resistant *Staphylococcus aureus* infection in a pet rabbit. *Vet Dermatol.* (2013) 24:370–2. doi: 10.1111/vde.12023
70. Sousa M, Silva N, Igrejas G, Sargo R, Benito D, Gómez P, et al. Genetic diversity and antibiotic resistance among coagulase-negative staphylococci recovered from birds of prey in Portugal. *Microb Drug Resist.* (2016) 22:727–30. doi: 10.1089/mdr.2015.0266
71. Yilmaz EŞ, Dolar A. Detection of extended-spectrum  $\beta$ -lactamases in *Escherichia coli* from cage birds. *J Exot Pet Med.* (2017) 26:13–8. doi: 10.1053/j.jepm.2016.10.008
72. Cortés-Cortés G, Lozano-Zarain P, Torres C, Castañeda M, Moreno Sánchez G, Alonso CA, et al. Detection and molecular characterization of *Escherichia coli* strains producers of extended-spectrum and CMY-2 type beta-lactamases, isolated from turtles in Mexico. *Vector Borne Zoonotic Dis.* (2016) 16:595–603. doi: 10.1089/vbz.2014.1725
73. Muñoz-Ibarra E, Molina-López RA, Durán I, Garcias B, Martín M, Darwich L. Antimicrobial resistance in bacteria isolated from exotic pets: the situation in the Iberian Peninsula. *Animals.* (2022) 12:1912. doi: 10.3390/ani12151912
74. World Health Organization. Global action plan on antimicrobial resistance. *Sixty-Eight World Health Assembly.* (2015). Available at: <https://www.emro.who.int/health-topics/drug-resistance/global-action-plan.html> (Accessed September 9, 2023).
75. Yarto E. Farmacología en animales exóticos: ¿qué podemos usar y qué no? Congreso LAVECCS. Punta del Este (2017). Available at: <https://docplayer.es/54106620-Farmacologia-en-animales-exoticos-que-podemos-usar-y-que-no-10mo-congreso-laveccs-punta-del-este-uruguay-2017.html> (Accessed September 21, 2023).
76. Lemus JÁ, Blanco G, Arroyo B, Martínez F, Grande J. Fatal embryo chondral damage associated with fluoroquinolones in eggs of threatened avian scavengers. *Environ Pollut.* (2009) 157:2421–7. doi: 10.1016/j.envpol.2009.03.013
77. Hrubá H, Abdelsalam EEE, Anisimov N, Bandouchova H, Havelkova B, Heger T, et al. Reproductive toxicity of fluoroquinolones in birds. *Vet Res.* (2019) 15:209. doi: 10.1186/s12917-019-1957-y
78. Brown SA. Fluoroquinolones in animal health. *J Vet Pharmacol Ther.* (1996) 19:1–14. doi: 10.1111/j.1365-2885.1996.tb00001.x
79. Martinez M, McDermott P, Walker R. Pharmacology of the fluoroquinolones: a perspective for the use in domestic animals. *Vet J.* (2006) 172:10–28. doi: 10.1016/j.tvjl.2005.07.010
80. Ministry of Health, Welfare, and Sport. Animal health register. The Netherlands (2023). Available at: [https://wetten.overheid.nl/BWBR0035238/2023-01-01/#Hoofdstuk5\\_Paragraaf2\\_Artikel5.8](https://wetten.overheid.nl/BWBR0035238/2023-01-01/#Hoofdstuk5_Paragraaf2_Artikel5.8) (Accessed October 18, 2023).
81. Staatsblad Belgisch. Koninklijk besluit betreffende de voorwaarden voor het gebruik van geneesmiddelen door de dierenartsen en door de verantwoordelijken van de dieren. (2016). Available at: [https://etaamb.openjustice.be/nl/koninklijk-besluit-van-21-juli-2016\\_n2016024152.html](https://etaamb.openjustice.be/nl/koninklijk-besluit-van-21-juli-2016_n2016024152.html) (Accessed October 18, 2023).
82. Ministry of Food, Agriculture and, Fisheries of Denmark., Danish Veterinary and Food Administration. Distribution and use of veterinary medicinal products. (2019). Available at: <https://en.foedevarestyrelsen.dk/animals/animal-health/veterinary-medicine/distribution-and-use-of-veterinary-medicinal-products> (Accessed October 11, 2023).