Aus dem Department für Nutztiere und öffentliches Gesundheitswesen in der Veterinärmedizin der Veterinärmedizinische Universität Wien

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(Leiter: Univ.-Prof. Dr. med. vet. Thomas Wittek Dipl. ECBHM)

Evaluation of antimicrobial substances used for most common diagnoses in New World Camelids at the University Clinic for Ruminants, University of Veterinary Medicine, Vienna

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Ursa Selan

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Betreuer 1: Univ. Prof. Dr. med. vet. Thomas Wittek Dip. ECBHM

Klinik für Wiederkäuer Veterinärmedizinische Universität Wien

Betreuer 2: Dr. med vet Hund, Alexandra, Dip. ECBHM

Landwirtschaftliches Zentrum für Rinderhaltung, Grünlandwirtschaft, Milchwirtschaft, Wild und Fischerei Baden-Württemberg (LAZBW)

Gutachter: Priv.-Doz. Dr. Joachim Spergser, Dipl. ECVM

I would like to dedicate this work to my grandfather, who was very much looking forward to this journey but did not make it to the finish line with me.

List of abbrevations:

ASG	Arzneispezialitätenregister - Official Registry, Austrian medicinal product index
EMA	European Medicine Agency
i.m	Intramuscular
i.v	Intravenous
NWCs	New World Camelids
GMON	Gesundheitsmonitoring code key
TGD	Tiergesundheitsdienst - Animal Health Service
BMSGPK	Bundesministerium für Soziales, Gesundheit, Pflege und Konsumentenschutz - Federal Ministry for Social Affairs, Health, Care and Consumer Protection
IU	International unit
AMR	Antimicrobial resistance

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1 INTRODUCTION

New World Camelids (NWCs) belong to the suborder Tylopoda (“padded foot”) which is distinct from ruminants, who are in the suborder Ruminantia (Fowler 2008).

The popularity of NWCs is on the rise in Austria. Thirty years ago there were around 100 animals in the country. Nowadays, the total number of llamas and alpacas is estimated to be close to 10,000 (Rappersberger 2020). However, the exact number is unknown.

They were first used for breeding and their wool. Especially alpacas were almost exclusively bred for fibre production for centuries. Now they are also used for hiking and as trekking animals and play an important role as therapy animals. Some are kept as pets (Rappersberger 2020, Trah 2010). Besides being selective eating animals that do not pluck out grass but instead bite it off, and with sure footing that do not cause trampling damage to the ground, both species make for good landscape maintenance, for example on steep surfaces (Rappersberger 2018). The llamas hefty appearance and paddock behavior, such as alerting calls and defense strategies, make them a good addition to other protective measures for watching over a herd of sheep or poultry (Rappersberger 2020). These are reasons for the increasing popularity of llamas and alpacas in Austria.

Their rising numbers also mean increasing demands for treatment and care, and a higher number of patients are putting more pressure on the veterinary teams providing healthcare. Not much was known one or two decades ago when treating patients, and the literature was sparse and insufficient. Even though camelids are taxonomically different from ruminants, their rumination makes them functionally similar (Gauly 2002). So a lot of treatments and applying medicine was based on the principles applied to ruminant patients, especially small ruminants.

Research has been done since and there has been more literature published with information on procedures involving camelids as patients (Björklund et al. 2019, Cebra 2014c). But there is still limited information regarding the dosages for the medicine used. Moreover, there are no officially approved antimicrobial substances for camelids, so every medicine currently used is approved for other animal species. There is no drug officially registered for NWCs in Austria (BASG 2021).

1.1 NEW WORLD CAMELIDS IN AUSTRIA

Native to South America the NWCs evolved from the wild forms of Guanaco (Lama guanicoe) and Vicuña (Vicugna vicugna). They went through a domestication process and generations of selective breeding, eventually leading to the domesticated animals as which we know them now: llamas and alpacas (Lama glama and Vicugna pacos). Molecular studies have shown that llamas (Lama glama) and guanacos (Vicugna vicugna) fall under the genus llama. The species alpaca (Vicugna pacos) and vicuña (*Vicugna vicugna*) can be traced to the genus vicugna (Kadwell et al. 2001). Differences between llamas and alpacas are shown in Table 1.

There are two alpaca breeds, Huacaya alpaca and the Suri alpaca, with their fleece characteristics being the only difference between them (Hoffman and Baum 2006). Huacayas have crimpy, springy fibre, which grows out and gives them a fluffy, wavy look. (Hoffman and Baum 2006, Petty and Petty 2021). They represent around 90% of the alpaca population. The remaining 10% Suri alpacas have a shiny, flat and smooth coat (Rappersberger 2018, Spring Farm Alpacas 2019).

Even if considered resilient to diseases NWCs may have health issues, especially if the owner does not meet the animals' demands for feeding and housing (Wittek 2020). The conditions in their homeland differ from Austria's, which can lead to diseases (Wittek and Franz 2021). They are considered herd and prey animals, meaning their defence mechanism inherently works in a way to disguise signs of weakness or disease (Rappersberger 2020). This means that a lot of owners do not see the signs of illness and health deterioration until much later, especially if they do not observe their animals as often as they should. Thus warning signs of the first stages of an incoming sickness can be missed, and a lot of times the illness turns out to have been present much longer than originally presumed (Rappersberger 2020, Wittek 2020, Wittek and Franz 2021).

Table 1: Difference between llamas and alpacas (Rappersberger 2020)

	Llama	Alpaca
Head	▪ long ears, mostly arched ▪ long, narrow nose	▪ short, pointy symmetrical ears ▪ short, stout nose ▪ well-defined forehead
Body	▪ large ▪ longer, straight back; tail in line ▪ with back	▪ small ▪ prominently angular hind legs ▪ shorter, sloping back; tail sloped down ▪ from back
Withers height	▪ 105 - 125 cm	▪ 75 - 100 cm
Weight	▪ 125 - 175 kg	▪ 50 - 80 kg
Colours	▪ white, beige, brown, grey, black ▪ monochromatic, spotted, striped	▪ white, beige, brown, grey, black ▪ mostly monochromatic
Fibre	▪ double coated fleece, long coarse outer guard hair	▪ single coated fine fleece

1.2 ANTIMICROBIAL THERAPY IN CAMELIDS

Antimicrobials is a term for a wider range of agents that work against a broad spectrum of microbes, including: bacteria, fungi, viruses and protozoa (Giguère et al. 2013). The focus of the study was to evaluate the antibiotic therapy given to the patients at the University Clinic for Ruminants, so every time the word "antimicrobial" is used in this study, what is meant are substances with antibacterial properties.

Antimicrobial drugs with antibiotic properties are commonly used in veterinary medicine for treating diseases caused by bacteria. There are many different classes of antibiotics available for use in animals, including penicillins, cephalosporins, aminoglycosides, quinolones, sulfonamides, tetracyclines, amphenicols and macrolides (Boothe 2021). They are often categorized as either broad-spectrum or narrow-spectrum drugs. This means: they are either effective against a wide range of organisms or working specifically against a specific bacterial infection.

An initial categorisation of antibiotics by the World Health Organisation in 2014 proposed three categories for antibiotic classification (WHO 2014). The ones classified as CIA – Critically Important Antimicrobials are the ones most relevant for human health. So the European Medicines Agency (EMA) compiled their own updated list of categorised antibiotics, which served as guidelines for veterinary medicine (European Medicines Agency 2020). EMA then collaborated with an Antimicrobial Expert Group (AMEG), which was created in 2013 and published the first refined list on categorisation of antibiotics in the European Union in 2014. It included all antibiotic classes, now ranked in four groups and labelled A to D. Their most recent list was published in 2020 (EMA 2020, European Medicines Agency 2020).

Veterinarians are advised to be prudent in their use of antibiotics to protect public and animal health; unsuccessful and/or prolonged exposure to antibiotic treatments can result in antibiotic resistance, which presents a clear and present world-wide threat (Palma et al. 2020). Antimicrobial resistance (AMR) has been described as the ability of bacteria, parasites, viruses, and fungi to survive and spread despite treatment with specific and/or combination therapies that are normally used against them (Founou et al. 2016).

The greater goal is to prevent widespread — and often inappropriate — use of antimicrobial agents. This can be achieved with correct antibiotic treatment that depends on identifying the disease-causing agent and selecting the appropriate drug for treatment, using antibiotics for the shortest effective duration given a particular clinical syndrome, and using narrow-spectrum antibiotics whenever possible (Boothe 2021, Leekha et al. 2011). Prolonged empiric antimicrobial treatment without clear evidence of infection as well as excessive use of certain antimicrobial agents are to be avoided (Leekha et al. 2011).

1.3 GUIDELINES FOR THE USE OF ANTIMICROBIAL AGENTS IN AUSTRIA

In 2018 the Republic of Austria's Federal Ministry for Social Affairs, Health, Care and Consumer Protection (BMSGPK - Bundesministerium für Soziales, Gesundheit, Pflege und Konsumentenschutz) published official guidelines on the treatment of antibacterial substances in veterinary medicine in Austria (BMASGK 2018). It contains specific instructions for the successful prevention of infections as well as criteria for good veterinary practice such as making correct diagnoses (Figure 1). The document also lists all antimicrobial agents and their respective properties, indications for usage and against which bacteria they are effective, as well as the registration of each antibiotic medicine in Austria. Prior to this document the German Federal Chamber of Veterinarians published their "Guidelines for the prudent use of veterinary antimicrobial drugs", containing instructions for correct animal-specific antibiotic treatment (BTK 2015). Then the Austrian Veterinary Chamber (Österreichische Tierärztekammer) published their own document in 2019 together with the BMSGPK about dealing with antimicrobial substances (Österreichische Tierärztekammer 2019). All of these documents share the same important goal: to reduce abuse of antimicrobial substances and prevent the emergence of antibiotic resistance.

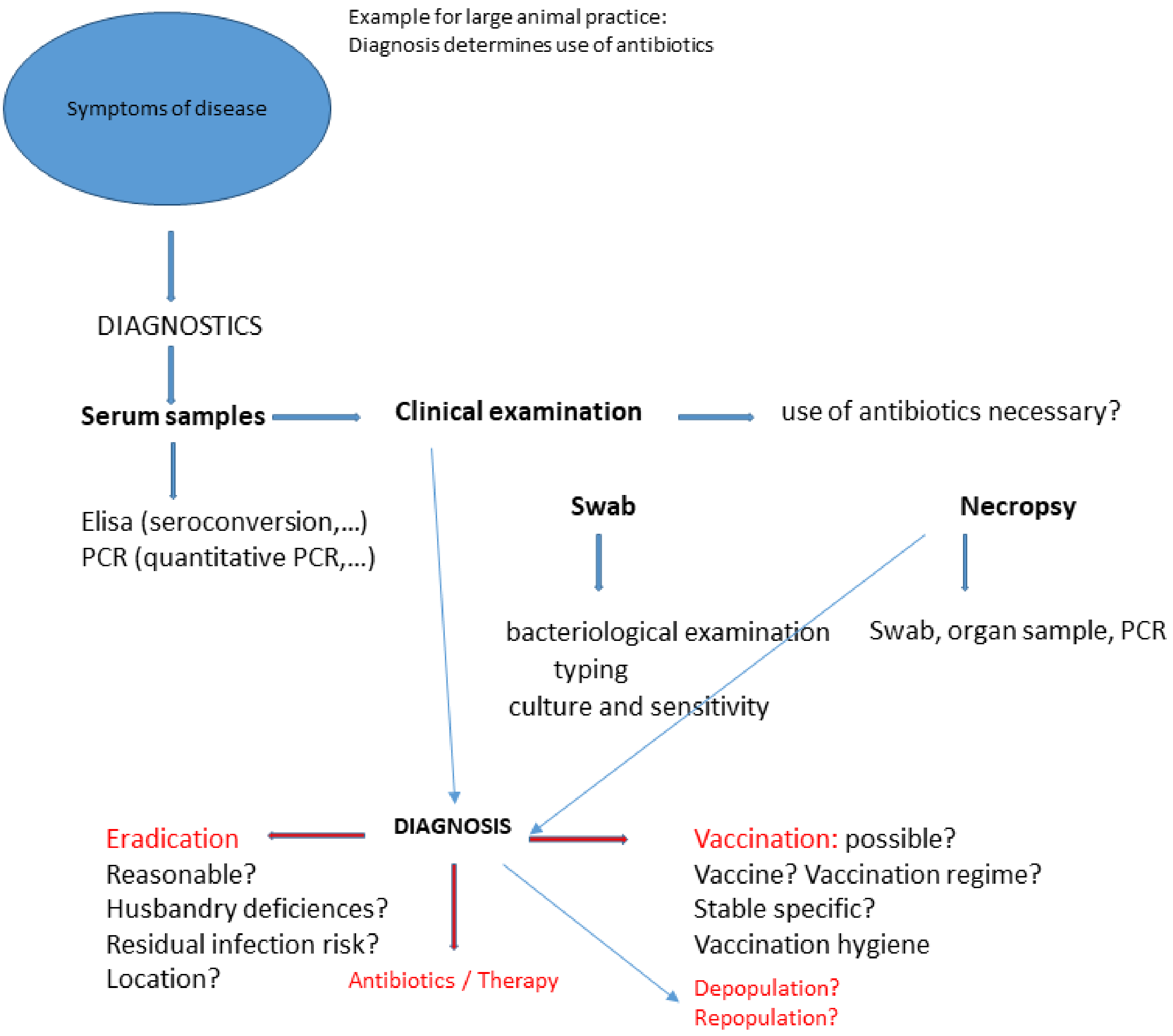

Figure 1: Example on correct setting of the diagnose and therapy in large animal practice (BMASGK 2018)

1.4 PHARMACEUTICAL GUIDELINES AND REGULATION FOR NWCs IN AUSTRIA

Llamas and alpacas are, even if seen as hobby animals, classified by law as food-producing animals in Austria, which means the veterinarian has to follow certain rules and regulations before administering medicine. This means that only active substances from (EU) regulation Nr. 37/2010 can be used. As there are no active substances officially approved for llama and alpaca patients, every veterinarian needs to start the treatment with a re-dedicated drug, following the rededication cascade. Withdrawal times also need to be regarded. As there is no dairy production from llamas and alpacas for human consumption only the meat withdrawal times need to be abided (Wittek and Franz 2021).

1.5 GOALS OF THE STUDY AND RESEARCH QUESTIONS

The aim of this retrospective study was to gather insight into antimicrobial treatment that New World camelids received as patients at the University Clinic for Ruminants, at the University of Veterinary Medicine, Vienna, Austria, in the years from 2005 till 2019.

The study engaged in answering the following questions:

- Are the recommendations on dealing with the antimicrobial substance respected and followed according to the published pharmaceutical guidelines?
- What were the most common diagnoses that required antimicrobial treatment in NWCs during the years 2005 till 2019?
- What were the antimicrobial classes mostly used during these years?
- Which dosages were used?
- How much antibiotics was used per year?
- Did each case have a plausible cause for antimicrobial therapy?

Hypotheses:

- Antimicrobial treatments for New World Camelids at the University Clinic for Ruminants – University of Veterinary Medicine, Vienna, Austria were justified according to established disease/diagnosis
- Application of antimicrobial drugs from group B (according to EMA classification) used in New World Camelids at the University Clinic for Ruminants – University of Veterinary Medicine, Vienna, Austria decreased over time according to the published guidelines

2 MATERIALS AND METHODS

2.1 PATIENTS AND DATA ACQUISITION - TIS

For the study, medical records of New World camelid patients at the University Clinic for Ruminants, University of Veterinary Medicine, Vienna in the years from 2005 till 2019 were used. Only those patients that received antimicrobial treatment were selected.

All data of the patients at the University Clinic for Ruminants was stored in a database named TIS (Tierspital - Informationssystem - Animal hospital system). In TIS all the information of the diagnosis, performed examinations, therapy and drugs used, dosages and the duration of treatment is stored. Information was gathered on the patients including the type of antibiotics used, how much and how many treatments the patient received.

2.2 WEIGHT

Most patients were weighed on admission, but 38% of the patients had no weight recorded. Approximated weight of those patients with no recorded information was compared to various articles including growth curves, following the growth of llamas an alpacas from month 0 to month 36 (Figure 2, Table 2 and Table 3)(Fowler 1998, Grund et al. 2018, Van Saun 2008).

After comparing the data gathered on their weight, the decision was made for purpose of the study to calculate the antibiotic therapy on approximated weight depending on the patient's age. For alpaca patients that were between one and two years of age, it was assumed the females weigh 50 kg and males weigh 60 kg. For those who were older than two years of age, it was presumed that the female patients weigh 60 kg and male patients 70 kg. As the vast majority of llama patients at the clinic were adult animals, the female patients were assumed to weigh 90 kg and males 120 kg.

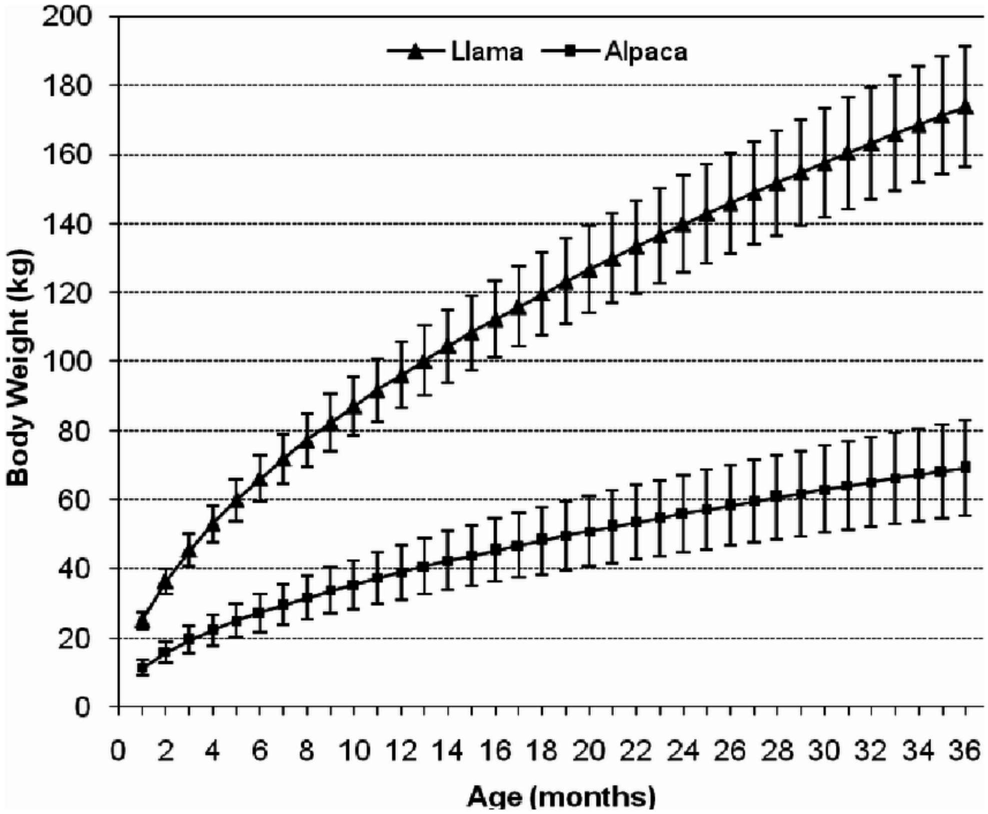

Figure 2: Growth curve of llama and alpaca based on their growth data (Van Saun 2008)

Table 2: Body weight of llama from birth till adulthood (Fowler 1998)

Llama	Male	Female
Weight at birth	8 - 18 kg	8 - 18 kg
Adult animals	130 – 243 kg	108 - 200 kg

Table 3: Body weight of alpaca from birth till adulthood (Fowler 1998)

Alpaca	Male	Female
Weight at birth	8 - 15 kg	8 - 15 kg
Adult animals	60 - 80 kg	Approx. 55 kg

2.3 DIAGNOSES

The patients of the University Clinic for Ruminants were admitted for various reasons. We included as diagnosis only the reasons for the administration of antimicrobial therapy. Other drugs used, such as pain medications and deworming medicine were not included.

For the diagnosis, the Gesundheitsmonitoring (GMON) code key (Table 4) was used, that was established for cattle. GMON code key is a part of a program by the Animal Health Service (Tiergesundheitsdienst – TGD). The program provides a tool to help monitor and record the health of cattle. The GMON diagnosis key classifies diagnoses in cattle with a number, according to the body system. For example, all of the diseases of the digestive system are united under one section and paired with numbers, according to the group they belong to. The diagnosis key starts with calf diseases, then follows with numbers for the digestive system, metabolic system, fertility and husbandry, udder, hoof and extremity diseases, airway and lungs, heart, bloodstream, blood and urinary diseases, then nervous system, skin and infectious diseases and finishes with miscellaneous, which includes numbers for various procedures and the description of conditions such as fever, weight loss etc. This study was a part of a larger project of the University Clinic for Ruminants where cattle, sheep, goats and camelids were included. The same diagnosis key was used in all species. As this diagnosis key was mainly focused on the diseases of cattle we included additional numbers, to account for diseases that are common in NWCs. The same codes were used in the evaluation of sheep and goats. An original GMON code key published by the TGD can be found in table 10 of the Annex.

Table 4: Adapted GMON diagnose key used in the study for most common diagnoses

Diagnosis code key GMON	
Calves (Cria in our case)	
11	Omphalitis
12	Umbilical hernia
17	Other calf diseases
171	Neutering
GI tract	
23	Compartment acidosis
26	Ileus
27	Other diseases of abdominal cavity
271	Peritonitis
273	Clostridium infection /Clostridium suspicion
28	Diseases of the mouth
281	Teeth extraction
29	Diseases of the oesophagus
Calving, Fertility	
41	Endometritis
45	Abortion and other disorders of gravidity
46	Dystocia
47	Injury during birth
99	Male genitalia
Udder	
52	Udder - chronic infection
Hoofs and extremities	
64	Fractures, dislocations and other limb injuries
68	Recumbency due to diseases of the locomotor system
Respiratory System	
71	Diseases of the upper respiratory system
72	Pulmonary inflammation
73	Other pulmonary diseases
Heart, Blood and Bloodstream, Urinary tract	
81	Heart diseases
82	Septicaemia, Anemia
88	Urinary obstruction, urolithiasis, diseases of the kidney and urinary tract, cystitis suspicion, ectopic ureter suspicion
CNS, Skin, Infection	
91	CNS disease
92	Diseases of the sensory organs
93	Parasites and skin infections
95	Other skin diseases
951	Abscess
952	Wounds, bite wounds, trauma
96	General infection
960	Tetanus
100	Zinc deficiency, zinc responsive dermatosis
Other	
3	Fever, feverish general diseases
0	No reason for antibiotic therapy
999	Perioperative infection prophylaxis
821	Mykoplasma haemolamae suspicion
1000	Palatoschisis

2.4 ANTIMICROBIAL CLASSIFICATION

Antimicrobial therapy used at the University Clinic for Ruminants was classified according to the European Medicines Agency - EMA classification system (categorisation of antibiotics used in animals), which now comprises four categories, using the letters from A to D (Figure 3).

Category A **Avoid**	**Category B** **Restrict**
▪ Antibiotics in this category are not authorised as veterinary medicines in EU ▪ Should not be used in food-producing animals ▪ May be given to companion animals under exceptional circumstances	▪ Antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health ▪ Should be considered only when there are no antibiotics in categories C or D that could be clinically effective ▪ Use should be based on antimicrobial susceptibility testing, wherever possible
Category C **Caution**	**Category D** **Prudence**
▪ For antibiotics in this category there are alternatives in human medicine ▪ For some veterinary indications, there are no alternatives belonging to Category D ▪ Should be considered only when there are no antibiotics in Category D that could be clinically effective	▪ Should be used as first line treatments, whenever possible ▪ As always, should be used prudently, only when medically needed

Figure 2: EMA categorisation of antimicrobials for use in animals (European Medicines Agency 2020)

2.5 DOSAGES

Two sources were used to determine the correct dosages of the drugs:

The Official Registry, Austrian medicinal product index (Austrian Federal Office for Safety in Health Care Austrian Medicines and Medical Devices Agency, ASG) (BASG 2021) where all the drugs that are registered in Austria are stored, together with their dosages and their proposed way of application. There are no official drugs and dosages registered for llamas and alpacas in Austria. All of the registered substances found in ASG are approved for cattle and sometimes for small ruminants. When ever possible we used dosages for small ruminants. If there was no other possibility, the dosages for cattle were used. The other source was the book with dosage recommendations by MemoVet, “Drug dose recommendations for small ruminants and South American Camelids” (Emmerich et al. 2016)

The information on the type and amount of drugs given to each patient were stored in TIS. The information was collected, additionally the recommended dosages out of the Official Registry and MemoVet were gathered (Table 5). The dosages were compared to the gathered recommendations and an evaluation followed, giving an overview on which recommended dosages were more commonly used.

2.6 CAUSE FOR ANTIMICROBIAL THERAPY

One of the goals of the study was to determine, if there was legitimate cause for administering antimicrobial therapy. This was established by thoroughly examining the medical records of all NWC patients in TIS and recording the diagnosis. In cases where animals had more than one diagnosis, the clinical problem most likely leading to an antibiotic therapy was selected.

2.7 STATISTICAL ANALYSIS

Data curation and descriptive data analysis was performed in Excel (Microsoft Corporation. (2016). Microsoft Excel.).

Table 5: Antimicrobial substances registered in Austria and recommended dosages used, using two different sources – ASG and MemoVet.

Class	Drug	Registered trade name	ASG	MEMOVET
Cephalosporine 3rd generation	Ceftiofur	Excenel RTU 50 mg/ml	1 mg/kg i.m	2,2 mg/kg i.v Llama : 2,2 – 2,8 mg/kg i.m / 2,2 mg/kg i.v Alpaca: 1,5 – 2,2 mg/kg i.m / 2,2 mg/kg i.v
		Excenel Flow 50 mg/ml	1 mg/kg i.m	Llama : 2,2 – 2,8 mg/kg i.m / 2,2 mg/kg i.v Alpaca: 1,5 – 2,2 mg/kg i.m / 2,2 mg/kg i.v
		Eficur 50 mg/ml	1 mg/kg i.m	Llama : 2,2 – 2,8 mg/kg i.m / 2,2 mg/kg i.v Alpaca: 1,5 – 2,2 mg/kg i.m / 2,2 mg/kg i.v
*CS 4th generation	Cefquinome	Cobactan 25 mg/ml, 45 mg/ml, 75 mg/ml	1 - 2 mg/kg i.m	1 mg/kg i.v 1 – 2 mg/kg i.m
Fluoroquinolones	Enrofloxacin	Baytril 25 mg/ml, 100 mg/ml	5 mg/kg i.v, s.c	5 mg/kg i.v, s.c
		Baytril RSI 100 mg/ml	5 mg/kg i.v, s.c	5 mg/kg i.v, s.c
	Marbofloxacin	Marbocyl 20 mg/ml, 100mg/ml	2 mg/kg s.c, i.m, i.v	No record for the substance
Aminoglycosides	Gentamicin	Gentavan 50 mg/ml	4 mg/kg i.m, i.v	4 - 6 mg/kg i.v, s.c

*CS - Cephalosporine

Class	Drug	Registered trade name	ASG	MEMOVET
Amphenicols	Florfenicol	Nuflor 300 mg/ml	20 mg/kg i.m	20 mg/kg i.m, s.c
		Selectan 300 mg/ml	20 mg/kg i.m	20 mg/kg i.m, s.c
Aminopenicillins, (with beta lactamase inhibitors)	Amoxicillin + Clavulanic acid	Synulox RTU 140/35 mg/ml	8,75 mg/kg i.m, s.c	32 mg/kg(A)+8 mg/kg(C) i.m
		Synulox 140/35 mg/ml	8,75 mg/kg i.m, s.c	32 mg/kg(A)+8 mg/kg(C) i.m
Aminopenicillins (no beta lactamase inhibitors)	Amoxicillin	Betamox 150 mg/ml	7 mg/kg i.m	7-10 mg/kg i.m
		Betamox Long Acting 150 mg/ml	7 mg/kg i.m	7-10 mg/kg i.m
	Ampicillin	Ampicillin „Vana“ 200 mg/ml	10 mg/kg i.m	Alpaca: 10 mg/kg i.m 2x per day; 15 mg/kg i.m, i.v Llama: 6-12 mg/kg i.v 2x per day; 15 mg/kg i.m, i.v
		Ampivet 100 mg/ml	10 mg/kg i.m	Alpaca: 10 mg/kg i.m 2x per day; 15 mg/kg i.m, i.v Llama: 6-12 mg/kg i.v 2x per day; 15 mg/kg i.m, i.v

Class	Drug	Registered trade name	ASG	MEMOVET
Tetracyclines	Oxytetracycline	Medicycline 200 mg/ml	20 mg/kg i.m	20 mg/kg i.v, s.c
		Vanacycline 100 mg/ml	20 mg/kg i.m	20 mg/kg i.v, s.c
		Terramycin prolongatum 200 mg/ml Terramycin 100 mg/ml Terramycin 92,7 mg/ml	20 mg/kg i.m	20 mg/kg i.v, s.c
		Tetrasol LA 200 mg/ml	20 mg/kg i.m	20 mg/kg i.v, s.c
		Oxycyclin 92,7 mg/ml	10 mg/kg i.m	20 mg/kg i.v, s.c
Sulfonamides, dihydrofolate reductase inhibitors and combinations	Sulfamethoxazole + Trimetoprim	Vanasulf 200 mg/ml	13,3 mg/kg (S) + 2,7 mg/kg (T) i.v, i.m, s.c	15 mg/kg p.o; 15 mg/kg (S) + 3 mg/kg (T) i.v or dose for sheep: 15-25 mg/kg (S) + 3-5 mg/kg (T) i.v, i.m
Natural, narrow- spectrum penicillins (beta lactamase sensitive penicillins)	Procain Benzylpenicillin	Vanaproc 333 mg/g intramammary inj.	1 inj. per day	
	Penethamate Hydriodide	Ingel – Mamyzin 269,5 mg/ml	10 mg/kg i.m (= 10.000 I.E)	15.000 I.E i.m
		Permacyl 236,3 mg/ml	14,2 mg/kg (=15.000 I.E) i.m	15.000 I.E i.m

Class	Drug	Registered trade name	ASG	MEMOVET
Combined preparation with natural, narrow - spectrum penicillins and aminoglycoside	Benzylpenicillin-Procain + Dihydrostreptomycinsulfat	Penistrepto 200/200 mg/ml Penistrep 200/250 mg/ml	8 mg/kg (B) + 8 mg/kg (DHS) i.m	Doses for sheep: 13 mg/kg (B) + 8 mg/kg (DHS) i.m

3 RESULTS

3.1 PATIENTS

In the time interval from 2005 till 2019, 341 NWC patients received antimicrobial therapy at the University Clinic for Ruminants. Of those, 203 were alpacas, and 138 were llamas (Figure 4). Patients such as camels and those that participated in research projects of the University were not included in this study.

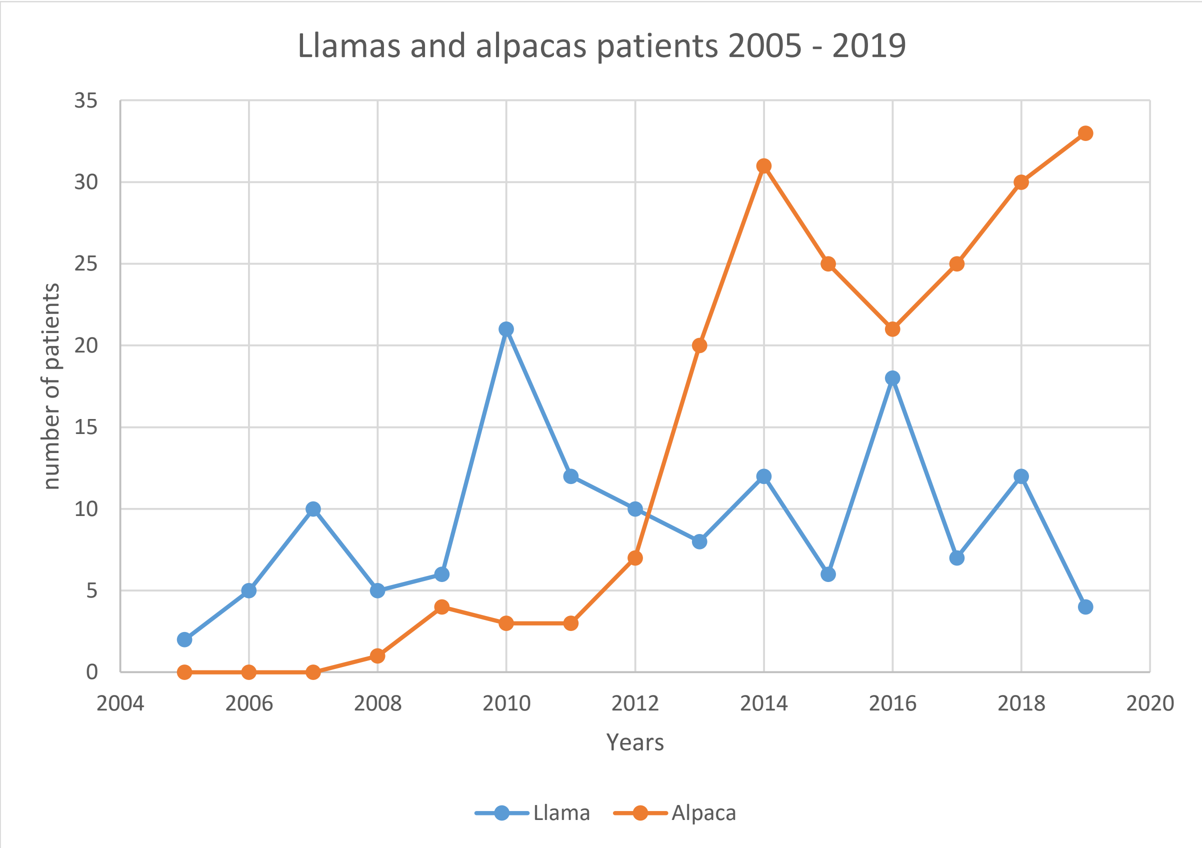

Figure 3: Number of both llama and alpaca patients that received antimicrobial therapy from 2005 to 2019

Especially the number of alpaca patients treated with antibiotics has been rising since 2012, whereas the llama patients have been more consistent in their numbers. The most llama patients were treated in year 2010, after that the number of llama patients slowly dropped. The highest number of alpaca patients being antibiotically treated at the clinic was in the year 2019. This makes them the majority of the NWCs patients. The highest number of all NWC patients that received antimicrobial therapy was 43 patients in the year 2014, with the number of NWC patients varying between 31 and 42 in the years that followed.

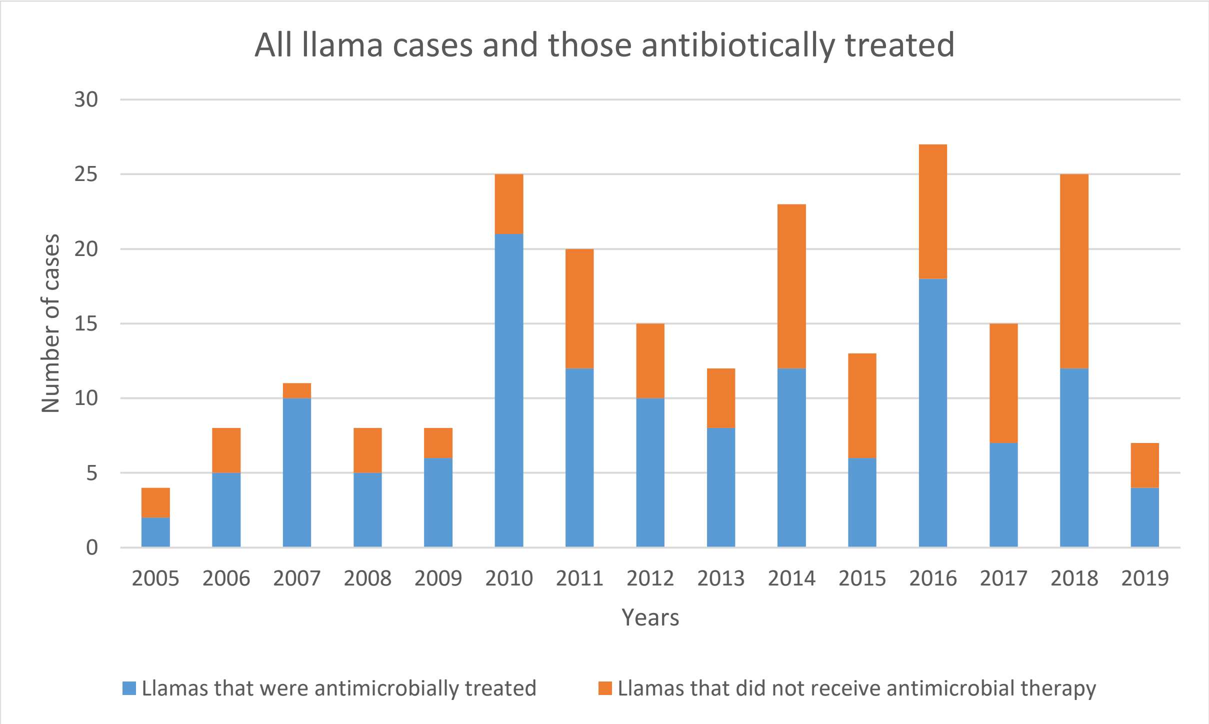

Figure 4: All llama cases at the University Clinic for Ruminants and those llama cases receiving antimicrobial treatment

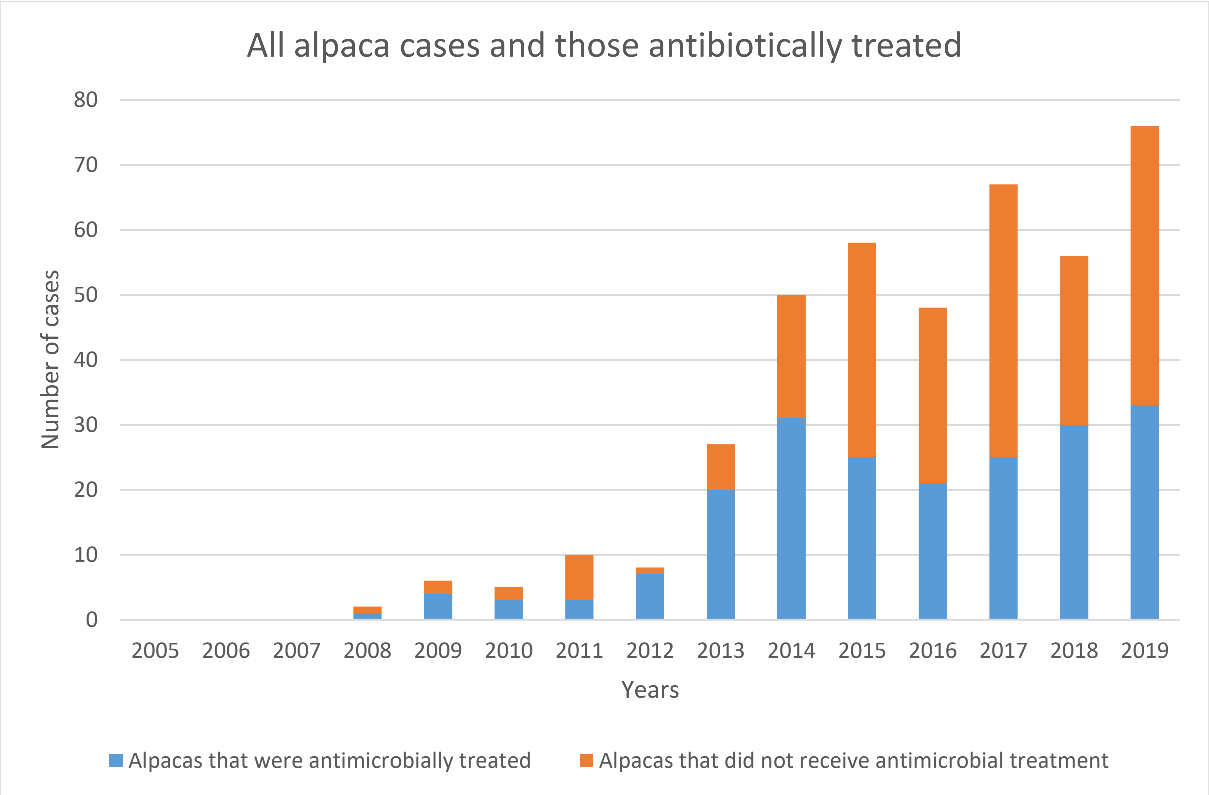

Figure 6: All alpaca cases at the University Clinic for Ruminants and those alpaca cases receiving antimicrobial treatment

The number of all NWC cases treated at the University Clinic for Ruminants in comparison to cases that were treated antibiotically can be seen in Figures 5 and 6, showing llama and alpaca patients separately. The cases shown are only those patients receiving treatment of any kind. Those animals that accompanied patients which were hospitalized were not treated and were excluded from the study.

3.2 AGE

Patients at the clinic ranged from juvenile Llamas and Alpacas (cria) to adult animals. The age of the alpacas ranged from two days to 16 years. The youngest Llama patient was only one-day old; the oldest Llama was 18 years old. There were 34 patients of both species where no age was entered into the main patient data system - TIS. The mean age of all the patients together was 3.9 years (standard deviation (SD) ± 3.6 years). Mean age of alpaca patients was 3.2 years, while the llama patients were older, their mean age being 4.9 years.

3.3 GENDER

Animals of both genders were included in the study, including castrated males. One llama patient had no gender entered into the database (Tables 6 and 7). Seven alpaca patients had no data on their gender. Llama female: male ratio was 1:3.1 whereas alpaca male: female ratio was 1:1.1.

Table 6: Number of male and female llama patients in the study

Llama male	Llama male - castrated	Llama female	Total
89	15	33	137

Table 7: Number of male and female alpaca patients in the study

Alpaca male	Alpaca male - castrated	Alpaca female	Total
78	25	93	196

3.4 COMMON DIAGNOSES/DISEASES FOR ANTIBIOTIC TREATMENT

Patients with the same diagnose code key were gathered under the same group, counted and recorded to evaluate the number of patients treated every year.

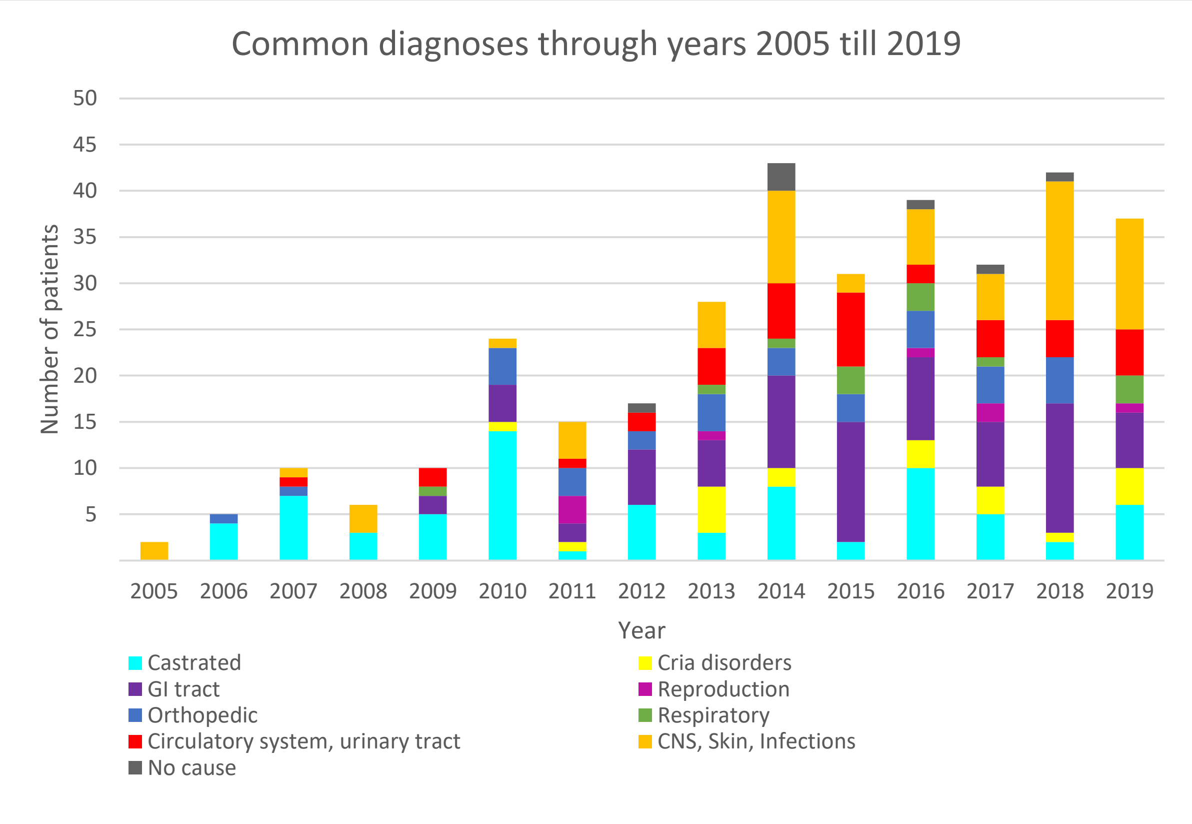

Figure 7: All of the patients receiving antimicrobial treatment through years 2005 till 2019 and the common diagnoses needing antimicrobial treatment

The most dominant diagnoses seen in llama and alpaca patients at the University Clinic for Ruminants can be seen in Figure 7. After year 2012 the most predominant diagnoses are those of GI tract, followed by diagnoses out of the group CNS, skin diseases and infections.

3.4.1 Castrations

It was observed that in the first years the most frequent reason for antimicrobial treatment was castration, where antibiotics were given as perioperative infection prophylaxis (Figure 8).

Most commonly used antimicrobial drug of choice until 2016 was a combination of benzylpenicillin and dihydrostreptomycin, administered i.m or s.c, with the recommended dosage of 16 mg/kg (ASG, used recommended dose for cattle) or 21 mg/kg (MemoVet, used recommended dose for sheep). After 2016 the patients undergoing procedure of castration received ampicillin. A few cases received amoxicillin-clavulanic acid.

Animals (n) that received antimicrobial substances as part of the perioperative infection prophylaxis were benzylpenicillin–dihydrostreptomycin (n = 51), amoxicillin–clavulanic acid (n = 2), cefquinome (n = 1), oxytetracycline (n =1), amoxicillin (n = 12) and ampicillin (n = 10).

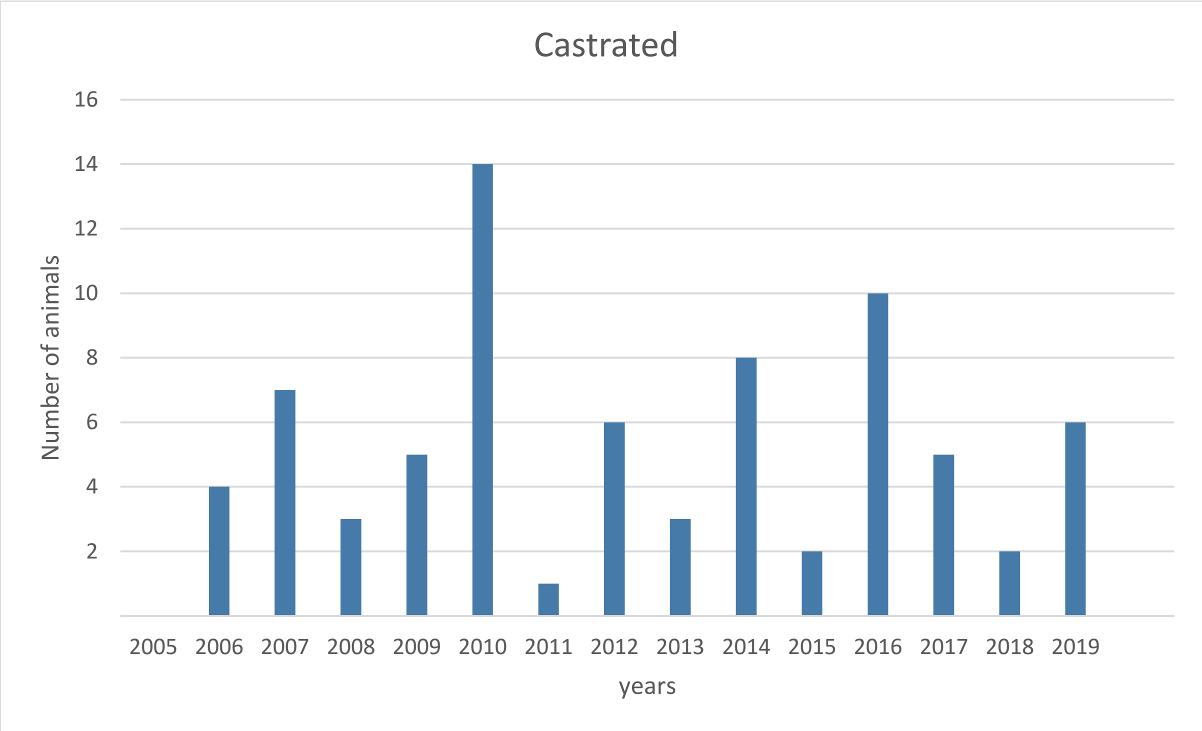

Figure 8: Number of castrated patients in the years 2005 till 2019

3.4.2 Diseases of crias

The most common cria disorder observed was septicaemia of the newborn, followed by complications related to the umbilical cord (GMON code key 11 and 12). All complications at birth such as aspiration pneumonia, premature birth, no suckling, organ defects at birth and other diseases appearing in the first months were recorded under the number 17 – “other calf (in our case cria) diseases. There were five cria patients receiving antimicrobial therapy in the year 2013, which is the highest number throughout the years (Figure 9).

Cria patients receiving antimicrobial therapy in this study were administered different antimicrobial substances. Antimicrobial substances used in cria (n) patients were amoxicillin–clavulanic acid (n = 5), ampicillin (n = 2), oxytetracycline (n = 1), enrofloxacin (n = 3), ceftiofur (n = 2) and cefquinome (n = 9).

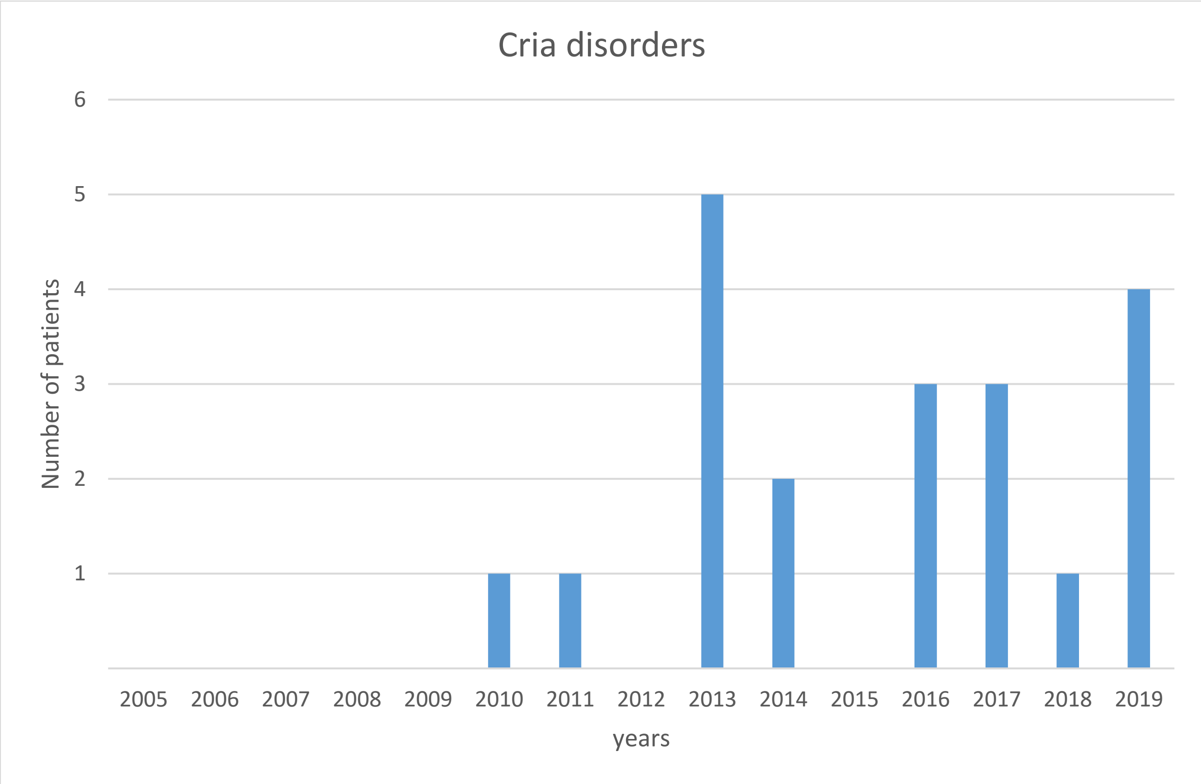

Figure 9: Number of cria patients that received antimicrobial treatment during the years 2005 till 2019

3.4.3 GI tract diseases

Under GI tract we gathered all the diseases of the digestion system, starting with diseases of the mouth (GMON code key 28). Most of the patients treated for diseases of the mouth were admitted for dental diseases. The cardinal symptom was mostly local swelling, with tooth root abscesses among the most commonly seen causes. Out of all 37 patients admitted for dental diseases during the years 2005 – 2019 all patients received surgical treatment and wound care. In 23 patients, surgical extraction of the affected teeth was performed (GMON 281). In eight other patients fistulating abscesses (GMON 951) were the main causes for receiving antibiotic treatment. All of the patients that were treated with antimicrobial substances during the years 2005 till 2019 can be seen in Figure 10.

Animals (n) received the following antimicrobial substance for diseases of the mouth, amongst which dental diseases were one of the most common concern: amoxicillin (n = 2), ampicillin (n = 8), amoxicillin–clavulanic acid (n = 12), enrofloxacin (n = 1), benzylpenicillin–dihydrostreptomycin (n = 1), ceftiofur (n = 4) and cefquinome (n = 14).

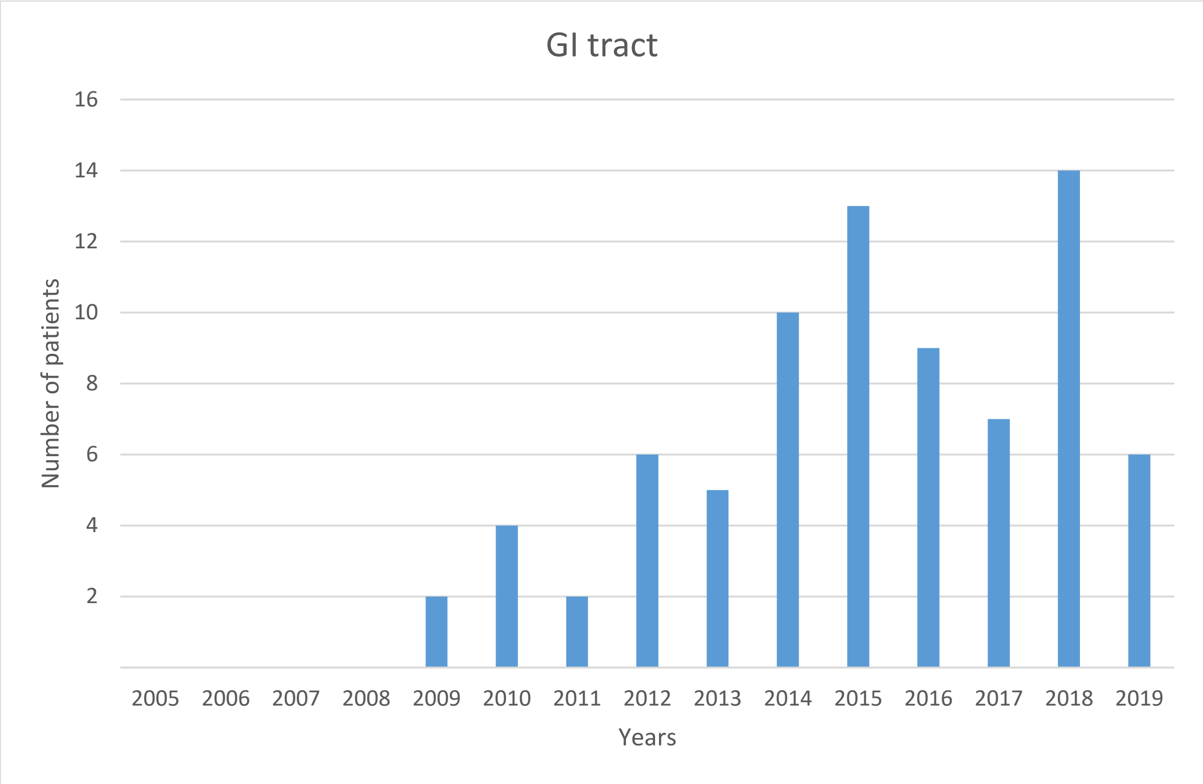

Figure 10: Patients with GI tract diseases which received antimicrobial treatment from 2005 till 2019

Other reasons for admitting patients with GI disorders were diseases of the oesophagus (5 patients with GMON 27). One patient suffered from an acidosis of compartment 1 of the stomach, three were diagnosed with peritonitis. There was one patient with ileus and four patients had other causes such as rectal prolapse, which were summarized in the category "other diseases of the abdominal cavity" as it did not have its own GMON code.

There were 27 patients that received treatment based on assumption or proven evidence of *Clostridium perfringens* (*C. perfringens*) infections (GMON 273, Figure 11). Patients showing symptoms such as fast onset of illness, diminished general behaviour, signs of colic, diarrhoea, dysentery, intestinal gas tympani, central nervous system disease symptoms such as convulsion, were dyspnoeic or were recumbent all had *C. perfringens* as differential diagnosis. Five cases were tested positive for *C. perfringens* Type A toxin. Together with thorough anamnesis and attempt of toxin verification some needed a fast response in treatment as *C. perfringens* has an aggressive progression. All of 27 patients with suspected enterotoxaemia that received treatment at the University Clinic for Ruminants were referred by another veterinarian and in most of them antibiotic treatment had already been initiated for their symptoms before referral. Others were treated with antibiotics at the University Clinic for

Ruminant before the result of bacterial examination was available. In all of the patients a faecal sample was taken for parasitic examination, and all samples contained different amount of endoparasites. This could have potentially played a part in bacterial proliferation in these patients.

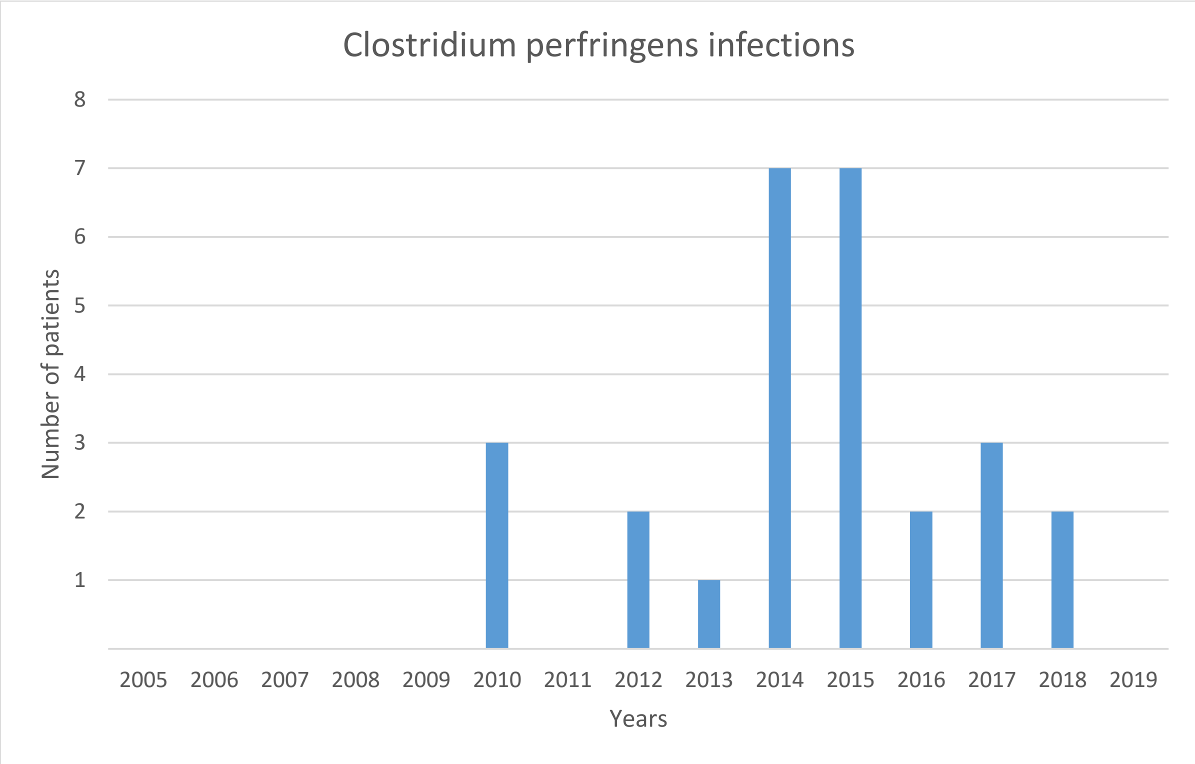

Figure 11: Patients with assumption or proven C. perfringens infection

Patients (n) with suspicion of *C. perfringens* at the University Clinic for Ruminants received antimicrobial substances such as amoxicillin–clavulanic acid (n = 5), enrofloxacin (n = 1), benzylpenicillin–dihydrostreptomycin (n = 1), ampicillin (n = 5), oxytetracycline (n = 3), trimethoprim–sulfamethoxazole (n = 1) and cefquinome (n = 14).

3.4.4 Orthopaedic diseases

During the years 2005 till 2019 there were 33 patients admitted with orthopaedic problems (Figure 12). All cases were identified with a GMON code key 64, for cases like fractures, luxations and other injuries of the limbs. There was one case where the patient was recumbent due to disease of the musculoskeletal system. Most patients were admitted because of lameness or visible infected wounds that needed antibiotic treatment. Other cases such as fractures received surgical treatment. Two patients needed their toes to be amputated; in one of these the front lateral phalanx media was affected by purulent inflammation and osteomyelitis. The other toe was amputated proximal to the front medial proximal phalanx. One other patient was admitted because of a traumatic exungulation.

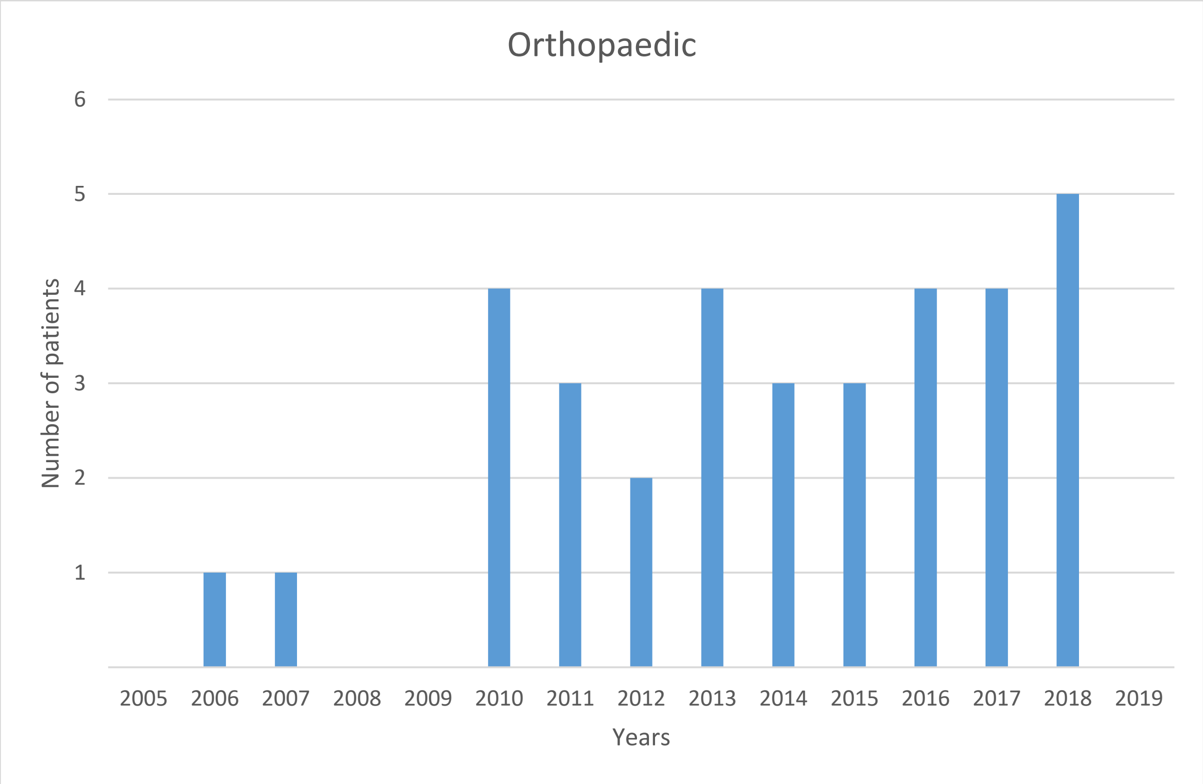

Figure 12: Patients in the years 2005 till 2019 which received antimicrobial treatment for orthopaedic conditions

Orthopaedic patients in this study received antimicrobial drugs such as combined drug of benzylpenicillin–dihydrostreptomycin (n = 11), in the first years, because of the broad spectrum the drug offered. Later it was replaced by amoxicillin-clavulanic acid (n = 4). Ampicillin was used, with a broad spectrum against gram–negative and gram–positive bacteria, and is often used in cases involving joints (n = 8). Gentamicin was also used for infections caused by gram–negative bacteria (n = 7). It was frequently applied locally. The most used antimicrobial substances in orthopaedic cases in this study were cephalosporines 3rd and 4th generation (ceftiofur (n = 5), cefquinome (n = 12).

3.4.5 Respiratory system diseases

Patients admitted for respiratory diseases received GMON code keys 71 = the diseases of the upper respiratory tract, 72 = pneumonia and 73 = other respiratory diseases that did not fall under the former categories. Together there were 13 such patients (Figure 13) with respiratory diseases, most (7 patients) were treated for inflammation of the lungs, with diagnoses such as bronchitis and bronchopneumonia. Years with the highest number of patients receiving treatment for respiratory disease were 2015, 2016 and 2019, with 3 cases each.

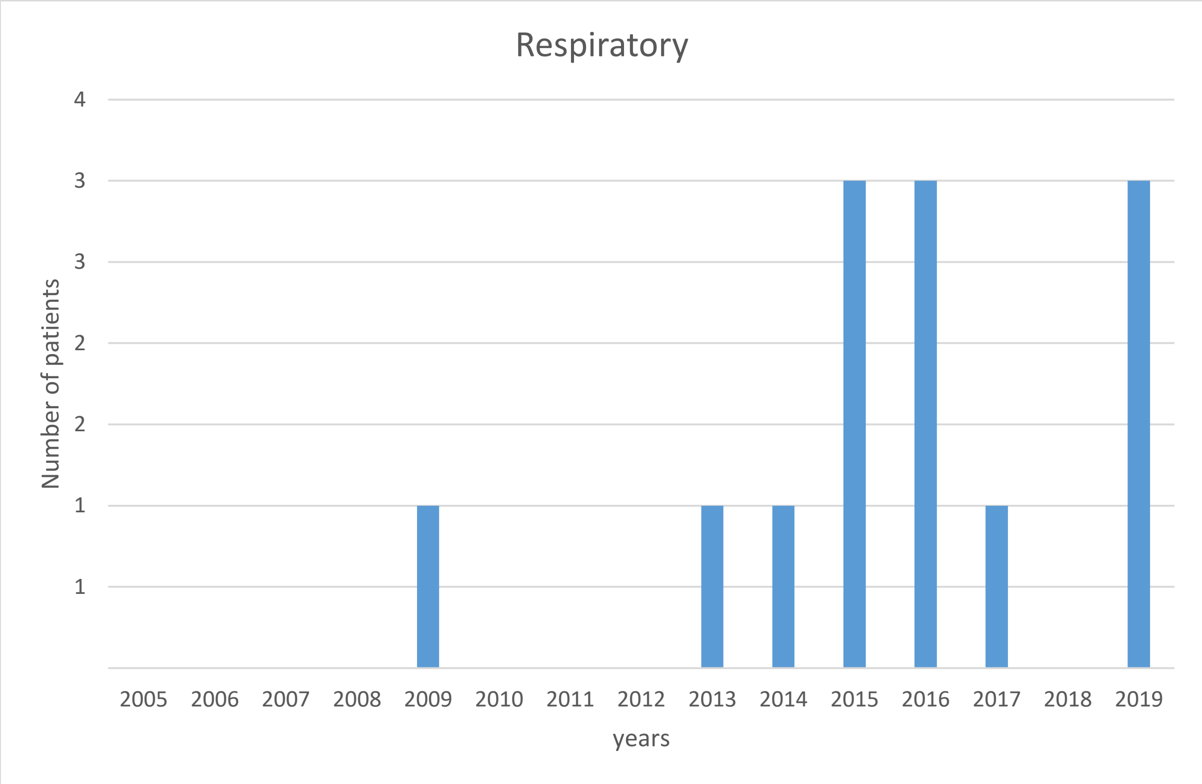

Figure 5: Patients with respiratory system diseases, which received antimicrobial treatment in the years 2005 till 2019

The most commonly used antimicrobial drug for treating patients with respiratory disease in this study was amoxicillin–clavulanic acid (n = 5). Patients (n) also received antimicrobial drugs such as ceftiofur (n = 2), cefquinome (n = 4), oxytetracycline (n = 1) and florfenicol (n = 1).

3.4.6 Circulatory system and urinary tract diseases

3.4.6.1 Circulatory

There were 30 patients between the years 2005 – 2019 admitted to the University Clinic for Ruminants with diseases of the circulatory system (Figure 14). Those with diseases of the heart were grouped as GMON diagnosis key 81 – there were two such patients, in the years 2013 and 2019. The two patients with a heart condition received treatment with cefquinome (n = 1) and ampicillin (n = 1).

Seventeen patients were grouped as GMON code key 82 with principal diagnoses being septicaemia or anaemia. Eight of the patients diagnosed with anaemia had a secondary presumptive diagnosis of *Candidatus Mycoplasma haemolamae (CMhl).*

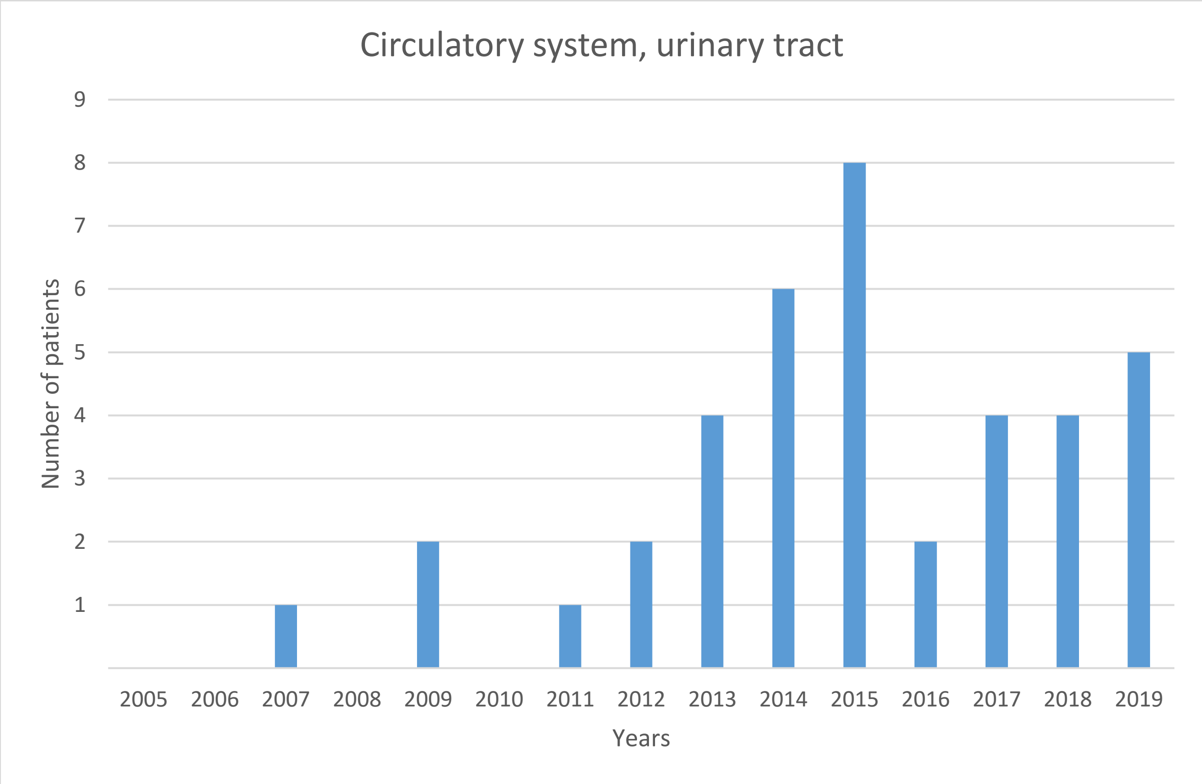

Figure 6: Number of patients with symptoms of circulatory system and urinary tract which received antimicrobial treatment

CMhl was also the principal diagnosis in 11 patients who received antibiotic treatment (Figure 15). The highest number of patients with the diagnosis of CMhl was in the years 2013 and 2014, with three such patients in each of the mentioned years.

Patients (n) receiving treatment for anaemia and suspicion or diagnosis of CMhl were primarily treated with oxytetracycline (n = 17). Other antimicrobial substances used were amoxicillin–clavulanic acid (n = 6), ampicillin (n = 3), amoxicillin (n = 5), marbofloxacin (n = 2), benzylpenicillin–dihydrostreptomycin (n = 3) and cefquinome (n = 7).

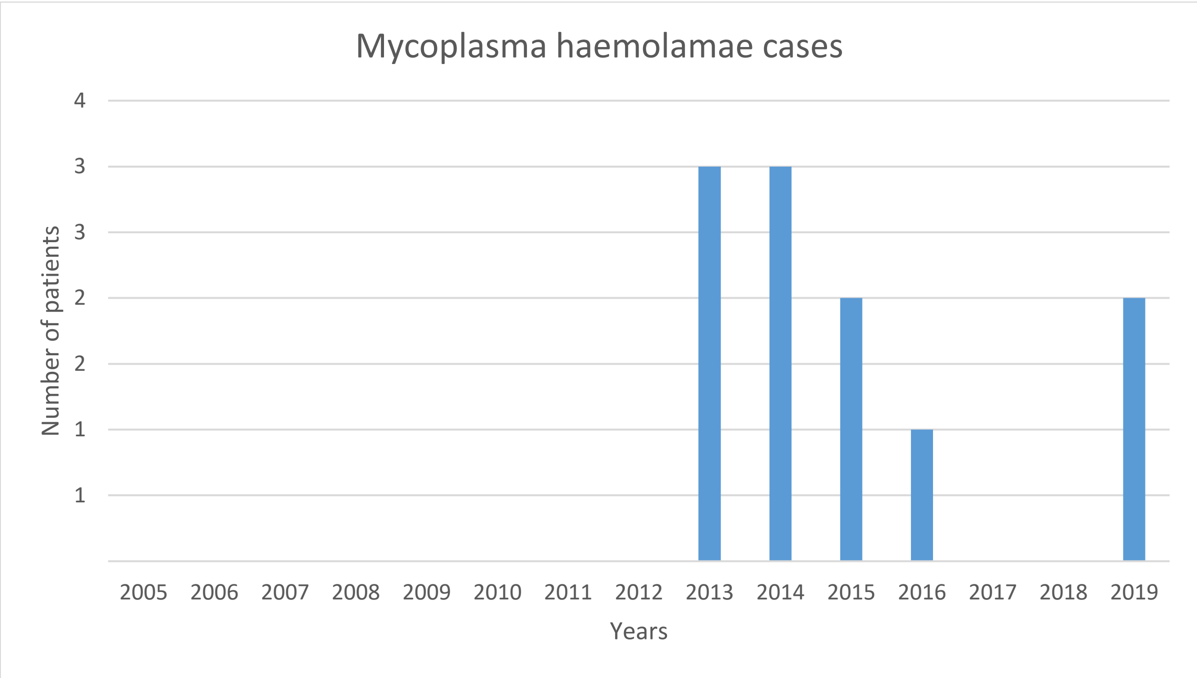

Figure 7: Patients with Candidatus Mycoplasma haemolamae, which received antimicrobial treatment

3.4.6.2 Urinary tract

There were together nine patients treated for diseases of the urinary system between the years 2005 and 2019. Diseases included cases such as urinary obstruction, urolithiasis, diseases of the kidney and urinary tract, suspected cystitis and suspected ectopic ureter. All were gathered under code key 88. Out of nine patients eight reported cases were treated because of urinary obstruction. One case was a cria patient with suspicion of ectopic ureter.

Treatment for diseases of the urinary system were antimicrobial substances amoxicillin–clavulanic acid (n = 4 animals), benzylpenicillin–dihydrostreptomycin (n = 2), oxytetracycline (n = 1), trimethoprim–sulfamethoxazole (n = 1) and cefquinome (n = 5).

3.4.7 Diseases of the central nervous system, skin and generalised infections

3.4.7.1 Diseases of central nervous system and skin

There were nine patients who received antimicrobial treatment for various diseases of the central nervous system (CNS, GMON code key 91). Patients (n) with CNS diseases received the following antimicrobial substances: cefquinome (n = 4), ampicillin (n = 1), amoxicillin–clavulanic acid (n = 2) and oxytetracycline (n = 4).

Patients with diseases of the eyes and ears were gathered under one code key for diseases of the sensory organs (GMON code key 92). Together there were 20 such patients, 15 of them were treated for various eye diseases or injuries, mostly keratoconjuctivitis and corneal ulcers. Five patients underwent enucleation. Five other patients with diseases of the sensory organs were patients admitted for ear problems, most commonly otitis, caused by psoroptes ear mites.

Animals (n) with diseases of the eyes that needed parenteral antimicrobial treatment received amoxicillin–clavulanic acid (n = 4), ampicillin (n = 3) and oxytetracycline (n = 6). Topical preparations contained oxytetracycline (n = 7), gentamicin (n = 1) and ofloxacin (n = 1). Patients (n) with diseases of the ears were treated with amoxicillin–clavulanic acid (n = 2), enrofloxacin (n = 1) and amoxicillin (n = 1). One topical ear preparation contained gentamicin (n = 1).

Patients with skin diseases received two different GMON code keys: number 93 was for those who had skin infections due to external parasites, there were ten such patients recorded. Those with other skin diseases that did not fall under the previous category were given number 95 for “other skin diseases”. We counted eight such patients. Together there were 18 patients presented for skin diseases.

Two common reasons for skin infections stood out, one being zinc deficiency, causing zinc responsive dermatitis. Other reasons were various abscesses of the skin, mostly caused by old wounds. Zinc deficiency was marked with GMON number 100 and was noticed in six patients in total; four patients showed signs of low zinc levels concurrently with skin infections due to external parasites. Two patients had low zinc levels in the category other skin diseases. An abscess was noticed five times as a secondary diagnosis with patients under the category other skin diseases. The most common symptom amongst the patients with skin diseases was dermatitis, with mange mites (both sarcoptis and chorioptis mange mites) being the most common observed ectoparasites.

Antimicrobial treatment for patients (n) with skin diseases consisted of amoxicillin (n = 4), ampicillin (n = 2), oxytetracycline (n = 3), benzylpenicillin (n = 2), amoxicillin–clavulanic acid (n = 5), benzylpenicillin–dihydrostreptomycin (n = 4), marbofloxacin (n = 1), cefquinome (n = 1) and ceftiofur (n = 1).

3.4.7.2 Generalised infections

There was one patient that presented with signs of generalised infection. We recorded three patients with tetanus in 2016, 2017 and 2018. Eight patients that received antibiotic treatment for various wounds or trauma were recorded under GMON code key 952. The majority of them were presented for different wounds, such as bite wounds after dog attacks or wounds sustained in the field or after fighting amongst themselves. Another seven patients received antibiotic treatment after being presented with fever.

All of the patients being treated with antimicrobial therapy for diseases of the CNS, Skin diseases and infections are presented in Figure 16.

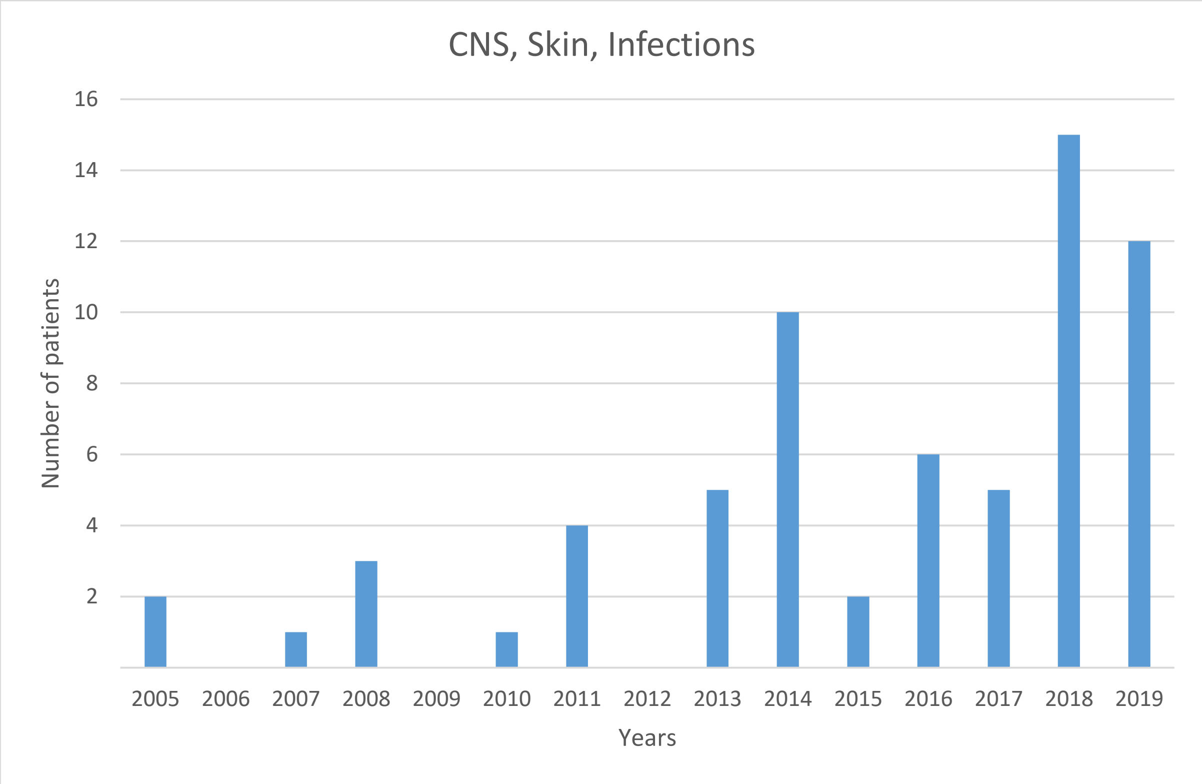

Figure 16: Patients with symptoms of CNS, skin diseases or infection, which received antimicrobial treatment

Patients (n) presented for signs of general infection received antimicrobial treatment with ampicillin (n =1). Those being treated for various wounds were treated with cefquinome (n = 1), ampicillin (n = 2), enrofloxacin (n = 1), gentamicin (n = 1), oxytetracycline (n = 2), amoxicillin (n = 1), florfenicol (n = 1) and benzylpenicillin–dihydrostreptomycin (n = 1). Patients being treated for tetanus all received penicillin (n = 3). Those presented for fever received treatment with cefquinome (n = 3), enrofloxacin (n = 1), florfenicol (n = 1), ampicillin (n = 3), amoxicillin–clavulanic acid (n =1) and oxytetracycline (n = 1).

3.4.8 Diseases of the reproduction system

There were eight patients (Figure 17) with diseases of the reproduction system at the University Clinic for Ruminants during the years 2005 - 2019, which makes them the smallest group of patients. Two of the female patients were admitted for metritis, two needed antibiotic treatment after a difficult birth, one patient had an abortion, one was admitted after injury during parturition and one had a chronic inflammation of the udder. There was one male patient treated for orchitis.

Antimicrobial substances used in patients (n) with diseases of the reproduction system were as follows: amoxicillin (n = 3), ampicillin (n = 1), penethamat (n = 1), amoxicillin–clavulanic acid (n = 1), benzylpenicillin–dihydrostreptomycin (n = 1) and cefquinome (n = 2).

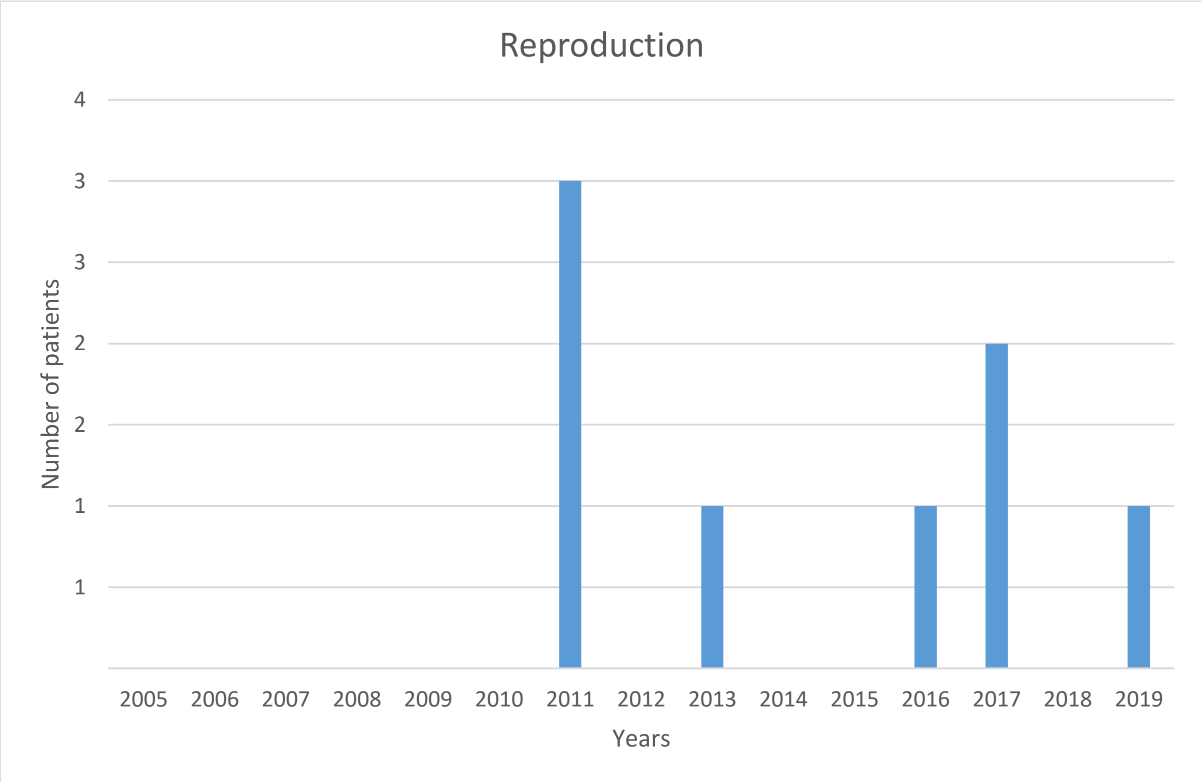

Figure 8: Patients with diseases of reproductive system, which received antimicrobial treatment from years 2005 till 2019

3.4.9 Treatment without obvious cause

There were a few cases in the TIS system where no obvious cause for antimicrobial treatment could be discovered. These were mostly patients where the therapy with antibiotics was initiated be their referring veterinarian and continued at the University Clinic. As this study was intended for evaluating reasons for antibiotic therapy we gathered such cases where no obvious reason for therapy was gathered under one group and labelled with number 0. There were seven such patients (Figure 18).

Patients (n) were treated with the following antimicrobial substances: cefquinome (n = 1), benzylpenicillin–dihydrostreptomycin (n = 1), amoxicillin–clavulanic acid (n = 2), oxytetracycline (n = 1) and ampicillin (n = 1).

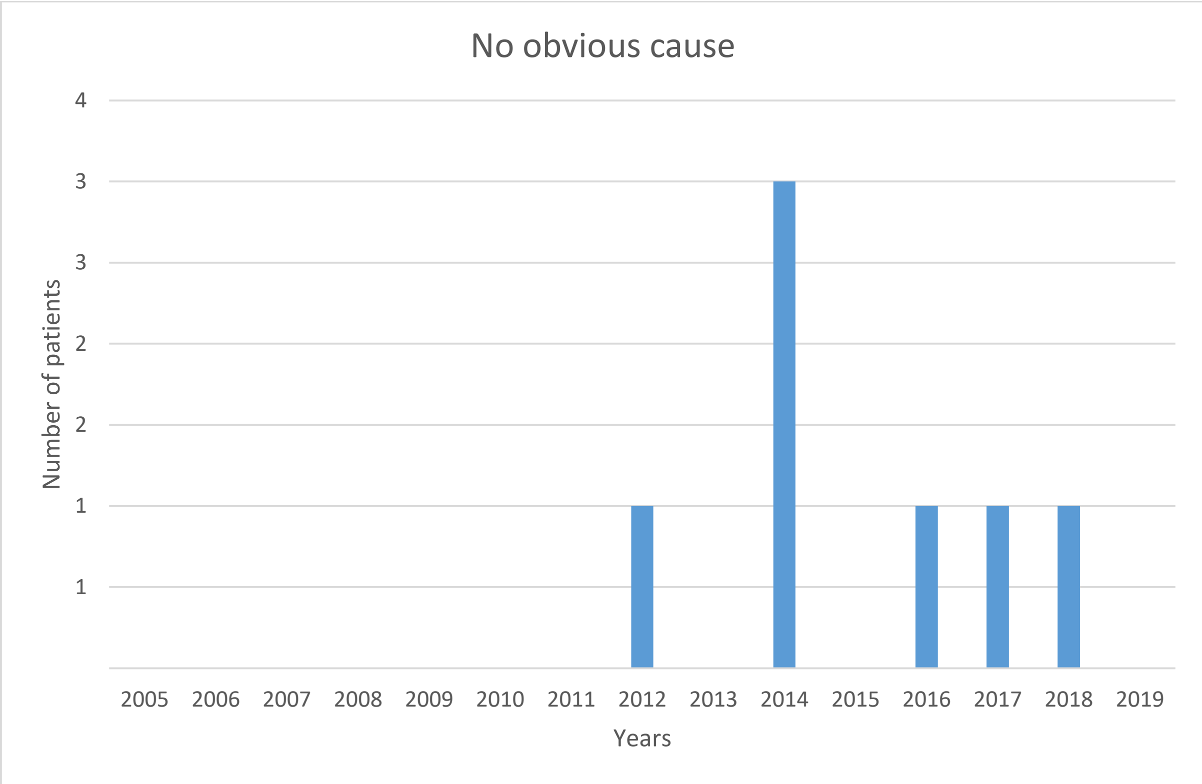

Figure 18: Cases where no valid cause for antimicrobial treatment has been observed

3.4.10 Local applications

Antimicrobial substances used for local therapy were gathered and evaluated separately (Table 8). Number of treatments were recorded along with the antimicrobial drug that was used. Most of the treatments involved eye drops or ointments, followed by local applications of antimicrobials during surgical peri- or postoperative management or during wound management, as a part of infection prophylaxis.

Most used antimicrobial substances for local therapy were aminopenicillins (no beta-lactamase), followed by aminoglycosides, tetracyclines and aminopenicillins in combination with beta–lactamase inhibitors. The most used substance for eye treatment was oxytetracycline, the same was observed amongst substances for local sprays.

Table 8: Number of local antimicrobial treatments by antibiotic class

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	All
Combo: penicillins + aminoglycosides	0	0	0	0	0	0	0	0	2	0	1	2	0	0	0	5
Aminopenicillins, no ß lactamase	3	0	0	0	1	0	1	0	0	3	0	0	2	2	4	16
Cephalosporines 3rd and 4th generation	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	2
Fluoroquinolones	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	2
Aminopenicillins + ß-lactamase	0	0	0	0	0	0	0	0	0	1	0	0	0	10	0	11
Tetracyclines	0	0	0	0	0	0	2	0	0	4	1	2	0	1	1	11
Aminoglycosides	0	0	0	0	0	0	0	1	2	0	4	0	5	2	0	14
Sulfonamides	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Amphenicols	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
																61

3.5 ANTIMICROBIAL SUBSTANCES USED

Antimicrobial substances from groups B through D and C/D according to EMA classification were used at the University Clinic for Ruminants (Table 9).

An outline of the antibiotic substances used through the years 2005 till 2019 is shown in Figure 20. In the first years of patient therapy, the most commonly used substance was a combined preparation of penicillins and aminoglycosides, which was the most frequently used substance in the year 2012. It was most often used in patients that came for castration, followed by orthopaedic cases. After the years 2012 its use started slowly declining, until it completely stopped being in use after the year 2016, as it was no longer available.

Table 9: Antimicrobial substances used in this study, according to EMA classification

EMA Category	Antibiotic class	Substance
B	Cephalosporine 3rd- and 4th-generation, with the exception of combinations with ß-lactamase inhibitors	cefquinome
		ceftiofur
	Quinolones: fluoroquinolones and other quinolones	enrofloxacin
		marbofloxacin
C	Aminoglycosides (except spectinomycin)	gentamicin
		streptomycin
	Aminopenicillins, in combination with beta lactamase inhibitors	amoxicillin + clavulanic acid
	Amphenicols	florfenicol
D	Aminopenicillins, without beta – lactamase inhibitors	amoxicillin
		ampicillin
	Tetracyclines	oxytetracycline
	Sulfonamides	trimethoprim
	Natural, narrow-sprectrum penicillins (beta lactamase-sensitivepenicillins)	benzylpenicillin
C/D	Aminoglycosides (except spectinomycin)	dihydrostreptomycin
	Natural, narrow-sprectrum penicillins (beta lactamase-sensitivepenicillins)	benzylpenicillin

Starting in 2010 and till 2015 (with a peak in 2013) the 3rd- and 4th generation cephalosporins were more frequently in use. The main diagnoses receiving treatment with cephalosporins were orthopaedic cases and dental treatments. Number of applications given to patients with orthopaedic or dental illness are shown in Figure 19. The third group of patients treated with cephalosporins were those with assumptive or proven *C. perfringens* infection.

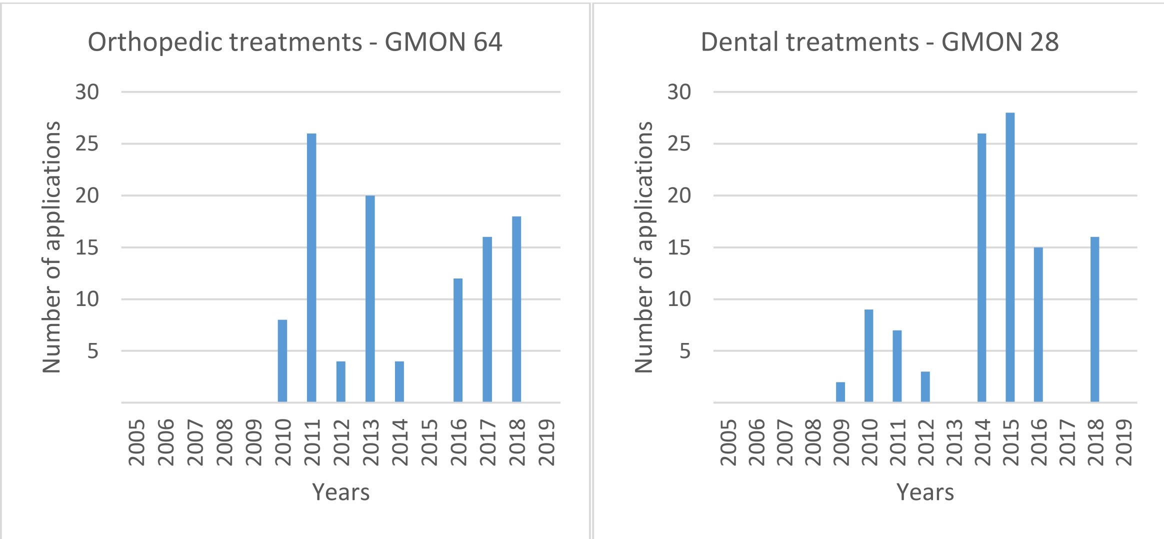

Figure 19: Most common reasons for antimicrobial treatment with cephalosporins

The other antibiotic substance from the EMA category B are fluoroquinolones. Their most common usage was for GMON diagnosis 952 – abscess (usually in skin diseases). Fluoroquinolones were not frequently a part of antibiotic treatment plan at the University Clinic for Ruminants.

There is an increase in the use of ampicillins (no beta lactamase inhibitors), as they became the drug of choice after the combined substance of penicillins and aminoglycosides was no longer available on the market. Together with natural narrow-spectrum penicillins (beta lactamase sensitive) out of the EMA group D their use peaked in 2018.

There is also a rise in the use of aminopenicillins in combination with beta-lactamase inhibitors, which are showing a steady rise since 2013. Tetracyclines seem to be in more or less constant use, mostly since the year 2013. Aminoglycosides, sulfonamides and amphenicols are the least used antibiotic substances in camelid patients at the University Clinic for Ruminants. An overview of the antimicrobial substances according to EMA classification can be seen in Figure 21.

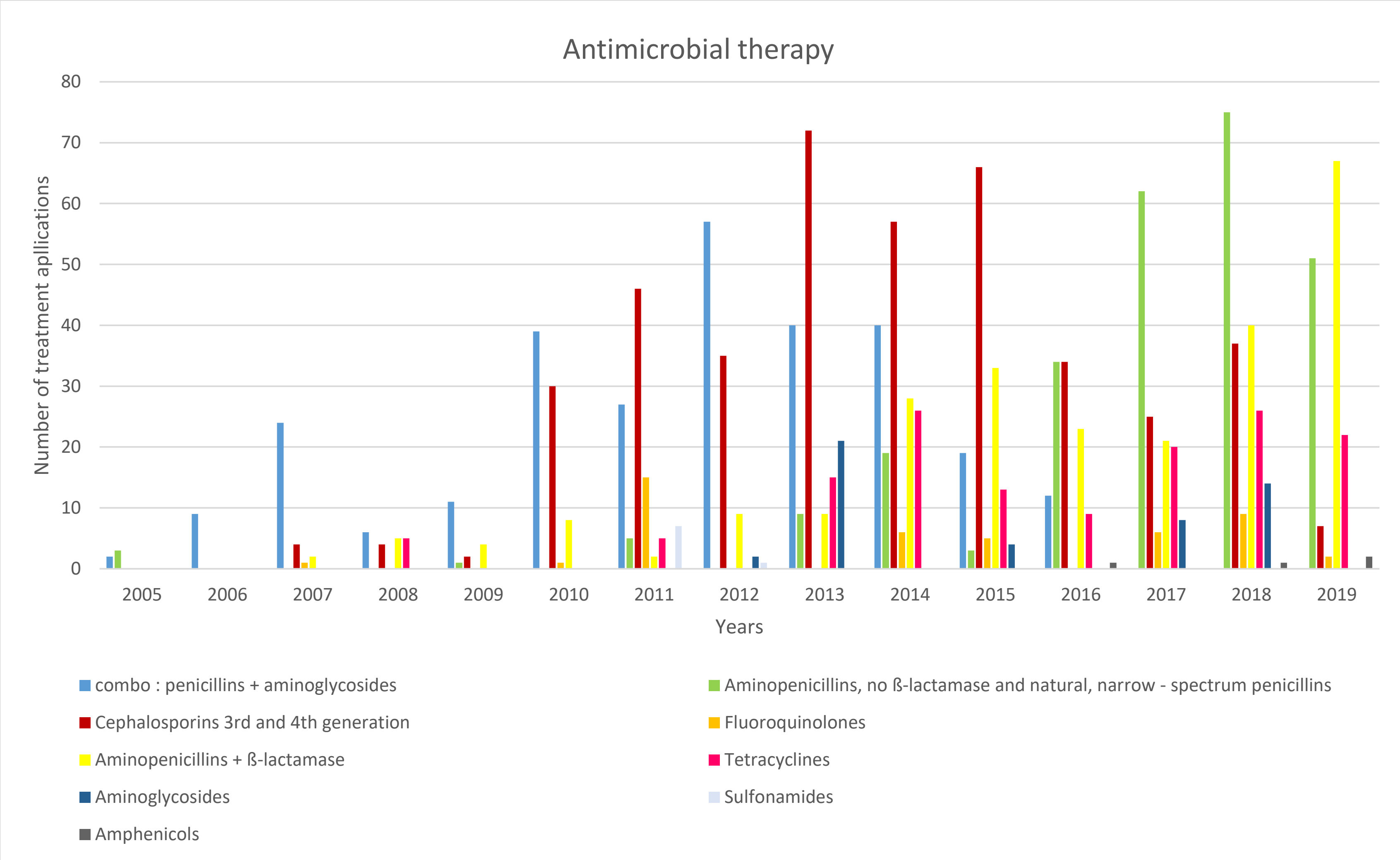

Figure 20: Number of applications of different antimicrobial substances from 2005 to 2019

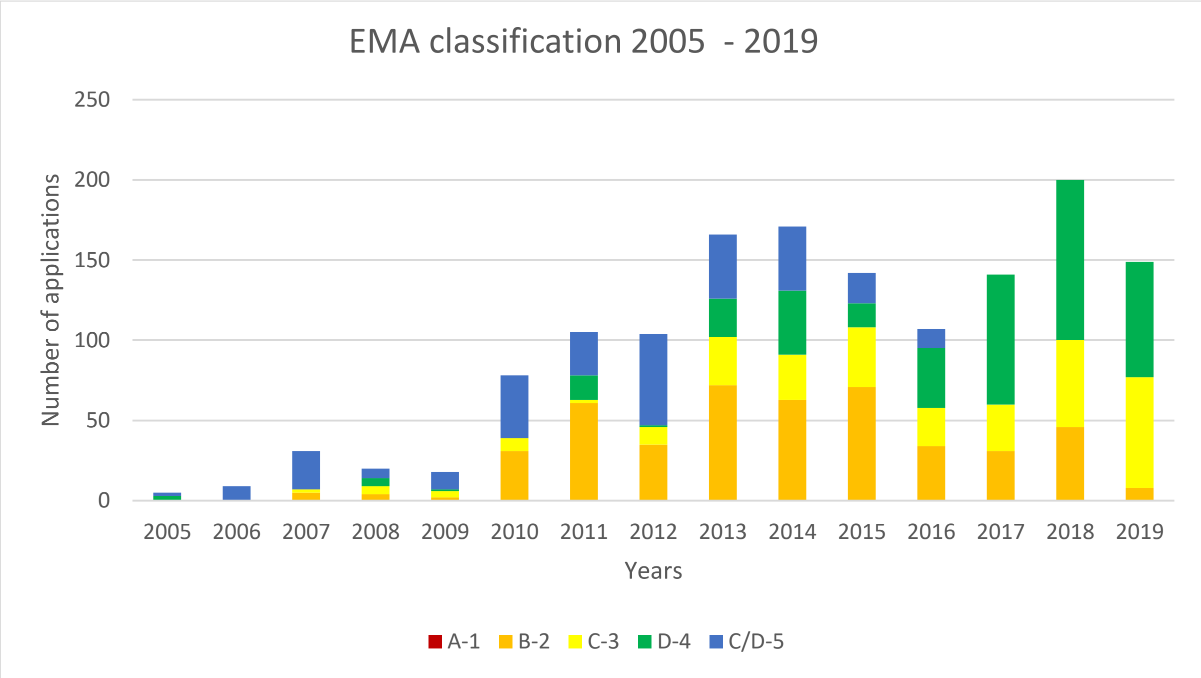

Figure 9: Antimicrobial substances used at the University Clinic for Ruminants, according to EMA classification

Every application and the amount of drug received by each patient was stored in TIS. The average amount of consumed antimicrobial drugs was calculated for an overview of how much antimicrobial substance was used (in mg/kg) each year (Figure 22). Local applications were exempt from the calculation, together with those treatments where the route of drug application was not recorded. Together those were 5% of all treatments. In 8% of patients the birth date was unknown and consequently no approximation of their weight was possible. These were also excluded.

A comparison was made between the dosages out of the ASG (BASG 2021) and the ones in MemoVet (Emmerich et al. 2016) to see if the dosages given were in the recommended range. Drugs out of EMA category B were taken into consideration and were evaluated (Figures 23 through 26). Marbofloxacin only had dosage out of one source, the ASG.

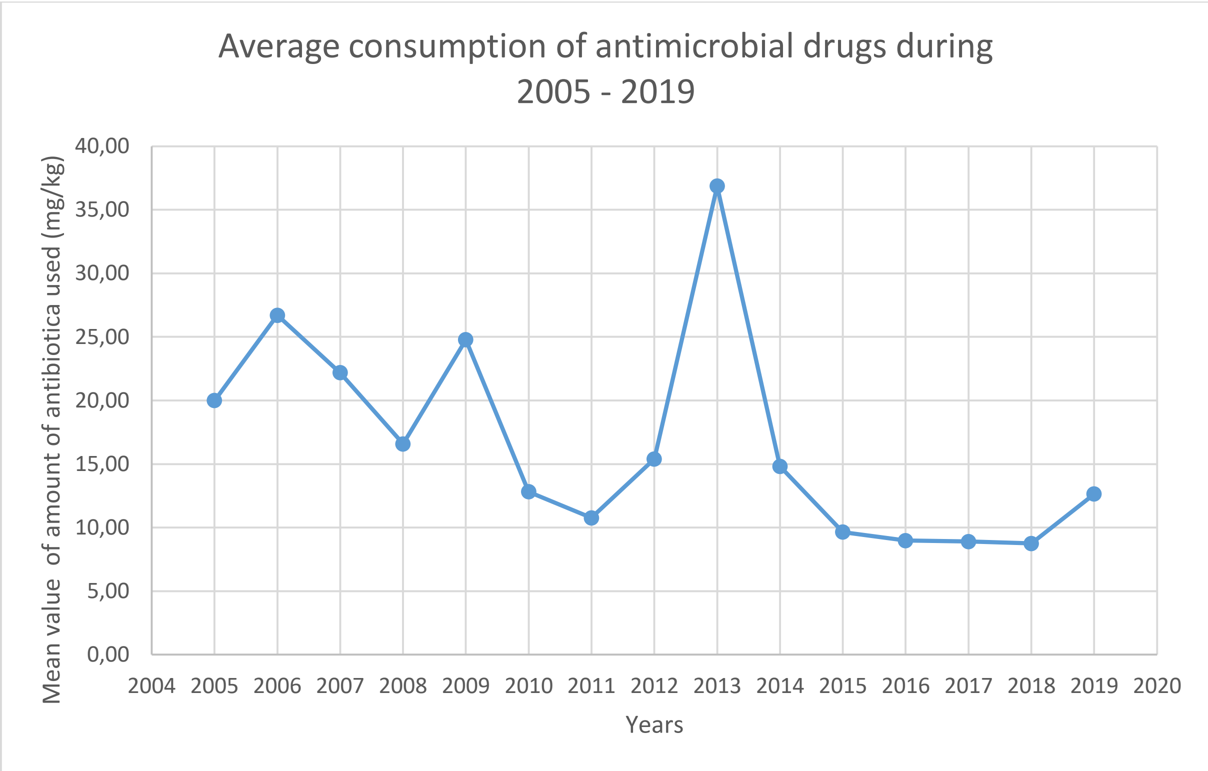

Figure 10: Average amount of antimicrobial substances used in the years 2005 till 2019, measured in mg/kg

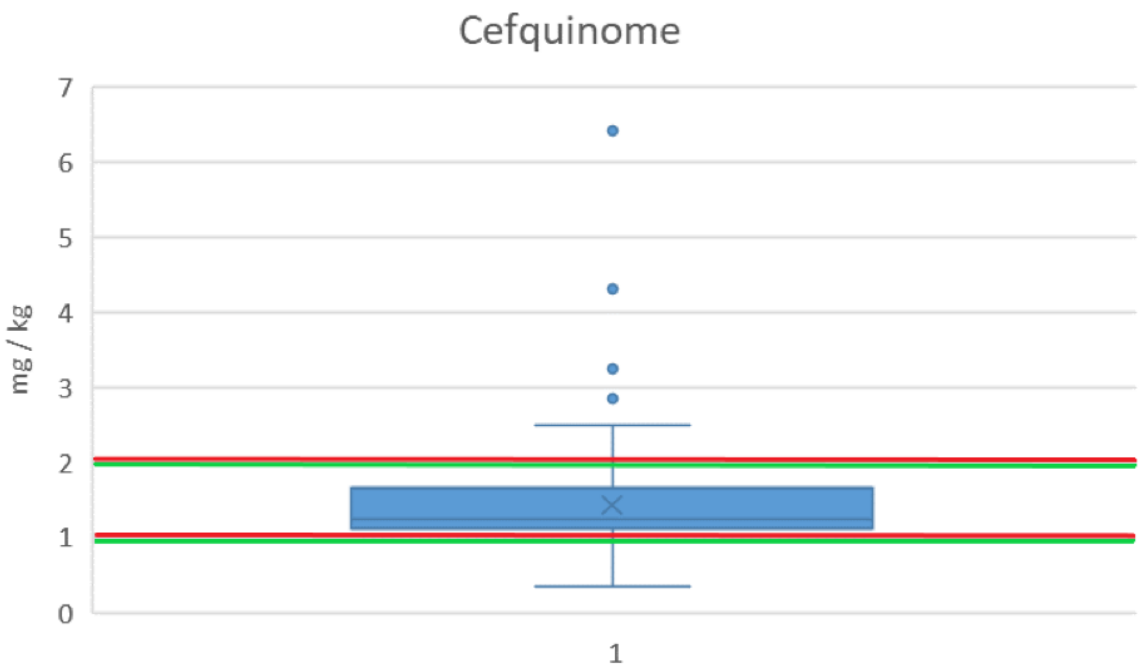

Figure 11: 4th generation cephalosporins– dosages used for cefquinome
Red lines represent the recommended minimal and maximal dosage for cattle/calves from ASG
Green lines represent the recommended minimal and maximal dosage for NWCs from MemoVet

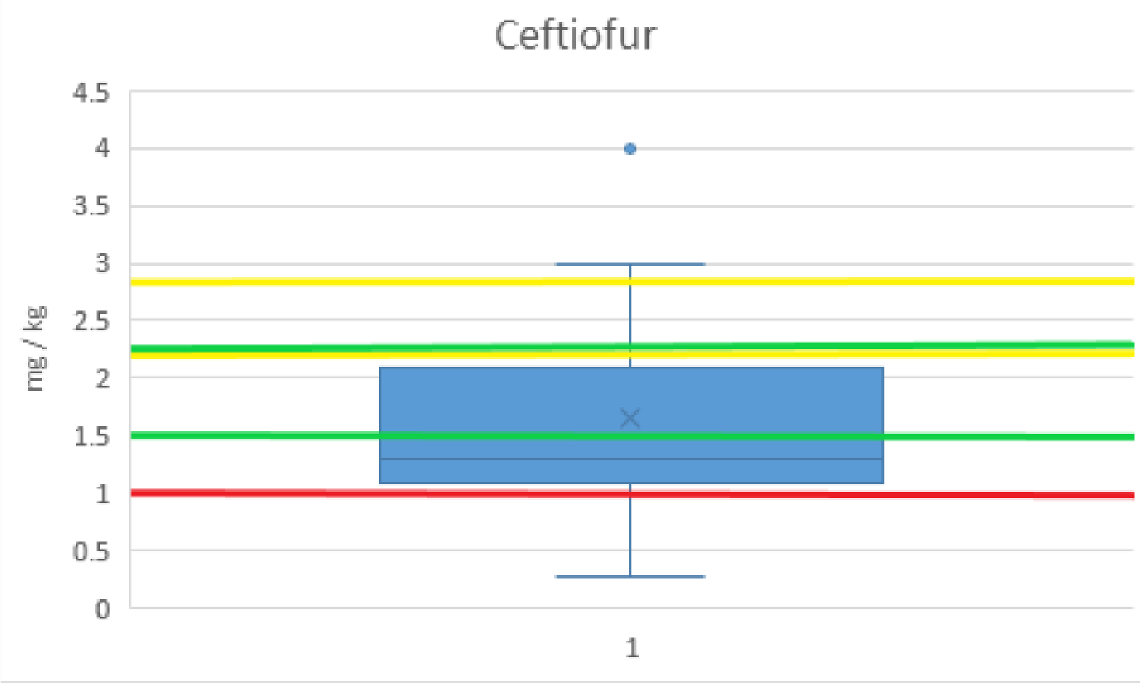

Figure 12: 3rd generation cephalosporins– dosages used for ceftiofur
The red line represents the recommended dosage for cattle from ASG
Green lines represent the recommended minimal and maximal dosage for alpacas from MemoVet
Yellow lines represent the recommended minimal and maximal dosage for llamas from MemoVet

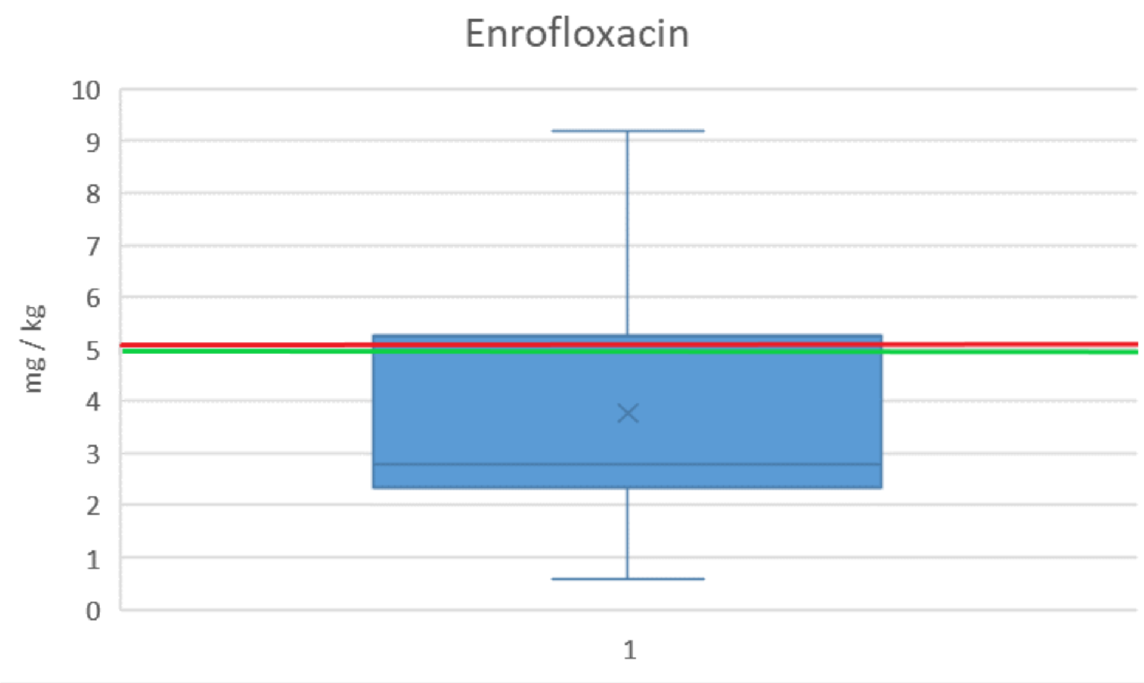

Figure 13: Fluoroquinolones – dosages used for enrofloxacin
The red line represents the recommended dosage for cattle/small ruminants from ASG
The green line represents the recommended dosage for NWCs from MemoVet

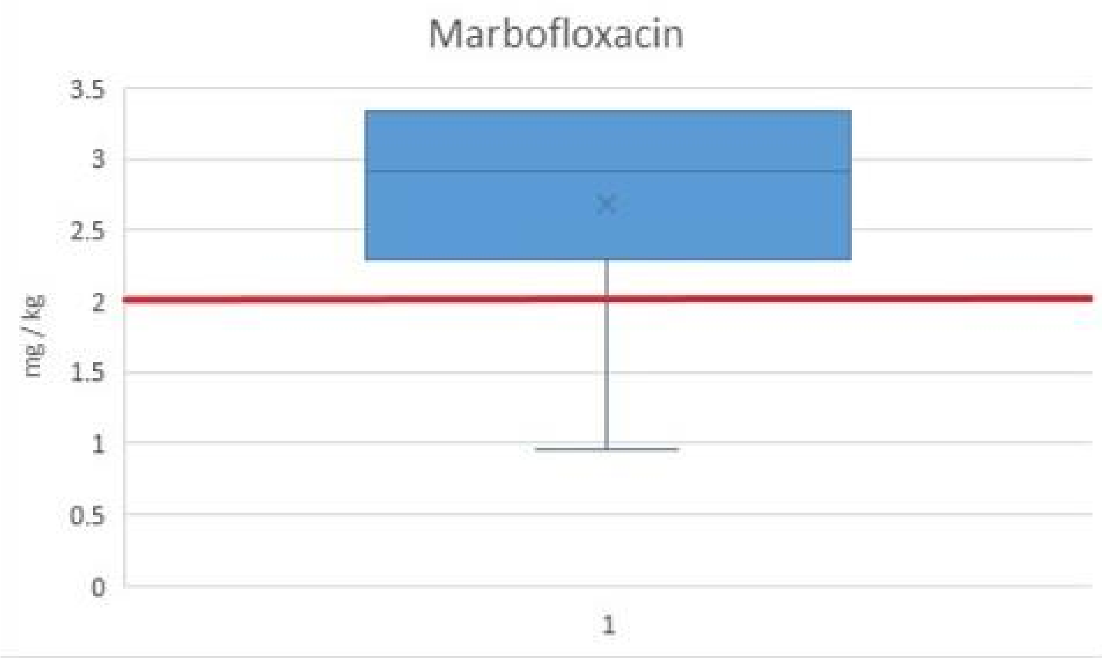

Figure 14: Fluoroquinolones – dosages used for marbofloxacin
The red line represents the dosage for calves from ASG
There is no recommendation for Marbofloxacin in MemoVet

4 DISCUSSION

Numbers of NWC patients at the University Clinic for Ruminants have been steadily increasing with the rise in their popularity in Austria. As the veterinary professionals encounter the problems of antibiotic resistance, the aim of this study was to confront the insufficiently explored area of antimicrobial therapy in NWCs, as there are no officially registered antimicrobials for use in NWCs. The goals were to evaluate the rising number of llama and alpaca patients receiving antimicrobial therapy at the University Clinic for Ruminants at the Veterinary University in Vienna, Austria in the years from 2005 till 2019, while exploring the most common diagnoses that needed antimicrobial therapy, the antimicrobial classes that were mostly used, what doses were preferred and how much of antimicrobial substances was used each year during this period of time. Causes for antimicrobial therapy were investigated while evaluating if the published pharmaceutical guidelines were abided. The results give an insight into the workings of the University Clinic for Ruminants with NWC patients that needed antimicrobial therapy.

It needs to be emphasized that the University Clinic for Ruminants is a referral clinic. This means mainly that veterinarians in private veterinary clinics and in the field sent patients to the University Clinic for Ruminants when they encountered cases where the initial treatment was unsuccessful or that need special care. Very few owners were unable to find veterinarians for primary care and therefore came to the clinic directly. The University is therefore no primary care facility and the cases do not reflect the situation of NWC patients in Austria.

4.1 ANTIMICROBIAL SUBSTANCES

To our knowledge, no antimicrobial substances have yet been officially approved for NWCs in EU. Veterinarians are facing a challenge while determining which drugs and which dosages to use for different situations because of lack of complete information on pharmacokinetics and proper dosages. Published materials found regarding antimicrobial substances used in NWCs are only considered basic guidelines and dosages are mere recommendations.

Antimicrobial substances used in our study at the University Clinic for Ruminants were according to EMA classification from groups B through D and C/D. No drugs from group A were used, which is considered the group to be avoided as it does not contain any antimicrobials authorised for veterinary medicine.

Antimicrobial substances used at the University Clinic for Ruminants during the years 2005 till 2019 were recorded and evaluated. The most used substance in the first years of this study till 2012 was a combined product containing benzylpenicillin and dihydrostreptomycin. It was taken off the market in 2016 and therefore not used after. An explanation on why this combination of substances was so often used is, that a combination of two different antimicrobial classes provided a broad spectrum of antibiotic coverage, as benzylpenicillin is effective against gram-positive bacteria and dihydrostreptomycin against gram-negative and in part also gram-positive bacteria. However, studies have shown that the situation of streptomycin regarding AMR is unfavourable, so the combined product has been replaced with other antimicrobial substances to avoid unwanted AMR (Rocha et al. 2021, van Overbeek et al. 2002).

At the University Clinic for Ruminants cephalosporins were used frequently between 2010 and 2015. Their usage started to decline after 2015 which correlates with antimicrobial guidelines that were published. Guidelines require restricted use of cephalosporins that are in the B category according to EMA, meaning they are critically important and should be used based on antimicrobial susceptibility testing whenever possible with AMR in mind (EMA 2020).

Instead, antimicrobial substances of group D such as aminopenicillins without beta–lactamase inhibitors, tetracyclines and narrow-spectrum penicillins became the drug of choice, followed by aminopenicillins with beta–lactamase inhibitors out of group C.

Average consumption of antimicrobial drugs was calculated, observing 2013 as the year with the highest consumption. An explanation for this is that the combination of benzylpenicillin and dihydrostreptomycin dosages are higher than others. After the year 2013 the average consumption started decreasing, correlating with benzylpenicillin–dihydrostreptomycin being taken off the market and with the published antimicrobial guidelines, which dictate reducing antimicrobial usage while fighting AMR. According to the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) of the EMA, in the years from 2019 and 2020 the use of antimicrobials such as cephalosporins, that are critically important in human medicine has decreased by 33%, together with fluoroquinolones, that are down by 13% in comparison to 10th ESVAC report that measured consumption between the years 2011 and 2018 (EMA 2021). The ESVAC report for 2019 and 2020 states that the county with the largest antimicrobial consumption of all antimicrobial classes is Cyprus (EMA 2021). Indicators of antimicrobial consumption are measured in mg/PCU (Population Correction Unit) which is a theoretical unit of measurement developed by the EMA to monitor antibiotic use and sales across Europe. Austria is well under the 50 mg/PCU mark while Cyprus is in comparison using almost 400 mg/PCU. Austria’s most commonly used antimicrobials seem to be tetracyclines and penicillins (EMA 2021). Romania seems to be the country with the highest consumption of antimicrobials from group B (EMA 2021). Antimicrobial consumption in animals has decreased in comparison to human consumption (ECDC et al. 2021).

A few sources have published their antimicrobial dosage recommendations for NWCs. Dosages in this study were the ones used for cattle and whenever possible, for small ruminants. Two different sources for dosages were inspected and dosages from MemoVet seem to be mostly higher than the ones from ASG, which are mainly principally recommended for cattle. Other sources agree on the higher dosages that were observed in MemoVet (Cebra et al. 2014, Jensen 2006, Marshall 2017). The reason that different dosages seem to be preferred in NWC compared to cattle could be found in factors that can influence pharmacokinetics, such as absorption rate, distribution of the drug and metabolism (Fajt 2014). More research is needed in this direction.

Four different antimicrobial agents from group B were evaluated, observing if they were in the range according to recommended dosages out of ASG and MemoVet. Most dosages used for cefquinome lie in the recommended values. Ceftiofur dosages used were mostly higher than the recommendation in ASG, but lower as the recommended dosages for llamas in MemoVet. It seems some intermediate dosage was preferred. Dosages for enrofloxacin that were used were lower than recommended and those for marbofloxacin were considerably higher than the recommended 2 mg/kg. Older sources recommended enrofloxacin in doses of 2.5 mg/kg. MemoVet does not include the information for marbofloxacin, the reason for it remains unknown.

4.2 STUDY POPULATION

There were 634 NWC patients treated at the University Clinic for Ruminants during the years 2005 through 2019, not counting companion animals. Approximately half of the patients needed antimicrobial treatment. After the year 2013 the number of patients increased and wavered between 70 and 90 patients per year. The rising numbers noticed in the study correlate with the rising popularity of NWCs in Austria and Germany (BMEL 2022, Neubert et al. 2021, Wittek and Franz 2021). While NWCs slowly gained popularity, the numbers at the University Clinic for Ruminants increased as people owned more NWCs that needed veterinary care and more attention was directed to their medical needs (Koenig et al. 2018). Interestingly, in 2019 when the number of patients in the study was the highest, alpacas were voted the most popular animal of the year, replacing the unicorn in that category (Marks 2019). With the rising numbers further research is needed to optimise animal husbandry and veterinarians role in their care (Neubert et al. 2021, Wittek and Franz 2021)

Patients of all ages were admitted to the University Clinic for Ruminants. Most of llama patients that came to the clinic and needed antimicrobial treatment were adult animals, while alpacas that were treated were younger on average. One of the challenges of this study was that in some of the medical records age or weight was not recorded. Cattle in Austria, for example, are fitted with two ear tags shortly after their birth and their data are put into a database that enables continuous tracking of their movement (AMA 2022). The NWC owners in comparison are only obligated to report any animal farming but individual animal identification is not enforced. Some breeding organisations require that the animals receive a subcutaneous transponder (microchip) (LARA 2021). Overall, it is likely that their database contains less precise information.

As for age and weight, both are important for making the right decision on choosing the antimicrobial substance, and even more importantly, the correct dosage and dose. When treated at the University Clinic for Ruminants, the attending veterinarian could estimate the weight of the animals based on their appearance. However, this was not possible in this retrospective study in hindsight. To find the most probable weight we consulted the growth curves and estimated the weight of the patients based on their age (Canaza-Cayo et al. 2015, Fowler 1998, Van Saun 2008).

Animals of both sexes were treated as patients at the University Clinic for Ruminants. In the llama patient population there were more male representatives, while the alpaca patients were more or less equal in numbers. In Austria, llama herds had predominantly more male animals in the herd, while alpaca herds had more female animals. This is probably because llamas are mostly used for trekking, some for herd protection, while alpaca herds are mostly for breeding and fiber production (Bauerstatter et al. 2018).

4.3 COMMON DIAGNOSES/DISEASES

With their rising popularity, NWCs received more attention regarding their health issues but were often grouped alongside small ruminants, even though they are phylogenetically different. Not much was known about their health at first, but their foregut fermentation made it simpler for them to be grouped in that category (Agnew 2018). There are, however, anatomic and physiologic differences between ruminants and NWCs (Fowler 2008). The same applies for their diseases. There are some ruminant diseases that NWCs are susceptible to and some that are specific for them.

To gain an insight into the most common diseases of NWC patients at the University Clinic for Ruminants the GMON code key was adapted for an easier and methodical evaluation of NWC diseases that required antimicrobial treatment. It needs to be kept in mind that these were the most common diseases at the University Clinic for Ruminants and do not necessarily reflect the most common diseases amongst NWCs in Austria.

The most common reason for antimicrobial therapy in patients at the University Clinic for Ruminants were GI tract disorders, followed by diseases of the CNS, skin and various infections. The third major group were patients being treated for diseases of the circulatory system and urinary tract. One other large group of patients was presented for castration and received antibiotic therapy as a part of perioperative infection prophylaxis.

The most commonly observed health issue identified in a survey amongst NWC owners in Germany were gastrointestinal parasites, together with other diseases of the digestive system like diarrhoea and dental issues. The authors also reported skin diseases, where ectoparasites were the most common reason. Abortions were reported as the most frequent issue in female animals and injuries due to ranking fights in male NWCs (Neubert et al. 2021). The authors of a retrospective Swedish study of necropsies reported that the digestive system was most frequently affected, especially noticing parasitic gastroenteritis and hepatic disease. Cardiovascular conditions, systemic diseases and perinatal deaths, including abortions and fatal septicaemia were also diagnosed. Other frequent findings were wasting, dermatitis and diseases of the central nervous system (Björklund et al. 2019). Overall findings of our study coincide with these studies on NWC health, which report intestinal diseases, parasitism, neonatal deaths, nutritional disorders and skin diseases amongst the major health concern in NWCs.

The findings in NWCs are different from those in a study surveying small ruminants receiving antimicrobials at the University Clinic for Ruminants. Here the most common causes for antimicrobial therapy were diseases of the urinary tract, followed by gastrointestinal diseases and systemic infections. Diseases of the musculoskeletal system and central nervous system together with sensory organs were also frequently diagnosed (Keppelmüller 2022).

4.3.1 Castrations

Many people that keep NWCs as hobby animals decide for castration to avoid behaviour issues if the animals are not intended for breeding. Herds with higher numbers of male intact animals sometimes confront the problem of higher injury probability due to rank fights (Bauerstatter et al. 2018, Neubert et al. 2021). We hypothesized that the number of patients being admitted for castrations at the beginning of our study were higher because the NWC herd management was in its early stages and still evolving. The veterinarians outside the University Clinic for Ruminants may not have had enough experience to perform such procedures at that time and the owners may have had more confidence in the University.

Broad spectrum treatment for perioperative prophylaxis was preferred and most commonly used antimicrobials for procedures of castration in this study were benzylpenicillin–dihydrostreptomycin, ampicillin and amoxicillin-clavulanic acid. Antimicrobial substances described by other authors are procaine penicillin G and oxytetracycline following a similar approach (Aubry et al. 2000, Lynch et al. 2020, Tibary 2007).

4.3.2 Diseases of crias

Not many cria patients were treated at the University Clinic for Ruminants between the years 2005 and 2019. We assume that the reason for the low number of young patients was that and the crias were mostly treated by the attending veterinarian in the field.

Crias at the University Clinic for Ruminants most often received treatment for septicaemia of the new born, which was commonly observed by other authors (Staples 2016). Neonatal and juvenile diarrhoea has been rarely reported in NWCs by other researchers (Cebra 2007, Whitehead 2009). For comparison, common diseases in calves are neonatal calf diarrhoea and respiratory diseases (Cho and Yoon 2014, Costa and Amaral-Phillips 2022, Stokstad et al. 2020). Complications related to the navel and umbilical cord, the second most frequent diagnosis in our study can be seen both in calves and crias (Blowey and Weaver 2011, Whitehead 2009). According to other authors, the most commonly observed cria problems seem to be related to environmental conditions such as hyper- or hypothermia and nutritional management such as failure to nurse and consequently dehydration and hypoglycaemia. Failure of passive transfer and sepsis are often observed too, together with prematurity and congenital conditions (McKenzie 2015, Whitehead 2009). These findings lead to the assumption, that some crias affected with neonatal diseases may not have survived in the field before intensive care could be initiated at the University Clinic for Ruminants.

Some sources recommend treating neonatal sepsis in NWCs with an antimicrobial regimen with a good spectrum of activity against gram-negative bacteria and suggest combined therapy of a penicillin with an aminoglycoside such as gentamicin (Whitehead 2009). In another study, the type of bacteria found in cria patients presented for sepsis were described and approximately half of the isolates were gram-positive bacteria (Dolente et al. 2007). This shows that each case warrants its own decision about the right antimicrobial drug choice and a broad spectrum drug is a good choice when there is a critically ill patient and the veterinarian has no time to wait for culture results.

4.3.3 GI tract diseases

Diseases of the digestive system were by far the most commonly observed diseases in the NWC patients at the University Clinic for Ruminants. Overall, 47% of all patients with GI disease were cases of dental disease with local swelling caused by tooth root abscesses. This also seems to be the most common problem observed by other authors (Cebra et al. 1996, Neubert et al. 2021, Niehaus 2009, Proost et al. 2020). In 62% of the stomatology cases in this study surgical intervention such as tooth extraction was performed, alongside antimicrobial treatment. Other sources conclude that surgical treatment was the most observed procedure in dental diseases of the NWCs, together with apicoectomy (Niehaus et al 2007). Aetiology of dental disease in NWC has not yet been established, but common observations suggest combination of genetic predisposition, diet and other management factors (Niehaus 2009). During our study, we had the impression that NWC patients with disease of the mouth tolerated the pain relatively well. Though some were under-conditioned, many kept eating even when the disease had already progressed. This might explain why the owners were late to observe any kind of discomfort in their animals and presented patients with severe cases of osteomyelitis in late stages of disease. To summarise, dental disease is commonly observed in NWCs. The prognosis depends on early diagnosis and treatment. Routine dental exams are advised to prevent development of advanced stages of dental and other diseases of the mouth (Niehaus 2009).

Many dental diseases seen in NWCs involve severe osteolytic changes, abscesses and actinomycosis with other bacteria involved such as *Fusobacterium spp.*, *Streptococcus spp., Bacterioides spp.,* so the choice of antimicrobial agent should be decided upon antimicrobial susceptibility testing (Wittek and Franz 2021). Most commonly used drug in veterinary medicine for dental diseases is amoxicillin-clavulanic acid as it has a broad spectrum against the bacteria commonly found in dental disease (Fraser 2012, Sarkiala and Harvey 1993). Cephalosporins with their spectrum of use were a common choice in this study, likely because of the amount of anaerobic bacteria found and severity of dental cases. It was decided upon as it is useful to treat infections of soft tissue and bone due to bacteria that are resistant to other commonly used antibiotics (Boothe 2015).

Another type of case that warranted antimicrobial treatment were animals with rapid onset of clinical signs suggesting enteric disease caused by *C. perfringens*. Most observed symptoms were enteritis with dehydration, weakness, sudden loss of appetite, indigestion and colic symptoms with cramps. Some animals showed signs of shock and CNS symptoms and some developed symptoms of kidney disease, ascites and subcutaneous oedema. These symptoms coincide with those described by De Perno, which were enteritis and oedema, together with high morbidity (DePerno et al. 2004). Enterotoxaemia resulting from *C. perfringens* is a condition that can have significant and lethal consequences causing severe systemic disease, so there can be no delay in treatment. Most reported strains of *C. perfringens* in NWCs were Type A, C, D and E (Staples 2016, Wittek and Franz 2021). All of the positive results for *C. perfringens* in samples taken from NWCs in our study that were sent to toxin analysis contained a type A strain. Additionally, all patients with suspected enterotoxaemia were affected by endoparasites. *C.perfringens* belongs to the natural gut flora but can proliferate due to changes in the gastro-intestinal tract balance caused by endoparasites, inadequate diet, ulcers in the gastro-intestinal tract and other diseases (Wittek and Franz 2021).

Some suspected cases were verified post mortem. It can be concluded that clostridial enterotoxaemia is a serious disease, which can end fatally. The only recommended protection against losses is to vaccinate the animals but even this does not fully provide protection against some of the toxins (Staples 2016).

Decision for starting antimicrobial therapy and selection of antimicrobial class depended on the symptoms upon admission and personal preference of the veterinarian. Antimicrobial guidance in Switzerland does not support choosing cephalosporins for cases of clostridial enteritis and justifies this claim with the explanation that cephalosporins aren’t suitable due to their pharmacokinetics (Vetsuisse-Fakultät 2022). The authors recommended benzylpenicillin in doses of 22.000 to 30.000 IU 1x per day s.c for five to seven days or longer (Vetsuisse-Fakultät 2022). In any case antimicrobial susceptibility test prior to treatment must be performed if possible, but with the fast onset of clostridial enterotoxaemia treatment sometimes requires a rapid decision.

4.3.4 Orthopaedic diseases

Even though NWCs are anatomically different, they have orthopaedic problems similar to cattle and small ruminants (Kaneps 1996). NWCs have triangular-shaped toenails and fat pad covered by a soft and flexible leathery pad in comparison to ruminants that have hooves and a sole (Fowler 2008). They bear their weight on both P2 and P3 and not just on P3 like most large animal species. The claw, located at the toe, corresponds to the hoof wall of ruminants but is not a weight bearing structure (Kaneps 1996, Malone et al. 2019). One author noted that NWCs show only reduced signs of pain in some cases when suffering from orthopaedic problems which could be a reason why owners detect the problems later than the original occurrence (Gunsser 2012). Our study cannot confirm this observation as all of the animals admitted to the clinic already showed signs of different and advanced stages of the disease. All of the orthopaedic cases in our study were grouped under the GMON "fractures, dislocations and other limb injuries", which summarized the most frequent orthopaedic problems of the NWCs treated at the University Clinic for Ruminants. Patients in the study suffered mostly from lameness caused by wounds that led to orthopaedic complications such as fistulation or contaminations of the joint and possibly infectious arthritis. Other diagnoses were fractures, luxations, rupture of the cruciate ligament, lesions of the tendon or trauma of the hooves. These findings correspond to other reports of orthopaedic cases, which were mainly related to trauma (Kaneps 1996, Malone et al. 2019, Wittek and Franz 2021). No case of foot rot, caused by *Dichelobacter nodosus*, was recorded amongst the NWC patients during the study. It seems that NWCs can contract the disease that is so contagious in sheep but it does not seem to have the same virulence in NWCs (Ardüser et al. 2020). They are more prone to interdigital dermatitis if the right conditions are met. (Malone et al. 2019). Even if their orthopaedic problems are similar to cattle and small ruminants NWCs are most often regarded as pets, so owners tend to have higher management expectations of their conditions. Being smaller in weight makes them excellent candidate for procedures that are not practical in larger animals (Kaneps 1996).

The most used antibacterial substance in orthopaedic cases in this study were 3rd and 4th generation cephalosporins, which are often used in cases involving soft tissue and bone (Boothe 2015). Cephalosporins are also regarded as good perioperative antimicrobial prophylactic treatment undergoing elective orthopaedic surgery (Whittem et al. 1999). For interdigital phlegmon the recommended drug of choice are penicillin and tetracycline (Vetsuisse-Fakultät 2022).

4.3.5 Respiratory system diseases

Sick or distressed NWCs commonly display abnormal respiratory signs, including dyspnoea and tachypnoea (Cebra 2014a). But in comparison to other ruminants and members of the horse family the problems in NWCs arise mostly from upper respiratory tract dysfunctions or are caused by other multisystemic diseases rather than from pneumonia (Cebra 2014a, Wittek and Franz 2021). In our study patients suffered mostly from primary lung diseases such as bronchitis and bronchopneumonia. The cases of upper airway disease such as rhinitis and laryngitis were rare during the study (n = 4). There is little information regarding clinical manifestation of neonatal cria pneumonia, which is in contrast to calf respiratory diseases that are one of the major causes for economic losses in the cattle industry (Bedenice 2011). Bacterial infection of the lung is relatively rare in NWCs and most commonly caused by *Streptococcus* and *Corynebacterium* spp. (Wiedner 2021). Overall, NWCs seem to be less prone to respiratory diseases compared to ruminants. The veterinarian needs to be prepared for diagnostics beyond thoracic auscultation and the respiratory tract altogether, as many systemic diseases of the NWCs are associated with troubled breathing, including hereditary predisposed and genetically conditioned disorders (Cebra 2014a, Wittek and Franz 2021).

Recommended for treatment of infectious of the respiratory tract are amphenicols, trimethoprim-sulfonamides, beta-lactam antibiotics and tetracycline (Vetsuisse-Fakultät 2022). Another recommendation for aspiration pneumonia are broad-spectrum antimicrobials, such as combinations of an aminoglycoside with a beta–lactam agent (Cebra 2014a).

4.3.6 Circulatory system and urinary tract diseases

Diseases of the circulatory system and urinary tract were categorised under one group in the study. There were only two patients with heart disease reported in the study, so any kind of conclusion is not possible due to the low number of patients. Cria patients that came to the University Clinic for Ruminants with weakness and being unable to stand on their own always had congenital heart diseases such as ventricular septum defect, atrial septum defect, persistent Ductus Botalli or congenital disorder of the bicuspid valve as a differential diagnosis. However, congenital heart diseases of crias and endocarditis in adult animals, including heart valve malfunction and diseases of the pericard and myocard are not common in NWCs (Wittek and Franz 2021).

Several patients (n = 17) were admitted with symptoms of anaemia, which is primarily caused by endoparasites, blood lost due to injury, gastrointestinal ulcers or acute infection with CMhl (Wittek and Franz 2021). CMhl is a disease exclusively found in NWCs and it was the principal diagnosis in 64% of the patients in this group, suggesting CMhl as one of the main reasons for anaemia in NWCs. Every patient in our study that was diagnoses with CMhl had a concurrent infection with one or more groups of internal parasites, which seems to have an impact on the severity of symptoms (Viesselmann et al. 2019). CMhl should be a differential diagnosis for every lethargic patient showing signs of chronic weight loss, decreased general demeanour with concurrent diseases and endoparasites with or without signs of anaemia (Evans and Six 2016, Marshall 2017). All of the patients in the study were adult animals and research is being done regarding vertical transfer to crias (Pentecost et al. 2012). As CMhl is a disease that can lead to severe anaemia and can be fatal if untreated, it is important to treat every case of anaemia as a potential case of CMhl.

A long acting oxytetracycline has been the recommended as antimicrobial drug of choice for treatment of CMhl. Recommended dosage is 20mg/kg (some propose 20 – 24 mg/kg) parenterally, some authors recommend additional oral treatment with oxytetracycline (Marshall 2017, Walker 2019, Wittek and Franz 2021). Suggested period of treatment differs with various authors; A minimum of 14 to 21 days is recommended. Some use long acting oxytetracycline registered for cattle and advise to treat every two or three days for five treatments or more (Marshall 2017, Walker 2019, Wittek and Franz 2021). NWCs may remain chronic carriers even after receiving treatment with oxytetracycline (Tornquist et al. 2009). Other research in treating CMhl with Artemisinin has been ongoing, as a way to clear the infection and not just improving anaemia and decreasing bacterial numbers as seen with oxytetracycline (Puccetti 2009).

Diseases of the urinary tract are one of the most commonly reported disorders in small ruminants, urolithiasis being the most common reason for treatment (Duesterdieck-Zellmer et al. 2014, Scully 2021). The publications on urinary tract disorders in NWCs are sparse and mostly consist of individual cases (Duesterdieck-Zellmer et al. 2014). However, urolithiasis is the most common cause for urinary tract obstruction in NWCs (Cebra 2014c). The reason behind the findings may be that NWCs reportedly drink less and urinate less compared to other ruminant species, a potential explanation being the GI conservation of water (Cebra 2014c). Other commonly mentioned causes for urinary tract diseases are those most often observed in other species, such as cystitis and nephritis. This concurs with our findings that the most commonly observed diagnosis in our patients was urinary obstruction, with suspicion of urolithiasis. It seems that male NWCs are more predisposed to urinary tract infections compared to females and literature reports that more castrated males suffer from urolithiasis (Cebra 2014c, Duesterdieck-Zellmer et al. 2014). Fowler (2010) disagrees and refers the intact, breeding males as the ones more commonly affected (Fowler and Bravo 2010). This study can neither confirm nor deny this observation as castrated (n = 4) and intact male (n = 3) representatives in the study were almost equal. According to Cebra, congenital malformations of the urinary tract seem to be more common in camelids that in other species of domestic livestock (Cebra 2014c). In this study there was only one suspected case of ectopic ureter recorded.

Recommended antimicrobial treatment for urinary infections and urolithiasis is amoxicillin or ampicillin. Trimethoprim-sulfonamid and gentamicin are also suggested while fluoroquinolones are regarded as critical antibiotics and are to be used only if there is no other option available and after an antimicrobial susceptibility test (Vetsuisse-Fakultät 2022, Wittek and Franz 2021). Patients in this study received trimethoprim-sulfonamid, amoxicillin–clavulanic acid, benzylpenicillin–dihydrostreptomycin and cefquinome after the antimicrobial susceptibility test was performed.

4.3.7 CNS, diseases of the skin and generalised infections

Neurological diseases are reportedly as common in NWCs as in other species. They show a wide number of symptoms with many different causes (Taylor 2013b). Different types of disease manifestations that can mimic metabolic and musculoskeletal conditions, which need to be distinguished from the true neurological origin of the disease (Anderson and Whitehead 2004, Whitehead and Bedenice 2009). Only nine patients needed antimicrobial treatment for various CNS diseases at the University Clinic for Ruminants, their numbers were again too low to for a sensible conclusion about neurological disease amongst NWCs in Austria. Most common cause for neurological symptoms in NWC patients taking part in the study originated from trauma from cervical vertebral injuries. These are fairly common and described as vertical body luxation, subluxation or cervical body fracture caused by trauma (Anderson and Whitehead 2004). Cervical luxation and subluxation seem to be more common in NWCs than in other species (Whitehead and Bedenice 2009). Diagnoses at the University Clinic for Ruminants were determined with the help of radiographs and sometimes additional diagnostic testing like CT or MRI. Owner’s compliance played a decisive part in setting the diagnosis.

One pregnant llama with neurological signs showed possible pregnancy related neurological signs, which is usually observed in sheep and goats as the so called pregnancy toxaemia, and rarely in NWCs (Paxson and Bedenice 2015). After treatment the animal regained normal neurological function but it opened a question on the occurrence of pregnancy toxaemia in NWCs.

Interestingly, *Parelaphostrongylus tenuis* (the "meningeal worm") is reportedly one of the most important diseases of NWCs in the eastern half of North America (Whitehead and Bedenice 2009). There have been no reported cases of it in Europe.

Penicillin, ampicillin and tetracycline have been discussed for treatment of *Listeria monocytogenes.* Fluoroquinolones and cephalosporines are advised only when no other alternative can be found (Vetsuisse-Fakultät 2022). Some recommend a broad spectrum antimicrobial agent where more differential diagnoses were possible to cover as many causes as possible (Balducci et al. 2020). Most patients in our study received oxytetracycline, ampicillin and amoxicillin-clavulanic acid.

Diseases concerning eyes and ears were grouped as one in this study. There were more patients admitted to the University Clinic for Ruminants for diseases of the eyes that suffered mostly from ocular trauma. Some of the patient's ocular diseases were due to other systemic disease. The University's own ophthalmologic specialists agreed with previous published studies that most commonly observed reasons for diseases of the eyes were either trauma, foreign body (like dust for example) or infectious agents (Gionfriddo 1994). Other reasons observed were congenital in nature or due to different types of allergies. In all of the cases in our study, the reason behind the infection was bacterial in nature.

Patients with diseases of the eye in this study received their treatment in the form of eye drops or ointments, which were in majority tetracycline ophthalmic preparations or those containing gentamicin. Those that additionally received parenteral antimicrobial therapy mostly received ampicillin or amoxicillin-clavulanic acid. Other sources suggest broad spectrum topical antimicrobial medication for conditions such as conjunctivitis, keratoconjunctivitis, ulcerative keratitis and conditions affecting the ocular surface (Czerwinski 2019).

Patients being treated for diseases of the ear at the University Clinic for Ruminants presented with symptoms of otitis, which was in most cases otitis externa, caused by ectoparasites (mites). One patient was diagnosed with otitis media with the differential diagnosis of neurological disease, with listeriosis as one possible cause. The animal recovered and no samples were available for further analysis. Previous studies agree that the origin of ear diseases was either neurological, bacterial, parasitic, traumatic or caused by foreign body (Franz et al. 2019, Koenig et al. 2001). Furthermore NWCs seem to be predisposed to developing otitis media/externa because of the characteristic anatomic conditions of the ear (Franz et al. 2019).

Diseases of the ear that were caused by ectoparasites received parenteral antimicrobial therapy only if the patient presented with fever and signs of diminished general demeanour. Infections in the ear were treated with topical antimicrobial substances. Thereby it needs to be kept in mind that otitis externa can consequently lead to perforation of the ear drum and otitis media, which causes neurological symptoms and needs to be treated accordingly (Wittek and Franz 2021)

Skin conditions in NWCs are reported as one of the most challenging and frustrating disorders veterinarians need to deal with (Cebra 2014b). The majority of patients seeking help for skin diseases at the University Clinic for Ruminants were diagnosed with infections caused by ectoparasites, such as mites, consequently developing mange. Other common observations were bacterial infections due to trauma or abscesses from old wounds or shearing accidents that developed into purulent skin infections, which required antimicrobial treatment and wound care. Zinc responsive dermatosis was also recorded and was in all cases diagnosed concurrently with some other skin disorder, often mites. One case was suspected as idiopathic necrolytic neutrophilic hyperkeratosis (INNH, known as “munge”). Ectoparasites are the most common cause of pruritus amongst NWCs (Taylor 2013a). Infectious problems and idiopathic hyperkeratosis / zinc responsive dermatosis are also noticed among the most common dermatopathies (Scott et al. 2011, Taylor 2013a). Moreover, zinc responsive dermatosis is reportedly one of the most perplexing conditions as some animals do not respond to supplementation (Rosychuk 1989). Skin lesions are reported to occur most likely in young breeding females because the mineral content in their diet is low. Also, dark fleeced animals may be more frequently affected because dark fleece contains higher levels of zinc and copper than white flees and exerts higher demands on mineral metabolism (Taylor 2013a). All of the animals being treated for zinc responsive dermatosis at the University Clinic for Ruminants were females, so the study can agree to the observation about the predisposition of the sexes. They did all respond positively to the oral zinc supplementation.

Alopecia as major clinical sign of skin disease has been reported to occur more frequently in dark haired animals which are more predisposed to alopecia on the light haired areas in comparison to light fleeced animals. One other possible reason is that insects prefer warmer surface of a darker background (Cebra 2014b, Wiedner 2021).

Those skin diseases in this study that needed systemic antimicrobial therapy were treated with ampicillin, amoxicillin, amoxicillin-clavulanic acid, oxytetracycline, gentamicin, benzylpenicillin-dihydrostreptomycin and ceftiofur. Other recommendations for bacterial skin infections are penicillin or trimethoprim–sulfadiazine (Rosychuk 1989).

4.3.8 Reproductive system

The smallest group of patients in the study were those treated for diseases of the reproductive system. Cases of metritis, dystocia, abortion, chronic inflammation of the udder and injury after parturition were observed. (Tibary et al. 2006) reported similar findings, namely that NWCs were most commonly affected by infertility, abortions, udder diseases and neonatal mortality, often caused by various infectious diseases. In comparison to other animals like cattle and small ruminants the NWCs seem to have similar diseases of the reproductive system, together with similarities of the infectious and non-infectious causes but they tend to have a lower predisposition towards diseases of the reproductive organs (Ali et al. 2019, SVF 2013, Wittek and Franz 2021). Few bacterial causes have been reported for pregnancy losses in NWCs and were similar to those in small ruminants, most commonly chlamydiosis, followed by leptospirosis, campylobacteriosis, and toxoplasmosis. These studies contained no information on bacteria culture tests (Gorman et al. 1999, Tibary 2021). There is an economic aspect of breeding so diagnostics and therapy of reproductive disorders, together with gestation examinations play an important part in the veterinary care of NWCs. Especially in alpacas we see a higher demand in reproductive measures as the breeding industry grows in its popularity. There was only one male llama so here can be no conclusion about the male NWC population in Austria and their reproductive system diseases.

4.3.9 Treatments without obvious cause

It is difficult to discuss why a few patients (n = 7) in this study received antimicrobial therapy while there was no obvious cause for it found in TIS. Plausible explanation could be, that TIS did not hold enough information on individual patient for this study to find a cause that would justify antimicrobial therapy. Or perhaps that patient was already treated before coming to the University Clinic for Ruminants, and the attending veterinarian decided it was sensible to continue the therapy because the patient possibly displayed symptoms that would warrant antimicrobial therapy and would be in the best interest of the patient. Sometimes admittance is during the night time or on weekends and decisions are needed which would benefit the patient. It also needs to be reminded that every veterinarian has its own preference and makes decisions according to them.

Even if the body of research regarding common maladies of NWCs is growing there is still much to be researched, including drugs being used and their dosages. Surveys have been done and 72% of the owners of NWCs feel that while there were very little NWC specialised practices, they were still well cared for by their veterinarians while almost 55% thought veterinarians do not have sufficient knowledge in the camelid field, agreeing they get insufficient information material provided by their veterinarian (Neubert et al. 2021). Another questionnaire showed only 10% of the owners were satisfied with the veterinary service they received and more than half of the participants thought veterinarians lacked sufficient knowledge while treating NWCs as something between a ruminant and a horse instead of a camelid (Björklund et al. 2019). Responses like these show the need of veterinary education supported by academic research of NWC diseases and needs for effective treatment (Björklund et al. 2019).

5 SUMMARY

Even with the rise of popularity of NWCs in the world and in Austria there are to our knowledge no antibiotic drugs on the market officially registered for NWCs. Veterinarians need to adapt and deal with these new patients as best as they can, using the existing drugs available for other species, including antimicrobial substances. With the ever rising threat of AMR, guidelines for using antimicrobial drugs need to be respected while combating diseases of NWCs. This retrospective study examined the most commonly observed diagnoses of 341 NWCs that received treatment at the University Clinic for Ruminants in the years between 2005 and 2019 and what antimicrobial drugs were used to treat them, while abiding to the published rules of correct conduct of antimicrobial usage.

Most commonly observed diagnoses that needed antimicrobial treatment were diseases of the GI tract, followed by diseases of CNS, skin and various infections. Another commonly observed problems were diseases of the circulatory system and urinary tract. Most common antimicrobial drug used in the first years of this study was a combined substance of benzylpenicillin and dihydrostreptomycin. It was later replaced by aminopenicillins (no beta lactamase) and narrow spectrum penicillins, followed by aminopenicillins with beta lactamase inhibitors. Their usage responds to the published guidelines on using antimicrobial substances in veterinary medicine in Austria in 2018 and those already published by colleagues in Germany in 2015. These findings comply with EMA categorisation of antibiotic classes as these substances fall under category D (prudent use).

Cephalosporins were mostly used in cases of dental disease and in orthopaedic patients. Their usage slowly declined after the published guidelines as they are registered in restricted group and should be only used where no other drugs are available and after antimicrobial susceptibility test.

There were several studies and articles published regarding NWCs and their health since NWCs first became popular, but the dosages published still serve only as guidelines and most of them are taken from those used for cattle or small ruminants. Further research in health issues and treatment is still needed so that veterinarians can feel confident treating these rising numbers of new type of patients.

6 ZUSAMMENFASSUNG

Trotz der zunehmenden Beliebtheit von NWK auf der Welt und in Österreich gibt es unseres Wissens noch keine offiziell für NWK zugelassenen Antibiotika auf dem Markt. Tierärzte müssen sich anpassen und mit diesen neuen Patienten so gut wie möglich umgehen, indem sie die für andere Tierarten verfügbaren Medikamente, einschließlich antimikrobieller Substanzen, verwenden. Angesichts der zunehmenden Bedrohung durch Antibiotikaresistenz müssen bei der Bekämpfung von Krankheiten bei NWK die Leitlinien für die Verwendung antimikrobieller Arzneimittel beachtet werden. Diese retrospektive Studie untersuchte die am häufigsten gestellten Diagnosen bei 341 NWK, die in den Jahren 2005 bis 2019 an der Universitätsklinik für Wiederkäuer behandelt wurden und welche antimikrobiellen Arzneimittel zu ihrer Behandlung eingesetzt wurden, und ob die veröffentlichten Leitlinien für deren korrekte Anwendung eingehalten wurden.

Die häufigsten Diagnosen, die eine antimikrobielle Behandlung erforderten, waren Erkrankungen des Magen-Darm-Trakts, gefolgt von Erkrankungen des ZNS, der Haut und verschiedene Infektionen. Ein weiteres häufig beobachtetes Problem waren Erkrankungen des Kreislaufsystems und der Harnwege. Das in den ersten Jahren dieser Studie am häufigsten verwendete antibiotische Präparat war eine Kombination aus Benzylpenicillin und Dihydrostreptomycin. Später wurde es durch Aminopenicilline (ohne Beta-Laktamase) und Schmalbandpenicilline ersetzt, gefolgt von Aminopenicillinen mit Beta-Laktamase-Hemmern. Diese antimikrobiellen Medikamente wurden in den letzten Jahren der Studie am häufigsten eingesetzt und ihre Verwendung entspricht den 2018 in Österreich veröffentlichten Leitlinien zum Einsatz antimikrobieller Substanzen in der Veterinärmedizin, sowie den bereits 2015 von Kollegen in Deutschland veröffentlichten Leitlinien. Diese Ergebnisse stehen im Einklang mit der EMA-Kategorisierung der Antibiotikaklassen, da diese Substanzen in die Kategorie D (umsichtige Verwendung) fallen.

Cephalosporine wurden hauptsächlich bei Zahnerkrankungen und orthopädischen Patienten eingesetzt. Ihr Einsatz ging nach der Veröffentlichung der Leitlinien langsam zurück, da ihre Verwendung nur noch eingeschränkt gestattet ist und sie nach einem Resistenztest nur dann verwendet werden sollten, wenn keine anderen wirksamen Arzneimittel zur Verfügung stehen.

Da NWK immer beliebter geworden sind, wurden deutlich mehr Studien und Artikel über deren Gesundheit veröffentlicht. Die angegebenen Dosierungen dienen nach wie vor nur als

Richtlinien und die meisten von ihnen sind von denen für Rinder oder kleine Wiederkäuer übernommen worden. Es sollten noch weitergehende Forschung zu Gesundheitsfragen und zur Behandlung angestellt werden, um Tierärzten bei der Behandlung dieser neuen Art von Patienten mehr Sicherheit geben zu können.

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ANNEX

Table 8: the original GMON code key published by the TGD (TGD - Tiergesundheitsdienst 2011)

Diagnoseschlüssel	
Kälber	
11	Nabelentzündung
12	Nabelbruch
13	Sehnenkontraktur
14	Missbildungen
15	Ikterus haemolyticus neonatorum
16	Kälberdurchfall
17	andere Krankheiten des Kalbes
171	Kastration
172	Kastration unblutig
173	Kastration blutig
174	Enthornung Kalb
175	Kastration und Enthornung
176	Kastration unblutig und Enthornung
177	Kastration blutig und Enthornung
Verdauungstrakt	
21	Durchfall
22	Tympanie
23	Pansenübersäuerung
24	Fremdkörpererkrankung
241	Fremdkörper-Vorbeugung (Prophylaxemagnet)
25	Labmagenverlagerung
26	Darmverschluss
27	andere Erkrankungen der Bauchhöhle
271	Peritonitis
273	Clostridiose, Clostridioseverdacht
28	Erkrankungen der Maulhöhle
281	Zahn Extraktion
29	Erkrankungen der Speiseröhre
Stoffwechsel	
31	Gebärparese, Hypocalcämie
311	Gebärpareseprophylaxe
32	Tetanie
33	Azetonämie
331	Ketoseprophylaxe
34	andere Stoffwechselkrankheiten
35	Vergiftungen
Abkalbung, Fruchtbarkeit	
400	Trächtigkeits-U. fraglich
401	Trächtigkeits-U. rektal negativ
402	Trächtigkeits-U. rektal positiv
403	Trächtigkeits-U. US negativ
404	Trächtigkeits-U. US positiv
405	Trächtigkeitstest PAG negativ
406	Trächtigkeitstest PAG positiv
407	Geburtsinduktion
41	Gebärmutterentzündung
411	Endometritis Vorbeugung
42	Stillbrunst, Azyklie

421	Brunstsynchronisation
422	Embryotransfer – Superovulation
43	Ovarialzysten
44	Scheidenvorfall
45	Abortus und andere Störungen der Gravidität
451	Abortusinduktion
46	Schwergeburt
461	Geburtshilfe konservativ
462	Fetotomie
463	Sectio caesarea
47	Geburtsverletzungen
48	Nachgeburtsverhaltung
49	puerperale Erkrankungen
491	Puerperalkontrolle
99	Männliche Geschlechtsorgane
	Euter
51	akute Euterentzündung
52	chronische Euterentzündung
53	Erkrankungen der Euter- und Zitzenhaut
54	Euterödem
55	Andere Eutererkrankungen
56	prophylaktisches Trockenstellen
560	prophylaktisches Trockenstellen
561	prophylaktisches Trockenstellen mit Antibiotikum
562	prophylaktisches Trockenstellen mit Zitzenversiegler
563	Kombinierte Anwendung Zitzenversiegler und Antibiotikum zum Trockenstellen
564	Bakteriologische Milchuntersuchung
	Klauen und Gliedmaßen
61	Panaritium, Mortellaro
62	Klauengeschwür; Krankheiten der Gelenke an den Klauen
621	Klauenkorrektur
63	Klauenrehe
64	Frakturen, Luxationen, andere Gliedmaßenverletzungen
65	Krankheiten von Muskeln und Sehnen, WMD
651	Vitamin E - Selen Prophylaxe
66	spastische Parese, Paralyse
67	Peritarsitis
68	Festliegen infolge Erkrankung des Bewegungsapparates
69	Krankheiten des Schwanzes
	Atemwege
71	Erkrankungen der oberen Luftwege
72	Lungenentzündung
73	andere Lungenerkrankungen
74	Pleuritis
	Herz, Kreislauf und Blut, Harntrakt
81	Herzerkrankungen
82	Septikämie, Anämie
83	Piroplasmose und andere Parasitosen des Blutes
84	Leukose
85	Erkrankungen der Gefäße und der Milz
86	Pyelonephritis
87	Erkrankungen der Harnblase
88	Harnabflusstörungen
	ZNS, Haut, Infektionen

91	ZNS-Erkrankungen
92	Erkrankungen der Sinnesorgane
93	Parasitosen und Infektionen der Haut
94	Erkrankung der Hörner
941	Enthornung erwachsenes Rind
95	andere Hauterkrankungen
951	Abszess
952	Wunde, Bissverletzungen, Trauma
96	Allgemeininfektionen
100	Zinkmangel, Zinkabhängige Dermatose
960	Tetanus
961	Schutzimpfung
	Sonstiges
1	Abmagerung, Kachexie
2	verminderte Fresslust, Inappetenz
3	Fieber, fieberhafte Allgemeinerkrankung
4	Anwendung von Antiparasitika, Coccidiostatika, Antiprotozoika, Repellentien
5	Metaphylaktische Tierarzneimittelanwendung
6	Prophylaktische Anwendung von Tierarzneimitteln, Futtermitteln
7	Sedierung, Immobilisation
0	ohne Diagnose, ohne Angabe
999	perioperative Infektionsprophylaxe
821	Mykoplasma, Mykoplasma verdacht
1000	Palatochisis

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