

Master of Public Health  
Integrative Learning Experience Report

***ANTIMICROBIAL STEWARDSHIP IN VETERINARY MEDICINE: PREVALENCE OF STEWARDSHIP  
PROGRAMS  
AND PRELIMINARY ANTIMICROBIAL USE DATA***

by

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## Abstract

This applied practice experience was undertaken for 242 hours at the Dispensary at the Veterinary Health Center at Kansas State University from September 2018 to March 2019. The Veterinary Health Center at Kansas State University (VHC) is a full-service veterinary hospital that provides routine, specialty, and emergency care. The Dispensary at the VHC plays a crucial role in providing unparalleled services filling prescriptions for their patients.

Antimicrobial resistance is defined by the Centers for Disease Control and Prevention as microorganisms that mutate to evade the antimicrobials used to treat them. Antimicrobial resistance is an international public health crisis because antimicrobial resistant infections may spread to others and increase mortality rates. As antimicrobial resistance becomes a growing public health concern in human health, the prevalence of antimicrobial stewardship programs in human hospitals has increased exponentially. Similar to human health, antimicrobial stewardship programs for veterinary use should integrate infection prevention and control, whilst implementing judicious antimicrobial prescribing. Although veterinary medicine would benefit from antimicrobial stewardship programs, lack of person power and time are major barriers hindering the implementation of these programs.

The Veterinary Health Center at Kansas State University prescribes a broad range of antimicrobials for therapeutic use as do most veterinary hospitals. The purpose of this applied practical experience was to analyze the frequency, dose, duration, indication and overall prescribing patterns of one of those antimicrobials, amoxicillin-clavulanate, in canine and feline patients at the VHC. The main objective was to help determine prescribing patterns of this medication, as baseline data to be used in the implementation of an antimicrobial stewardship program at the VHC. In addition to analyzing these data, a survey was sent to veterinary teaching hospitals across the United States and Canada to develop a deeper understanding of veterinary antimicrobial stewardship programs in these settings. Applying the knowledge gained from this applied practical experience has provided me with a deeper One Health understanding of antimicrobial resistance.

**Subject Keywords:** Antimicrobial resistance, stewardship, amoxicillin-clavulanate, veterinary teaching hospitals, One Health

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## **Acronyms and Abbreviations**

AMDUCA- American Medicinal Drug Use Clarification Act

AVMA- American Veterinary Medical Association

ASPs- Antimicrobial Stewardship Program

BEPHI- Bureau of Epidemiology and Public Health Informatics

CVM- Center for Veterinary Medicine

CDC- Centers for Disease Control and Prevention

EU- European Union

ESBL- Extended Spectrum  $\beta$ -lactamase

ELDU- Extra Label Drug Use

Federal Drug Administration- FDA

Kansas Department of Health and Environment- KDHE

Kg- Kilograms

MRN- Medical Record Number

Mg- Milligrams

mL- milliliters

PBP- Penicillin-binding Protein

PO- Per os

Spp.- species

BID- "bis in die" which means twice a day

USP- United States Pharmacopeia

VCPR- Veterinarian-Client Patient Relationship

VDL- Veterinary Diagnostic Laboratory

VHC- Veterinary Health Center- VHC

World Health Organization- WHO

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## Chapter 1- Field Experience Scope of Work

### Antimicrobial Resistance

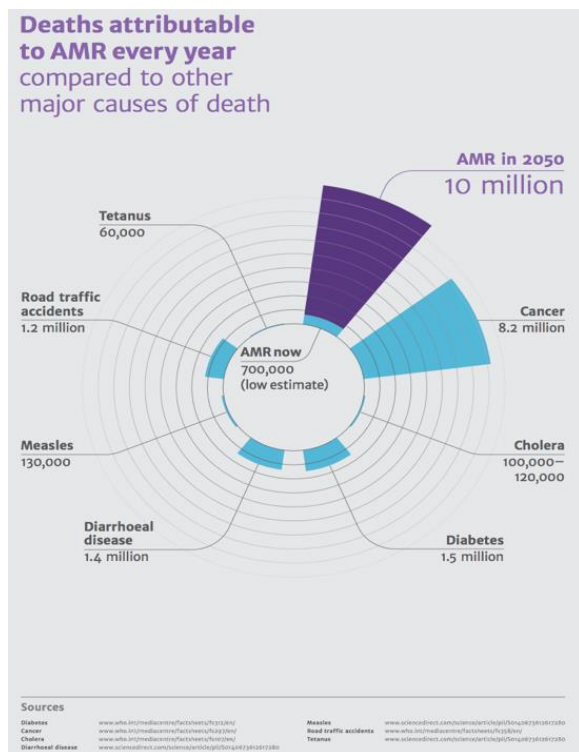
An antimicrobial is an agent that inhibits the growth of microorganisms such as viruses, fungi, or bacteria. Their primary function as bacteriostatic or bactericidal agents makes them critical tools used for treating infections in both human and veterinary health.<sup>1</sup> The terms “antibiotic” and “antimicrobial” are often used interchangeably and although they are similar in function, they do not possess identical definitions. According to the American Veterinary Medical Association (AVMA), antibiotics are a subset of antimicrobials that perform a narrower spectrum of functions, inhibiting bacterial growth only.<sup>1</sup> The discovery of penicillin in 1928 marked the beginning of the modern era of antibiotics. Penicillin was found to substantially increase survival rates from 10% to 90% in patients with pneumonia and bacteremia.<sup>2</sup> Penicillin was widely prescribed to treat serious infections; however, within a thirty-year period penicillin became less effective for treating infections due to resistance developed by its targeted bacteria. Penicillin resistance became a substantial clinical problem, and as a response, a new generation of antimicrobials called beta-lactamase inhibitor antibiotics, such as amoxicillin-clavulanic acid, were discovered and utilized in a clinical setting.<sup>2</sup>

Any use of antimicrobials increases selective pressures in a population of bacteria, resulting in the promotion of resistant bacteria while killing vulnerable bacteria.<sup>3</sup> Many pathogenic microorganisms naturally mutate to evade the bactericidal drugs used to kill them, and the misuse of antimicrobials has resulted in an increased rate of developed antimicrobial resistance.<sup>4</sup> Resistance genes can be found within the microorganisms’ plasmids. A plasmid is a small circular DNA strand in the cytoplasm of the microorganism that can replicate independently of the chromosomes. Bacterial organisms possessing plasmids with resistance genes can survive and replicate in the face of certain antimicrobial agents, share these plasmids with other pathogenic or normal flora, and can cause resistant infections in people or animals.<sup>4</sup>



## Global Burden of Antimicrobial Resistance

New resistance mechanisms are rapidly emerging globally along with new associated barriers to treat common infectious diseases.<sup>5</sup> Antimicrobial resistant bacteria are emerging and proliferating faster than antimicrobials are being developed; within the last decade only one antimicrobial has been developed and approved for use. The World Health Organization published a report in 2011, stating only 15 of 167 antimicrobials under development presented a new mechanism of action that had the potential to overcome the challenge of multidrug resistance.<sup>6</sup> Without effective antimicrobials available as a method of treatment for standard medical procedures there is a direct increase in the risk of adverse events and mortality in patients. This increase in risk of adverse events and mortality is due to prolonged treatment of infectious diseases and chronic infections. In 2017, the Centers for Disease Control and Prevention (CDC) reported antimicrobial resistance was annually responsible for: 25,000 deaths in the European Union, 58,000 infant deaths from resistant bacterial infections in India, 38,000 deaths in Thailand and 23,000 deaths in the United States of America.<sup>7,8</sup> Based on the current global census, and accounting for hospitalizations due to antimicrobial resistance, a total of 700,000 deaths are estimated to be attributed to antimicrobial resistance annually by 2050 (see Figure 1.1).<sup>9</sup> The mortality rates will potentially be higher in developing countries due to the misuse of antimicrobials in human medicine. Misuse of antimicrobials is facilitated in these developing countries due to their availability, they are available over the counter, without any necessary prescription through supply chains that are unregulated in developing countries.<sup>10</sup> Antimicrobials in Africa have been dispensed on the streets to individuals who cannot afford to seek care, and those antimicrobials have been found to have 46% less potency than the antimicrobials dispensed by a licensed physician.<sup>10</sup> The global projected estimated cost of antimicrobial resistance and the associated treatment methods have been estimated to escalate to 100.2 trillion dollars.<sup>9</sup>



**Figure 1-1 Global Projected Human Deaths Attributable to Antimicrobial Resistance Annually by 2050 Projected by the Government of the United Kingdom<sup>9</sup>**

### Antimicrobial Stewardship Programs

In response to a global public health concern, antimicrobial stewardship programs have been established in human hospitals across the world beginning in 1996.<sup>11</sup> Antimicrobial stewardship programs (ASPs) are plans implemented by a multidisciplinary team of health care professionals seeking to optimize antimicrobial prescribing to improve overall patient care.<sup>11</sup> The CDC published seven core elements of antimicrobial stewardship that all established ASPs must adhere to in order to be recognized by the CDC: Leadership commitment, accountability, drug expertise, action, tracking, reporting and education.<sup>11</sup> Leadership commitment is defined as dedicating necessary human, financial, and information technology resources to the antimicrobial stewardship program. Accountability is appointing a leader responsible for program outcomes. Action is implementing at least one recommended action such as systemic evaluation of ongoing treatment. Tracking is monitoring antimicrobial prescribing and resistance patterns. Reporting is reporting information on antimicrobial use and resistance to physicians,

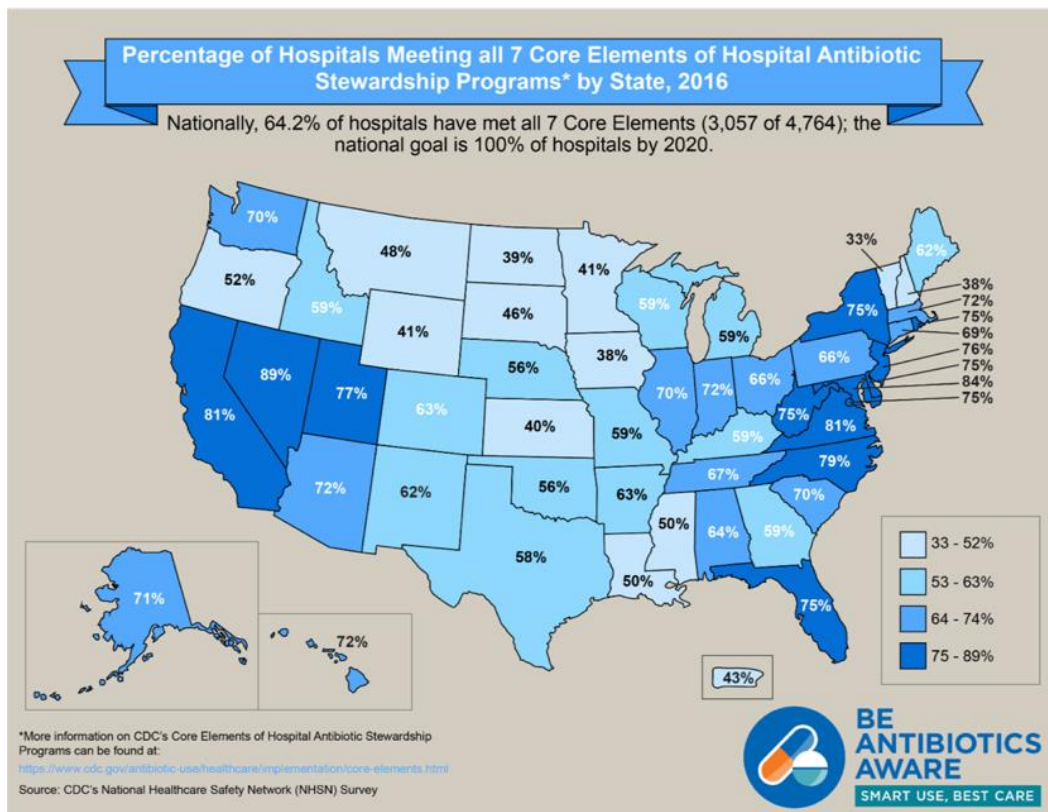
nurses and relevant clinical staff. Education is educating clinicians, hospital faculty, and the general public about resistance and optimal prescribing.<sup>11</sup> Nationally 58.2% of human hospitals have established ASPs and adhere to the CDC's seven core elements (see Figure 1.2).<sup>11</sup> Established ASPs should implement policies that support optimal antimicrobial prescribing including: implementing facility specific treatment recommendations, documenting dosage, duration, and indication.<sup>12</sup> Evidence has demonstrated a link between improved antimicrobial use and optimizing treatment of infections, in addition to a reduction in all antimicrobial related adverse events in hospitals adhering to the CDC's seven core elements.<sup>11</sup>

Human health has an abundance of comprehensive ASPs that have been widely implemented within the last two decades.<sup>12</sup> There has been a strong push for ASP implementation in veterinary practices through global action plans by organizations such as the American Veterinary Medical Association (AVMA). Despite the push for implementation, it has been found that comprehensive ASPs are uncommon in veterinary practice.<sup>13</sup> The Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) has publicly voiced their support for the establishment of veterinary ASPs to be widely implemented in veterinary hospitals.<sup>14</sup> As of September 2018, the FDA released a five-year plan for supporting antimicrobial stewardship in veterinary settings partnered with the AVMA.<sup>14</sup>

The AVMA published five core principles that parallel the importance of the CDC's seven core elements in human health. The purpose of these core principles is to integrate maintaining animal health and welfare with a variety of preventive and management strategies and utilizing evidence-based approaches in prescribing choices.<sup>15</sup> AVMA lists the core principles of ASPs in veterinary medicine as commit to stewardship, advocate for a system to prevent common diseases, select and use antimicrobial drugs judiciously, evaluate microbial drug use practices, and educate and build expertise.<sup>15</sup> Commit to stewardship is defined as developing stewardship plans that incorporate dedication and accountability for disease prevention and that also optimize the prescribing, administration, and oversight of antimicrobial drugs. Advocate for a system of care to prevent common diseases is identifying diseases and working with clients to adopt preventive strategies to minimize the need for antimicrobial drugs. Select and use antimicrobial drugs judiciously is using an evidence-based approach for making a diagnosis and

determining whether an antimicrobial drug is indicated. Evaluate antimicrobial drug use practices is encouraging the development of a program for the evaluation of antimicrobial drug prescribing at the veterinary-practice level. Educate and build expertise is making resources available to encourage expertise in antimicrobial stewardship and keeping up to date on strategies for disease prevention.<sup>15</sup>

The FDA CVM aims to achieve three major goals: align microbial drug product use with the principles of antimicrobial stewardship, foster stewardship of antimicrobials in the veterinary setting, and enhance monitoring of antimicrobial resistance and antimicrobial drug use in animals.<sup>14</sup>



**Figure 1-2 Percentage of human hospitals meeting all 7 core elements of antimicrobial stewardship programs in the United States by state as of 2016 <sup>11</sup>**

## One-Health Perspective

The One Health triad identifies and recognizes the relationship between the health of humans, animals, and the environment. Initiatives have been implemented to address the global concern of antimicrobial resistance. Internationally (WHO), nationally (CDC), and locally the Kansas Department of Health and Environment and the Kansas Healthcare-Associated Infections & Antimicrobial Resistance Advisory Group have implemented initiatives such as World Antibiotic Awareness Week, US Antibiotic Awareness Week, and Be Antibiotics Aware Week in Kansas. These initiatives aim to educate the public about the development of antimicrobial resistance and risks associated in relation to human and animal health.

Antimicrobial use in companion animal health is discussed; however, a greater emphasis and focus is on antimicrobials used in food-producing animals for growth purposes, specifically reducing antimicrobial-resistant bacteria transmission between animals and humans through food.<sup>16</sup> These initiatives have proven effective in public education regarding appropriate disposal of antimicrobials to prevent antimicrobial resistant bacteria developing in the environment and affecting livestock. Unfortunately, most individuals are not aware of the importance of antimicrobial resistance in companion animals as well. The CDC and AVMA emphasize the importance of understanding not all infections or illnesses, in both humans and animals, require antimicrobials as a method of treatment. There is an established bias between human health and animal health that blames animals for transmitted diseases between the animal and human sector of the One Health triad. For an antimicrobial stewardship program to be effective and implement a One Health perspective, both human health clinicians and veterinarians should clarify any misconceptions and work together towards a positive change. The CDC has an entire website dedicated to parasites that are transmitted from animals to humans, the most common vectors of transmission are birds, pigs, and insect-borne vectors.<sup>17</sup> Individuals reading this may misinterpret the message, and this increases fear while diminishing the human-animal bond. Increasing public knowledge of steps that can be taken to reduce the spread in both directions would be most effective in preventing development of antimicrobial resistant bacteria and transmission between the three sectors of the One Health triad.

The relationship between the One Health triad and reducing antimicrobial resistance is commonly discussed in various health care platforms and is analyzed to determine methods to eliminate factors that are driving resistance. Utilizing a One Health approach to view antimicrobial resistance as more than just a human health concern will allow for appropriate rectification and overall reduction of adverse events. The common tips that are shared for human antimicrobial use such as not sharing antibiotics, taking an antimicrobial agent as prescribed by a clinician and recognizing not all infections require an antimicrobial has to be applied to animal health as well. A One Health perspective is a logical method when addressing antimicrobial resistance, as the drivers of antimicrobial resistance extend far beyond human health and include antimicrobial use and abuse in all three sectors of the One Health triad.

### Resistance Mechanisms

Antimicrobials are categorized based on their principal mechanisms of action. These mechanisms include the interference with cell wall synthesis, inhibition of protein synthesis, interference with nucleic acid synthesis, inhibition of a metabolic pathway and disruption of bacterial membrane structure.<sup>18</sup>  $\beta$ -lactams are classified by their principal mechanism of action which is cell wall synthesis.  $\beta$ -lactamases are a family of enzymes produced by microorganisms that are responsible for the development of resistance to  $\beta$ -lactam antibiotics such as penicillin and extended spectrum cephalosporins.<sup>19</sup> In an attempt to overcome  $\beta$ -lactamase resistance,  $\beta$ -lactamase inhibitors were clinically introduced. Commonly known  $\beta$ -lactamase inhibitors are clavulanate, sulbactam, and tazobactam.<sup>18</sup>  $\beta$ -lactamase inhibitors paired with  $\beta$ -lactam drugs such as amoxicillin or ampicillin, increase the  $\beta$ -lactam bactericidal activity.<sup>18</sup>

For microorganisms to develop resistance to  $\beta$ -lactam and  $\beta$ -lactamase inhibitors there are three major mechanisms of resistance: destruction of  $\beta$ -lactam rings by  $\beta$ -lactamase enzymes, altered targets in penicillin binding proteins (PBPs), and decreased uptake in the porin channel formation.<sup>20</sup> Upon the destruction of the  $\beta$ -lactam ring, the antimicrobial being used for treatment will not be able to bind to the PBP and, subsequently interfere with cell wall synthesis. Altering the PBP through mutations in the original PBP or acquired PBPs leads to the inability of the antimicrobial to bind and inhibit cell wall synthesis. A decrease in the porin channel formation

is a resistance mechanism as the  $\beta$ -lactams use this channel to cross the outer membrane of the cell in order to reach the PBP and any change in this channel results in reduced  $\beta$ -lactam uptake.<sup>20</sup> If the microorganism achieves any or all three of these mechanisms of resistance, the  $\beta$ -lactam drug is no longer effective in treatment. This applies to all classes of  $\beta$ -lactam drugs including  $\beta$ -lactamase inhibitors. The antimicrobial that was analyzed in this project was amoxicillin-clavulanic acid. Amoxicillin-clavulanic acid is an aminopenicillin with a  $\beta$ -lactamase inhibitor; therefore, understanding the mechanisms of resistance for the  $\beta$ -lactamase inhibitors is crucial.

### Amoxicillin-clavulanic acid

#### Microbiology

Amoxicillin is a commonly used bactericidal antimicrobial in human and veterinary medicine. Amoxicillin by itself has been shown to have activity against penicillin-sensitive bacteria as well as gram-negative bacteria.<sup>21</sup> Amoxicillin is sensitive to destruction by  $\beta$ -lactamases and is not effective by itself against microorganisms that produce  $\beta$ -lactamases.<sup>21</sup> Clavulanic acid is a naturally occurring inhibitor of  $\beta$ -lactamase and is effective against  $\beta$ -lactamase of gram-negative and gram-positive microorganisms. When paired the combination of amoxicillin-clavulanic acid results in an extension of amoxicillin activity and prevents destruction by  $\beta$ -lactamase. The clavulanic acid is referred to as a suicide inhibitor and results in destruction of the microorganisms after binding to the  $\beta$ -lactamase the microorganism produces. However, other resistance mechanisms such as altered PBP binding sites are not affected.<sup>21</sup> The combination of amoxicillin-clavulanic acid is labeled for use in dogs and cats and commonly prescribed in veterinary medicine.

#### Pharmacology

Amoxicillin-clavulanic acid is a time-dependent antimicrobial. Time-dependent antimicrobials' bactericidal activity is based on the time that the drug maintains an appropriate concentration at the binding site of the microorganism. Amoxicillin-clavulanic acid is effective due to extensive time at the binding site. When amoxicillin-clavulanic acid is above the minimum inhibitory concentration (MIC) this allows for the beta-lactamase inhibitor to effectively work against the microorganism. Time-dependent antimicrobials have to be dosed more than once in

a 24-hour period, because once the free antimicrobial concentration in the patient's plasma goes below the MIC, the antimicrobial's bactericidal activity is not as effective. This results in dosing amoxicillin-clavulanic acid and other time-dependent antimicrobials twice or three times a day depending on the antimicrobial and indication.

#### Labeled Dose information

Amoxicillin-clavulanic acid is available in several strengths ranging from 62.5-mg to 375-mg. This applied practical experience focused on four strengths of amoxicillin-clavulanic acid tablets and one oral suspension prescribed to both canine and feline patients the Veterinary Health Center: 62.5-mg, 125-mg, 250-mg, 375-mg and the oral suspension 62.5-mg/mL.

Amoxicillin-clavulanic acid tablets are indicated for the treatment of skin and soft tissue infections such as abscesses, cellulitis, dermatitis, superficial and deep pyoderma, and wounds due to susceptible bacteria in canine and feline patients.<sup>21</sup> Periodontal infections due to susceptible bacteria can also be treated with amoxicillin-clavulanic acid in canine patients, as well as urinary tract infections caused by susceptible *E. coli*.<sup>21</sup>

The labeled dose of amoxicillin-clavulanic acid was obtained from the FDA approved drug label. The labeled dose for canines is 6.25 mg/lb or 13.75 mg/kg administered twice a day by mouth. For canine superficial skin and soft tissue infections such as abscesses, wounds, cellulitis, and periodontal infections the approved duration is 5-7 days.<sup>21</sup> The labeled dose is 62.5-mg per cat administered twice a day by mouth. For feline skin and soft tissue infections such as abscesses and cellulitis the approved duration is 5-7 days.<sup>21</sup>

#### A Brief Introduction to the Veterinary Health Center at Kansas State University

The VHC is a veterinary hospital that treats more than 23,000 patients per year across the Midwest. The VHC provides a wide range of services including: routine and specialty care for small and exotic animals, a range of equine and livestock services, shelter medicine, 24-hour emergency care and clinical trials. The VHC describes the goal of their facility "To provide superior veterinary medical education, quality patient care, and exceptional customer service in a caring environment."



I worked directly with the Dispensary at the VHC during my applied practice experience. The Dispensary is licensed by the Kansas State Board of Pharmacy as an Institutional Drug Room with a DEA registered hospital and clinic. The Dispensary plays a crucial role in the daily activities of the VHC. Clients, clinicians, and fourth-year veterinary students are able to order and pick up prescribed medications for their patients in a timely and efficient manner. The Dispensary has recently been remodeled to add United States Pharmacopeia (USP) standard compounding suites for non-sterile compounding (USP <795>), sterile compounding (USP <797>), and sterile hazardous drug compounding (i.e. chemotherapy) (USP <800>).<sup>22</sup> The remodel was also designed to improve workflow and patient safety outside of the compounding areas.

During my experience, I had interactions with pharmacy staff including pharmacists, pharmacy interns, pharmacy technicians, and student workers to develop a basic understanding of veterinary dispensaries in veterinary medicine. However, my primary job at the Dispensary was to collect and analyze amoxicillin-clavulanic acid data from the VHC. As a result of this, I had several interactions with the College of Veterinary Medicine's Computer and Technical Support group to gain access and familiarity with VetStar, which is the VHC's health information system.

### Project Introduction

A multi-disciplinary team of Kansas State CVM and VHC faculty and staff have joined together to develop and implement an ASP in the VHC. They understand the necessity of monitoring antimicrobial use data as a first step to determine if changes in antimicrobial prescribing behavior are needed and to guide those changes. This applied practical experience was the first step in collecting antimicrobial data for this initiative. Due to the demand of establishing an ASP in the VHC the pharmacy director, Dr. Colvin-Marion and Dr. Kate KuKanich created a project that would build the necessary foundation for the first stage of a multi-phase project to develop an ASP.

I worked with the VHC Director of Pharmacy, Dr. Colvin-Marion, and the College of Veterinary Medicine's Computer and Technical Support group, Nancy Hawkins and Daniel Cutting, to determine prescribing patterns of amoxicillin-clavulanic acid at the VHC. Dr. Colvin-Marion and I worked closely together to improve my understanding of veterinary pharmacy and how it differs from human pharmacy. She also dedicated time to discuss dosing guidelines,

weight-based dosing, and available literature for amoxicillin-clavulanic information with me. With the assistance of the information technology department at the VHC, five amoxicillin-clavulanic acid products were exported from VetStar for data analysis purposes. This information was exported into a Microsoft Excel sheet that provided client information and strength of amoxicillin-clavulanic acid prescribed. Utilizing my access to VetStar enabled me to collect further information on each patient including: weight, date seen, diagnosis, dose prescribed, duration, frequency, and susceptibility. This data analysis will build as a foundation for the next phase of this project. In addition to analyzing prescribing data, Dr. KuKanich and I designed a survey that was sent to veterinary hospitals across the United States and Canada to inquire about their ASPs and any barriers or successes they wanted to share.

## Chapter 2- Learning Objectives

1. Gain a deeper understanding of the role that dosage, frequency and duration have in antibiotic prescribing patterns
2. Understand the background of both human and veterinary antimicrobial stewardship programs
3. Understand how frequently amoxicillin-clavulanic acid is being prescribed at the Veterinary Health Center at Kansas State University
4. Learn how veterinary schools across the United States of America and Canada implement antimicrobial stewardship programs
5. Utilize responses from surveys to build a deeper understanding on how to begin an antibiotic stewardship program at the Veterinary Health Center at Kansas State University
6. Use knowledge obtained from data analysis to apply towards human health and antibiotic stewardship programs
7. Have a deeper understanding of the role under and overprescribing of antibiotics has on development of antimicrobial resistance
8. Create a foundation for the next phase of development for an antimicrobial stewardship program at the Veterinary Health Center at Kansas State University

### Activities Performed

**Table 2:1 Activity Table**

Objective	Activity
1, 3, & 8	Export five different strengths of amoxicillin-clavulanate prescription data from VetStar 4/2/18 to 11/19/18
1 & 7	Compare actual dose prescribed to approved label dose from drug insert
1	Determine appropriate indication and which diagnoses require amoxicillin-clavulanic acid prescriptions
4, 5, 2 & 6	Create a survey inquiring about antimicrobial stewardship programs to veterinary teaching hospitals across the United States of America and Canada
1 & 8	Attempt to understand the reason behind varying durations between clinicians at the VHC

2 & 6	Spoke with representatives from two human hospitals in Kansas with established antimicrobial stewardship programs to learn what data they collect, hurdles they have, changes that have resulted from antimicrobial stewardship implementation
4 & 5	Analyze data from the surveys and write an abstract and poster based on those responses

**Products Developed**

My major professor, Dr. Kate KuKanich, and I designed a cross-sectional online survey that was sent to 26 veterinary teaching hospitals across the United States of America and Canada. This survey requested information from veterinary teaching hospitals inquiring about current established ASP's in their hospital. If they had established ASPs, the survey prompted a series of questions inquiring about the following: length of the program, shared data with clinicians, data collected regarding antibiotic use, observed changes in prescribing behavior, and restricted use of antibiotics. If the hospital did not have an established ASP, the survey prompted a series of questions inquiring about barriers preventing implementation and any additional details about stewardship efforts. Whether the veterinary teaching hospital had an established ASP or not, their responses were very helpful in understanding potential barriers of implementation and furthermore barriers that are preventing these ASPs to be successful.

All responses were returned to Dr. KuKanich and were subsequently forwarded to me for data collection and analysis. Once all survey responses were collected and recorded, Dr. KuKanich and I wrote and submitted an abstract titled Prevalence of Antimicrobial Stewardship Program in Veterinary Teaching Hospitals for the Phi-Zeta Research Day at Kansas State University. The abstract was accepted for presentation, and a poster was created for the Phi-Zeta Research presentation. The survey, abstract and poster are all attached in the Appendix.

My preceptor, Dr. Colvin-Marion had a student working in the VHC pharmacy who was very interested in my applied practical experience. Courtney Howell provided me with an opportunity to present my applied practical experience data and analysis to the University of Kansas Veterinary Pharmacy Club. At this presentation, I also brought the poster titled

“Prevalence of Antimicrobial Stewardship Programs in Veterinary Teaching Hospitals” to share these results as well.

I work at the Kansas Department of Health and Environment in the Bureau of Epidemiology and Public Health Informatics (BEPHI). I have shared my presentation with the epidemiologists at KDHE, so that they will further understand my role in the stewardship efforts at Kansas State. KDHE already has a strong working relationship with several veterinarians at Kansas State CVM (including Drs. Apley and KuKanich) to collaborate on One Health stewardship. This collaboration and community effort on One Health and stewardship was furthered by our creation of a flyer intended for lay people to understand that both people and animals can carry antimicrobial resistance bacteria, and that we all share responsibility for minimizing risk of further development of resistance in our community. This flyer is located in the Appendix.

### Chapter 3: Capstone Project Literature Review

#### Veterinary Antimicrobial Resistance

Veterinary antimicrobial resistance has been studied globally within the last decade, but specifically in the last 5 years there has been an increase in veterinary antimicrobial resistance literature both in farm and companion animals. A concept that has been repeated throughout the literature states that antimicrobials are essential for veterinary medicine but should be handled prudently to protect their efficacy in fighting infections. The European Union (EU) has driven antimicrobial use in food-producing livestock down by 27% since 2005, through actively monitoring antimicrobial use in food-producing livestock, utilizing susceptibility data, and European parliament interventions such as restriction of specific antimicrobial agents.<sup>23</sup> European parliament restricts the use of monensin in cattle, salinomycin in piglets, avilamycin, and flavophospholol in livestock.<sup>23</sup> The EU has conducted numerous studies investigating attitudes and behaviors towards initiatives focusing on reducing the use of antimicrobials.<sup>23</sup> A survey was conducted across the EU to determine the cause of higher antibiotic use in food-producing animals despite the known consequences of antimicrobial overuse, and the implementation of antimicrobial restriction placed by the European Parliament in 2017.<sup>24</sup> Results

showed that increased antimicrobial consumption in food-producing livestock was due to fear of economic impact on food production, jeopardizing livestock health by reducing antimicrobial use, and individual farm profits.<sup>26</sup> Countries such as the Netherlands and Iceland are diligent regarding reduced antibiotic use, and have adhered to these initiatives prior to the EU's law enactment restriction of animal antibiotic use in 2018.<sup>24</sup> However, countries such as Italy, Republic of Cyprus, and Spain had rates ranging between 375-450 (mg/kg of estimated biomass) of overall consumption of antimicrobials in one year.<sup>24</sup> Implementation of surveillance and antimicrobial susceptibility databases have proven to be successful in the EU since 1998, resulting in a decrease in antimicrobial resistant bacteria emergence within their country and the EU.<sup>23</sup>

Currently antimicrobial usage data in the United States of America is monitored more closely in food-producing animals rather than companion animals. The WHO published a report in 2018 reviewing an early implementation study they have been conducting reviewing antimicrobial consumption in 65 countries. This report only outlined antimicrobial use in food animals rather than from an animal health or welfare perspective.<sup>25</sup> Tetracycline (71%), penicillin (9%), and macrolide (6%) compose the most clinically significant antimicrobials that are used in food animals.<sup>25</sup> To improve judicious use of antimicrobials in animals, the FDA amended animal drug regulations and implemented a veterinary feed directive (VFD) stating that certain drugs are only intended for use in animal feeds and the administration or use of a VFD is permitted only under direct supervision of a licensed veterinarian.<sup>26</sup> The FDA has created a list of the drugs requiring a VFD, some of these include neomycin, sulfamerazine, tylosin, erythromycin, and florfenicol.<sup>26</sup> FDA defines judicious drug use as practices that aim to maximize therapeutic efficacy while ultimately minimizing selection of resistant microorganisms, and it is a crucial part of veterinary medicine.<sup>26</sup>

#### Efficacy of amoxicillin-clavulanic acid based on indication

Due to amoxicillin-clavulanic acid's function as a  $\beta$ -lactamase inhibitor, it is found to be more effective against resistant infections than a traditional  $\beta$ -lactam drug. When attempting to treat resistant infections caused by extended-spectrum  $\beta$ -lactamase(ESBL) producing microorganisms, such as some strains of *Escherichia coli*, veterinarians might prescribe amoxicillin-clavulanic acid.<sup>27</sup>

Literature has been published within the last five years examining the efficacy of amoxicillin-clavulanic acid in veterinary medicine. In 2012 a study was conducted that concluded administration of amoxicillin-clavulanic acid resulted in the most effective treatment for feline patients with clinical upper respiratory tract infections housed in an animal shelter in comparison to doxycycline and cefovecin.<sup>28</sup> The amoxicillin-clavulanic acid was administered at 12.5 mg/kg, twice a day orally for a duration of 14 days.<sup>28</sup> Comparative studies of amoxicillin-clavulanic acid to fluoroquinolones resulted in higher therapeutic successes of recurrent urinary tract infections in canines (96.2%) with treatment using amoxicillin-clavulanic acid than the studied fluoroquinolone (84%).<sup>29</sup> The cause of increased efficacy is due to the  $\beta$ -lactamase inhibitor activity working against a  $\beta$ -lactamase producing microorganism that would cause urinary tract infections in canines such as *Staphylococcus spp.* and *Escherichia coli*.<sup>27</sup>

Skin infections in companion animals are most commonly associated with coagulase-positive *Staphylococcus spp.*, a causative agent of canine pyoderma.<sup>30</sup> In 2012, seventeen peer-reviewed controlled trials were conducted to review the systemic antimicrobial treatment of canine pyoderma. Results identified a fair level of evidence supporting increased efficacy of cefovecin in superficial pyoderma, and oral administration of amoxicillin-clavulanic acid in treating deep pyoderma in canines in comparison to clindamycin, oral cefadroxil and trimethoprim–sulfamethoxazole.<sup>31</sup> The administered dose in this study was 12.5-25 mg/kg orally twice a day for 14 days with an emphasis on rechecking pyoderma status after completion of amoxicillin-clavulanic acid.<sup>33</sup>

Periodontal disease is prevalent amongst dogs, and investigations have been conducted to evaluate the aerobic and anaerobic subgingival flora susceptibility to a wide range of antibiotics.<sup>33</sup> It was found that anaerobic bacteria had a higher resistance to antibiotics than aerobic bacteria. Aerobic bacteria such as *Streptococcus spp.*, *Escherichia coli* and *Pasteurella multocoda* were found to be susceptible to amoxicillin-clavulanic acid.<sup>33</sup> The authors of the study concluded that amoxicillin-clavulanic acid was an acceptable treatment for oral soft tissue infections in canine and feline patients.<sup>33</sup> There is a fair amount of evidence concluding amoxicillin-clavulanic acid can be effective in treating companion animals with bites from dogs and cats. A study conducted in 2000 isolated several aerobic species including *Pasteurella spp.*,

*Streptococcus spp.*, and *Staphylococcus spp.* from the wounds caused by dog bites.<sup>34</sup> Cat bites were found to contain both *Staphylococcus spp.* and *Pasteurella multocoda*.<sup>34</sup> Treatment of a bite would should be based on culture and susceptibility of the wound itself. While culture is pending, either oral amoxicillin-clavulanic acid or its intravenous equivalent ampicillin-sulbactam would be appropriate.<sup>32,33,34</sup>

### Consequences of inappropriate prescribing on antimicrobial resistance

There is an abundance of available literature regarding inappropriate prescriptions of broad-spectrum antimicrobials in human medicine and the direct consequence inappropriate antimicrobial prescribing has on increasing resistance; however, few studies review the consequences in veterinary medicine. In 2011, a study was conducted to determine antimicrobial prescribing in ambulatory human pediatric patients in the United States; this study found that 21% of patient visits resulted in an antimicrobial prescription, and subsequently 50% of the prescribed antimicrobials were classified as broad-spectrum antimicrobials. After further review, broad spectrum antimicrobials were not appropriately prescribed and led to development of resistance to amoxicillin in 3.4% of the patients seen.<sup>35</sup> In 2014, the British Journal of General Practice published an article reviewing the antimicrobial consumption by people in the United Kingdom and what consequences were associated with overprescribing. The authors discussed microorganisms, such as *Staphylococcus aureus*, have demonstrated resistance to more than 50% of currently approved antimicrobials and determined that implementing a One Health approach to reducing antimicrobial consumption is an effective method to reduce the drivers of antimicrobial resistance.<sup>35</sup> In 2015, a systematic review was conducted on the antimicrobial crisis as a whole globally.<sup>4</sup> Inappropriately prescribed antibiotics are proven to contribute to the promotion of resistant bacteria in human patients, and have been incorrectly prescribed in 30% to 50% of cases reviewed.<sup>4</sup> One cause of the development of drug resistance has been use of antibiotics for growth-promotion within livestock.<sup>4</sup> Based on a report published by the FDA in 2010, the authors conclude that more than half (80%) of the United States' antimicrobial consumption is attributed to food animals.<sup>36</sup> It is predicted by 2030 there will be a 67% increase to antimicrobial consumption in food animals to match global food demand, if no changes or policies are implemented immediately.<sup>37</sup> Results conclude that the presence of  $\beta$ -lactamase



resistant pathogenic strains develop through horizontal gene transfer between resistant microorganisms to other microorganisms.<sup>38</sup> Prescribing amoxicillin-clavulanic acid under the standard dose have been shown to contribute to strain diversification in organisms including *Pseudomonas aeruginosa*.<sup>39</sup> As amoxicillin-clavulanic acid was developed as an alternative agent and should be used for treatment of resistant bacteria, there is little to no evidence to support that amoxicillin-clavulanic acid is frequently inappropriately prescribed in veterinary patients. A study conducted in 2011 concluded 48% of human infections treated with amoxicillin-clavulanic acid could have been treated with a narrow-spectrum antibiotic and would have been just as effective.<sup>40</sup> There are currently no published studies revealing evidence of a direct relationship between over prescribing amoxicillin-clavulanic acid in canine or feline patients and increased antimicrobial resistance.

## Materials and Methods

### Identifying Prevalence of Antimicrobial Stewardship Programs in Veterinary Teaching Hospitals

In order to join the One Health stewardship efforts, major organizations such as the AVMA, American Association of Bovine Practitioners, American Association of Equine Practitioners, and American Association of Feline Practitioners have created initiatives and guidelines for veterinary hospitals to follow to establish antimicrobial stewardship programs and to promote judicious use of antimicrobials. To determine the prevalence of antimicrobial stewardship programs in veterinary teaching hospitals, an online cross-sectional survey was designed by a pharmacy student at the VHC originally, and then edited by myself and Dr. KuKanich. This survey was then sent to 26 veterinary teaching hospitals in the United States and Canada. The survey was sent to pharmacists, infection control, or pharmacology faculty that would have a deep understanding of hospital stewardship programs and policies. The survey consisted of questions requesting information about the following: established stewardship programs, which antimicrobials are monitored, sharing data with clinicians, changes in prescribing behavior, restricted use of antimicrobials, and hurdles of implementing a program.

## Identifying Successes of Antimicrobial Stewardship Programs in Human Hospitals in Kansas

Human hospitals in the United States of America have been required to establish antimicrobial stewardship programs by the Joint Commission as of January 2017. Leading public health organizations such as the CDC, along with state health organizations such as KDHE have been working diligently together to establish effective antimicrobial stewardship programs. Although these programs are prevalent in Kansas human hospitals, their hurdles nor successes have been published for public knowledge. To determine these successes and hurdles, five human hospitals in Kansas were contacted via phone to discuss their antimicrobial stewardship programs. These calls were placed to infection prevention, infection control, and infectious disease pharmacists in each hospital. This informal conversation consisted of questions requesting information regarding antimicrobial stewardship program establishment, barriers or hurdles faced prior to implementation, actions that were taken to reduce or eliminate these hurdles, observed successes, and which antimicrobials were being prescribed frequently prior to antimicrobial stewardship program establishment.

## Methods of amoxicillin-clavulanic acid use monitoring

To determine prescribing patterns of amoxicillin-clavulanic acid at the VHC, baseline data had to be collected and analyzed. The College of Veterinary Medicine Computer and Technical Support group, Nancy Hawkins, exported a list of all canine and feline patients prescribed amoxicillin-clavulanic acid at the VHC from April 2, 2018- November 19, 2018. This data export provided the medical record number (MRN), date of birth, species, breed, type of visit, frequency, duration, and strength of amoxicillin-clavulanic acid prescribed. First the data had to be sorted by medical record number to determine which patients were prescribed amoxicillin-clavulanic acid more than once in this seven-month period. Once it was sorted, then each patient's MRN was entered into the VHC's health information system, VetStar, to determine dose, frequency, duration, indication, and prescribing clinician.

The original data export included patient durations and frequencies for respective amoxicillin-clavulanic acid prescriptions. After searching each patient chart, it was determined that the original data export included incorrect durations and frequencies for each patient. The durations and frequencies were deleted from the original data entirely and entered based on the

patient's chart. To access this information, the view chart tab in VetStar was utilized to collect the correct duration and frequencies. Utilizing the PP function in VetStar displayed the date the amoxicillin-clavulanic acid was dispensed, how many tablets were dispensed, and frequencies that were not explicitly listed in the discharge summary of the patient chart. Weight was not exported; therefore, each patient's weight had to be collected from the patient chart and inputted into the Microsoft excel sheet. Patient weight was charted in the health information system for 764/795 (96%) patients, however 31/795 (3.9%) patients required paper charts to be pulled to determine weight.

Once patient weight, frequency, duration, date of prescription, indication and prescribing clinician were all collected, the patient dose could be calculated. Utilizing the Microsoft excel sheet, the mg per dose was recorded (375mg tablet administered twice a day= 375mg). The mg per dose was divided by the kg of each patient to determine mg/kg for each prescription. These data were entered into a separate column for later comparison of labeled dose to actual dose prescribed.

To complete data analysis several functions in Microsoft excel were utilized to accurately calculate and sort the data for reporting. To determine prevalence of amoxicillin-clavulanic acid prescriptions for each species at the VHC, utilizing the sort and count function in Excel allowed for an accurate count of each species. Frequency of tablets prescribed was analyzed by sorting between the frequencies that have been manually input to the Excel sheet from patient chart. The average dose for each species was calculated by using the summation function in Excel for the mg/kg calculated previously.

## Results

### Identifying Observed Successes and Hurdles to Antimicrobial Stewardship Programs in Human Hospitals

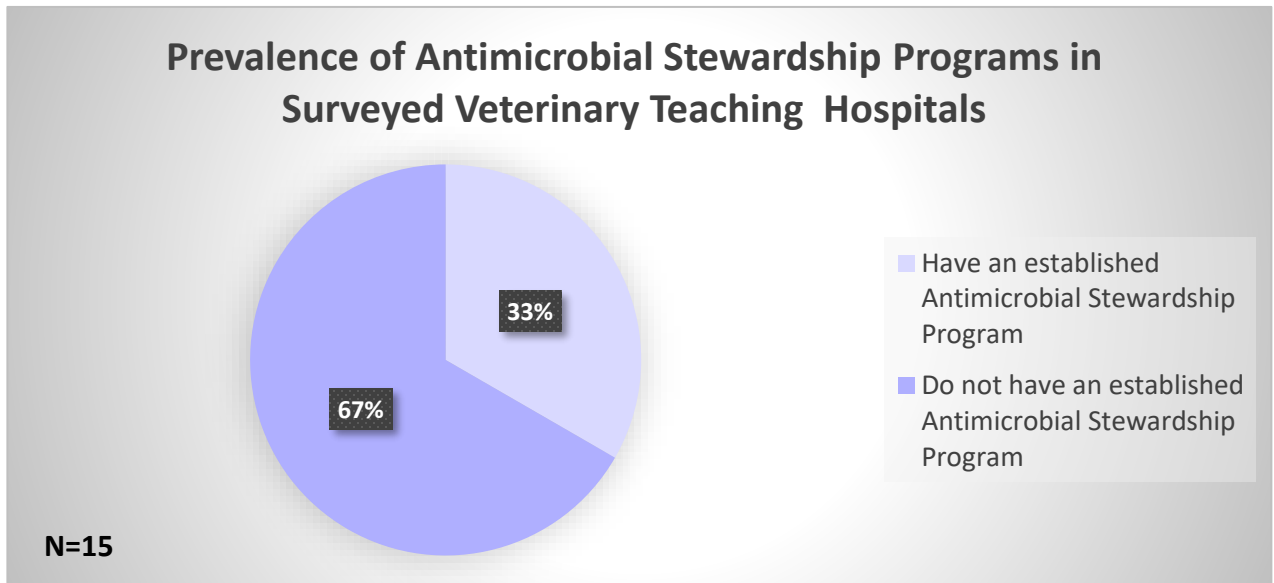
Two hospitals out of the five hospitals contacted, Lawrence Memorial Health and Shawnee Mission Medical Center, informally discussed their antimicrobial stewardship programs. Shawnee Mission Medical Center reported their antimicrobial stewardship program has shown substantial success in reducing antimicrobial use in their hospital and increased clinician-pharmacist consults when prescribing antimicrobials. Shawnee Mission Medical Center

reported clinician reluctance to altering their prescribing behaviors as a major barrier when the program was first implemented; however, through numerous meetings and one-on-one meetings with clinicians, overall clinician reluctance has decreased. Shawnee Mission Medical Center reported success in antimicrobial stewardship by monitoring their prophylactic antimicrobial agents; in-depth data mining showed many antimicrobial agents were being prescribed when there was an alternate drug that could have been used. Lawrence Memorial Health discussed the success they have found in implementing an antimicrobial stewardship program at their hospital, especially in their walk-in clinic. Lawrence Memorial Hospital has monitored the antimicrobials being prescribed in their walk-in clinic to ensure that their patients are receiving an appropriate antimicrobial without any diagnostic tests being conducted. Lawrence Memorial hospital did not disclose any barriers to implementation, nor how they were able to determine which antimicrobials were appropriate without diagnostic tests being conducted.

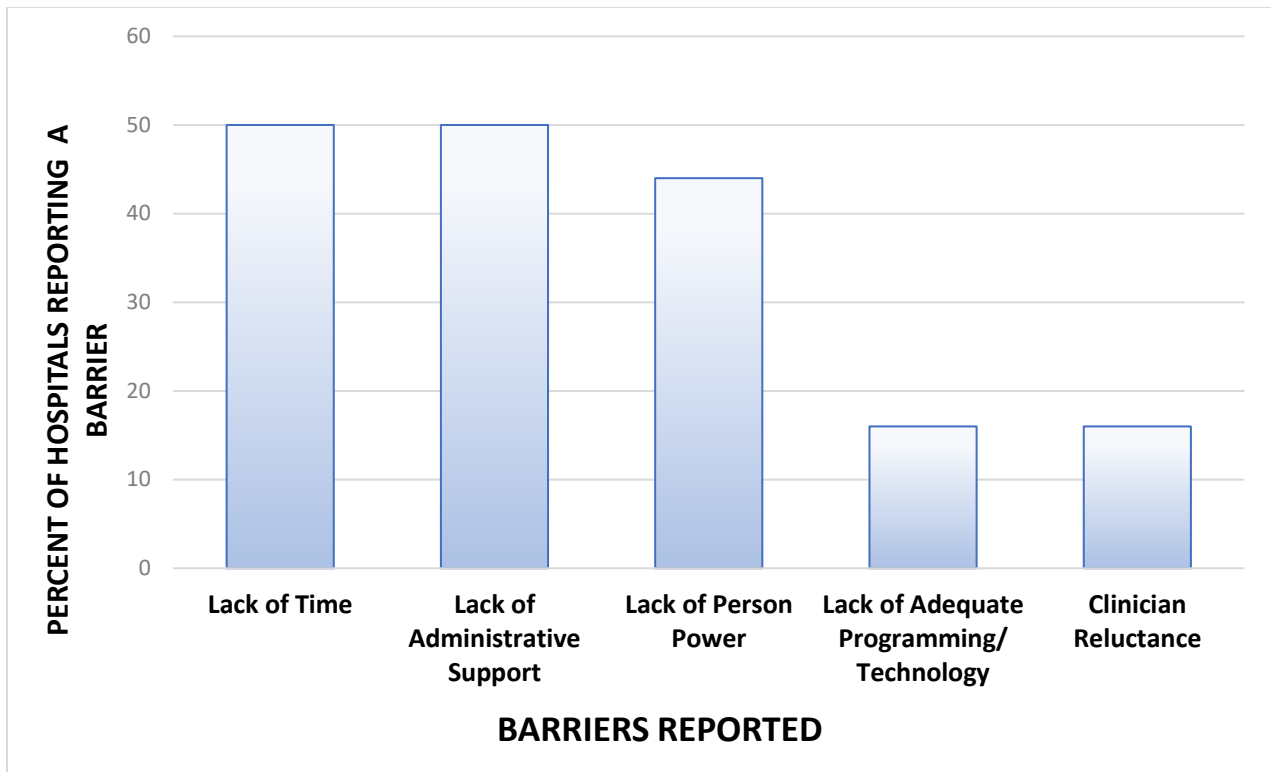
#### [Identifying Prevalence of Antimicrobial Stewardship Programs in Veterinary Teaching Hospitals](#)

Fifteen surveys (15/26, 57.8%) were completed and returned. Five out of fifteen (33%) veterinary teaching hospitals reported having an established ASP that monitored antimicrobial use as of January 2019 (see Figure 3.1). Three hospitals reported sharing collected antimicrobial use data with clinicians and indicated this had resulted in improved prescribing behavior. Several reported formats that were implemented for antimicrobial data collection were resistance patterns for all common organisms for respective antimicrobials, frequency of antimicrobial prescriptions, periodic review of perioperative dosing, indication, site of infection, targeted pathogen, culture, susceptibility, patient comorbidities, and concurrent medications. Five responding hospitals (33%) reported monitoring antimicrobials including: standard antimicrobials on standard minimum inhibitory concentration panel, carbapenems, vancomycin and chloramphenicol. Six hospitals had considered implementing a stewardship program. These

six hospitals reported barriers such as lack of person power, training, time, and resistance from clinicians to alter prescribing patterns (see Figure 3.2 and Figure 3.3)



**Figure 3-2: Prevalence of Antimicrobial Stewardship Programs in Surveyed Veterinary Teaching Hospitals Across the United States and Canada (N=15)**



**Figure 3-3: Barriers to Antimicrobial Stewardship Program Implementation Reported by Surveyed Veterinary Teaching Hospitals in the United States and Canada (N=6)**

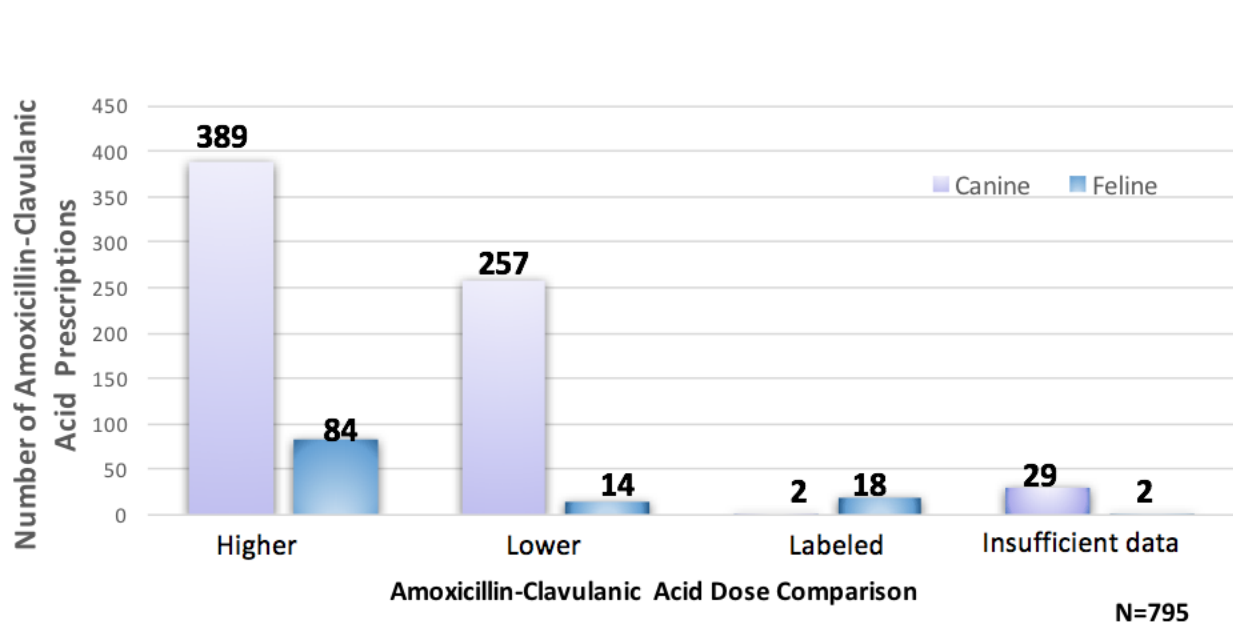
[Amoxicillin-clavulanic acid use monitoring](#)

**Dosing Results**

The labeled dose of amoxicillin-clavulanic acid is 13.75 mg/kg administered twice a day by mouth for canines and 62.5 mg twice a day by mouth per cat for feline patients. Amoxicillin-clavulanic acid milligrams divided by patient weight was calculated for each patient to determine whether the dose prescribed adhered to the labeled dose (see Figure 3.4). Dogs received a dose that varied from the labeled dose more commonly than feline patients did. Paper charts had to be pulled for 31/795 (0.3%) patients because weight was not documented in the VetStar chart, and due to time constraint were not evaluated in the comparison.

The average dose prescribed for canines was calculated as 14.43 mg/kg with a wide range of 5.97mg/kg to 49.86 mg/kg. The canine patient that was prescribed 5.97 mg/kg weighed 10.98 kg and was prescribed a 62.5-mg tab administered twice a day with a charted

indication of abrasions due to motor vehicle accident. The canine that was prescribed 49.86 mg/kg was 7.59 kg and was prescribe a 375-mg tab with a charted indication of subacute melanic diarrhea. The standard deviation for canines was calculated as 5.64. The average dose for felines was 14.48mg/kg with a standard deviation of 4.37. The feline dose range was from 6.43 mg/kg-24.47 mg/kg. The patient who received 6.43 mg/kg weighed 9.732 kg and was prescribed a 62.5-mg tab with a charted indication of open wounds. The patient that received a 24.47mg/kg dose weighed 10.36 kg and was prescribed a 250-mg tab with a charted indication of chronic urinary tract infection. A total of 103/118 (87.2%) feline patients were prescribed 62.5-mg/mL oral suspension (80 patients) or 62.5-mg tablets (23 patients), and a total of 18/118 (15.2%) were dosed in accordance to labeled dose.



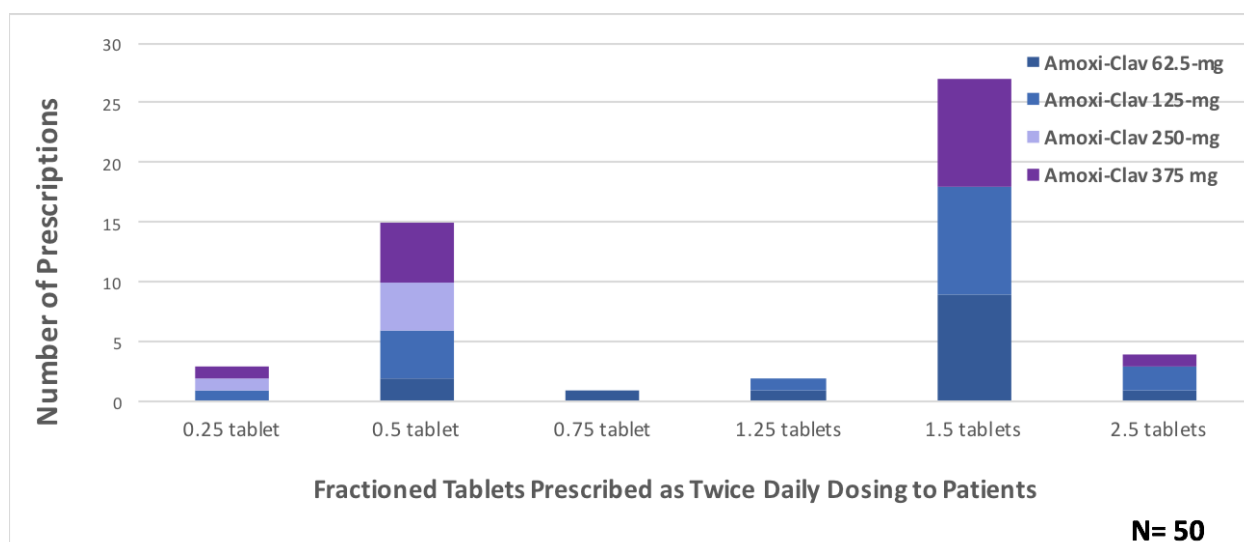
**Figure 3-4: Comparison of Amoxicillin-Clavulanic Acid Dose Prescribed at the Veterinary Health Center to the Labeled Dose in Feline (N=118) and Canine (N=677) Patients**

#### Frequency Results

Amoxicillin-clavulanic acid is labeled for administration to dogs and cats twice a day. The VHC exhibited precision in prescribed frequency. Prescriptions with twice a day frequency were prescribed to 794/795 (99.8%) of VHC patients. One patient (0.2%) was prescribed a one-time dose of amoxicillin-clavulanic acid and this was given as a prophylactic antimicrobial prior to a dental procedure.

### Fractioned Tablet Results

The product used at the VHC during the analyzed study period was a non-scored, non-chewable tablet generic (Putney/Dechra) amoxicillin-clavulanic acid. The chewable tablet manufactured by Zoetis pharmaceutical company was not analyzed in this study as it is not currently available on the market. Out of 795 patients, 50 (6%) patients were prescribed a fractioned amoxicillin-clavulanic acid dose (see Figure 3.5). All four tablet strengths were prescribed in a fractioned dose. Both dogs 39/50 (78%) and cats 11/50 (22%) received fractionated tablets. All doses were prescribed to be administered twice a day by mouth.



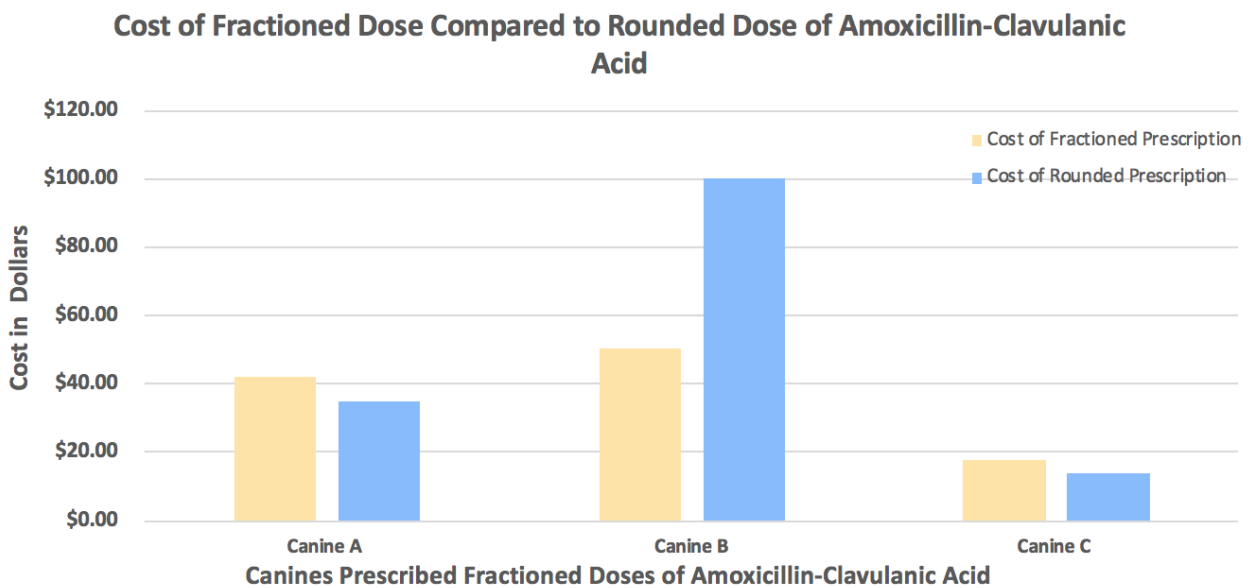
**Figure 3-5: Frequency of Fractioned Amoxicillin-Clavulanic Acid Tablets Prescribed to Canine and Feline Patients at the Veterinary Health Center at Kansas State University**

### Fractioned Dose Cost Analysis

A total of 50 patients were prescribed fractioned doses of amoxicillin-clavulanic acid at the VHC. Of these, three canine's charts were pulled to develop a cost analysis. Amoxicillin-clavulanic acid per tablet costs: \$0.60 for the 62.5-mg tablet, \$1.20 for the 125-mg tablet, \$2.00 for the 250-mg, and \$2.50 for the 375-mg. These prices were provided by the VHC dispensary as cost per tablet as of April 2019. These three canines were prescribed 2.5 125-mg tablets BID for 7 days, 1.5 125-mg tablets BID for 14 days and 0.5 375-mg tablets BID for 7 days respectively (see Figure 3.6). At the prescribed dose, Canine A received 2.5 of the 125mg tablets twice a day



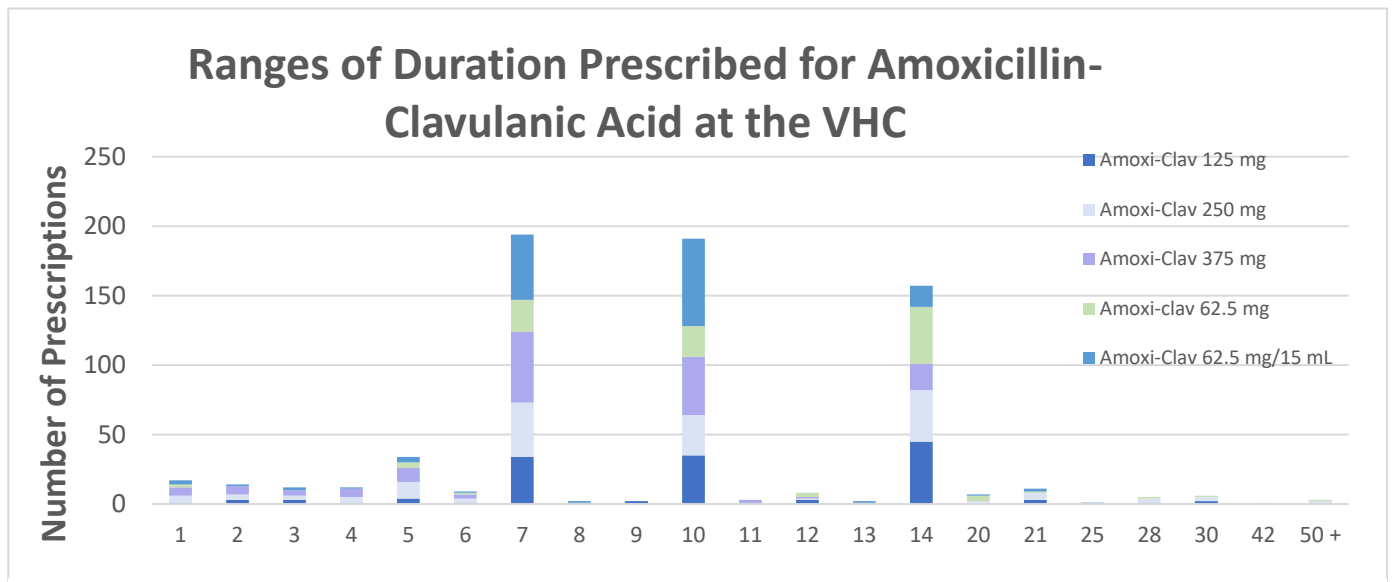
for 7 days, for a total cost of \$42, and owner challenge of administering 3 tablets or fragments twice daily. For comparison, Canine A could have been administered a 375mg tablet twice daily for 7 days for a lower cost (\$35). Canine A weighs 20.7 kg, with the fragmented dose (312.5mg) the canine is receiving 15.09 mg/kg, in comparison to the nearest rounded dose rounding up to the 375-mg tablet, the canine would receive 18.11 mg/kg. Canine B received 1.5 of the 125-mg tablets twice a day for a total cost of \$50.40, and having the owner administer 4 tablets or fragments twice daily. In comparison, Canine B could have been administered a 125-mg tablet and a 62.5-mg tablet twice a day, however this would be a higher overall cost (\$100.40) and still administering two tablets twice a day. Canine B weighs 12.8 kg and receives 14.65 mg/kg with the fragmented dose (187.5-mg), in comparison to the rounded dose (250-mg) the canine would receive 19.53 mg/kg. Canine C received 0.5 tablets of the 375-mg tablets twice a day for a total cost of \$17.50, and creating a challenge for the owner to administer a fragmented tablet twice a day. Canine C could have been administered a 125-mg tablet, this would be easier for the owner to administer rather than a fragmented tablet however the total cost would decrease to \$14.00. Canine C weighs 13.1 kg and receives 14.31 mg/kg with the fragmented dose (187.5-mg), the rounded dose has to be rounded up to the nearest tablet size (250-mg) and the canine would receive 19.08 mg/kg.



**Figure 3-6: Cost of Fractioned Tablets Prescribed Compared to Nearest Rounded Tablet of Amoxicillin-Clavulanic Acid Prescribed at the Veterinary Health Center**

Duration Results

Duration for all five strengths of amoxicillin-clavulanic acid (62.5-mg, 125-mg, 250-mg, 375-mg, and 62.5mg/ mL), were extrapolated from patient charts (see Figure 3.7). Clinicians had recorded duration prescribed in 691/795 (87%) patient charts obtained through the VetStar health information record. The pharmacy dispensary tab of VetStar documents the duration of the prescription if it is not explicitly stated in the discharge summary or in the health information record. The results of duration analysis at the VHC ranged from 1 day to 54 days for antimicrobial administration. One day durations were prescribed to 20/795 (0.25%) of patients, and their indications were listed as prophylactic prior to procedures such as mass removal, dental procedure, mandibulectomy, mast cell tumor excision, foreign body removal and suture dehiscence. Durations of 52 and 54 days were prescribed to 2/795 (0.002%) patients, and the indications charted for those patients were chronic wound management and sinusotomy, respectively.



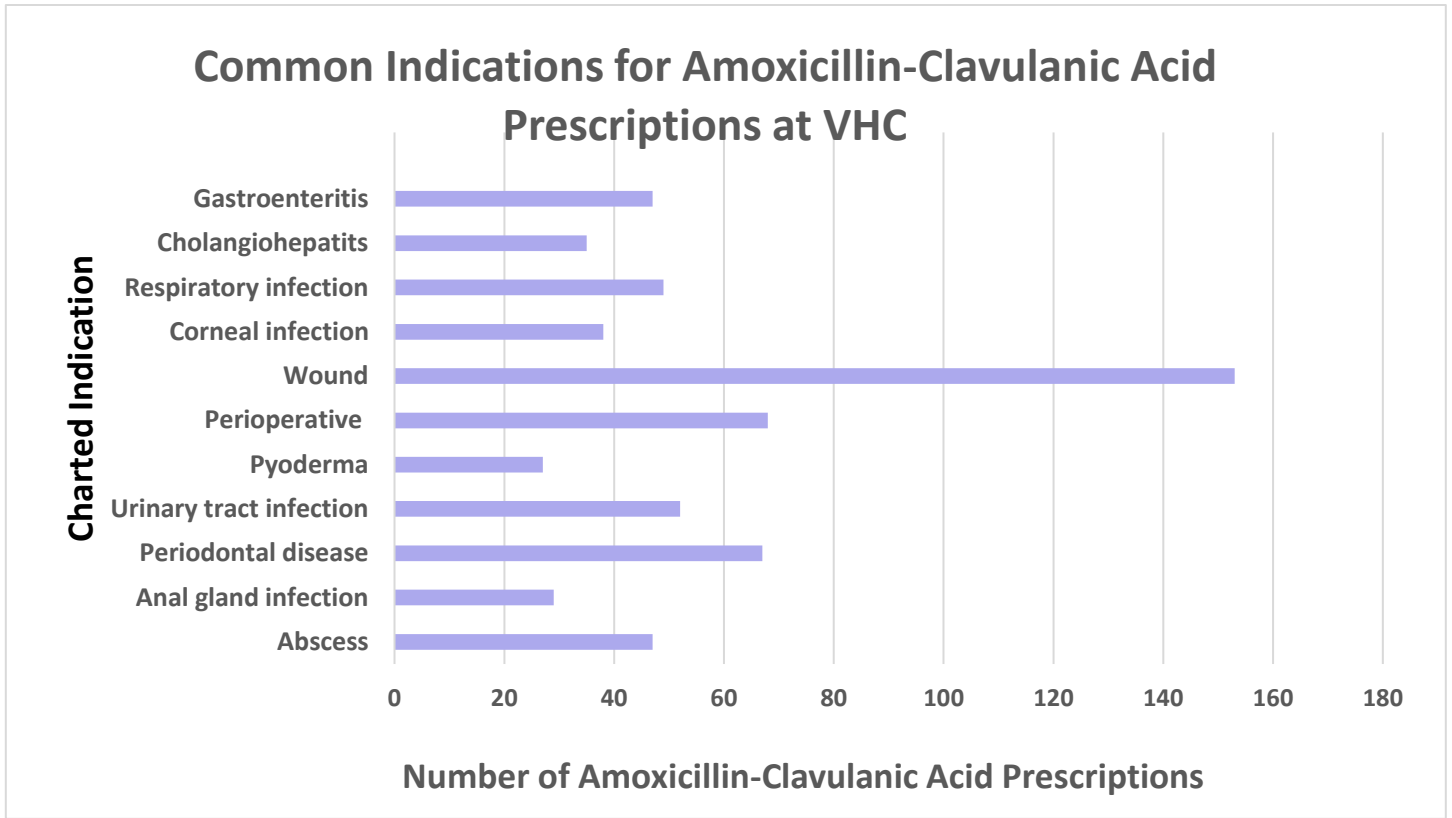
**Figure 3-7: Range of Durations Prescribed for Amoxicillin-Clavulanic Acid for Canine and Feline Patients at the Veterinary Health Center at Kansas State University**

## Species Prevalence Results

Prevalence data were analyzed to determine which species has a higher rate of amoxicillin-clavulanic acid consumption within the seven-month period of this project. Analysis showed the species on the amoxicillin-clavulanic acid prescriptions was 118/795 (13.3%) feline and 677/795 (86.7%) canine; as some patients might have had more than one prescription for this medication during this time, the number of prescriptions might not accurately represent the number of patients receiving this medication. Since the KSU VHC sees approximately 5 canine patients for every feline patient yearly (12,571 dogs and 2,589 cats in 2018), the percentage of amoxicillin-clavulanic acid prescriptions per species compares well to the patient population at the VHC.

## Indication Results

The VetStar patient charts indicated a wide range of diagnoses that prompted clinicians to prescribe amoxicillin-clavulanic acid (see Figure 3.8). The majority [792/795 (99.6%)] of patient charts documented indication prompting amoxicillin-clavulanic acid prescription; however, 3/795 (0.003%) patient charts had no documented indication in the VetStar chart and required paper charts to be pulled. Charted indications that were not reported in Figure 3.8 included: mass removal (4.6%), fracture (2.8%), and hernia repair (2.6%). Less common diagnoses that prompted clinicians to prescribe amoxicillin-clavulanic acid included: abdominal surgery, cholecystectomy, urethral blockage, pyometra, kennel cough, arytenoid lateralization, bloody discharge or stool, and cystitis (<1.4%).



**Figure 3-8: Most Common Indications Prompting Amoxicillin-Clavulanic Acid Prescriptions for Canine and Feline Patients at the Veterinary Health Center at Kansas State University**

**Discussion**

**Prevalence of Antimicrobial Stewardship Programs**

There is a strong encouragement from organizations such as the American Veterinary Medical Association for veterinarians to take the next step and implement action towards an ASP. The results of this project have shown despite this push for stewardship, only five veterinary teaching hospitals reported having an existing ASP in their veterinary teaching hospitals at the time of the survey. All other respondents recognize the need for implementation, yet there are noted challenges to overcome. The VHC is ahead of the curve, by already developing an understanding of what challenges other veterinary teaching hospitals have faced and recognizing these hurdles prior to implementation. Veterinary teaching hospitals with established antimicrobial stewardship programs reported monitoring and reviewing antimicrobials such as

vancomycin, carbapenems, imipenem, chloramphenicol and antimicrobials on the facility's standard minimum inhibitory concentration panel.

Veterinary teaching hospitals that plan on implementing an antimicrobial stewardship program should understand the barriers to implementation to succeed in their efforts. Human hospitals have an immense amount of support from federal agencies and stakeholders to develop antimicrobial stewardship programs. Veterinary teaching hospitals lack funding to support stewardship programs; although there is moral support behind the push for these programs, federal agencies do not provide any funding for program implementation in veterinary medicine. Lack of administrative support and supportive faculty was reported from three hospitals when asked about barriers to implementation from other veterinary hospitals. If a veterinary teaching hospital does not have the appropriate support from both administration and surrounding faculty there is potential for failure. Noting barriers reported including clinician reluctance to altering prescribing behaviors and lack of time for data export and analysis, is important to note to reduce these barriers for the VHC.

Despite barriers to implementation, three hospitals with ASPs reported positive observed changes in clinician prescribing behavior. Reported changes included first line empirical and prophylactic antimicrobials have changed, increased number of proactive clinician consults with pharmacists, and a decrease in prescribed fluoroquinolones in the hospital. This positive change in prescribing behavior also was reported to give clinicians further insight to antimicrobial stewardship programs and that it is a process to optimize patient care rather than restricting clinician prescribing. Sharing antimicrobial data collection resulted in clinicians receiving a visual representation of how frequently antimicrobials are being used, and this has prompted them to prescribe antimicrobials with an appropriate indication, duration, dose, frequency and route of administration. The changes in prescribing behavior that these three veterinary teaching hospitals have experienced should be known by veterinary teaching hospitals who reported barriers to implementation. Thus, allowing the 6 (40%) hospitals that reported barriers to understand the efforts towards antimicrobial stewardship programs can produce a positive change.

## Limitations

There are many specific hurdles involved in collecting antimicrobial use data, as encountered throughout this study, in comparison to human hospital medical record systems where stewardship data are often linked and might be easier to collect. Implementing an antimicrobial stewardship program requires baseline data collection such as which antimicrobials are prescribed frequently, dose prescribed, indication, duration and respective prescribing clinicians. Collecting these data initially may be a major hurdle for many veterinary teaching hospitals without a robust health information system. These hospitals may lack the person power to manually extract these data for each antimicrobial and therefore, must hold off on implementing an antimicrobial stewardship program despite knowing the importance. To overcome this barrier, veterinary teaching hospitals should initially create a multi-disciplinary team including individuals from their health information technology department. Working diligently with information technology to determine a way to export the data and collate the data sets into one spreadsheet would potentially reduce time spent data mining. Allocating individuals that are responsible for certain aspects of an antimicrobial stewardship program (data mining, further investigation in patient charts, susceptibility cultures, data analysis, determining trends in data, and proposed changes) would benefit these veterinary teaching hospitals substantially to create an effective antimicrobial stewardship program.

Funding may also be a barrier to implementation for an antimicrobial stewardship program in veterinary teaching hospitals. To overcome this hurdle, collecting and analyzing baseline data for the most frequently used antimicrobials could potentially highlight the need for an antimicrobial stewardship program at the hospital. Discussing the need for an antimicrobial stewardship program with administrators at the veterinary teaching hospital that is supported with data from frequently prescribed antimicrobials would clearly demonstrate the benefit of an antimicrobial stewardship program. Creating a cost-benefit analysis would also be beneficial, to show administration the cost of treating an antimicrobial resistant infection in diagnostic tests and patient cost versus the cost per patient of implementing an antimicrobial stewardship program.

## Extra Label Drug Use

The American Medicinal Drug Use Clarification Act of 1994 (AMDUCA) provided veterinarians that are acting within a veterinarian-client-patient-relationship (VCPR), with a wider prescribing and dispensing range for animals to receive effective treatment. Extra-label drug use (ELDU) is the use of an approved drug in veterinary medicine that varies from the labeled dose for an indication that is not in accordance to labeled dose indications. ELDU's are classified as: a prescription that is not for the species listed on the label, for an indication that is not listed on the label, for a different dose or frequency than listed on the label, or a different route of administration than listed on the label. AMDUCA provides veterinarians with greater flexibility to prescribe antimicrobials to their patients. The AVMA provides a list for veterinarian review of antimicrobials that are restricted from ELDU, examples of when ELDU is necessary, and how to keep records of ELDU.<sup>41</sup> At the VHC, ELDU is practiced often by clinicians.

Veterinarians at the VHC are focused on the well-being of their patients, as physicians are in human health. Antimicrobial resistance is a concept that is intangible; the implications may be understood but the direct effect they, as prescribing clinicians, have on antimicrobial resistance may not be understood. Although they are practicing ELDU, there are an abundance of other factors to be considered when comparing the labeled dose prescription frequency to the actual prescription. These factors include consensus statements, pharmacy or pharmacology recommendations or published literature indicating the use of an antimicrobial in their patients will be effective and improve their overall health.

## Duration

There is very limited evidence-based literature on recommended durations for amoxicillin-clavulanic acid in veterinary medicine. Clinicians at the VHC have most commonly prescribed amoxicillin-clavulanic acid for 7, 10 or 14 days. The labeled dose recommends a duration of 5-7 days; however, veterinarians treat a variety of infections, some of which require a longer course of antimicrobial therapy. Indications such as kidney infections and pneumonia are recommended by consensus guidelines to be treated for 30 days for effective treatment.<sup>42</sup> The duration for amoxicillin-clavulanic acid at the VHC varied widely from 1 days to 58 days between feline and canine patients. This range in duration is due to the lack of published

literature and guidelines for veterinary medicine. This puts veterinarians in a position to prescribe durations based on their knowledge of the antimicrobial, microorganism they are attempting to treat and site of infection, consultations with pharmacologists, and published veterinary literature. When reviewing data for implementing an ASP it is important to understand how much of the antimicrobial is necessary to be effective, prescriptions that were administered unnecessarily, and administration of treatment after the infection has resolved. Although these data have been collated based on the export, there is no definitive simple guideline or standard that can be applied to these concerns.

Determining how long antimicrobials need to be administered in order to be effective has no single answer, each indication varies in treatment duration. Beyond just indication each patient can be vastly different from the other; therefore, clinicians balance a multitude of factors when prescribing an antimicrobial. Administration of treatment after resolution of the targeted infection is a controversial topic in both human and veterinary health. Organizations such as the CDC and WHO publish fact sheets briefly reviewing methods that individuals can reduce the risk of their own natural flora developing resistance mechanisms to antimicrobials. Previously those fact sheets had included recommendations to always complete the course of antimicrobials; however, within the last year the CDC and the WHO have replaced that with taking antimicrobials exactly as prescribed. Unfortunately, this misconception has been established in many individuals in both the human and animal sector. Many pet owners will receive an antimicrobial agent for their companion animal and continue to administer the medication beyond when the animal shows no signs of infection; and this is the current recommendation unless their veterinarian tells them otherwise. They are not likely to return to the veterinarian's office or hospital because of this established misconception. It falls on the clinicians to determine how long the antimicrobial needs to be administered, and to inform clients about follow-up visits or signs of improvement. Antimicrobials for humans and animals should be taken as prescribed by their respective clinician to reduce the development of antimicrobial resistant bacteria. Further research to determine optimal duration of specific bacterial infections in companion animal medicine is warranted.



## One Health

The goal in any ASP is to improve patient outcomes, increase efficacy of antimicrobials and reduce further development of antimicrobial resistance. Developing a One Health approach to implementing an ASP in any inpatient setting requires compliance from all three sectors of the One Health triad to be successful. There are misconceptions between each sector of the One Health triad and biases that exist; therefore, a multidisciplinary team is the best way to remove these biases and clarify any misconceptions to have a positive impact on both veterinary and human health. Integrating these three sectors reduces possible adverse events in health care and optimizes patient care both animals and humans.

There is no single group or sector that is responsible for the development of antimicrobial resistance. Through discussions with leaders of antimicrobial stewardship programs at Shawnee Mission Medical Center and Lawrence Memorial Hospital, there is a difference in which antimicrobials are commonly used in humans in comparison to companion animals. Antimicrobials such as vancomycin, carbapenems, piperacillin, and penicillin G are used regularly in human health intravenously. Whereas, in this applied practice experience, in several meetings it was discussed with Dr. Colvin-Marion and Dr. KuKanich, that antimicrobials such as vancomycin, imipenem and penicillin are rarely prescribed for dogs and cats at the VHC. Clinicians in veterinary medicine are taking major steps towards reducing antimicrobial resistance in their own patients. Vancomycin was reported as being formally monitored and restricted in five survey responses from veterinary teaching hospitals, while in human medicine vancomycin is used for a wide range of indications from unknown source of fever to sepsis. This frequent, overuse, or misuse of any antimicrobial can contribute to the development of resistance mechanisms in humans.

## Strengths

As a leader in veterinary medicine, the VHC has demonstrated strengths in prescribing patterns of amoxicillin-clavulanic acid. Clinicians at the VHC prescribe a consistent frequency of twice a day by mouth for their patients; there was one patient that was prescribed a one-time dose, and after further investigation it was deemed as appropriate. Durations prescribed had a wide range, however 586/795 (78%) of clinicians prescribe a duration of 7, 10 or 14 days. The

variation is due to lack of evidence-based research in which to base their prescribing decisions. Charted indications had a wide range as well; however, clinicians do not base their therapeutic-dosing strictly off of the medication label. There were derivations from the label in indications; however, clinicians at the VHC utilize resources such as consensus statements, pharmacology consults, and available literature. There were no indications that were considered as outliers, although they were uncommon indications not listed on Figure 3.6 (mass removal, fracture and hernia repair) that were documented 8 or more times and could also be deemed as appropriate use of this medication. Thus, showing although there are less common indications the clinicians at the VHC are consistent in their prescribing patterns. Consistency was also shown in the feline amoxicillin-clavulanic acid tablet and oral suspension prescriptions; 103/118 feline patients were prescribed 62.5-mg tablets or the oral suspension of amoxicillin-clavulanic acid. The dose prescribed was the labeled dose 18/118 of these feline patients.

The VHC's primary strength is the willingness of clinicians such as Dr. KuKanich and the Dispensary director Dr. Colvin-Marion to rectify any inappropriate prescribing they come across. They are both determined to facilitate change and implement a stewardship program as leaders in veterinary medicine. Although this veterinary hospital is not as large as some facilities in the country, the VHC has been monitoring antimicrobial use informally and this will allow for the stewardship program to be implemented efficiently and successfully.

#### Future considerations for VHC antimicrobial stewardship implementation

The VHC does display several strengths in prescribing patterns of amoxicillin-clavulanic acid, however there are some inconsistencies that should be investigated further to determine if a change in prescribing behavior should be made. A study was conducted to determine the potency of doxycycline when fragmented and showed that as the medication is fragmented the potency decreases respectively.<sup>43</sup> The generic tablet manufactured by Dechra/Putney that is dispensed at the VHC is not scored, and no studies are currently published examining analysis to determine the potency in each fragment when the tablet is halved or quartered. There was a total of 50 patients (6.2%) that were prescribed fractioned doses at the VHC. Prescribing fractioned doses may not be of clinical significance if the patient is still receiving the appropriate dose. However, further research is warranted as it might be of significance if they are getting sub

therapeutic dose or overdose leading to adverse effects. With the current dosing guidelines having a range for dogs and cats up to 25mg/kg by mouth every 12 hours, discussions should be had within the VHC whether fractionated doses could be avoided completely. Rounding the dose to the nearest full tablet would enable clinicians to be sure their patients are receiving the full dose prescribed. Rounding doses could potentially create financial burdens for clients as the cost of the rounded dose is higher than the prescribed fragmented tablets. Clients are paying for their prescriptions out of pocket, and an increased cost of medication could potentially deter them from purchasing the prescription entirely.

The labeled dose is not a gold standard prescribing guideline, and as discussed there is a limited amount of literature regarding appropriate antimicrobial dosing for companion animals. AMDUCA, consensus statements, pharmacology consults and ELDUs are all sources that provide veterinarians with a wider range of prescribing and dispensing due to the substantial lack of available literature. However, for an antimicrobial stewardship program determining a range of mg/kg is necessary to decide whether clinicians are prescribing amoxicillin-clavulanic acid inappropriately. The range of amoxicillin-clavulanic acid doses in canine and feline patients had a very wide range, the standard deviation determined that this was an expected variation and there are other factors to consider. Tablet rounding, weight of patient, indication, antimicrobial being prescribed are all to be considered when examining these data.

Establishing a completely electronic health information system with synchronization to other diagnostic systems at the VHC will promote efficacy in the data collection stage. The VHC, alike all veterinary teaching hospitals, has a wide range of antimicrobials that are prescribed, and it is not possible to analyze them in an efficient manner with the current system. Susceptibility results are imperative to have when analyzing antimicrobial data to determine when the antimicrobial is appropriate and if there are any antimicrobial resistant microorganisms that clinicians are attempting to treat. In the next phase of this project, I believe the most efficient way to aid the VHC in implementing an antimicrobial stewardship program is to introduce a new system with a wider range of export functions. This would allow for multiple antimicrobials to be analyzed at once and will ultimately aid the VHC in establishing an antimicrobial stewardship program in the near future.

Chapter 4- Competencies

**Table 4-1: Summary of MPH Foundational Competencies**

Number	Competency	Description
3	<b>Analyze quantitative and qualitative data using bioinformatics, computer-based programming and software</b>	A majority of the data analysis for this applied practice experience was exported into a Microsoft Excel 2013 spreadsheet from the VHC’s electronic health record system, VetStar. I used VetStar to collect amoxicillin-clavulanic acid prescription data on each patient. As I went through each patient, I noticed patterns in amoxicillin-clavulanic acid prescribing and acknowledged questions I stated in my objectives earlier in this project. Although there were a lot of data to analyze, I learned how to present patterns in data in a concise and simple format.
7	<b>Assess population needs, assets and capacities that affect communities’ health</b>	Creating a survey that was sent to 26 teaching veterinary hospitals and collecting respective responses regarding barriers hindering implementation and current dilemmas in established ASPs enabled me to understand the needs and capacities that affect veterinary health. These survey responses allowed me to view the veterinary health population from a broader perspective. Understanding the various components that affect veterinary health, and moreover assessing their needs allowed me to understand what affects veterinary health across the nation.
19	<b>Communicate audience-appropriate public health content, both in writing and through oral presentation</b>	This competency was addressed through the several presentations that are planned throughout this project. The presentation for the University of Kansas Veterinary Pharmacy Club will have applicable information to the future careers of respective club members. Antimicrobial stewardship programs in veterinary medicine are coming to the forefront with new initiatives from CVM and AVMA. This presentation will allow University of Kansas Veterinary Pharmacy Club students to understand the beginning stages of developing an ASP. I have shared my presentation with the epidemiologists at KDHE, so that they will further understand my role in the stewardship efforts at KSU. KDHE already has a strong working relationship with several veterinarians at KSU CVM (including Drs. Apley and KuKanich) to collaborate on One Health stewardship. This collaboration and community effort on One Health and stewardship was furthered by our creation of a flyer intended for lay people to understand that both people and animals can carry antimicrobial resistance bacteria, and that we all share

		responsibility for minimizing risk of further development of resistance in our community. The poster titled “Prevalence of Antimicrobial Stewardship Programs in Veterinary Teaching Hospitals” was presented at the Phi-Zeta Research day, I was able to present our findings to individuals ranging from DVMs to undergraduate biology majors.
<b>21</b>	<b>Perform effectively on interprofessional teams</b>	I have been provided with an amazing opportunity to work with a variety of health care professionals in both human and veterinary health. I have spent a great deal of time with a veterinarian, Dr. Katherine Stenske-KuKanich, and a veterinary pharmacist, Dr. Landa Colvin-Marion. Both have been influential in my understanding of the importance of ASPs in veterinary health and furthermore they have provided me with a deeper understanding of the relationship between dose and indication. Speaking with human hospital pharmacists, I gained an alternative insight on ASPs and their importance, I found that they are standard in human hospitals and are essentially taken for granted. Although infectious disease pharmacists are aware of the importance, most times clinicians in human health are irritated with the overall process of antibiotic consults with pharmacists to reduce resistance development. Working on an interprofessional team allowed me to develop a more effective method of analyzing my data and moreover enabled me to view all aspects of health from a one-health perspective.
<b>22</b>	<b>Apply systems thinking tools to a public health issue</b>	Although I was not involved in policymaking, one goal of this field experience is to build towards implementing an ASP at the VHC. There are various unintended consequences that have to be accounted for when developing a program such as an ASP for a veterinary hospital. Working with various health professionals involved in veterinary and human health allowed me to focus on applying systems thinking approaches and models toward the overall outcomes.

Student Attainment of Infectious Diseases and Zoonoses

**Table 4-2: MPH Emphasis Area Competencies**

<b>MPH Emphasis Area: Infectious Diseases and Zoonoses</b>	
<b>Number and Competency</b>	
<b>Description</b>	
1	<p><b>Pathogens and Pathogenic Mechanisms</b></p> <p><u>Understand and be able to describe the ecology and modes of disease causation and infectious agents such as bacteria, viruses, parasites and fungi:</u> I addressed this competency through reading literature on microorganisms and resistance mechanisms. I also had the opportunity to develop a deeper understanding of pathogenic mechanisms in the required Microbiology course (BIOL 570).</p>
2	<p><b>Host response to pathogens and immunology</b></p> <p><u>Describe the current understanding of host immune response to infection and understand the role of vaccination in infectious disease control:</u> This competency was addressed through gaining a deeper understanding of infectious disease transmission between animals in veterinary health. An in-depth analysis of prescription indication, enabled me to understand some infectious diseases could have been prevented entirely through primary prevention such as vaccination. An example of a vaccine preventable disease in canines is Parvovirus, which predisposes secondary bacterial infections. Amoxicillin-clavulanic acid is not prescribed for Parvovirus as it is a viral disease; however the medication serves as a treatment to the secondary bacterial infections.</p>
3	<p><b>Environmental and ecological influences</b></p> <p><u>Understand the influence of space/geography, insect vectors, toxic plants and other toxin sources as well as infectious agents on infectious disease and food safety:</u> This competency was addressed in my field experience indirectly regarding the role of antimicrobial resistant bacteria thriving in optimal environmental conditions. Certain areas of the world have a higher rate of resistant bacteria outbreaks or better known as “superbugs” due to optimal growth and survival conditions. Although not directly addressed in my</p>

		integrated learning experience report, I read an extensive amount of literature regarding animal-human transmission, and human-animal transmission of infectious diseases through insect vectors. This enabled me to understand the severity of antimicrobial resistant bacteria survival and the subsequent consequences they have on the One Health triad.
4	<b>Disease surveillance and quantitative methods</b>	<u>Understand how disease events and risk factors for disease are quantified and compared:</u> Throughout my field experience, I analyzed the exported data to understand risk factors linked to common diagnoses for canine and feline patients. Understanding risk factors associated with disease events allows for disease surveillance as a preventive measure for adverse events for both human and veterinary medicine.
5	<b>Effective communication</b>	<u>Develop and demonstrate effective strategies to communicate public health/ infectious disease issues to a variety of audiences:</u> I have prepared several presentations for different audiences to demonstrate effective strategies to communicate this applied learning experience to a variety of audiences. By presenting the information to a varied audience, while making sure the key points are addressed it enables each respective audience to capture the message of the presentation and integrate it into their everyday roles in public health.

**Appendix 1: Survey Sent to Veterinary Teaching Hospitals Across the United States and Canada**

**Antimicrobial Stewardship Survey: Veterinary Teaching Hospitals**

- 1) Does your teaching hospital have a stewardship program in place that monitors antibiotic use? Yes/no
- 2) If so, when was this program implemented? (approximate date) \_\_\_\_\_
- 3) Which antibiotics do you monitor?  
\_\_\_\_\_
- 4) What data/information do you collect regarding antibiotic use?  
\_\_\_\_\_
- 5) Do you share antibiotic use data with clinicians? Yes/no
  - a. If yes, what is the format and does it work well?  
\_\_\_\_\_
- 6) Has your stewardship program led to changes in antibiotic prescribing behavior? Yes/no
  - a. If yes, how?  
\_\_\_\_\_
- 7) Do you restrict use of certain antibiotics in your hospital? Yes/no
  - a. If so, please provide details if possible  
\_\_\_\_\_
- 8) If you do not monitor antibiotic use, have you considered it? Yes/no
  - a. What hurdles do you face or have prevented you from starting one?  
\_\_\_\_\_
- 9) Any other details you'd like to share about stewardship efforts at your hospital?  
\_\_\_\_\_



## Appendix 2: Abstract Accepted for Kansas State University College of Veterinary Medicine Phi Zeta Research Day

Jovita Ramjisingh

1

Prevalence of Antimicrobial Stewardship Program in Veterinary Teaching Hospitals

2

Katherine Stenske Kukanich, DVM, PhD, DACVIM (SAIM)

3

Landa Colvin-Marion, B.S., M.P.H., PharmD, Veterinary Health Center at Kansas State University, Manhattan, KS, USA; Elynn Mulcahy PhD, M.P.H., Diagnostic Medicine and Pathobiology, Kansas State University, Manhattan, KS, USA; Michael D. Apley, DVM, PhD, DACVCP, Production Medicine and Clinical Pharmacology, Kansas State University, Manhattan, KS, USA.

4

5

Key Words: Antimicrobial; Stewardship; Veterinary Hospitals

### BACKGROUND

Antimicrobial stewardship programs provide hospital strategies to optimize the responsible use of antimicrobials, to minimize the development of resistance, and to improve patient outcomes. While stewardship programs are required in human healthcare, there is no requirement for such programs in veterinary healthcare, and the prevalence of such programs is unknown.

### METHODS

A cross-sectional online survey was sent to 26 veterinary teaching hospitals in the United States and Canada. The survey was addressed to infection control and/or pharmacology faculty who would be knowledgeable regarding hospital stewardship programs and policies. The survey consisted of nine questions requesting insight about the following: established stewardship programs, which antimicrobials are monitored, sharing data with clinicians, changes in prescribing behavior, restricted use of antimicrobials, and hurdles to implementing a program.

### RESULTS

Twelve surveys were returned. Three out of twelve (25%) teaching hospitals reported having an established antimicrobial stewardship program that monitored antimicrobial use as of January 2019; all three hospitals reported sharing collected antimicrobial use data with clinicians and indicated this had resulted in improved prescribing behavior. Two hospitals without a program reported restriction of antimicrobials such as vancomycin, carbapenem, imipenem, and third-generation cephalosporins. Five hospitals (55%) had considered implementing a stewardship program. These five hospitals reported barriers such as lack of person power, training, time, and resistance from clinicians to alter prescribing patterns.

### CONCLUSION

Establishing antimicrobial stewardship programs and monitoring antimicrobial use requires overcoming logistic hurdles in veterinary teaching hospitals, but can have a positive influence on responsible antimicrobial prescribing.

# Appendix 3: Poster Presented at the Kansas State University College of Veterinary Medicine Phi Zeta Research Forum, March 2019, Titled "Prevalence of Antimicrobial Stewardship Programs in Veterinary Teaching Hospitals"



## PREVALENCE OF ANTIMICROBIAL STEWARDSHIP PROGRAMS IN VETERINARY TEACHING HOSPITALS

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KANSAS STATE UNIVERSITY | Master of Public Health Interdisciplinary Program

### ABSTRACT

Antimicrobial stewardship programs provide hospital strategies to optimize the responsible use of antimicrobials, to minimize the development of resistance, and to improve patient outcomes. While stewardship programs are required in human healthcare, there is no requirement for such programs in veterinary healthcare, and the prevalence of such programs is unknown. A cross-sectional online survey was sent to 26 veterinary teaching hospitals in the United States and Canada. The survey was addressed to infection control and/or pharmacology faculty who would be knowledgeable regarding hospital stewardship programs and policies. The survey consisted of nine questions requesting insight about the following: established stewardship programs, which antimicrobials are monitored, sharing data with clinicians, changes in prescribing behavior, restricted use of antimicrobials, and hurdles of implementing a program. Fifteen surveys were returned, and five (33%) veterinary teaching hospitals reported having an established antimicrobial stewardship program that monitored antimicrobial use as of January 2019; all five hospitals reported sharing collected antimicrobial use data with clinicians and indicated this had resulted in improved prescribing behavior. Five hospitals reported restriction of antimicrobials such as vancomycin, carbapenem, imipenem, and third-generation cephalosporins. Six hospitals had considered implementing a stewardship program; however, they reported barriers such as lack of person power, training, time, and resistance from clinicians to alter prescribing patterns. Establishing antimicrobial stewardship programs and monitoring antimicrobial use requires overcoming logistic hurdles in veterinary teaching hospitals, but can have a positive influence on responsible antimicrobial prescribing.

#### BACKGROUND

- Major veterinary organizations including the American Veterinary Medical Association (AVMA) have created initiatives to promote judicious use of antimicrobials in veterinary medicine. Judicious use of antimicrobials aids in safeguarding the efficacy for both human and veterinary medicine<sup>1</sup>
- The AVMA has developed core principles for antimicrobial stewardship and has recently joined the Centers for Disease Control and Prevention in their attempt to reduce antimicrobial resistance in both human and animal health<sup>2</sup>
- Veterinary hospitals are encouraged to implement antimicrobial stewardship programs and to follow AVMA core principles to help minimize antimicrobial resistance in both human and animal health.

#### OBJECTIVES

- To determine the prevalence of antimicrobial stewardship programs in veterinary teaching hospitals across the United States and Canada
- To gain insight into which antimicrobials are restricted
- To analyze the relationship between restricting antimicrobial use and clinician prescribing behaviors
- To understand barriers hindering the implementation of an antimicrobial stewardship program in hospitals without an established program

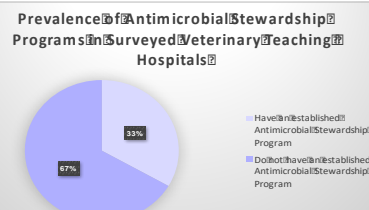
#### METHODS

- A cross-sectional online survey was sent to 26 veterinary teaching hospitals in the US and Canada.
- The survey was addressed to pharmacists, infection control, and/or pharmacology faculty who would be knowledgeable regarding hospital stewardship programs and policies.
- The survey consisted of questions about the following: established stewardship programs, which antimicrobials are monitored, sharing data with clinicians, changes in prescribing behavior, restricted use of antimicrobials, and hurdles of implementing a program.

#### RESULTS

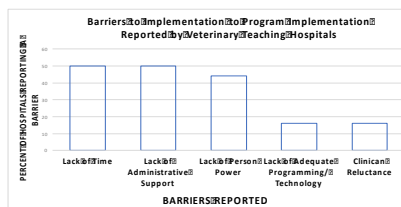
- 15/26 surveys were returned (57.8% response)**
- Antimicrobial stewardship programs remain rare among veterinary teaching hospitals**
  - As of 2019, 33% (5/15) of responding veterinary hospitals reported having an established antimicrobial stewardship program implemented between 2004 to 2016 (see Figure 1)
  - An additional veterinary teaching hospital monitored antimicrobial use but did not consider itself an established stewardship program
  - Of the remaining hospitals, 6 had considered implementing a program in their hospital
- Several formats were implemented for antimicrobial data collection:**
  - Resistance patterns for all common organisms for respective antimicrobials
  - Frequency of antimicrobial prescriptions
  - Periodic review of perioperative dosing
  - Indication
  - Site of infection
  - Targeted pathogen
  - Culture/ Susceptibility
  - Patient comorbidities and concurrent medications
- Monitoring antimicrobials can lead to changes in antimicrobial prescribing behavior**
  - 5 responding veterinary teaching hospitals monitor antimicrobial use
  - 5 veterinary teaching hospitals reported sharing antimicrobial use data with clinicians through presentations, periodic updates and prescribing use reviews
  - Reported antimicrobials monitored included:
    - Antimicrobials on standard MIC panel
    - Carbapenems
    - Vancomycin
    - Chloramphenicol

Figure 1. Prevalence of antimicrobial stewardship programs as reported by surveys sent to veterinary teaching hospitals.



- Antimicrobial restriction within veterinary hospitals**
  - Five hospitals (including 2 without an established antimicrobial stewardship programs) reported restriction of antimicrobials such as:
    - Vancomycin
    - Carbapenems
    - Imipenem
    - Third-generation cephalosporins

Figure 2: Reported barriers to implementation of antimicrobial stewardship programs in veterinary teaching hospitals.



#### CONCLUSIONS

- Despite encouragement from the AVMA for veterinarians to take action towards antimicrobial stewardship, few veterinary schools reported having an existing antimicrobial stewardship program in their teaching hospitals.
- Many recognize the need, yet there are noted challenging hurdles to overcome.
- Recognizing and addressing these hurdles is important for veterinary leadership if stewardship programs are to succeed.
- Where programs have been established in veterinary teaching hospitals, monitoring and reviewing antimicrobial use has been well received and has resulted in positive change for antimicrobial use within those hospitals.

#### ACKNOWLEDGEMENTS

- The authors would like to thank all the veterinary hospitals and veterinarians who contributed to this project by completing the survey.
- The authors would also like to thank Courtney Howell for her contribution to this project

#### REFERENCE

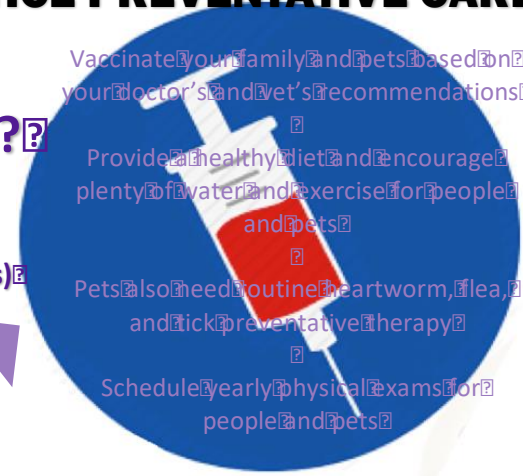
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Appendix 4. Flyer created for KDHE dissemination to general public

**WASH YOUR HANDS**



**PRACTICE PREVENTATIVE CARE**



**What is One Health?**

Working together to keep all individuals in our families and communities (people and animals) healthy and happy



Only give medication to the patient it was prescribed for  
Don't reuse leftover medication  
Dispose of old medication appropriately  
Learn more about disposing medication:  
[www.vet.k-state.edu/chc/med-disposal.html](http://www.vet.k-state.edu/chc/med-disposal.html)

**USE MEDICATION RESPONSIBLY**

When people or pets are sick, visit the doctor or vet for help  
Allow tests to be performed to determine an early diagnosis  
Ask your doctor and vet questions  
Remember only bacterial infections need antibiotics (not viral infections)

**SEE A DOCTOR WHEN SICK**

**Appendix 5: Acknowledgement of Individuals Who Provided Time and Resources for My Applied Practice Experience**

Barta Stevenson

Bryna Stacey

Courtney Howell

Daniel Cutting

Daniel Neises

Dr. Ellyn Mulcahy

Dr. Kate KuKanich

Dr. Landa Colvin-Marion

Dr. Michael Apley

Heidi Calvin-

Justin Blanding

Nancy Hawkins

Participants of the Veterinary Teaching Hospital Survey

Sheri Tubach

Susan M. McGann-

Theresa Hill

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