

**ANTIMICROBIAL USE, PREVALENCE OF EXTENDED SPECTRUM BETA-LACTAMASE
PRODUCING *ESCHERICHIA COLI* AND ECONOMIC EFFECTS ON CATTLE AND
POULTRY IN DAR ES SALAAM TANZANIA**

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**A THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENTS FOR THE
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EXTENDED ABSTRACT

Antimicrobial usage (AMU) in livestock production provides a basis for improving animal health and productivity. However, it is evident that the over-dependence of animal production on antimicrobial agents is one of the major factors driving the emergence of antimicrobial resistance (AMR) in bacteria that can be transmitted via the food chain or environment to humans. This thesis aims to assess antimicrobial use in cattle and poultry production in relation to resistance in Extended Spectrum Beta-Lactamase (ESBL) producing *Escherichia coli* (*E. coli*) and also gain insight into economic effects (cost and benefit) of antimicrobial use reduction in animal production in Ilala, Kinondoni and Ubungo districts which form part of the Dar es Salaam region, Tanzania with the following objectives. (i) To conduct a systematic review on the methods and metrics used to quantify and assess MU in cattle and poultry production in Sub-Saharan Africa, (ii) To determine the quantity, quality and pattern of antimicrobial use in cattle and poultry production in Dar es Salaam, Tanzania, (iii) To assess antimicrobial consumption in food-producing animals in Dar es Salaam, Tanzania, (iv) To determine the prevalence and antimicrobial resistance pattern of ESBL producing *E.coli* isolates from cattle and poultry production, and (v) To estimate the economic effects (costs and benefits) of antimicrobial use reduction in cattle and poultry production.

In view of these objectives, the findings of this thesis are presented in five scientific papers. Paper 1: A systematic literature review was conducted to provide an overview of methods of measuring AMU and metrics used, reviewing existing data on AMU in cattle and poultry production in order to identify gaps in Sub-Saharan Africa. The study revealed a deficit of studies on estimate of quantity and quality of antimicrobials used in food-producing animals in Sub-Saharan Africa.

Paper 2: A cross-sectional study was conducted on 116 farms (51 poultry and 65 small-scale dairy cattle) in Ilala, Kinondoni and Ubungo Districts of Dar-es-Salaam region, Eastern Tanzania from 15th August to 30th September 2019 to investigate the level of antimicrobial use practice, type and quantity (amount) of antimicrobials consumed. The study revealed that 23 (19.8%) of the farms visited had records while 93 (80.2%) relied on recall, 58.6% of the livestock farmers had adequate level of practices (favorable) in accordance to antimicrobial use based on their responses, the most commonly used class of antimicrobials in poultry production were: Fluoroquinolones (25.5%), sulphonamides (21.6%), tetracycline (11.8%) while in the small-scale dairy farms, tetracycline (20.0%), beta-lactams (18.5%), sulphonamides (12.3%) were most commonly used. Quantitatively, in the poultry farms, the frequently used antimicrobial class sulphonamides (46.1%), tetracycline (19%) and Macrolides (14.2%). In the small-scale dairy farms, the use beta-lactams (36.4%), sulphonamides (22.3%), tetracycline (14.3%) were predominant.

For Paper 3: a cross-sectional study, using data extraction form to collate antimicrobial use data from sales records (three consecutive years) of five established licensed veterinary pharmaceutical wholesales/outlets which were purposively selected in Ilala, Kinondoni and Ubungo. The study revealed that 178.4 tonnes of antimicrobials (by weight of active ingredients) were consumed during the 3 year study period (2016-2018), with an average of 59.5 ± 3.8 tonnes/year. The commonly sold antimicrobials were tetracycline (44.4%), sulphonamides (20.3%) and aminoglycosides (10.3%). Regarding veterinary antimicrobial use importance to human medicine, 34.4% were critically important antimicrobials; 4.1% were reserve and 51% were watch groups according to AWaRe categorization of WHO. Overall, a

mean of 7.44 ± 0.81 mg/PCU (population correction unit) was consumed by food-producing animals during the three-year study period.

Paper 4: A cross-sectional study was conducted in 54 of the previously visited farms where a pre-tested questionnaire on antimicrobial (antibiotics) usage was completed. A total of 121 *E. coli* isolates were obtained from 201 sampled small-scale dairy cattle rectal swabs. Looped rectal swab specimens from Stuart transport medium, were streaked directly onto plain MacConkey agar (Oxoid, Basingstoke, UK) and aerobically incubated at 37°C for 24 hours. Presumptive *E. coli* colonies were Gram stained and then subjected to biochemical tests (Indole test, Methyl red test, Voges-Proskauer test and Citrate Utilisation test; IMViC test) for identification. *E. coli* strain ATCC 29522 was used as a reference organism. Antimicrobial susceptibility testing (AST) was performed against eight types of antimicrobials: (Tetracycline, (TE) (30 µg), Ampicillin, (AMP) (10 µg), Gentamicin, (GN) (10 µg), Ciprofloxacin, (CIP) (5 µg), Cefotaxime, (CTX) (30 µg), Nalidixic Acid, (NA) (30 µg), Trimethoprim/Sulfamethoxazole, (SXT) (1.25/23.75µg) and Chloramphenicol, (C) (30 µg)). The highest prevalence of AMR was against AMP (96.7%), CTX (95.0%), TE (50.4%) and SXT (42.1%). The 121 isolates of *E. coli* belong to 41 different phenotypes showing a variation of resistance. The most frequently observed phenotypes were AMP-SXT-CTX with a prevalence of 12.4%, followed by the combination AMP-CTX with 10.7% and TE-AMP-CTX and NA+TE+AMP+CTX with 8.3% each. Fifteen different phenotypes that produce Extended Spectrum Beta-Lactamases (ESBLs) were detected with a prevalence of 42.9% and 74.4% of *E. coli* isolates exhibited multidrug resistance (MDR). This probably confirms that antimicrobial use is unregulated and thus inappropriate use which led to the emergence and development of resistance.

Paper 5: A cross-sectional study was conducted on randomly sampled broiler farms which were in production for one year in Kinondoni and Ubungu Districts in Dar es Salaam region of Tanzania from February to March 2021. A pre-tested questionnaire was used to capture data required to complete the model for the estimation of the economic effects (costs and benefits) on reduction of antimicrobial use. Data collected included: number of chicks bought and dead on the farm (mortality), observed clinical signs; signs of respiratory infections (coughing, wheezing, sneezing and nasal discharge), enteric infection (diarrhea) and lameness (locomotive signs) (morbidity). A McInerney model built on biological and economic parameters of disease effects on livestock production was used to analyze the data. The net costs and benefits were estimated within a partial budgeting framework in the model. The results of this study showed that antimicrobial use reduction will have an effect on mortality and morbidity and thus increase the cost of production due to changes in additional management changes (animal health management and technical management).

Findings from this thesis recommend that rational AMU should be emphasized by targeting cattle and poultry production in Tanzania in general and Dar es Salaam in particular.

DECLARATION

I, ROGERS RUYU AZABO, do hereby declare to the Senate of Sokoine University of Agriculture that, this thesis is my own original work and that it has neither been submitted nor concurrently being submitted for a degree award in any other institution.

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DEDICATION

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- Paper I:** **Azabo, R.,** Dulle, F., Mshana, SE., Matee, M., Kimera, S. Quantity and quality of antimicrobial use on occurrence of multidrug resistant *Escherichia coli* in cattle and poultry production in Sub-Saharan Africa: Systematic Review.
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LIST OF ABBREVIATIONS AND SYMBOLS

AAI	Active Antimicrobial Ingredient
AMC	Antimicrobial Consumption
AMP	Ampicillin
AMR	Antimicrobial Resistance
AMU	Antimicrobial Use/Usage
ARB	Antibiotic Resistant Bacteria
ARG	Antibiotic Resistant Gene
AST	Antimicrobial Susceptibility Test
ATCC	American Type Culture Collection
ATCvet	Anatomical Therapeutic Chemical Classification of Veterinary Medicinal Products
AWaRe	Access Watch and Reserve
BA	Boronic Acid
BelVet-SAC	Belgian Veterinary Surveillance Antimicrobial Consumption
BLRA	Binary Logistic Regression Analysis
C	Chloramphenicol
°C	Degree centigrade
C _a	Cost on reduction
CA	Clavulanate
CAZ	Ceftazidime
C _f	Cost of increased Feed Conversion Ratio
C _{rw}	Cost of reduced weight
CD	Destruction Costs
Cis	Confidence Intervals
CIA	Critically Important Antimicrobials
CIP	Ciprofloxacin
CLSI	Clinical and Laboratory Standards Institute
CN	Gentamicin
CoP	Community of Practice
CRG	Cost of Reduced Growth
CTM	Cost of Technical Measure
CTX	Cefotaxime
CUHAS	Catholic University of Health and Allied Sciences
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DCD	Defined Course Dose
DDD	Defined Daily Dose
DDDA	Defined Daily Dose Animal
DDD _{vet}	Defined Daily Dose veterinary
DPRTC	Directorate of Postgraduate Studies, Research, and Technology Transfer and Consultancy
<i>E. coli</i>	<i>Escherichia coli</i>
ECDC	European Centre for Disease Prevention and Control
EDTA	Ethylene Diamine Tetra acetic Acid.
EEA	European Economic Area
EMA	European Medicines Agency

ESBL(s)	Extended Spectrum Beta-Lactamase(s)
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agricultural Organization
FAOSTAT	Food and Agricultural Organization Global Statistical Database
FCR	Feed Conversion Ratio
g	gram
HIA	Highly Important Antimicrobial
HGT	Horizontal Gene Transfer
IA	Important Antimicrobial
INV	Cost of an Investment
IU	International Unit
IMViC test	Indole, Methyl red, Voges-Proskauer and Citrate Utilisation test
LMB	Total Loss due to Morbidity
LMICs	Low- and Middle-Income Countries
LMR	Loss due to Mortality
LS	Lifespan
MBR	Morbidity Rate
MDR	Multidrug Resistance
mg	milligram
mg/kg	milligram/kilogram
mg/ml	milligram/milliliter
mg/PCU	milligram/ Population Correction Unit
ml	milliliter
MoHCDGEC	Ministry of Health Community Development Gender Elderly and Children
MR	Mortality
MRT	Mortality Rate
MS	Microsoft Excel
MUHAS	Muhimbili University of Health and Allied Sciences
n/N	Number
N_{area}	Stocking density
N_{rounds}	Number of rounds per year
N_{total}	Total number of chickens per farm
NA	Nalidixic acid
NaLIRRI	National Livestock Resources Research Institute
NARO	National Agricultural Research Organisation
NIMR	National Institute of Medical Research
OR	Odds Ratio
OIE	Office International des Epizooties (World Health Organization for animals)
P	Price
P_{doc}	Purchase price (day old chick)
P_f	Price of feed
P_m	Price of meat
$P_{\text{probiotics}}$	Purchase price of probiotics per chick per treatment
P_{vitamin}	Purchase of vitamins per chicken per treatment
PCU	Population Correction Unit
P-value	Probability value
RC	Replacement Cost
SACIDS	Southern African Centre for Infectious Disease Surveillance

SANVAD	Southern African National Veterinary Surveillance and Monitoring Programme for Resistance to Antimicrobial Drugs
SPSS	Statistical Package for Social Sciences
SUA	Sokoine University of Agriculture
SXT	Trimethoprim/sulfamethoxazole
t	Tonnes
TE	Tetracycline
TVM	Total Value at Mortality
UDD	Used Daily Dose
UDD _{vet}	Used Daily Dose veterinary
VCIA _s	Veterinary Critically Important Antimicrobials
VGT	Vertical Gene Transfer
VHIA _s	Veterinary Highly Important Antimicrobials
VIA _s	Veterinary Important Antimicrobials
WHIS	World Animal Health Information System
WHO	World Health Organisation
W	Weight
ΔFCR	Increase in Feed Conversion
ΔFCRA	Decrease in feed conversion rate due to antibiotic reduction
μl	Microlitre
μg	Microgram
%	Percentage
% W	Relative reduction in weight

CHAPTER ONE

GENERAL INTRODUCTION

1.1 Background

Antimicrobials are essential for preventing and control of infectious diseases as well as therapeutics (Phillips *et al.*, 2004; Pagel and Gautier, 2012; Rushton, 2015; Kirchhelle 2018). They also contribute to livestock productivity and sustainability, food security, foodsafety, animal welfare, and protection of livelihoods and animal resources (Rushton, 2015). This has led to the control of animal infections that can infect humans through the food chain (Phillips *et al.*, 2004). However, the effectiveness of antimicrobial agents is hampered by the emergence of antimicrobial resistance (AMR) in bacterial strains in humans, food producing animals and the environment (Finley *et al.*, 2013; Aiken *et al.*, 2014; Van Boeckel *et al.*, 2015). Antimicrobials are routinely used by livestock farmers in animal feeds at sub-therapeutic doses as growth promoters (Onu *et al.*, 2004) to improve feed efficiency in poultry and cattle production (Dibner and Richards, 2005). Several studies have reported the selection of antimicrobial resistance through subtherapeutic use of antimicrobials (Andersson and Hughes, 2014). Since then, the addition of antimicrobials to livestock feed has been barred in European countries to limit the emergence of AMR in microbial populations (Anadón, 2006). Although AMR is a naturally occurring phenomenon since ancient times (D'Costa *et al.*, 2011), the widespread use of antimicrobials in humans and animals has significantly accelerated the process of AMR emergence and spread. It is clear in humans (Goossens *et al.*, 2005) and veterinary medicine (Chantziaras *et al.*, 2014).

Worse still, some resistance genes in some pathogens, such as *Escherichia coli* (*E. coli*) are encoded and co-selected with virulence genes (Woolhouse *et al.*, 2002). *E. coli* is a mutualistic bacterium in humans and animals, which constitutes about 99% of the intestinal bacterial flora (Diarra *et al.*, 2007). This bacterium was preferred in this study as a model organism because of the following properties: i) Relative abundance in animal and human guts as they form part of the commensal flora and can be isolated easily from the faecal samples ii) Easily exchange genetic material with bacteria of the same or of different species (Coque *et al.*, 2008), iii) It has the ability to thrive aerobically and anaerobically (Tenaillon *et al.*, 2010). Because of the above, *E. coli* is used as an indicator organism for monitoring and surveillance which is the basis for decision making and mitigation strategies (Djuikoue *et al.*, 2022). This bacterium has the capacity to shrink the action of numerous antimicrobial agents due to its ability to develop several resistance mechanisms among which include production of extended spectrum β -lactamases (ESBLs) (Djuikoue *et al.*, 2022). ESBLs are enzymes which render antimicrobials especially those with Beta-lactam rings in-effective when used to treat infections caused by ESBL producing organisms (Kim *et al.*, 2002). Several studies have shown that ESBL-producing *E. coli* have been isolated particularly from poultry (Smet *et al.*, 2008) and cattle (Liebana *et al.*, 2006).

The emergence and spread of drug-resistant pathogens continue to be amplified by the economic boom and international travel, threatening the ability to treat and contain common infectious diseases (Jasovsky *etal.*, 2016; Frost *et al.*, 2019).

Antimicrobial use and its concern about resistance have received significant consideration from both the scientific world and the public in general, but astonishingly information from researchers on the economics in animal husbandry is missing (Miller *et al.*, 2006). Although commonly used

in food producing animals, there is paucity of data on the details of the economics of using antimicrobials in animals. Therefore, with appropriate data collection, understanding the economics of AMU in animal husbandry, correlating human and animal health risks linked with their use in animals, will aid in the development of effective policy actions (Miller *et al.*, 2006).

To address these relationships, requires development of a complex relational database. The quality of the data in the database is important to provide the information. The reliability and validity of the antimicrobial use information reported by the manufacturer determines the accuracy of the model (Barber *et al.*, 2003). Data AMU should be collected at the farm level, along with animal productivity and underlying disease data, cost data (including the cost or price of antibiotics used), and production data.

Many decisions regarding the use of antimicrobial agents in livestock are generally determined by cost-benefit relationships, and decision to support antimicrobial efficacy have economic implications (Miller *et al.*, 2006). Economists need user data, resistance data, and other farm management / production data before they can suggest effective alternatives to current AMU, and ideally, develop an economic production model or other economic models. The use of antimicrobial agents on farms is a cost of production. Economists can develop models that can predict how specific antimicrobial usage regimens influence measures of productivity (Miller *et al.*, 2006). In this study, the McInerney model (McInerney, 1996) was used to determine the cost-benefit analysis on reduction of AMU in livestock production. This model was used because it was built on reductionism.

In Tanzania, Karimuribo *et al.* (2005) and Mubito *et al.* (2014) reported that dairy cattle and exotic chicken production accounts for most of the antimicrobial drugs used. In view of preserving the therapeutic effectiveness of antimicrobials and preventing continued emergence of AMR among bacteria, various public health international bodies and many countries have put mitigation strategies like appropriate antimicrobial use, formulation of policies that limit antimicrobial use in animals (Maron *et al.*, 2013) and research funding in various aspect of AMR and development of alternative approaches (Hulscher *et al.*, 2010). However, antibiotic misuse is on the rise, particularly among middle- income countries such as China, Brazil, South Africa, Russia and India (Van Boeckel *et al.*, 2015). This study is therefore designed to assess AMU in cattle and poultry in relation to prevalence of ESBL producing *E. coli* and also gain insight in its economic effects. The findings from this study will add value to empirical knowledge on responsible antimicrobial stewardship and thus prolonging the benefits derived from them in livestock production.

1.2 Antimicrobial Classification According to WHO and OIE

According to World Health Organization (WHO) classification which is based on two criteria and three categories. The criteria used are: (1) Whether it is the sole drug or among the few options for treating human infections which are serious; and (ii) whether the antimicrobial drug is used for fighting disease causing organisms that can be conveyed from non-human sources, or disease causing organisms that may acquire resistance genes from non-human sources. The three categories are: (1) Critically important antimicrobials (CIAs) (criteria 1 and 2). (2) Highly important antimicrobials, (HIAs) (neither criteria 1 or 2) and (3) Important antimicrobials, (IAs) (neither criteria 1 nor 2) (FAO, 2007).

The Office International des Epizooties (OIE) has also grouped antimicrobials into three categories based on two criteria: (i) Whether the 50% response rate by the respondents to the questionnaire regarding Veterinary Critically Important Antimicrobials (VCIAs) was met and (ii)

whether the antimicrobial was recognized as essential against specific infections and there were no appropriate alternatives. The three groups are: (1) VCIA, (criteria 1 and 2), (2) Veterinary highly important antimicrobials, VHIA (criteria 1 or 2) and (3) Veterinary important antimicrobials, VIA (criteria 1 nor 2) (FAO 2007).

The main difference between WHO and OIE definitions lies in the CIAs category. In the WHO categorization, a number of antimicrobial classes which include ansamycins, carbapenems, glycopeptides, oxazolidinones and streptogramins only appear in the WHO list; whereas sulfonamides, phenicols, diaminopyrimidines, and tetracyclines were considered only as critically important for animal health by OIE (FAO, 2008).

Most antimicrobials used in food producing animals are closely related to those used in humans. This has been demonstrated by the WHO and OIE list that CIAs are equally essential in the treatment of both human and food animals. However, there is a guideline on CIAs usage in food producing animals that recommends veterinary therapy to farmers and food industry to avoid routine antimicrobial use for growth enhancement and prevention of disease in healthy animals. The guideline aims at preserving the efficacy of antimicrobials by reducing their use in animals as they are of importance in human medicine (WHO, 2017).

1.3 Mechanisms of generation and transmission of AMR

Since the introduction of antimicrobial (antibacterial) agents, microorganisms have gradually become resistant with time (Reygaert, 2018). The resistance mechanisms may occur either through natural mutation or acquired. The acquired resistance can occur in two main ways: that is vertical (VGT) and horizontal gene transfer (HGT). In the former, genes are transferred from generation to the next by cell division (Dantas and Sommer, 2014) and in the latter, genes are transferred from external sources by contact either directly or indirectly (Dantas and Sommer, 2014). Among bacterial cells (Antibiotic Resistant Genes (ARGs) are transferable through 'conjugation', 'transformation' or 'transposition'). Four major resistance mechanisms have been identified and these include: (i) restriction of antibiotic uptake, (ii) modification of cellular targets, (iii) inactivation of antimicrobial agent, and (iv) efflux of antimicrobial agents (leakage) (Reygaert, 2018). The transfer of AMR bacteria and genes may occur through complex pathways across systems. These systems include humans, animals and the environment (Da Costa *et al.*, 2013; Woolhouse *et al.*, 2015; Graham *et al.*, 2019). A range of bacterial (commensals or pathogenic) species and ARGs (mobile genetic elements like plasmids) may be exchanged among humans, animals (farms and livestock) and environment (Baquero *et al.*, 2019). The transfer of resistant organisms between animals, humans or across species may be through direct contact i.e., exposure to infected individuals/animals, handling and consumption of contaminated food/ products) or indirect i.e., environment/ contaminated water with untreated human waste/animal manure) contact (Da Costa *et al.*, 2013).

1.3.1 Surveillance of AMU in animal production

The first cross-border system of surveillance on AMU in animal production called European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), was launched in September 2009 by European Medicine Agency (EMA). ESVAC provided an approach which is harmonized for collection and reporting data on AMU in animals of the European Union (EU) and European Economic Area (EEA) member countries (EMA 2009). Antimicrobial agents used / consumed in each country refer to animal populations using the mg / PCU AMU metric.

$$\text{AMU(mg/PCU)} = \frac{\text{Antimicrobial agents required (mg)}}{\text{Population Correction Unit}}$$

The numerator represents the sales data of each active antimicrobial ingredient (AAI) and the denominator the country level animal population which is expressed as 'Population Correction Unit' (PCU) (Nguyen, 2021). One PCU corresponds to 1 kg of treated animal. The total number of PCUs per country, year and animal category is based on a number of different animal categories (number of livestock, number of animals slaughtered, number of animal imported/exported) and their average weight at treatment, projected as a consensus value for each species across the EU.

The average treatment weight values used to calculate PCU are given in the first ESVAC report (EMA, 2011). The ESVAC report now provides global estimates for all animal species combined. In most EU countries, industry provides data on AMUs and this sales information is combined with animal production statistics (expressed as PCUs). EMA has also established standardised units of measurement for reporting antimicrobial consumption in specific animal species, called the 'defined daily dose' (DDD) and 'defined course dose'(DCD) for animals. This metric is expected to be used in future reports of ESVAC, alongside mg/PCU (EMA,2020).

The OIE has played a leading role in the Global Action Plan on Antimicrobial Resistance (OIE, 2016) by developing a global database on antimicrobial use in animals. In their fourth OIE annual report (2020b) on the use of veterinary antimicrobials. Data on AMU in 2018 were provided by 153/184 (84%) OIE member countries, but only 118(64%) were able to provide specific quantitative information. By OIE region, the proportion of countries participating in the survey was highest in the Americas (94%) and Europe (91%) and lowest in Africa (81%), Far Asia Oceania (78%) and in the Middle East (50%).

The main obstacles to data collection on AMU have been lack of regulatory frameworks for veterinary antimicrobials and the lack of IT tools, funding and human resources (OIE, 2020b). In the OIE report, quantitative antimicrobial sales data for animal biomass has been adjusted using the following metrics:

$$\text{AMU(mg/PCU)} = \frac{\text{Antimicrobial agents required (mg)}}{\text{animal biomass (Kg)}}$$

Antimicrobial use quantities in animals are categorized as 'all animal species', companion animals', aquatic food animals, 'all food animals', and 'terrestrial food animals'. In contrast to the EU "PCU", the OIE animal "biomass" is calculated as the total weight of all livestock raised in a given area in a year (OIE, 2020). It is used as a proxy that could represent people exposed to reported antimicrobials. This method of animal biomass calculation was developed by the OIE based datasets available globally, such as the OIE World Animal Health Information System (WAHIS) and Statistics from the United Nations Food and Agriculture Organization (FAOSTAT) (Góchez et al., 2019). By OIE region, the quantities adjusted by animal biomass of those countries which participated in the survey in 2016. The highest amounts were from Asia-Far East-Oceania (240.5mg/kg), followed by the America (138.0mg/kg), Europe (68.5mg/kg) and lowest in Africa (45.2mg/kg). This report included global estimates for 2014 and 2015, but due to errors found in previous reports, these results do not need to be compared and interpreted (OIE, 2020).

1.3.2 Challenges of antimicrobial use monitoring

The main challenges of AMU monitoring are diverse and rate of change in production systems. Monitoring of AMU in animal production has a variety of purposes: Monitoring AMU over time; comparison between different populations; as a benchmark to facilitate AMU reduction over time and to examine the association between AMU and AMR. However, the different indicators used in different studies and surveillance systems pose additional challenges to data comparability (Collineau *et al.*, 2017). A recent study, which comprehensively examined 38 active farm-level AMU monitoring systems in 16 countries, found that these systems included many types of data collected, analyzes performed, and corresponding results were included (Sanders *et al.*, 2020).

1.3.3 Quantifying antimicrobial use

In the process of assessing the impact of strategies associated with reducing the risk arising from AMU in food producing animals, antibiotic use should be adequately quantified so that differences or variations can be correctly interpreted. Internationally, data on antimicrobial agent use is quite scarce. According to the OIE survey of 178-member states, 73% of these do not have formal systems for collecting quantitative data on antibiotic use in animals (Diaz, 2013). Collection of data is particularly difficult in developing nations due to over-the-counter sales of antibiotics (Morgan *et al.*, 2011). Proper quantification of AMU remains a problem in Europe, where quantitative data are widely available. A project by ESVAC has so far collected data on the total amount of antimicrobials sold together for all food animal types (EMA, 2015). It does not assess the actual use of antimicrobials and does not provide information on how, why or who used antimicrobials. The comparison of the cross-country is faced with serious problems, especially demographic differences in animal, production types and treatment practices (Bondt *et al.*, 2013).

There are a variety of metrics and technical units of measurements available for AMU in food animals, each with its own merits and demerits. In Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), (DANMAP, 2013), total consumption is expressed in kg or tons of active substance, with the actual biomass of the animal population at risk is used as the denominator data (Ungemach *et al.*, 2006).

Another way of quantifying consumption data is to express consumption in terms of the dose used per animal species. Due to variances in daily doses between antimicrobials, formulations, animal species and countries, standardized doses recommended by ESVAC or regulated defined daily doses for animals (DDDA) are required. The ESVAC consortium defined the Defined Daily Dose Animal (DDDA) as "the estimated average maintenance dose per kg body weight per day for the primary target in a given animal species" (EMA, 2009).

1.3.4 Monitoring antimicrobial resistance in *Escherichia coli*

In addition to data on antimicrobial consumption, monitoring of AMR in livestock is an important step in a strategy to limit resistance (Moreno *et al.*, 2000). This is because it provides an effective intervention to fight against tolerance to infections that threaten animal health or welfare by developing guidelines for selecting appropriate therapies in clinical settings. Resistant zoonotic bacteria are of interest because in addition to compromising the health of animals and/or humans, they can also transmit the resistance genes acquired to pathogenic or commensal bacteria in humans directly through contact with animals or humans or indirectly via consumption of food animal products or environment (Hesp *et al.*, 2019).

1.4 Problem Statement

In order to meet the increasing demand for animal products like milk, eggs and meat in urban and peri-urban areas, AMU in livestock production is inevitable. As a consequence of this livestock is exposed to antimicrobial agents. Antimicrobials have been proposed to greatly contribute to livestock sustainability and productivity, and economic returns by reducing disease incidence, morbidity and mortality (Barlow, 2013). Equally, they are used for non-therapeutic purposes such as growth promotion and feed efficiency enhancers (Ellerbroek *et al.*, 2010). Nonetheless, these activities can promote the growth of drug-resistant bacteria, thereby reducing the efficacy of common antimicrobials used for the treatment of bacterial diseases in food producing animals (Speksnijder *et al.*, 2015; Wall *et al.*, 2016). In Dar es Salaam region in particular and Tanzania in general, cattle and poultry production contributes greatly to the total antimicrobial use in livestock production (Karimuribo *et al.*, 2005; Mubito *et al.*, 2014). This probably translates into abuse and overuse of broad-spectrum antimicrobials, thus contributing to selection and emergence of ESBL-producing *Enterobacteriaceae* in animals. This is further reinforced by inadequacy in enforcement of legislations regarding antimicrobial drug application in farm animals as well as monitoring of their residues (Nonga *et al.*, 2009). Several studies have reported about antimicrobial resistance in animals to commonly used antimicrobials in Tanzania (Nonga and Muhairwa, 2010; Kashoma *et al.*, 2015; Katakweba *et al.*, 2018). However, there is paucity of information on quantity and quality of antimicrobials used in livestock production despite being one of the drivers of agricultural AMR.

1.5 Justification

Resistance to antimicrobials is likely to be one of the public health concerns of the next decade (Pidcock, 2012). Resistance is an ancient phenomenon due to several factors (D'Costa *et al.*, 2011) among which include excess AMU in both human and veterinary medicine (Hecker, 2003) and cross transmission of resistant strains from humans to humans and from animals to humans. Widespread livestock (cattle and poultry) AMU has been associated with the emergence of antimicrobial resistant bacteria ((WHO 2000), and evidence exists which links antimicrobial resistant human infections to foodborne pathogens from animals (Swartz, 2002). The potential human health and ecological impacts of these emerging contaminants calls for more epidemiological surveillance in small-scale dairy cattle and poultry farms. Therefore, there is need to assess AMU (practice, type, quantity and its quality) in cattle and poultry production in relation to prevalence of AMR in ESBL producing *E. coli* and also gain insights in economic effects on reduction of antimicrobial use. This study may provide analytical information which is evidence based to preserve the potential benefits of antimicrobial usage in food animal production with jeopardy to public health.

1.6 Research Questions

- i. What and how antimicrobials are used in cattle and poultry production in Dar es Salaam region of Tanzania?
- ii. How is the antimicrobial consumption profile of food producing animals in Dar es Salaam, region of Tanzania?
- iii. What is the prevalence and pattern of antimicrobial resistance of ESBL *E. coli* isolates from the cattle and poultry production in Dar es Salaam region?
- iv. What is the economic effect (costs and benefits) on reduction of antimicrobial usage in cattle and poultry production farms in Dar es Salaam region, Tanzania?

1.7 Study Objectives

1.7.1 General objective

To assess antimicrobial use in cattle and poultry production in relation to prevalence in ESBL producing *E. coli* and also gain insight in its economic effects.

1.7.2 Specific objectives

- i. To conduct systematic review on quantity and quality of AMU in cattle and poultry production in Sub-Saharan Africa.
- ii. To determine the quantity, quality and pattern of AMU in cattle and poultry production in Dar es Salaam, Tanzania.
- iii. To assess antimicrobial consumption in food producing animals in Dar es Salaam, Tanzania.
- iv. To determine the prevalence and antimicrobial resistance pattern of ESBL producing *E. coli* isolates from the cattle and poultry production in Dar es Salaam, Tanzania.
- v. To estimate the economic effects (costs and benefits) of antimicrobial use reduction in cattle and poultry production in Dar es Salaam, Tanzania.

1.8 General Methodology and Thesis Outline

This thesis details the approach used to assess antimicrobial use in cattle and poultry production in relation to prevalence of ESBL producing *E. coli* and also gain insight in economic effects (costs and benefits) of reducing antimicrobial use in broiler farms in Dar es Salaam, Tanzania. The study involved both literature search and extensive field investigation for both data and sample collection. Data were collected using various techniques: questionnaire administration to household heads with cattle/poultry, data extraction form for collation of data from sales records of established licensed veterinary pharmaceutical outlets, cattle rectal swab collection using sterile cotton swabs, isolation of *E. coli* and analysis of AMR pattern and prevalence of *E. coli* isolates from small-scale dairy cattle production. Various analytical skills were applied to process, analyze and interpret data using Microsoft™ Excel application, McInerney model and IBM Statistical Package for Social Science (SPSS) software version 20.

The thesis consists of five manuscripts and has the following structure: Chapter One presents the study context of the thesis and sets the scene for the work. It is followed by chapter two which comprises of manuscripts anchored in distinct research questions. The results in each manuscript are presented in accordance with the objectives of the thesis. Chapter Three, presents discussion of the findings of the five manuscripts in relation to the overall aim of the thesis, conclusions and recommendation for future research.

CHAPTER TWO

Paper I

Antimicrobial use in cattle and poultry production on occurrence of multidrug resistant *Escherichia coli*. A Systematic Review with Focus on Sub-Saharan Africa

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Paper II**Antimicrobial usage in cattle and poultry production in Dar es Salaam, Tanzania:
pattern and quantity****Rogers Azabo**^{1, 2,3*}, Stephen Mshana⁴, Mecky Matee^{3,5}, and Sharadhuli I Kimera^{3,6}.

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Paper III

**Assessment of Antimicrobial Consumption In Food Animals in
Dar es Salaam, Tanzania**

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Paper IV

Antimicrobial Resistance Pattern of Escherichia coli isolates from Small scale dairy cattle in Dar es Salaam, Tanzania

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Paper V

Farm costs and benefits of antimicrobial use reduction on broiler farms in Dar es Salaam, Tanzania

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CHAPTER THREE

General Discussion, Conclusion and Recommendations for Future Research

3.1 General Discussion

The aim of this PhD study was to assess AMU (pattern/practice, types of antimicrobials, quantities consumed) in small-scale dairy cattle and poultry production in relation to prevalence and antimicrobial resistance pattern in ESBL producing *E. coli* and also gain insight in economic effects on reduction of AMU in these species in Dar es Salaam, Tanzania. Dar es Salaam, is one of the regions in Tanzania with intensive livestock keeping activities due to urban and peri-urban market demand for livestock products (Katakweba *et al.*, 2018). *E. coli* is among the “One Health” bacterial species. It is a commensal bacterium of the intestinal flora of humans and animals which is frequently used as a sentinel organism for AMR (Aslam *et al.*, 2021). In this study, it was hypothesized that human anthropogenic activities such as antimicrobial use in livestock production may involve emergence of resistant genes which may spread to humans either through direct contact or food-animal products.

Results from paper 1, indicate paucity of information on the quality and quantity of veterinary drugs in Sub-Saharan Africa and yet they have a role to play in the overall picture of antimicrobial resistance. This finding calls for future research as far as resistance and MDR is concerned in food producing animals.

Results from paper 2 show that the use of antimicrobials is common among the poultry and cattle farmers, with the most frequently used antimicrobials being tetracyclines, sulphonamides, fluoroquinolones, macrolides, beta-lactams and aminoglycosides. When faced with antimicrobial treatment failure, farmers may look for new treatment courses with new antimicrobial classes, resulting in more AMU.

This is of a particular concern given the widespread practice and the affordability and availability over the counter (Dung *et al.*, 2020). In this study, veterinarians were the most common source of advice on AMU, most of whom owned private veterinary pharmacies/outlets and were the primary source of supply of antimicrobials and related products in the region. To increase profitability, these private pharmacies/outlets are more likely to sell antimicrobial products even in situations where they don't need them. This agrees with the study by Phu *et al.*, 2019 who reported that high level of AMU is associated with high density of the veterinary pharmacies. The study also found that recording and recalling were the most common methods of AMU data collection. There are differences in the sources of AMU data collection between different studies. These include electronic veterinary treatment records (Firth *et al.*, 2017; Hyde *et al.*, 2017a), farmers' treatment records (Redding *et al.*, 2014; Nobrega *et al.*, 2017), invoices of veterinary practices (Kuipers *et al.*, 2016), surveys (Glasgow *et al.*, 2019; Lambrou *et al.*, 2021; Mudenda *et al.*, 2022), national antimicrobial sales data (Bryan and Hea, 2017), wholesales data (Azabo *et al.*, 2021), and bin audits (Saini *et al.*, 2012a) have been used to collect data on AMU in food producing animals. Treatment registration was one of the criteria used for entry to this study. Although the farmer's treatment record was poor, most of them had adequate (favorable) level of AMU practices/pattern in poultry and cattle production. Understanding antimicrobial use pattern is important for developing rational antimicrobial use and mitigation options that can potentially reduce AMR risks in animal production (Lekagul *et al.*, 2019).

Furthermore, results in this paper indicate that the main purpose of AMU in all categories of farmers (poultry and cattle) are therapeutics (83.6%), therapeutics and prophylaxis (13.8%), prophylaxis (1.7%) and growth promotion (0.9%). In addition to sustaining production, farmers may use antimicrobials as a surrogate for biosecurity, unsanitary practices and poor environmental hygiene that can facilitate the emergence and spread of antibiotic-resistant pathogens (Graham *et al.*, 2009). Most of the commonly used antimicrobials used on both poultry and small-scale dairy cattle farms visited, were classified either as critically important (fluoroquinolones) or highly important (sulphonamides, tetracyclines).

Fluoroquinolones use in food animals is of concern because they are effective in treating intestinal infections in humans. In livestock where it is used, it has been reported to be linked with increased resistance in exposed populations (Adebowale *et al.*, 2016). The use of prohibited substances such as colistin is of concern as they are among the last antimicrobial agents of choice for human nosocomial infections (Kadar *et al.*, 2013). Quantitatively in both poultry and small-scale dairy cattle, the most frequently used antimicrobial classes were sulphonamides, tetracyclines, macrolides, fluoroquinolones, beta-lactam and aminoglycosides (Tables 4 and 5 in paper 2). In this study, antimicrobial consumption (AMC) was also expressed in terms of dose-based metrics (Tables 4 and 5 in paper 2). Estimates of AMC based on chosen metrics depend on several factors, among which include the type of data collected, the type of analyses conducted and their respective output (Mills *et al.*, 2018; Sanders *et al.*, 2020).

Results on quantification show that quantitative AMU data can be collected from a cross-sectional survey, especially when farmers are asked about AMU in their flocks/herds over a short period (one week). This method can be applied at the national level since it is appropriate and affordable.

Results from paper 3 showed that 178.4 tonnes of active antimicrobial ingredients were consumed by food-producing animals during the three years study period (2016-2018). A recent study demonstrated global antimicrobial consumption of 93309 tonnes of active antimicrobial ingredient in 2017 (Tiseo *et al.*, 2020). Antimicrobial use consumed by food animals in this study (7.44mg/PCU) was lower than the estimates in Vietnam (247.3 mg/PCU) (Carrique-Mas *et al.*, 2020). Food producing animal consumption of CIAs (34.4%) was significantly lower than that in Vietnam (71.8%) (Cuong *et al.*, 2021). Vietnam has large numbers of 'market season farms' which only raise flocks targeting specific festivals. These flocks/herds usually experience high disease incidence and mortality risks thus high AMU (Delabougliise *et al.*, 2019).

The commonly used route of antimicrobial administration in this study was the oral route (68.1%), lower than the 73.1% previously reported in Cameroon (Mouiche *et al.*, 2020). The oral route permits solid, semi consistent and liquid forms of antimicrobials to be taken through drinking water and with feed (Tsutsui *et al.*, 2018). Reporting data on antimicrobial consumption promotes reduction and more responsible use by benchmarking the dispensing and prescribing behaviour of farmers and veterinarians (Stevens, 2016).

Results from paper 4 showed an isolation rate of 60.2% of *E. coli* from rectal swab of apparently healthy small-scale dairy cattle. A recent study reported an isolation rate of up to 84% from a rectal swab of an apparently healthy dairy cattle (Gupta *et al.*, 2017). The widespread occurrence of *E. coli* highlights the potential for spread through human, animal, environment sources (Aworh *et al.*, 2021), with consequential flow of resistomes and virulence genes (Ogundipe *et al.*, 2020).

Determination of antimicrobial resistance using phenotypic methods revealed high levels of insensitivity of *E. coli* to a number of commonly used antibiotics such as nalidixic acid, tetracycline, gentamicin, ciprofloxacin, ampicillin, trimethoprim/sulfamethoxazole, chloramphenicol and cefotaxime. *E. coli* isolates from small-scale dairy cattle showed a high resistance to ampicillin (96.7%), cefotaxime (95.0%) and tetracycline (50.4%). Given the common practice of AMU in the study area, a high prevalence was shown of AMR in commensal *E. coli* against tetracycline (63.5%), nalidixic acid (53.7%), and ampicillin (52.3%) (Kimera *et al.*, 2021). A further concern is that these antimicrobials have been found in studies investigating residues in foods of animal origin in Tanzania and elsewhere, posing a risk to public health (Sahu and Saxena, 2014; Patel *et al.*, 2018; Bilashoboka *et al.*, 2019). Almost all classes of antibiotics are used in agriculture, including those closely related to clinically relevant antibiotics such as penicillin, cephalosporins, fluoroquinolones, tetracyclines, sulfonamides and aminoglycosides (Marshall and Levy 2011; Mboera *et al.*, 2018). The unfortunate part is that according to the National Sample Survey, only 20% of Tanzanian farmers utilise extension services for treatment (Michael *et al.*, 2017). The emergence of a high-level antimicrobial resistance levels in *E. coli* isolates from the healthy small-scale dairy cattle examined indicates the possible roles these bacteria play in the transmission. *Escherichia coli*'s natural habitat is the digestive tract/intestine (Jeffrey *et al.*, 2012). Commensal *E. coli* is widely used to monitor AMR in surveillance systems due to their ubiquity and ability to develop AMR after AMU. It is an important indicator of drug-resistant link between animal sources and human transmission, especially when resistance to CIA antibiotics such as polymyxins, quinolones or 3rd - 4th generation cephalosporins (WHO, 2019).

Results in this paper further revealed several susceptibility patterns in *E. coli* isolated from small-scale dairy cattle ranging from one to eight antimicrobial agents. A recent study revealed up to seven classes of antimicrobials (Mgaya *et al.*, 2021) in the study area. This indicates that the *E. coli* isolates in this study varied in their antimicrobial resistance spectrum.

Several MDR *E. coli* isolates showed different phenotypic resistance patterns. The most common combinations were AMP-SXT-CTX (Ampicillin, Trimethoprim/ sulfamethoxazole and Cefotaxime), which differed with the recent study in the same region, which reported a combination of TE-SXT-AMP (Tetracycline, Trimethoprim/ sulfamethoxazole and Ampicillin) (Mgaya *et al.*, 2021). A possible explanation for the MDR levels in this study could undoubtedly be due to the selection pressure due to uncontrolled use of various veterinary antimicrobial agents. Surprisingly, it has been observed that *E. coli* isolates had a high resistance to cefotaxime (95.0%) which are not commonly used in farm animals in Tanzania.

This can be elucidated by the cross-transfer of resistant bacterial strains between livestock and humans, where cephalosporins are widely used. Exchange of resistance genes between humans and animals can occur when cattle drinks contaminated water or pastures with effluents during the rainy season (Katakweba *et al.*, 2018). Therefore, the 95.0% resistance to cefotaxime could pose a significant threat to public health. Results from paper 5 reveal that it is still expensive to use antimicrobials in the broiler farms compared to avoidable disease costs and additional management costs.

3.1.1 Summary of the thesis finding

- i) There is paucity of information on the quality and quantity of veterinary antimicrobial usage in the Sub-Saharan Africa and yet have a role to play in the overall picture of antimicrobial resistance.
- ii) The most commonly used classes of antimicrobials in poultry and cattle production are sulphonamides, tetracyclines, fluoroquinolones, macrolides, beta-lactams and aminoglycosides.
- iii) Farmers do not keep up to-date treatment records despite the fact that they have adequate level of AMU practices and are literate.
- iv) Consumption of critically important antimicrobials (CIAs) in farms animals for instance fluoroquinolones has been linked to increased resistance in people exposed to them.
- v) There are high levels of non-susceptibility to a number of commonly used antibiotics such as nalidixic acid, tetracycline, gentamicin, ciprofloxacin, ampicillin, trimethoprim/ sulfamethoxazole, chloramphenicol and cefotaxime.
- v) There is a high level of resistance to cefotaxime which is not commonly used in farm animals in Tanzania but with wide spread use in human medicine.
- vi) Bacterial infections due to *E. coli* are difficult to treat with the currently used antimicrobials.
- vii) Finally, although AMU in broiler farms is expensive, its use cannot be ruled out **compared to the type of disease being controlled.**

3.1.2 Scientific contribution of this thesis

In this thesis, I assessed AMU (practices, types of antimicrobials, quantities used) in small-scale dairy cattle and poultry production in Dar es Salaam region, Tanzania. The thesis also revealed a high prevalence of AMR and MDR and ESBL producers in *E. coli* isolates in small-scale dairy farms previously visited where a pre-tested questionnaire on antimicrobial usage was completed in Dar es Salaam region of Tanzania. Based on the findings in this thesis, effective intervention strategies to curb excessive antimicrobial consumption may be designed thus minimising the risks of selection, development and spread of antimicrobial resistance.

Secondly, it is the first study of its kind in Tanzania to work on the economics of antimicrobial usage and antimicrobial resistance in animal husbandry.

This study provides analytical information which is evidence based, for policy makers to use as a guide during the formulation of policies on monitoring and control of antimicrobial use in livestock production in Tanzania.

3.1.3 Limitation of this thesis

- i) Language bias in paper 1 (Systematic review, only articles in English) as some journal articles may report similar or different findings on AMU in cattle and poultry production in Sub-Saharan Africa.
- ii) Since most farmers relied on self recall, it is influenced by reporting and social desirability. This must have affected the outcome of the study (paper 2).
- iii) Poultry and small-scale dairy cattle farms, and veterinary pharmaceutical wholesales/outlets involved in the study, were not representative of the farms and pharmaceutical outlets in the study districts (data for papers 2 and 3).

This may have limited validity of the AMU estimates/ quantification. Although the farms were not representative, it is likely that the major increase in AMU was driven by increased number of intensification of livestock production. Secondly, there are several antimicrobials used in cattle farms in Tanzania, which were not tested in this study. In addition, molecular characterization of resistant strains was not performed (paper 4). This would have revealed the most predominant resistant genes in the study areas. The observed high resistance can be explained on the basis of the Clinical Laboratory Standard Institute (CLSI) (CLSI, 2021) protocol which are internationally accepted guidelines that reflect the actual size and pattern of AMR in the study settings.

- iv) Due to the sensitivity of the nature of the information requested, most importers/ wholesalers were reluctant to provide the information since they thought that it was an indirect way of assessing their non-compliance to tax returns during the study period (paper 3). This might have affected the outcome of the AMU estimates.
- v) The model used in the estimation of the farm cost and benefits of AMU reduction had several assumptions which might have affected the outcome of the study.

3.2 Conclusion

This research has yielded a number of important results.

- i) Most of the respondents had adequate level of practice of AMU. This could be related to availability of veterinary services. Adequate practices are important in developing mitigation options for rational AMU, that can potentially reduce AMR risks in animal products.
- ii) The 'dose based' and 'weight based' indicators resulted in quantitatively different estimates of AMU in levels. It is imperative to consider the issue of metrics when comparisons on AMU data are made across studies.
- iii) A broad picture of antimicrobials administered to poultry (chicken) flocks and small-scale dairy cattle herds, showed that AMU in these species consists of CIAs, which are associated with increased resistance to humans exposed to them.
- iv) Using the One Health approach, AMU can be assessed from a relatively simple cross-sectional survey, although results vary with the indicator chosen. This method can be used in AMU surveillance in low-resource settings, allowing to focus reduction efforts and AMU in particular animal species.

3.3 Recommendations for Future Research

Based on the results of this research, the following recommendations are put forward for the next steps in monitoring and reducing AMU in Tanzania.

- i. Establishment of a surveillance system for AMU which will help in comparisons of AMU in different production types and locations, and even monitor changes in AMU over time.
- ii. There is need for molecular characterization so that the genes in circulation are known such that decisions can be made for reducing the burden associated with them.
- iii. Studies should be conducted on the quality of AMU as low- or poor-quality antimicrobials are associated with treatment failure due to incorrect AAI.

- iv. Implementation of sustainable long-term training programmes by relevant authorities targeting different stakeholders (veterinarians, feed producers, farmers,) to increase their awareness of the problem of AMR and the importance of AMU reduction.
- v. Review policies and guidelines that discourage use of CIAs. Antimicrobials intended for animal use are affordable and readily available over the counter, so the use of alternative antimicrobial products on the market should be promoted.
- vi. Research on the development and efficiency of additional management measures and other methods to produce poultry meat without high levels of AMU are needed.
- vii. Policy briefs on AMU which encourage its rational use in livestock production to minimise the effects of AMR on public health and feedback on the concluded studies.

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Appendix 2: Paper 1: Supplementary Table 2; Characteristics of eligible studies included

Country	Food animal	Sample type	Study site	% AMU	Resistance determined		Grade	Reference
					R	MDR		
Nigeria	Poultry	n/a	Farm	100	n/a	n/a	4	Adebowale, Adeyemo, Awoyomi, Dada & Adebowale, 2016
Nigeria	Poultry	F/droppings	Farm	100	+	n/a	4	Awogbemi, Adeyeye & Akinkunmi, 2018
Uganda	Poultry	n/a	Farm	96.7	n/a	n/a	3	Bashahun & Odoch, 2015
Ghana	Poultry	n/a	Farm	98	n/a	n/a	4	Boamah, Agyare, Odoi & Dalsgaard, 2016
Cameroon	Poultry	n/a	Farm	100	n/a	n/a	4	Kamini, Keutchatang, Mafo, Kansci & Nama, 2016
Nigeria	Poultry	n/a	Farm/drug shop	100	n/a	n/a	3	Geidam et al., 2012
Nigeria	Poultry	n/a	Farm	100	n/a	n/a	4	Oluwasile, Agbaje, Ojo & Dipeolu, 2014
Nigeria	Cattle/sheep/goats	n/a	Pastoralists	100	n/a	n/a	4	Alhaji & Isola, 2018
Nigeria	Cattle/Goats/Sheep	n/a	Drug shops	----	n/a	n/a	4	Adesokan, Akanbi, Akanbi & Obaweda, 2015
Nigeria	Poultry/Goats/Sheep	F/droppings	HH	100	+	+	4	Okpara et al., 2018
Sudan	Poultry/Cattle/Goats	n/a	Farm/HH	95	n/a	n/a	4	Eltayb, Barakat, Marrone, Shaddad & Lundborg, 2012
South Africa	Poultry/Cattle/Goats/Sheep	n/a	Pharmaceuticals/Drug shops	----	n/a	n/a	4	Eagar, Swan, & Van Vuuren, 2012
Nigeria	Poultry & Pigs	n/a	Farms	67	n/a	n/a	4	Amaechi, 2014
Zambia	Cattle	Faecal	Farm/drug shops	----	+	n/s	4	Mubita et al., 2015
Tanzania	Cattle/Goats/Sheep	n/a	Pastoral herds	74	n/a	n/a	4	Caudell et al., 2017
Uganda	Cattle/Pigs/goats/Chicken	Faecal	Farms	100	+	+	4	Okubo et al., 2018
Ghana	Cattle /Goats/pigs/Chicken & Sheep	Faecal	Farms	98	+	+	3	Donkor, Newman & Yeboah-Manu, 2012
Ethiopia	Cattle/ Poultry	n/a	Farms	80	n/a	n/a	4	Tufa et al., 2018
Zambia	Cattle	Faecal	Pastoral herds	100	+	n/s	4	Mubita et al., 2008
Sudan	Poultry	n/a	Farms	93	n/a	n/a	3	Sirdar, Picard, Bisschop & Gummow, 2012
Cameroon	Poultry	Chicken tissues	Farms	80	+	n/s	4	Guetiya et al., 2016
Cameroon	Cattle	Penicillin & tetracycline	Pastoral herds	69	n/a	n/a	4	Vougat Ngom et al, 2017
Tanzania	Poultry	Chicken liver	HH/Farms	100	n/a	n/a	4	Nonga, Mariki, Karimuribo & Mdegela, 2009
Nigeria	Cattle/poultry/sheep Goats/Rabbits	n/a	Farms	99.1	n/a	n/a	4	Olufemi, Eniola, Ademola & Morenike, 2015

AMU, Antimicrobial use; F, Faecal; HH, House Hold; MDR, Multidrug resistance; n/a, not applicable; n/s not specified; +, positive; R, Resistance

Appendix 3: Paper 2: Antimicrobial use records and those that relied on recall data and list of active antimicrobial ingredients used in poultry and cattle production in Dar es Salaam, Tanzania

Additional file Table 1: Poultry Data

Farm ID	Records/Recall	No. of animals treated	Antimicrobials frequently used
PP001	Recall	1600	Oxytetracycline
PP002	Recall	816	Tylosin
PP003	Recall	600	Oxytetracycline
PP004	Recall	1500	Tylosin
PP005	Recall	490	Oxytetracycline
PP006	Recall	1000	Enrofloxacin
PP007	Recall	1050	Oxytetracycline
PP008	Records	20000	Coridix
PP009	Records	8000	Oxytetracycline
PP010	Recall	200	Fluquin
PP011	Recall	600	Enrofloxacin
PP012	Records	1441	Enrofloxacin
PP013	Recall	102	Fluquin
PP014	Records	4500	Tylosin
PP015	Recall	600	Anticox
PP016	Recall	500	Flumequine
PP017	Recall	200	Agracox
PP018	Recall	200	Oxytetracycline
PP019	Recall	600	Tylosin
PP020	Records	2000	Tylosin
PP021	Recall	100	Enrofloxacin
PP022	Recall	500	Coridix
PP023	Recall	1700	Flumequine
PP024	Recall	200	Enrofloxacin
PP025	Recall	3000	Coridix
PP026	Recall	1700	Enrofloxacin
PP027	Records	1500	Enrofloxacin
PP028	Recall	300	Enrofloxacin
PP029	Recall	110	Flumequine
PP030	Recall	500	Ciprofloxacin
PP031	Records	500	Coridix
PP032	Records	1500	Colistin
PP033	Recall	500	Ganadexil
PP034	Recall	300	Ciprofloxacin
PP035	Recall	2003	Coridix
PP036	Recall	200	Coridix
PP037	Recall	200	Doxycycline
PP038	Records	5003	Coridix
PP039	Recall	780	Anticox

PP040	Recall	100	Tylo-dox
PP041	Recall	400	Keproceryl
PP042	Records	1000	Typhoprim
PP043	Recall	300	Fluban
PP044	Recall	520	Trimazin
PP045	Recall	300	Tylo-dox
PP046	Recall	200	Tylosin
PP047	Recall	600	Tylo-dox
PP048	Records	2400	Ganadexil
PP049	Records	5000	Fluban
PP050	Records	4000	Enrofloxacin
PP051	Records	3500	Oxytetracycline

Table 2: List of Active Antimicrobial Ingredients (AAI's) included in the 17 antimicrobials used in the Poultry farms in Dar es Salaam, Tanzania Farms with records

Farm ID	Product Type	Antimicrobial drug	AAI's	Strength/ Unit of product	Type of formulation	Administra tionroute	Dilution Factors (g/l of water) or g/kg feed intake	Water consumption by 1 kg chicken	DDD (mg/kg)	No. of birds treated	UDD (mg/kg)
PP008	Vet.Med	Coridix	Sulfamethoxypyridazine	125mg/g	Powder	Water	1	0.225	28.1	20000	168.8
PP008	Vet.Med		Trimethoprim	25mg/g	Powder	Water	1	0.225	5.6	20000	33.8
PP008	Vet.Med		Tylosin	30mg/g	Powder	Water	1	0.225	6.8	20000	40.5
PP009	Vet.Med	Oxytetracycline	Oxytetracycline	100mg/g	Powder	Water	2	0.225	45	8000	135
PP012	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/l	liquid	Water	0.5	0.225	11.3	1441	33.8
PP014	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Water	0.3	0.225	13.5	4500	40.5
PP020	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Water	0.3	0.225	13.5	2000	40.5
PP027	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/l	liquid	Water	1	0.225	22.5	1500	67.5
PP031	Vet.Med	Coridix	Sulfamethoxypyridazine	125mg/g	Powder	Water	1	0.225	28.1	500	84.4
PP031	Vet.Med		Trimethoprim	25mg/g	Powder	Water	1	0.225	5.6	500	16.9
PP031	Vet.Med		Tylosin	30mg/g	Powder	Water	1	0.225	6.8	500	20.3
PP032	Vet.Med	Colistin	Colistin	4800000iu	Powder	Water	0.1	0.225	5.3	1500	15.8
PP038	Vet.Med	Coridix	Sulfamethoxypyridazine	125mg/g	Powder	Water	1	0.225	28.1	5003	84.4
PP038	Vet.Med		Trimethoprim	25mg/g	Powder	Water	1	0.225	5.6	5003	16.9
PP038	Vet.Med		Tylosin	30mg/g	Powder	Water	1	0.225	6.8	5003	20.3
PP042	Vet.Med	Typhoprim	Sulfadiazine	250mg/g	Powder	Water	0.2	0.225	11.3	1000	33.8
PP042	Vet.Med		Trimethoprim	50mg/g	Powder	Water	0.2	0.225	2.3	1000	6.8
PP048	Vet.Med	Ganadexil	Enrofloxacin	100mg/l	liquid	Water	1	0.225	22.5	2400	67.5
PP049	Vet.Med	Fluban	Enrofloxacin	100mg/l	liquid	Water	1	0.225	22.5	5000	67.5
PP050	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/l	liquid	Water	1	0.225	22.5	4000	67.5
PP051	Vet.Med	Oxytetracycline	Oxytetracycline	500mg/g	Powder	Water	0.4	0.225	45	3500	135
PP001	Vet.Med	Oxytetracycline	Oxytetracycline	500mg/g	Powder	Water	0.4	0.225	45	1600	135
PP002	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Water	0.3	0.225	13.5	816	40.5
PP003	Vet.Med	Oxytetracycline	Oxytetracycline	200mg/g	Powder	Water	0.6	0.225	27	600	81
PP004	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Water	0.3	0.225	13.5	1500	40.5

Recall farms											
Farm ID	Product Type	Antimicrobial drug	AAI's	Strength/ Unit of product	Type of formulation	Administ-ration route	Dilution Factors (g/lof water) or g/kg feed intake	Water consumpti onby 1 kg chicken	DDD (mg/kg)	No. of birds treated	UDD (mg/kg)
PP005	Vet.Med	Oxytetracycline	Oxytetracycline	200mg/g	Powder	Water	0.6	0.225	27	490	81
PP006	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/g	Powder	Water	1	0.225	22.5	1000	67.5
PP007	Vet.Med	Oxytetracycline	Oxytetracycline	200mg/g	Powder	Water	0.6	0.225	27	1050	81
PP010	Vet.Med	Fluquin	Enrofloxacin	100mg/g	Liquid	Water	1	0.225	22.5	200	67.5
PP011	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/g	Liquid	Water	2	0.225	45	600	135
PP013	Vet.Med	Fluquin	Enrofloxacin	100mg/g	Liquid	Water	0.5	0.225	11.3	102	33.7
PP015	Vet.Med	Anticox	Sulfadimidine	740mg/g	Powder	Water	0.2	0.225	33.3	600	99.9
PP016	Vet.Med	Flumequine	Flumequine	100mg/g	Powder	Water	0.8	0.225	18	500	54
PP017	Vet.Med	Agracox	Oxytetracycline	100mg/g	Powder	Water	0.5	0.225	11.3	200	33.8
PP017	Vet.Med		Sulfadiazine	25mg/g	Powder	Water	0.5	0.225	2.8	200	8.4
PP017	Vet.Med		Sulfadimerazine	200mg/g	Powder	Water	0.5	0.225	22.5	200	67.5
PP018	Vet.Med	Oxytetracycline	Oxytetracycline	50mg/g	Powder	Water	3.3	0.225	37.1	200	111.4
PP019	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Water	0.3	0.225	13.5	600	40.5
PP021	Vet.Med	Enrofloxacin	Enrofloxacin	200mg/g	Powder	Water	0.3	0.225	13.5	100	40.5
PP022	Vet.Med	Coridix	Sulfamethoxypridazine	125mg/g	Powder	Water	1	0.225	28.1	500	84.4
PP022	Vet.Med		Trimethoprim	25mg/g	Powder	Water	1	0.225	5.6	500	16.9
PP022	Vet.Med		Tylosin	30mg/g	Powder	Water	1	0.225	6.8	500	20.3
PP023	Vet.Med	Flumequine	Flumequine	100mg/g	Powder	Water	1	0.225	22.5	1700	67.5
PP024	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/g	liquid	Water	0.5	0.225	11.3	200	38.8
PP025	Vet.Med	Coridix	Sulfamethoxypridazine	125mg/g	Powder	Water	1	0.225	28.1	3000	84.4
PP025	Vet.Med		Trimethoprim	25mg/g	Powder	Water	1	0.225	5.6	3000	16.9
PP025	Vet.Med		Tylosin	30mg/g	Powder	Water	1	0.225	6.8	3000	20.3
PP026	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/g	liquid	Water	0.5	0.225	11.3	1700	33.8
PP028	Vet.Med	Enrofloxacin	Enrofloxacin	100mg/g	liquid	Water	0.5	0.225	11.3	300	33.8
PP029	Vet.Med	Flumequine	Flumequine	100mg/g	Powder	Water	1	0.225	22.5	110	67.5
PP030	Vet.Med	Ciprofloxacin	Ciprofloxacin	200mg/g	Powder	liquid	0.3	0.225	13.5	500	40.5
PP033	Vet.Med	Ganadexil	Enrofloxacin	100mg/g	Powder	liquid	0.5	0.225	11.3	500	33.8

Farm ID	Product Type	Antimicrobial drug	AAI's	Strength/ Unit of product	Type of formulation	Administration route	Dilution Factors (g/lof water) or g/kg feed intake	Water consumption by 1 kg chicken	DDD (mg/kg)	No. of birds treated	UDD (mg/kg)
PP034	Vet.Med	Ciprofloxacin	Ciprofloxacin	200mg/g	Powder	liquid	0.3	0.225	13.5	300	40.5
PP035	Vet.Med	Coridix	Sulfamethoxy pyridazine	125mg/g	Powder	Water	2	0.225	56.3	2003	170.9
PP035	Vet.Med		Trimethoprim	25mg/g	Powder	Water	2	0.225	11.3	2003	33.8
PP035	Vet.Med		Tylosin	30mg/g	Powder	Water	2	0.225	13.5	2003	40.5
PP036	Vet.Med	Coridix	Sulfamethoxy pyridazine	125mg/g	Powder	Water	2	0.225	56.3	200	168.8
PP036	Vet.Med		Trimethoprim	25mg/g	Powder	Water	2	0.225	11.3	200	33.8
PP036	Vet.Med		Tylosin	30mg/g	Powder	Water	2	0.225	13.5	200	40.5
PP037	Vet.Med	Doxycycline	Doxycycline	100mg/l	liquid	Water	0.3	0.225	6.8	200	20.3
PP039	Vet.Med	Anticox	Sulfadimidine	740mg/g	Powder	Water	0.2	0.225	33.3	780	99.9
PP040	Vet.Med	Tylo-dox	Doxycycline	200mg/g	Powder	Water	0.5	0.225	22.5	100	67.5
PP040	Vet.Med		Tylosin	100mg/g	Powder	Water	0.5	0.225	11.3	100	33.8
PP041	Vet.Med	Keproceryl	Colistin	225000iu	Powder	Water	1	0.225	2.5	400	7.4
PP041	Vet.Med		Oxytetracycline	50mg/g	Powder	Water	1	0.225	11.3	400	33.8
PP041	Vet.Med		Erythromycin	35mg/g	Powder	Water	1	0.225	7.9	400	23.6
PP041	Vet.Med		Streptomycin	35mg/g	Powder	Water	1	0.225	7.9	400	23.6
PP043	Vet.Med	Fluban	Enrofloxacin	100mg/g	liquid	Water	1	0.225	22.5	300	67.5
PP044	Vet.Med	Trimazin	Trimethoprim	50mg/g	Powder	Water	0.9	0.225	10.1	520	30.4
PP044	Vet.Med		Sulfadiazine	250mg/g	Powder	Water	0.9	0.225	50.6	520	151.8
PP045	Vet.Med	Tylo-dox	Doxycycline	200mg/g	Powder	Water	0.5	0.225	22.5	300	67.5
PP045	Vet.Med		Tylosin	100mg/g	Powder	Water	0.5	0.225	11.3	300	38.8
PP046	Vet.Med	Tylosin	Tylosin	200mg/g	Powder	Feed	3.5	0.0634	44.4	200	132.3
PP047	Vet.Med	Tylo-dox	Doxycycline	200mg/g	Powder	Water	0.5	0.225	22.5	600	67.5
PP047	Vet.Med		Tylosin	100mg/g	Powder	Water	0.5	0.225	11.3	600	33.8

Vet.Med; Veterinary medicine

CATTLE DATA**Table 3:** Small-scale dairy farms with antimicrobial use records and those that relied on recall

Farm ID	Records/Recall	No. of animals treated	Antimicrobials frequently used
CC001	Recall	5	Tetracycline
CC002	Recall	1	Penstrep
CC003	Recall	8	Tylosin
CC004	Recall	4	Tetracycline
CC005	Recall	4	Enrofloxacin
CC006	Records	10	Penstrep
CC007	Recall	4	Gentamicin
CC008	Recall	5	Tetracycline
CC009	Records	4	Tetracycline
CC010	Recall	2	Tetracycline
CC011	Recall	6	Sulphonamide
CC012	Recall	5	Tetracycline
CC013	Recall	2	Gentamicin
CC014	Recall	5	Tetracycline
CC015	Recall	2	Tylosin
CC016	Recall	2	Ampicillin
CC017	Records	18	Tetracycline
CC018	Recall	2	Neomycin
CC019	Recall	2	Tetracycline
CC020	Recall	3	Penicillin
CC021	Recall	7	Tetracycline
CC022	Recall	4	Enrofloxacin
CC023	Recall	7	Ampicillin
CC024	Recall	15	Tetracycline
CC025	Recall	13	Gentamicin
CC026	Recall	5	Tetracycline
CC027	Recall	2	Penstrep
CC028	Recall	5	Tetracycline
CC029	Records	7	Gentamicin
CC030	Records	4	Sulphonamide
CC031	Recall	6	Tylosin
CC032	Recall	5	Sulphonamide
CC033	Recall	7	Tylosin
CC034	Recall	5	Enrofloxacin
CC035	Recall	5	Enrofloxacin
CC036	Recall	6	Tylosin
CC037	Recall	5	Ampicillin
CC038	Recall	13	Penstrep
CC039	Recall	14	Penstrep
CC040	Recall	10	Penstrep
CC041	Records	9	Enrofloxacin
CC042	Recall	10	Sulphonamide
CC043	Records	12	Penicillin
CC044	Recall	20	Tylosin
CC045	Recall	13	Penicillin
CC046	Recall	11	Gentamicin
CC047	Recall	6	Tylosin
CC048	Recall	11	Neomycin

Farm ID	Records/Recall	No. of animals treated	Antimicrobials frequently used
CC049	Recall	8	Penicillin
CC050	Records	12	Sulphonamide
CC051	Records	35	Penicillin
CC052	Recall	12	Sulphonamide
CC053	Recall	8	Penicillin
CC054	Recall	9	Penicillin
CC055	Recall	13	Penicillin
CC056	Recall	6	Sulphonamide
CC057	Recall	8	Tylosin
CC058	Recall	8	Penicillin
CC059	Recall	5	Penstrep
CC060	Recall	8	Penicillin
CC061	Recall	7	Penicillin
CC062	Recall	13	Gentamicin
CC063	Recall	6	Sulphonamide
CC064	Recall	8	Gentamicin
CC065	Recall	5	Penicillin

Table 4: List of Active Antimicrobial Ingredients (AAI's) in 13 antimicrobials used in the small-scale dairy farms, Dar es Salaam, Tanzania Farms with records

Farm ID	Product Type	Antimicrobial drug	AAI's	Strength/unit	Formulation	Route	Amount used (ml(s)/kg)	DDD (mg/kg)	No. of animals treated	mls/cc	No. of treatment days	UDD (mg/kg)
CC006	Vet.Med	Penstrep	Procaine G Penicillin	200mg/ml	Suspension	Intramuscular	1ml /25 kg	8	10	17	3	24
CC006	Vet.Med		Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml /25 kg	10	10	17	3	30
CC009	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2mls/10kg	10	4	30	4	14
CC017	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	18	25	3	17.6
CC029	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	7	21	3	14.8
CC030	Vet.Med	Sulphonamide (Intertrim)	Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/15kg	2.7	4	28	3	7.9
CC030	Vet.Med		Sulfamethoxazole	200mg/ml	Solution		1ml/15kg	13.3	4	28	3	39.5
CC041	Vet.Med	Enrofloxacin (Baytril 10%)	Enrofloxacin	100mg/ml	Solution	Subcutaneous	7.5ml/10kg	7.5	9	31	3	21.9
CC043	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	12	28	3	59.3
CC050	Vet.Med	Sulphonamide (Kombitrim)	Sulfamethoxazole	200mg/ml	Solution	Intramuscular	1ml/10kg	20	12	25	3	35.3
CC050	Vet.Med		Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/10kg	4	12	25	3	7.1
CC051	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	35	28	3	59.3
Recall farms												
CC001	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	5	15	3	10.6
CC002	Vet.Med	Penstrep	Procaine G Penicillin	200mg/ml	Suspension	Intramuscular	1ml/25kg	8	1	20	3	28.2
CC002	Vet.Med		Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml/25kg	16.7	1	20	3	35.3
CC003	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution		1ml/15kg	13.3	8	15	3	21.2
CC004	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2ml/10kg	10	4	25	3	8.8
CC005	Vet.Med	Enrofloxacin (Baytril 10%)	Enrofloxacin	100mg/ml	Solution	Subcutaneous	5ml/100kg	5	4	21	3	14.8
CC007	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	4	21	3	14.8
CC008	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	5	15	3	10.6
CC010	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2ml/10kg	10	2	25	3	8.8
CC011	Vet.Med	Sulphonamide (Norodine)	Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/16kg	2.5	6	25	3	7.1
CC011	Vet.Med		Sulfadiazine	200mg/ml	Solution	Intramuscular	1ml/16kg	12.5	6	25	3	35.3
CC012	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	5	15	3	10.6
CC013	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	2	20	3	14.1
CC014	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2ml/10kg	10	5	24	3	8.5
CC015	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution	Intramuscular	1ml/15kg	13.3	2	15	3	21.2
CC016	Vet.Med	Ampicillin	Ampicillin	500mg/ml	Solution	Intramuscular	1ml/45kg	11.1	2	10	3	35.3

CC018	Vet.Med	Neomycin	Neomycin	200mg/ml	Solution	Intramuscular	1ml/10kg	20	2	15	3	21.2
CC019	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	2	15	3	10.6
CC020	Vet.Med	Penicillin	Procaine Benzylpenicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	3	20	3	42.4
CC021	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2ml/10kg	10	7	15	3	5.3
CC022	Vet.Med	Enrofloxacin (Baytril 10%)	Enrofloxacin	100mg/ml	Solution	Subcutaneous	5ml/100kg	5	4	15	3	10.6
CC023	Vet.Med	Ampicillin	Ampicillin	500mg/ml	Solution	Intramuscular	1ml/45kg	11.1	7	8	3	28.2
CC024	Vet.Med	Tetracycline	Oxytetracycline	50mg/ml	Solution	Intramuscular	2ml/10kg	10	15	20	3	7.1
CC025	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	13	20	3	14.1
CC026	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	5	15	3	10.6
CC027	Vet.Med	Penstrep	Procaine G Penicillin	250mg/ml	Suspension	Intramuscular	1ml/25kg	10	2	17	3	30
CC027	Vet.Med		Dihydrostreptomycin	200mg/ml	Suspension	Intramuscular	1ml/25kg	8	2	17	3	24
CC028	Vet.Med	Tetracycline	Oxytetracycline	100mg/ml	Solution	Intramuscular	1ml/10kg	10	5	20	3	14.1
CC031	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution	Intramuscular	1ml/15kg	13.3	6	15	3	21.2
CC032	Vet.Med	Sulphonamide (Ashulpha)	Sulfadimidine	333mg/ml	Solution	Subcutaneous	3ml/10kg	33.3	5	13	3	28.2
CC033	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution	Intramuscular	1ml/40kg	5	7	11	3	15.5
CC034	Vet.Med	Enrofloxacin (Baytril 10%)	Enrofloxacin	100mg/ml	Solution	Subcutaneous	7.5ml/100kg	7.5	5	28	3	19.8
CC035	Vet.Med	Enrofloxacin (Baytril 10%)	Enrofloxacin	100mg/ml	Solution	Subcutaneous	5ml/100kg	5	5	20	3	14.1
CC036	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution	Intramuscular	1ml/15kg	13.3	6	15	3	21.2
CC037	Vet.Med	Ampicillin	Ampicillin	500mg/ml	Solution	Intramuscular	1ml/45kg	11.1	5	8	3	28.2
CC038	Vet.Med	Penstrep	Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml/25kg	10	13	20	3	35.3
CC038	Vet.Med		Procaine Benzylpenicillin	200IU/ml	Suspension	Intramuscular	1ml/25kg	8	13	20	3	28.2
CC039	Vet.Med	Penstrep	Procaine Benzylpenicillin	200mg/ml	Suspension	Intramuscular	1ml/25kg	8	14	18	3	24.4
CC039	Vet.Med		Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml/25kg	10	14	18	3	31.8
CC040	Vet.Med	Penstrep	Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml/25kg	10	10	21	3	37.1
CC040	Vet.Med		Procaine Penicillin	200mg/ml	Suspension	Intramuscular	1ml/25kg	8	10	21	3	29.6
CC042	Vet.Med	Sulphonamide (Intertrim)	Sulfamethoxazole	200mg/ml	Suspension	Intramuscular	1ml/25kg	13.3	10	20	3	28.2
CC042	Vet.Med		Trimethoprim	40mg/ml	Suspension	Intramuscular	1ml/25kg	2.6	10	20	3	5.6
CC044	Vet.Med	Tylosin	Tylosin	200mg/ml		Intramuscular	1ml/10kg	20	20	25	3	28.2
CC045	Vet.Med	Penicillin	Procaine Benzylpenicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	13	21	3	44.5
CC046	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	11	20	3	14.1
CC047	Vet.Med	Tylosin	Tylosin	200mg/ml	Solution	Intramuscular	1ml/15kg	13.3	6	18	3	25.4
CC048	Vet.Med	Neomycin	Neomycin	200mg/ml	Solution	Intramuscular	1ml/10kg	20	11	20	3	28.2

CC049	Vet.Med	Penicillin	Procaine Benzylpenicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	8	15	3	31.8
CC052	Vet.Med	Sulphonamide (Co-Trimoxazole)	Sulfamethoxazole	200mg/ml	Solution	Intramuscular	1ml/16kg	12.5	12	18	3	25.4
CC052	Vet.Med		Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/16kg	2.5	12	18	3	5.1
CC053	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	8	18	3	38.1
CC054	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	9	18	3	38.1
CC055	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	13	18	3	38.1
CC056	Vet.Med	Sulphonamide (Intertrim)	Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/15kg	2.6	6	18	3	5.1
CC056	Vet.Med		Sulfamethoxazole	200mg/ml		Intramuscular	1ml/15kg	13.3	6	18	3	25.4
CC057	Vet.Med	Tylosin	Tylosin	200mg/ml	Suspension	Intramuscular	1ml/15kg	13.3	8	25	3	35.3
CC058	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	8	20	3	42.4
CC059	Vet.Med	Penstrep	Dihydrostreptomycin	250mg/ml	Suspension	Intramuscular	1ml/25kg	10	5	20	4	47.1
CC059	Vet.Med		Procaine Penicillin	200mg/ml	Suspension	Intramuscular	1ml/25kg	8	5	20	4	37.6
CC060	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	8	15	4	42.4
CC061	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	7	15	3	31.8
CC062	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	13	20	3	14.1
CC063	Vet.Med	Sulphonamide (Intertrim)	Trimethoprim	40mg/ml	Solution	Intramuscular	1ml/15kg	2.7	6	15	3	4.2
CC063	Vet.Med		Sulfamethoxazole	200mg/ml	Solution	Intramuscular	1ml/15kg	13.3	6	15	3	21.2
CC064	Vet.Med	Gentamicin	Gentamicin	100mg/ml	Solution	Intramuscular	1ml/20kg	5	8	20	3	14.1
CC065	Vet.Med	Penicillin	Procaine Benzyl penicillin	300mg/ml	Suspension	Intramuscular	1ml/15kg	20	5	22	3	46.6

Vet.Med; Veterinary Medicine

Appendix 4: Paper 2: Antimicrobial drugs and types used among the 51 and 65 poultry and cattle farms respectively in Dar es Salaam, Tanzania

Table 1: Antimicrobial drugs used among the 51 chicken farms surveyed in Dar es Salaam, Tanzania.

Trade name	composition
Agracox	Oxytetracycline 100 mg/g, Pyrimethamine 25 mg/g, Sulfadiazine sodium 25 mg/g, Sulfadimerazine sodium 200mg/g, and Vitamins A: 15.000 IU; K3: 5mg
Anticox	Sulfadimidine (sodium form) 74g and Diaveridine 8g
Coridix	Sulfamethoxypyridazine 125 mg/g, Trimethoprim 25 mg/g, Tylosin 30 mg/g, Sodium sulphate
Colistin	Colistin sulphate 4800000 IU Excipients ad 1g
Ciprofloxacin	Ciprofloxacin 200 mg. Excipients ad 1 ml
Doxycycline	Doxycycline (as hyclate) 100 mg Excipients ad 1 ml
Enrofloxacin	Each ml contains 100mg Enrofloxacin
Fluban	Enrofloxacin 100mg Excipient q s 1ml
Flumequine	Each 100 gr contains: Flumequine 50 gr
Fluquin	Flumequine 200 mg, solvents 1 ml
Ganadexil 10%	Enrofloxacin, 100 mg; Excipient q.s. 1 ml.
Keproceryl wsp	Colistin (sulfate): 225000 IU, Oxytetracycline HCl: 5000 mg Erythromycin thiocyanate: 35 mg Streptomycin sulfate: 35 mg and Vitamins: A, D3, E, K3, B1, B2
Oxytetracycline	Oxytetracycline 50%
Trimazin	Trimethoprim 50 mg – Sodium sulfadiazine eq. 250 mg; Excipients up to 1 g
Tylo-dox Extra wsp	Contains per gram powder Doxycycline hyclate 200 mg. Tylosin tartrate 100 mg. Excipients ad 1 g
Tylosin	Tylosin tartrate 200 mg/g
Typhoprim	Sodium sulfadiazine, 250 mg/g; Trimethoprim 50 mg/g

Table 2: Type of antimicrobials used in the 51 chicken farms surveyed in Dar es Salaam, Tanzania

Class of antimicrobial	Antimicrobial name	Number of drugs (%) administered containing antimicrobials	Number of farms (%) using the antimicrobial
Aminoglycosides	Streptomycin	1 (5.9)	1 (2.0)
Diaminopyrimidines	Trimethoprim	3 (17.6)	9 (17.6)
Fluoroquinolones	Ciprofloxacin	1 (5.9)	19 (37.3)
	Enrofloxacin	3 (17.6)	
	Flumequine	2 (11.8)	
Macrolides	Erythromycin	1 (5.9)	10 (19.6)
	Tylosin	2(11.8)	
Polymyxins	Colistin	2 (11.8)	2 (3.9)
Sulphonamides	Sulfadiazine	3 (17.6)	12 (23.5)
	Sulfadimidine	1 (5.9)	
	Sulfadimerazine	1 (5.9)	
	Sulfamethoxypyridazine	1 (5.9)	
Tetracyclines	Doxycycline	2 (11.8)	13 (24.5)
	Oxytetracycline	4 (23.5)	

Table 3: Antimicrobial drugs used among 65 small scale dairy farms surveyed in Dar esSalaam, Tanzania

Antimicrobial class	Antimicrobial name	composition
Beta-lactamase	Penicillin	Procaine Benzyl penicillin 300mg/ml
	Ampicillin	Ampicillin trihydrate 500mg/ml
Aminoglycosides	Gentamicin	Gentamicin sulphate 100000 I.U. Excipientsup to 1 ml.
	Neomycin	Each mL contains 200 mg of neomycin sulfate equivalent to 140 mg neomycin base.
	Penstrep	Dihydrostreptomycin Sulphate 250mg/ml Procaine Penicillin 200mg/ml
Fluoroquinolones	Enrofloxacin	Baytril 10% Injectable Solution Enrofloxacin 100mg/ml
Macrolides	Tylosin	Tylosin Tartrate 200mg/ml
Sulphonamides	Ashulpha	Sulfadimidine 333mg/ml
	Co-Trimoxazole	Sulfamethoxazole 200mg/ml Trimethoprim 40mg/ml
	Intertrim	Trimethoprim 40 mg/ml Sulfamethoxazole 200 mg/ml
	Kombitrim	Sulfamethoxazole 200 mg/ml Trimethoprim 40 mg/ml
	Norodine	Trimethoprim 40 mg/ml Sulfadiazine 200mg/ml
Tetracyclines	Oxytetracycline	Oxytetracycline Hydrochloride 100 mg/ml

Table 4: Type of antimicrobials used in the 65 small scale dairy farms surveyed in Dar esSalaam, Tanzania

Class of Antimicrobial	Name of antimicrobial	Number of drugs (%) administered containing antimicrobials	Number of farms (%) using the antimicrobial
Beta-lactam	Procaine Benzyl penicillin	1 (7.7)	12 (18.5)
	Ampicillin	1 (7.7)	3 (4.6)
Aminoglycosides	Gentamicin	1 (7.7)	7 (10.8)
	Neomycin	1 (7.7)	2 (3.1)
	Penstrep	1 (7.7)	7 (10.8)
Diaminopyrimidines	Trimethoprim	3 (23.1)	6 (9.2)
Fluoroquinolones	Enrofloxacin	1 (7.7)	5 (7.7)
Macrolides	Tylosin	1 (7.7)	8 (12.3)
Sulphonamides	Sulfadiazine	1 (7.7)	1 (1.5)
	Sulfadimidine	1 (7.7)	1 (1.5)
	Sulfamethoxazole	3 (23.1)	6 (9.2)
Tetracycline	Oxytetracycline	1 (7.7)	13 (20.0)

Appendix 5: Paper 2: Questionnaire on antimicrobial use practices among the poultry and cattle farmers in Dar es Salaam, Tanzania

Questionnaire

This questionnaire is meant to assess the level of practice of antimicrobial usage among cattle and poultry farmers in Dar-es-Salaam, Tanzania. Participation is voluntary and all information given will be kept strictly confidential. **PLEASE tick one or more appropriately and write where necessary.**

Identification

Date: _____ Name of interviewer: _

Region: _____ District: _____ Ward: _____

Farm (Household) Characteristics/ Demographic Information

1. Name of interviewee: _____
2. Age (in years): _____
3. Gender: a. Male () b. Female ()
4. Level of education:
 - a. Informal () b. Primary () c. Secondary () d. Tertiary ()
5. Main Occupation of respondent: a. Livestock () b. Others ()
6. Experience in livestock rearing/ management.
 - a. Less than six years ()
 - b. More than six years ()
7. Type of domestic animal/poultry do you keep
 - a. Cattle ()
 - b. Chicken ()
 - c. Cattle & chicken ()

Cattle Section

A Practices regarding Antimicrobial usage in Dairy Cattle

A1. Have you used antimicrobials on your dairy farm? a.

Yes ()

b.

No () A2. Do you get

them over the counter? a. Yes ()

b. No ()

b. If yes who prescribes them for you? a. Self () b. Neighbour () c. Veterinarian

A3. Which of the following antibiotics have ever been used at this farm?

Antimicrobial	Tick		Antimicrobial	Tick
Tetracycline (any)			Ampicillin	
Penicillin			Enrofloxacin	
Gentamicin			Chloramphenicol	
Neomycin			Penstrep	
Ciprofloxacin			Unknown	
Sulfur based (any)			Other specify	

A4. Which antibiotics among the mentioned above do you use most and why_

A5. Who treats your cattle once they fall sick?

- a. Self () b. Neighbour () c. Veterinarian ()

A6. What amounts were administered in Q.A4 above? _____

A7. Where do you normally buy veterinary antibiotics?

- a. Veterinary drug shop () b. Veterinary clinic () c. Individual veterinarian ()

A8. Do drug sellers usually ask for prescription when selling veterinary antibiotics?

- a. Yes () b. No () c. Sometimes

A9. Do you keep antimicrobials on your farm? a. Yes ()

- b. No ()

A10. If yes, where do you store them?

- a. Cupboard () b. Open shelf in doors () c. Shelf direct sunlight ()

A11. Do you usually comply with antimicrobial drug withdraw periods?

- a. Yes () b. No ()

A12. What is the purpose of antimicrobial use?

- a. Treatment () b. Prevention () c. Treatment & Prevention ()
d. Growth Promotion ()

Poultry Section

B. Practices regarding Antimicrobial usage

B1. Have you used antimicrobials on your poultry farm? a. Yes () b. No ()
B2. Do you get them over the counter? a. Yes () b. No ()

Bb. If yes who prescribes them for you?

- a. Self () b. Neighbour () c. Veterinarian ()

B3. Please specify the common antibiotics you use?

Antimicrobial	Tick
Tetracycline	
Penicillin	
Amoxicillin	
Streptomycin	
Gentamicin	
Ciprofloxacin	
Enrofloxacin	
Tylosin	
Polymyxins	
Trimethoprim	
Others specify	

B4. Where do you usually buy the antimicrobials from?

- a. Veterinary drug shops () b. Veterinary clinic () c. Individual veterinarian ()

B5. Do drug sellers ask for prescriptions?

- a. Yes () b. No () c. Sometimes ()

B6. Who administers antimicrobials used on poultry in your flock?

- a. Self () b. Neighbours () c. () Veterinarian

B7. For what purpose are antimicrobials used for?

- a. Treatment () b. Prevention () c. Treatment & Prevention ()
d. Growth Promotion ()

B8. What common route of antimicrobial administration do you use?

- a. Parenteral route () b. Orally () c. Feed ()

B9. Do you Keep records? a. Yes () b. No ()

- Bb. If yes, which one? a. Treatment () b. Purchase ()

B10. Do you record the volumes or quantities of antimicrobial used? a. Yes () b. No ()

B11. Do you observe the withdrawal period?

- a. Yes () b. No

B12. Do you store antimicrobials on your farm? a. Yes () b. No ()

- b. If yes how? A. Cupboard () b. Shelf in doors () c. Shelf direct sunlight

B13. Do drug sellers usually ask for Prescriptions? a. Yes () b. No ()

- c. Sometimes

Thank you for the
kind responses

For further information, contact:

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654 641 180

Appendix 6: Paper 2: Questionnaire to small-scale dairy cattle and poultry (chicken) keepers on antimicrobial use and related practices poultry in Dar es Salaam, Tanzania

Date _____ Interviewer _____

District _____ Ward _____ Interviewee _____ Sex _____

No	Questions	Levels	Responses
1	Do you consume milk/eggs from dairy cattle/Poultry that were just treated with antimicrobials?	Desirable (1)	No
		Undesirable (0)	Yes
2	Do you consume meat from dairy cattle /poultry that was just treated with antimicrobials?	Desirable (1)	No
		Undesirable (0)	Yes
3	How long do use antimicrobials in dairy cattle/poultry?	Desirable (1)	As advised
		Undesirable (0)	Until cattle/poultry is cured; Until the bottle/vial/package is empty; As long as I can afford; Once(one) time treatment; Continuously over extended period
4	What do you do with expired veterinary antimicrobials?	Desirable (1)	Dispose of; Return to the veterinary drug shop/pharmacy; Refuse to receive it
		Undesirable (0)	Give it to other farmers; Use it for intended treatment; Nothing
5	How do you use manure?	Desirable (1)	Used as fertilizer; used as fuel (biogas); Sold for cash (fuel)
		Undesirable (0)	Leave on farm in open air; discard into the environment
6	Do you have isolation unit for sick animals/birds?	Desirable (1)	Yes
		Undesirable (0)	No
7	Do veterinary drug sellers ask for prescriptions?	Desirable (1)	No
		Undesirable (0)	Yes, sometimes
8	What do you do when cattle/poultry dies on the farm?	Desirable (1)	Bury, burn
		Undesirable (0)	Leave as it is; give to the dog; home consumption
9	Who provides source of drug information to the farmer?	Desirable (1)	Veterinarian; Livestock health practitioner
		Undesirable (0)	Myself; neighbour; fellow farmer
10	Where do you purchase antimicrobials?	Desirable (1)	Veterinary drug shops; Agro-vet shops; Veterinary clinics, Individual veterinarians
		Undesirable (0)	Livestock market vendors; informal drug sellers/dealers
11	Who administers the antimicrobials?	Desirable (1)	Veterinarian; Livestock health practitioner
		Undesirable (0)	Myself, neighbour
12	Where do you store antimicrobials bought/brought on the farm?	Desirable (1)	Cupboard (cool & dry place)
		Undesirable (0)	Open shelf indoor; Shelf direct sunlight

Appendix 7: Paper 3: Quantities of veterinary antimicrobials (antibiotics), tonnes of active ingredient used in food-producing animals by route of administration in Dar es Salaam, Tanzania (2016-2018)

Route of administration	Antimicrobial class	Year			
		2016	2017	2018	2016-2018
Topical	Aminoglycosides	0.1(6.7)	0.1(5.6)	0.1(4.8)	0.3 (5.6)
	Beta-lactam	0.3 (20.0)	0.4 (22.2)	0.6 (28.6)	1.3 (24.1)
	Polypeptides	0.0 (0.0)	0.0(0.0)	0.0 (0.0)	0.0 (0.0)
	Sulphonamide	0.7 (46.7)	0.8 (44.4)	0.8 (38.1)	2.3 (42.6)
	Tetracycline	0.4 (26.7)	0.5 (27.8)	0.6 (28.6)	1.5 (27.8)
	Total	1.5 (100)	1.8 (100)	2.1(100)	5.4 (100)
Oral	Beta-lactams	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.6 (0.5)
	Tetracyclines	19.6 (52.5)	22.6 (53.3)	21.3 (52.0)	63.5 (52.6)
	Aminoglycosides	2.3(6.2)	2.6(6.1)	2.5(6.1)	7.4(6.1)
	Macrolides	2.4 (6.4)	2.8 (6.6)	3.0 (7.3)	8.2 (6.8)
	Nitrofurans	0.9 (2.4)	0.8 (1.9)	1.0 (2.4)	2.7 (2.2)
	Quinolones	3.2 (8.6)	3.5 (8.3)	3.4 (8.3)	10.1(8.4)
	Polymyxins/ polypeptides	1.6 (4.3)	1.8 (4.2)	1.7 (4.1)	5.1 (4.2)
	Sulphonamides	6.6 (17.7)	7.5 (17.7)	7.3 (17.8)	21.4 (17.7)
	Ionophores	0.5 (1.3)	0.6 (1.4)	0.6 (1.5)	1.7 (1.4)
	Total	37.3 (100)	42.4 (100)	41.0 (100)	120.7 (100)
Parenteral	Beta-lactams	3.5 (21.6)	3.8 (20.7)	3.4 (20.5)	10.7 (20.9)
	Tetracyclines	4.1(25.3)	5.0 (27.2)	4.3 (25.9)	13.4 (26.2)
	Aminoglycosides	3.4 (20.9)	3.8 (20.7)	3.4 (20.5)	10.6 (20.7)
	Macrolides	0.8 (4.9)	0.8 (4.3)	0.7 (4.2)	2.3 (4.5)
	Quinolones	0.4 (2.5)	0.5 (2.7)	0.4 (2.4)	1.3 (2.5)
	Sulphonamides	4.0 (24.7)	4.5 (24.5)	4.4 (26.5)	12.9 (25.2)
Total	16.2 (100)	18.4 (100)	16.6 (100)	51.2 (100)	

Appendix 8: Paper 3: Quantities of veterinary antimicrobials (tonnes of active ingredient) consumed by galenic form in Dar es Salaam, Tanzania (2016-2018)

Galenic form	Antimicrobial class	Year			
		2016	2017	2018	2016-2018
Solid dosage forms (powder/bolus)	Beta-lactams	0.2(0.6)	0.2(0.5)	0.2(0.5)	0.6(0.5)
	Tetracyclines	19.7(57.1)	22.7(57.6)	21.4(56.2)	63.8(57)
	Aminoglycosides	2.3(6.7)	2.6(6.6)	2.5(6.6)	7.4(6.6)
	Macrolides	2.4(7.0)	2.8(7.1)	3(7.9)	8.2(7.3)
	Nitrofurans	0.9(2.6)	0.8(2.0)	1(2.6)	2.7(2.4)
	Quinolones	0.1(0.3)	0.1(0.3)	0.1(0.3)	0.3(0.3)
	Polymyxins/polypeptides	1.6(4.6)	1.8(4.6)	1.8(4.7)	5.2(4.6)
	Sulphonamides	6.8(19.7)	7.8(19.8)	7.5(19.7)	22.1(19.7)
	Ionophores	0.5(1.4)	0.6(1.5)	0.6(1.5)	1.7(1.5)
	Total	34.5(100)	39.4(100)	38.1(100)	112(100)
Liquid dosage forms (suspensions/solutions)	Beta-lactams	3.8(18.4)	4.2(17.9)	3.9(17.9)	11.9(18.1)
	Tetracyclines	4.5 (21.8)	5.5 (23.5)	4.9 (22.6)	14.9 (22.7)
	Aminoglycosides	3.5 (16.9)	4.0(17.1)	3.5(16.1)	11.0 (16.7)
	Macrolides	0.8 (3.9)	0.8 (3.4)	0.7 (3.2)	2.3 (3.5)
	Quinolones	3.5 (16.9)	3.9 (16.7)	3.8 (17.5)	11.2(17.0)
	Polymyxins/polypeptides	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
	Sulphonamides	4.5 (21.8)	5.0 (21.4)	4.9 (22.6)	14.4 (21.9)
Total	20.6 (100)	23.4 (100)	21.7 (100)	65.7 (100)	

Appendix 9: Paper 3: Trends of food- producing animal population included in quantitative data reported in Tanzania, 2016-2018

Species	Year	Animal population	Number of animal slaughtered /year	Carcass Weight (kg)	Live Weight (kg)	Animal Biomass (tonnes)
Cattle	2016	26935923	3177658	101.9	181.9	4899644.4
	2017	26519776	3121863	126.4	225.7	5985513.4
	2018	27282702	3204778	147.2	262.9	7172622.4
Sheep	2016	5751090	1566343	12.0	25.5	392956.3
	2017	7332299	2001054	12.0	25.5	500896.6
	2018	7945775	2172878	12.0	25.5	542697.6
Goats	2016	18779631	3590171	12.0	25.5	1320513.1
	2017	18017462	3428777	12.0	25.5	1267304.6
	2018	18497912	3504103	12.0	25.5	1301492.8
pigs	2016	515901	369584	39.9	51.2	27837.4
	2017	518023	371415	40.0	51.3	28005.0
	2018	520853	373757	39.9	51.2	28136.6
Chicken	2016	37272000	15871000	6.5	8.3	309357.6
	2017	37518000	16000000	3.9	5.0	187590.0
	2018	37992000	16121000	4.8	6.2	235550.4

Appendix 10: Paper 5: Structured questionnaire on in-puts for mclnerney model for economic modeling on broiler farm production

Date _____ Interviewer _____
_____ District _____ Ward _____
_____ Interviewee _____ Sex _____

Restocking

- 1. How many chicks do you bring per batch? ..
.....
.....
- 2. How batches do you bring in a year? ..
.....
- 3. Where do they buy the chicks and at what price?.

Health Status of broilers on the farm

- 4. Have you ever experienced any of these risks in your flock?
a) Respiratory b) digestion c) locomotion d) 1st week problem
- 5. At what age did the bird experience these risks?
a) Week 1 b) Week 2 c) Week 3 d) Week 4 e) Week 5 f) Week 6 g) Week7
- 6) Who treats the bird when sick?
a) Veterinarian b) Self c) Neighbour
b. Which antibiotics did you use, what volumes and for how many days?.....
- 7. Did you witness any death in your flock due to any of the risk problems mentioned above?
a) Respiratory b) digestion c) Locomotion d) 1st week problem

Health costs

- 8. What was the cost of the antibiotics you used for the treatment of any of the above condition? ____

Health management

- 9. In the event of above risks did you invest in any of the following?
a) New drinking water system b) New ventilation system c) Floor cooling and heating
d) None of the above
- 10. If so how much did it cost? ..

Technical management

- 11. Apart from antibiotics did you use any other veterinary drug?
a) Yes b) No
- 12. Which one and how much did it cost?
- 13. What was it intended for and how long did you use it?
- 14. Did you provide the birds with any supplements?
a) Yes b) No

Feeds

- 15. If yes for how long and how much does it cost?_____
- 16. On introduction of day-old chicks on the farm, which type of feed do you provide to them?
a) Pellets b) Mash c) Mixture of mash & pellets
- 16.b) From which manufacturer and why?..
.....
- 17. How many bags do you buy and for how long do you feed them?..
- 18. What is the cost of each bag?
- 19. When do you start feeding them on either growers' pellet/mash?..
- 20. How many bags do you feed them on and for how long?..
.....
- 21. What is the cost of each bag?
- 22. When do you introduce the birds to finishers pellets/ mash and how many bags?
.....
- 23. What is the cost of each bag?
- 24. At what age do you dispose off the birds?..
- 25. By the time you dispose them off how much do they weigh?..
.....

Thank you for the kind responses

For further information, contact:

E-mail: rogersazabo@gmail.com; **Mobile Tel no:** +255
654 641 180

Appendix 11 Informed consent statement (English Version)



NATIONAL INSTITUTE FOR MEDICAL RESEARCH 2448, Ocean Road, Junction of Luthuli/Sokoine Drive P.O.Box 9653, Dar es Salaam Tanzania

	<p>SOKOINE UNIVERSITY OF AGRICULTURE (SUA) SACIDS Africa Centre of Excellence for Infectious Diseases of Humans and Animals in Eastern and Southern Africa College of Veterinary Medicine and Biomedical Sciences P.O Box 3015, Chuo Kikuu, Morogoro, Tanzania Tel: +255 23 264 0037; +255 787 011 677</p>	
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Informed consent explanation

RESEARCH TITLE Antimicrobial Use and Prevalence of Resistant Extended Spectrum Beta Lactamase (ESBL) producing *Escherichia coli* in cattle and poultry production in Tanzania.

Institution: Sokoine University of Agriculture

Student/ principal investigator: Rogers Ruyu Azabo (PhD Student), Sokoine University of Agriculture (SUA), Morogoro, Tanzania.

Supervisor: Prof. Sharadhuli. I. Kimera, Sokoine University of Agriculture (SUA), P.O. Box 3021, Morogoro, Tanzania.

Co-supervisors: Prof Mecky Matee, Muhimbili University of Health and Allied Sciences (MUHAS), P.O BOX 65001, Dar es Salaam, Tanzania; Prof. Stephen Mshana, Catholic University of Health and Allied Sciences (CUHAS), P.O BOX 1464, Mwanza, Tanzania.

Introduction

Antimicrobial usage in food producing animals (poultry and cattle) provides a basis for improving animal health and productivity. This in turn contributes to food security, food safety, animal welfare, protection of livelihoods and animal resources. However, the high dependence of animal production on antimicrobial agents is one of the major factors driving the emergence of antimicrobial resistance in bacterial strains. This has generated concern over the potential sources of Antibiotic Resistant Bacteria (ARB) impacting on human health.

The objective of this study is to assess the extent to which antimicrobials are used in cattle and poultry production in relation to resistance in ESBL producing *E.coli* and also gain insight in optimal use of animal health inputs.

Procedures (Methodology)

This study will be conducted in Ilala, Kinondoni and Ubungo Districts in Dar-Es- Salaam region. The research study has been granted permission by the Regional and District administrative Officers of the above-mentioned region and districts respectively. A survey will be conducted in the study areas to ascertain the type of antimicrobials (antibiotics) commonly administered to the small-scale dairy cattle and purpose of usage using a structured questionnaire. Sampling of small-scale dairy cattle for collection of faecal rectal swab faecal.

Benefits from the Study

- 1). Participants will be aware of the consequences of uncontrolled use of antimicrobials in food producing animals and thus its effects on public health.
- 2). The study will also provide evidence-based information to researchers on the effects of antimicrobial use in the overall picture of antimicrobial resistance.

Confidentiality

The collected data and their findings will be treated confidentially. Since participation is Voluntary, respondents will be anonymized at the time of data collection.

Incentives to Livestock Keepers

Free of charge consultations on the farm related problems and interventions within the study capacity.

Participation Rights

- 1) It is entirely voluntary. You are free to decide whether to participate or not.
- 2) You also have a right to withdraw from the study at any point of the study.

Whom to Contact

Principle investigator (Rogers Ruyu Azabo) will be contacted through his phone number and E-Mail address (0654641180) rogers.azabo@sacids.org.

Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask a question /question about the research and they have been satisfactorily answered. I consent voluntarily that I will participate in this study.

Name: _____ Date and signature: _____

If illiterate

Name of independent literate witness: _____ Date and signature of witness: _____

Name of Study Staff: _____ Date and Signature of Researcher: _____

Appendix 12: Ethical clearance certificate for conducting medical research in Tanzania

THE UNITED REPUBLIC OF TANZANIA



Institute Institute for Medical Research
1 Baraka House Street
P.O. Box 7072
11144 Dar es Salaam
Tel: 255 22 2111444
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E-mail: imr@imr.ac.tz
IMR@IMR.ac.tz



Ministry of Health, Community Development, Gender, Elderly & Children
University of Dodoma, College of Business Studies and Law
Building No. 11
P.O. Box 767
3278 Dodoma
17th November 2019

NO. ETHICAL CLEARANCE CERTIFICATE FOR CONDUCTING MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled "Antimicrobial use and prevalence of resistant bacterial species from Tanzania (2018) conducting a study in cattle gender and environment in Tanzania" (Number 001/2019) in its various local organizations in Prof. Mwanuzi S. Kumbiwa's Institute of Agriculture University of Agriculture, has been granted ethical clearance to be conducted in Tanzania.

The Principal Investigator will ensure that the following conditions are fulfilled:

1. Progress report to be submitted to the Ministry of Health, Community Development, Gender, Elderly & Children and the National Institute for Medical Research, Regional and District Medical Officers after every six months.
2. Permission to publish the results to be obtained from Tanzania Institute for Medical Research.
3. Copies of final publications are made available to the Ministry of Health, Community Development, Gender, Elderly & Children and the National Institute for Medical Research.
4. Any researcher who contravenes or fails to comply with these conditions shall be guilty of an offence and shall be liable on conviction to a fine or up to 10000 TSh or 20% of the net turnover of the business (as per Section 182C).
5. None. See in relevant report.

Approved in light of the law given: 17th November 2019 to 16th November 2019.

Name: Prof. Yusef Fazel Mjema



**CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY & CHILDREN**

Name: Prof. Mwanuzi S. Kumbiwa



**CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY & CHILDREN**

CC: Director, Health Services T. MUMBELE, Dodoma
RMB of Dar es Salaam region
DIRECTOR of Data, Statistics and Change Division