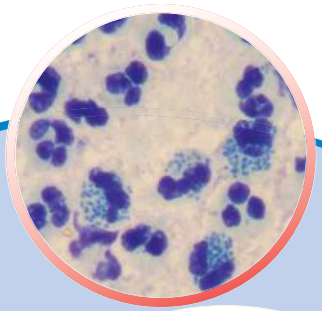
Sciences for Prosperity

UGANDA NATIONAL ACADEMY OF SCIENCES

Antibiotic Resistance in Uganda:
Situation Analysis and Recommendations



CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy WASHINGTON DC • NEW DELHI

Global Antibiotic Resistance Partnership

Sciences for Prosperity

Uganda National Academy of Sciences
A4 Lincoln House Makerere University P.O. Box 23911, Kampala, Uganda
Tel: +256-414-53 30 44 Fax: +256-414-53 30 44
E-mail: unas@unas.or.ug

www.ugandanationalacademy.org

This is a report of the Uganda National Academy of Sciences (UNAS). UNAS works to achieve improved prosperity and welfare for the people of Uganda by generating, promoting, sharing, and using scientific knowledge and by giving evidence-based advice to government and civil society. UNAS was founded in 2000 and was granted a Charter by His Excellency the President of Uganda in 2009. It is an honorific and service-oriented organization founded on principles of objectivity, scientific rigor, transparency, mutual respect, linkages and partnerships, independence, and the celebration of excellence.

Suggested citation:

UNAS, CDDEP, GARP-Uganda, Mpairwe, Y., & Wamala, S. (2015). Antibiotic Resistance in Uganda: Situation Analysis and Recommendations (pp. 107). Kampala, Uganda: Uganda National Academy of Sciences; Center for Disease Dynamics, Economics & Policy.

ISBN: 978-9970-424-10-8

ACKNOWLEDGEMENTS

Antimicrobial resistance (AMR) has been classified as a global health threat that threatens the gains achieved by anti-infectives. The world is therefore coming together to mobilize efforts to combat the problem. In May 2015, the WHO member countries passed a resolution and approved a Global Action Plan for combating that clearly outlines actions member countries should take to combat the problem (WHO, 2015). The Global Health Security Agenda (GSHA) further subscribes mechanisms to contain the same with leadership from the USA CDC (CDC, 2014). The country assessment by GHSA, done in early 2014, reported absence of coordinated actions in the country addressing the problem. The country had no national plan that brings together all stakeholders to take action. The Uganda National Academy of Sciences (UNAS) is therefore pleased for the timely financial support from the Center for Disease Dynamics, Economics & Policy (CDDEP) under the Global Antibiotic Resistance Partnership (GARP) to undertake the baseline information required to inform the next actions to combat the problem. CDDEP supported UNAS to put in place a standing committee on Antimicrobial resistance that constituted itself into GARP-Uganda Working Group to oversee the collection analysis and make recommendations for further actions

We heartily acknowledge the two consultants: Dr. Yusuf Mpairwe and Dr. Samuel Wamala who collected analyzed and compiled this report. We thank the reviewers and editors who volunteered their time to provide candid and critical comments to ensure that the report is accurate, effective and credible. We acknowledge serious gaps in the quality of data that was available. Nevertheless it is our sincere hope that this report provides a starting point and will be serve as a baseline and stimulate various stakeholders to come together to take actions aimed at containing the problem.

Prof. Denis K. Byarugaba
Chair, GARP-Uganda Working Group

Prof. Nelson K. Sewankambo
President UNAS

PREFACE

Antibiotic resistance was initially viewed as only being a human medical problem in hospital-acquired infections, and usually only in critically ill and immunosuppressed patients. Today, the antibiotic resistance (ABR) phenomena has spread to the point that the general population is considered to be at risk, bringing about an era where many common bacterial infections are becoming increasingly difficult to treat. Of concern, in addition to the use in human beings, is the expanding use of antibiotics in poultry and livestock not only for treating disease, but to promote growth and prevent disease.

The ABR phenomenon has become a global concern as geographic borders among countries and continents have become less distinct due to increasing global trade, expanding human and animal populations, societal advances and technological developments. Because of this increasing global connectivity, we now see rapid transport of infectious agents and their ABR genes. This means that ABR, in any obscure microscopic niche anywhere in the world, may consequently exert an impact on the rest of the world.

UNAS, with support from the Center for Disease Dynamics, Economics & Policy (CDDEP), has formed a multi-disciplinary committee to study antibiotic resistance and access in Uganda and to participate in an evidence-based policymaking process. This report covers the efforts made by UNAS and CDDEP in constituting an independent expert Global Antibiotic Resistance Partnership (GARP-Uganda) committee, and the production of the situational analysis report on antibiotic resistance and access in Uganda. This report will guide interventions that will be put in place to tackle the problem of antibiotic resistance in Uganda.

Dr Mpairwe Yusuf and Dr Wamala Samuel.

TABLE OF CONTENTS

List of Tables

List of Figures

List of Abbreviations and acronyms

%	Percent
+ve	Positive
AIDS	Acquired Immunodeficiency Syndrome
AMR	Antimicrobial Resistance
ARDC	Aquaculture Research and Development Centre
ASF	African Swine Fever
ASR	Antibiotic Sensitivity Report
CBPP	Contagious Bovine Pleuropneumonia
CDDEP	Center for Disease Dynamics, Economics & Policy
CHS	College of Health Sciences
CM	Clinical Mastitis
CoVAB	College of Veterinary Medicine, Animal Resources and Biosecurity
CPHL	Central Public Health Laboratory
CSBAG	Civil Society Budget Advocacy Group
ECF	East Coast Fever
ELISA	Enzyme-Linked Immunosorbent Assay
ENT	Ear, Nose and Throat
ESBL	Extended Spectrum Beta-Lactamase
FAO	Food and Agriculture Organisation
FMD	Foot and Mouth Disease
FY	Financial Year
GARP	Global Antibiotic Resistance Partnership
GDP	Gross Domestic Product
GNI	Gross National Income
GoU	Government of Uganda
HC II	Health Centre II
HC III	Health Centre III
HC IV	Health Centre IV
HCWs	Healthcare Workers
Hib	*Haemophilus influenzae* Type b
HIV	Human Immunodeficiency Virus

LSD	Lumpy Skin Disease
MAAIF	Ministry of Agriculture, Animal Industry and Fisheries
MDGs	Millennium Development Goals
MDR	Multi-Drug Resistant
MMA	Mastitis, Metritis and Agalactia
MoH	Ministry of Health
MRSA	Methicillin-Resistant *Staphylococcus aureus*
NAADS	National Agricultural Advisory services
NAGRC	National Animal Genetic Resource Centre
NAMELA	Naguru Medical Laboratory
NARO	National Agricultural Research Organisation
NCD	Newcastle Disease
NCD	Non-Communicable Disease
NCRI	Natural Chemotherapeutics Research Institute
NDA	National Drug Authority
NDP/A	National Drug Policy and Authority
NGO	Non-Governmental Organisation
NMS	National Medical Stores
Obs & Gynae	Obstetrics and Gynecology
PPF	Procaine Penicillin Fortified
RDT	Rapid Diagnostic Test
SCM	Subclinical Mastitis
TB	Tuberculosis
UBOS	Uganda National Bureau of Statistics
UGX	Uganda Shillings
UNAS	Uganda National Academy of Sciences
UNHRO	Uganda National Health Research Organisation
US	United States
USD	United States Dollar
Ushsbns	Uganda Shillings in Billions
UTI	Urinary Tract Infection
WHO	World Health Organisation
Yr	Year

Executive Summary

The problem of antimicrobial resistance has reached alarming levels. If measures are not taken to reverse the trends, the means to treat infectious diseases will become ever more limited. Of particular concern in Uganda and other low-income countries, treatment will be out of reach financially for many people, as newer, expensive antibiotics will be the only effective treatment options.

Antimicrobial resistance concerns resistance to all infectious agents, including viruses, bacteria and parasites. This situation analysis from the Global Antibiotic Resistance Partnership (GARP)-Uganda focuses on resistance in bacteria (ABR) in Uganda. It is intended to lay the groundwork for developing a national strategic plan for addressing antibiotic resistance and access. It comes at an opportune time, with the World Health Organization's Global Action Plan on Antimicrobial Resistance calling for national action plans, and the Global Health Security Agenda and other regional initiatives that bear on antibiotic resistance coming to prominence.

Uganda, like many countries in Sub-Saharan Africa, suffers from a high burden of infectious diseases. HIV/AIDS, with a prevalence of 7 percent, has compromised the ability of the population to fight off infections naturally. The burden of respiratory infections, diarrheal diseases, sepsis, urinary tract infections, meningitis, and sexually-transmitted infections, also remain high. Pneumonia, particularly caused by *Streptococcus pneumoniae,* causes up to 34,000 deaths annually, according to the Ministry of Health, most of them in infants and young children. The situation is similar in animal health, with a high burden of bacterial diseases whose treatment is compromised by ABR.

One aspect of the problem is the widespread availability of antibiotics without prescription. They can be bought over the counter, in unlicensed drug stores and in open vans in markets, for example. Healthcare workers also overprescribe antibiotics for a variety of reasons. Without greater awareness that overuse of antibiotics risks losing them to resistance, this situation is unlikely to change.

With no systematic national antibiotic resistance surveillance, information is scarce for determining the rates and trends of resistance over the years. Nevertheless from the available studies, both published in peer reviewed journals and in grey literature, there is evidence of an increasing trend of resistance among the major pathogens. A broad range of bacteria show high rates of resistance (over 50 percent in many cases) to commonly used antibiotics such as penicillin, tetracyclines and co-trimoxazole. Of particular concern is the high prevalence of multi-drug resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum beta-lactamase (ESBL)-producing bacteria, which confers resistance to some advanced antibiotics. The prevalence of MRSA in hospital studies is highly variable, from as low as 2 percent to as high as 90 percent, and ESBL ranges from 10 to 75 percent of isolates recovered. Furthermore, resistance to carbapenems—last-

resort antibiotics—is growing, with levels of 4 to 30 percent reported. These high levels of resistance are indicative of the scale of the problem, but also throw light on the challenges of documenting exactly what the situation is.

Documentation of the resistance problem in animal health is even more deficient. The condition most commonly reported on is mastitis in bovines, with over 50 percent of pathogens resistant to common antibiotics. It is well documented that bacteria, including resistant bacteria, are shared between animals and humans, suggesting that "One Health" strategies and interventions are called for.

It is important that Uganda move to put in place an integrated action plan involving all sectors and stakeholders to address antibiotic resistance. Six components are needed for a comprehensive plan. These are:

1. Reduce the need for antibiotics through improved public health measures
2. Improve hospital infection control and antibiotic stewardship
3. Rationalize antibiotic use in the community
4. Reduce antibiotic use in agriculture
5. Educate health professionals, policy makers and the public on sustainable antibiotic use
6. Ensure political commitment to meet the threat of antibiotic resistance

These measures are consistent with the WHO Global Action Plan. Specific interventions that contribute to each component are discussed in detail in this report.

I INTRODUCTION

Antibiotic resistance was initially viewed as only being a human medical problem in hospital-acquired infections, and usually only in critically ill and immunosuppressed patients. Today, antibiotic resistance has spread to the point that the general population is considered to be at risk, bringing about an era where various common bacterial infections are becoming increasingly difficult to treat. In addition to the use in humans, use of antimicrobials has expanded to include poultry and other livestock not only for treating disease, but also to promote growth and prevent disease.

Antibiotic resistance (ABR) is part of the all-encompassing antimicrobial resistance problem, which includes resistance to other organisms, such as viruses, malaria and other parasites, fungi and other atypical pathogens. The Global Antibiotic Resistance Partnership (GARP) is focused on resistance to the common antibiotics not because resistance of other organisms is not important, but to give weight to the importance of bacterial infections and the great benefits of everyday antibiotics. ABR has become a global concern as geographic borders among countries and continents have become less distinct due to increasing global trade, expanding human and animal populations, societal advances and technological developments. Because of this increasing global connectivity, we now see rapid transport of infectious agents and their ABR genes. This means that ABR, in any obscure microscopic niche anywhere in the world, may consequently exert an impact on the rest of the world.

The Global Antibiotic Resistance Partnership (GARP) is an initiative of the Center for Disease Dynamics, Economics & Policy (CDDEP), a non-profit organisation that conducts independent research. The programme began in 2009 to address the challenge of antibiotic resistance in low- and middle- income countries.

GARP working groups are country-led with guidance and collaboration from CDDEP. Research and policy directions are driven by local data, evidence and priorities. Country partners take the lead in managing the GARP process, with support from CDDEP. The GARP-Uganda secretariat is located at Uganda National Academy of Sciences (UNAS) and the working group is a standing committee of UNAS.

GARP Phase 1 culminated in the 1st Global Forum on Bacterial Infections: Balancing Treatment Access and Antibiotic Resistance, in New Delhi, India. Since GARP Phase 2 commenced in 2012, national working groups have been established in Mozambique, Nepal, Tanzania and Uganda.

The GARP Secretariat at CDDEP in Washington, DC and New Delhi provides technical support to each working group, creates links within the GARP network, and involves the working groups in global discussions and policy development.

GARP objectives

- Mobilise a critical mass of local expertise across various sectors for development of antibiotic resistance prevention and control policies
- Develop the evidence base for policy action on antibiotic resistance, identify policy opportunities where research dissemination, advocacy, and information can have the greatest impact in slowing the development and spread of resistance
- Collaborate and or cooperate with global and local initiatives to develop and implement actionable national strategies to address the challenge of antibiotic resistance

Formation of the GARP-Uganda committee

Experts with a track record of achievement in the fields relevant to antibiotic access and resistance were approached and invited as members of the committee. The biographies of those who accepted the invitation were assessed for potential bias and conflict of interest to ensure that any biases were balanced and conflicts of interest declared. This was crucial to guarantee the creation of a balanced and impartial committee capable of generating objective policy recommendations, with no personal gains or profit to institutions with which they are affiliated. They were also asked to serve on a voluntary basis. The committee aimed to include 15 members, with members serving in their individual capacity and not as representatives of the organisations to which they belong (a complete list of members is provided in the appendix).

II METHODOLOGY

This report is based on information obtained from a review of online publications, reports from government ministries, departments and agencies as well as from interviews conducted with key informants in various institutions as indicated here below:

- MoH (annual reports and interview)
- MAAIF (report and interview)
- Central Public Health Laboratory (interview)
- Mulago Hospital (Microbiology Laboratory - interview)
- CHS (Microbiology Laboratory - interview)
- CoVAB (Microbiology Laboratory - interview)
- Uganda Wildlife Education Centre (interview)
- National Medical Stores (interview)
- National Drug Authority (interview)
- Aquaculture Research and Development Centre (interview)
- Veterinary practitioners (interview)
- Naguru Medical Laboratory (extraction of information from records)

III POPULATION AND HEALTH BACKGROUND (HUMAN AND ANIMAL)

3.1 Human demographics

The current population of Uganda is 34.9 million comprising mainly persons under the age of 18.

Table 1 shows the mid-year demographic features of Uganda in the year 2012. The figures have been extracted from the Uganda Government Annual Health Sector Performance Report 2012/13 FY and in that report they were calculated from the annual population projection figures issued by the Uganda Bureau of Statistics. Figure 1 illustrates the population distribution by age and sex, while figure 2 shows the population census result from 1969 to 2013.

Table 1: Projected population of Uganda by age by 2015

Age (Years)	2002 Census	2015 Estimate			Percent of the Population
		Males	Females	Total	
Births in 2015				1,470,800	
10 - 14	3,509,151	2,707,800	2,469,300	5,177,100	14.8
15 - 24	4,883,723	2,844,000	2,963,200	5,807,200	16.6
3 - 5	2,642,407	1,941,400	1,805,200	3,746,600	10.7
6 - 12	5,378,678	4,206,400	3,882,800	8,089,200	23.1
13 - 19	3,995,884	2,724,800	2,605,600	5,330,400	15.2
15 - 49	5,478,502		6,965,300		38.7
< 18	13,708,263	10,320,200	9,553,800	19,874,000	56.7
18 - 30	5,472,062	2,997,300	3,440,100	6,437,400	18.4
60 & Above	1,101,039	664,200	817,400	1,481,600	4.2

Source: (UBOS, 2014)

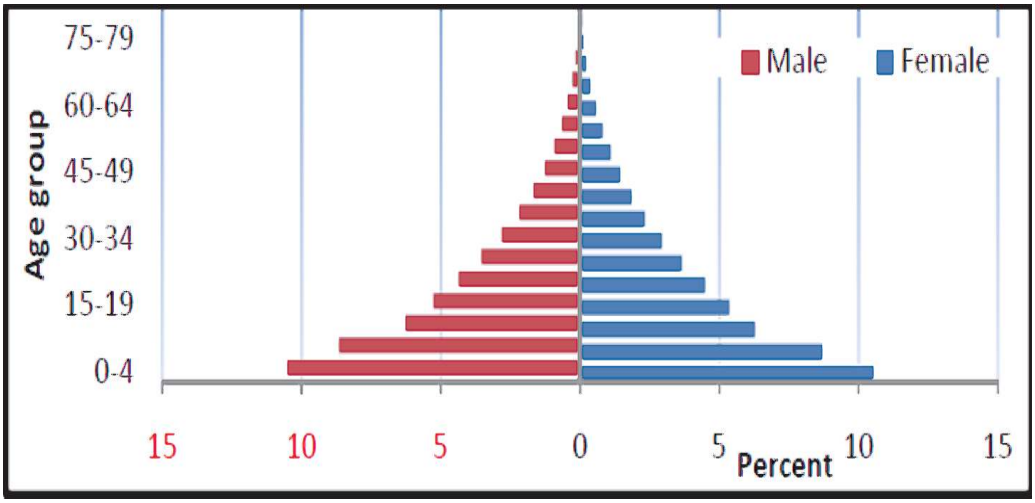


Figure 1: Population distribution by age and sex (in five year age groups).
Source: UBOS, Statistical Abstract 2013

According to provisional data of the recently concluded 2014 Uganda National Census, the current population of Uganda is approximately 34.9 million. The data also shows that the population size reduces as age increases; thus 50% of the population is under 20 years of age.

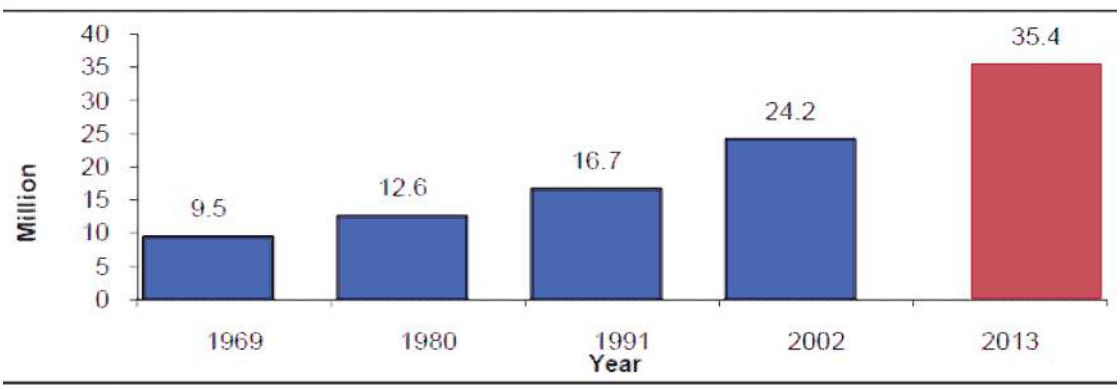


Figure 2: Population census (1969, 1980, 1991, 2002 and 2013).
Source: UBOS, Statistical abstract 2013

3.2 Uganda economic indices

GNI per capita, Atlas method (current US$) was $528 in 2011.

Life expectancy at birth was 59 years in 2012.

According to Wolfgang (2012) and based on per capita income, Uganda is the poorest of the East African countries, as indicated in Table 2 below, and is likely to remain so for some time to come.

Table 2: Income and income growth in East Africa

	Per capita income (end 2011)	Average growth 2000-2009	Average population growth 2000-2009	Per Capita Income in 2020 if past trends continue	Year Kenya will be overtaken if past trends continue
Kenya	784	3.7	2.6	862	N/A
Rwanda	556	7.7	3.1	828	2022
Tanzania	546	6.8	2.7	783	2024
Uganda	528	7.2	3.2	751	2025

Source: (Wolfgang, 2012)

3.3 National health policy

From the Ministry of Health document entitled, "The Second National Health Policy July 2010" the focus of the National Health Policy is directed towards:

- Health promotion,
- Disease prevention,
- Early diagnosis, and
- Disease treatment.

Emphasis is being placed on efficient use of available health resources; effective delivery and attainment of the Uganda National Minimum Health Care Package, which includes Health Promotion, Disease Prevention and Community Health Initiatives; Maternal and Child Health; Prevention and Control of Communicable Diseases; and Prevention and Control of Non-Communicable Diseases.

It is also directed towards effecting equitable and sustainable financing mechanisms and the realisation of the internationally adopted MDGs, three of which – reduction of child mortality, improvement of maternal health and combating HIV/AIDS, malaria and other diseases – are directly related to health.

3.3.1 Human health budgetary expenditure

Information from the Uganda Annual Health Sector Performance Report 2012/13 indicates that health service delivery is financed by the government, some private firms that pay medical insurance for their employees, private households, as well as by donors. The government funds public health facilities and also contributes some funding for the running of the Private-Not-for-Profit sector such as the faith-based health institutions. Private health institutions are largely patient-funded with help from employers where arrangements exist for employers to fund health expenditures of their employees.

The National Health Accounts Study for the health expenditures for the financial year 2009/10 showed that the government financed only 22%[1] of total health expenditure. Fifty percent (50%[1]) was contributed by private funds with 42% coming from household incomes, while external donors contributed 34%[1]. Total health expenditure per capita was estimated at USD 51 and was below the WHO recommended expenditure of USD 60 needed to provide the minimum health care package.

3.3.2 Health financing trends

Information from the Annual Health Sector Performance Reports 2012/2013 (MoH, 2013), and 2013/2014 (MoH, 2014a) indicates that although there had been an apparent and steady increase in budget allocation to the health sector in absolute terms since the year 2000, the proportion of the government budget allocated to this sector stagnated at an average 8% of total government expenditure, which is short of the Abuja Declaration target of 15% set 14 years ago. Government Health Financing Trends in Uganda (2010 to 2014) are shown in Table 3 below.

1 This Report notes that the sum of these figures exceeds 100%

Table 3: Government Health Financing Trends in Uganda

Year	GoU Funding (Ushsbns)	GoU Projects And GHIs (Ushsbns)	Total (Ushsbns)	Per capita Public Health exp (UGX)	Per capita Public Health exp (US $)	GoU health Expenditure As % of total Government expenditure
2010/11	569.56	90.44	660	20,765	9.4	8.9
2011/12	593.02	206.10	799.11	25,142	10.29	8.3
2012/13	630.77	221.43	852.2	23,756	9	7.8
2013/14	710.82	416.67	1127.48	32,214	12	8.7

Source: Annual Health Sector Performanace Report 2013/2014 (MoH, 2014a)

3.3.3 Infrastructure

Health facilities in the country may be classified according to ownership. Some are owned by the government, some by NGOs (mainly faith-based) and some are private. There are two National Referral Hospitals – Mulago and Butabika – both located in Kampala, the capital city, and 14 Regional Referral Hospitals, namely Arua, Fort Portal, Gulu, Hoima, Jinja, Kabale, Lira, Masaka, Mbale, Mbarara, Mubende, Moroto, Naguru and Soroti.

There were a total of 4,478 health units of varying levels of capacity in 2013. Of these, 66% were government owned, 20% were owned by NGOs and 14% were privately owned. In addition, there are a growing number of Village Health Teams. The total number and of distribution of these facilities are shown in Table 4 below.

Table 4: Health Facility Inventory 2013

OWNERSHIP				
LEVEL OF FACILITY	**GOVERNMENT**	**NGO**	**PRIVATE**	**TOTAL**
Hospital	65	63	27	155
HC IV	182	17	7	206
HC III	969	323	22	1,314
HC II	1,722	494	587	2,803
Total	**2,938 (66%)**	**897 (20%)**	**643 (14%)**	**4,478 (100%)**

Source: (MoH, 2013)

The health units are said to be in good condition, with few requiring minor repair, and are within a five-kilometre distance of 87% of the population.

3.3.4 Staffing

The 14 Regional Referral Hospitals have an approved staff allocation totaling 4,678 workers. However, only 72% of these posts were filled. There is a staff deficit averaging 28% and ranging between 10% and 54%. Although information about the staffing situation in other health units was not obtained, there is no reason to believe that the situation there is any better.

Professional healthcare workers are regulated under the Uganda Medical and Dental Practitioners Statute, the Allied Health Professionals Act, the Nurses and Midwifery Act and the Pharmacy Act. Inadequacy of remuneration and other amenities which affects most cadres in public service was cited as a serious constraint in the recruitment and retention of microbiologists and technical staff in microbiology laboratories in public health units. Professional cadres authorised to prescribe antibiotics are limited to registered medical practitioners, dental surgeons, clinical officers and midwives as well as veterinary surgeons.

3.4 The animal sector

3.4.1 Animal demographics - livestock and pets

According to the results of the National Livestock Census of 2008 (MAAIF & UBOS, 2010) the population of domestic animals in Uganda was as shown in Table 5 below.

Table 5: Livestock and pet population of Uganda in 2008

Animal type	No. in millions
Cattle	11.4
Goats	12.5
Sheep	3.4
Poultry	37.4
Other birds	2.1
Pigs	3.2
Rabbits	0.37
Dogs	1.6
Cats	0.64
Horses	0.002

Source: MAAIF and UBOS (2010): The National Livestock Census Report 2008

The cattle population was estimated at 11.4 million in 2008. If the trend has been maintained, the cattle population as of 2014 is well over 15 million.

3.4.2 Ministry of Agriculture, Animal Industry and Fisheries (MAAIF)

Agriculture has remained the major sector in Uganda's economy, contributing approximately 23% to the national GDP as of 2013 (CIA, 2014). Agricultural activities in the country are coordinated by the Ministry of Agriculture, Animal Industry and Fisheries. The ministry is mandated, as derived from the national objectives of the 1995 Constitution of the Republic of Uganda XI (ii), to formulate and review national policies, plans, legislation, standards and programmes relating to the sector. It also controls and manages crop and animal epidemic diseases affecting production (MAAIF, 2007). The ministry supports, promotes and guides the production of crops, livestock and fish in order to ensure improved quality and increased quantity of agricultural produce and products for local consumption, food security and export. The above objectives are fulfilled through three different directorates which are: Crop Resources, Livestock Resources and Fisheries Resources (MAAIF, 2015). The Directorate of Animal Resources is managed under a joint directorate arrangement combining Livestock and Fisheries. This is mandated to support sustainable animal disease and vector control, market oriented animal production, and food quality and safety for improved food security and household income (MAAIF, 2015).

MAAIF is mandated to facilitate agricultural production by playing a variety of functions, including regulating the use of veterinary drugs. However, the ministry does not have enough experienced manpower to efficiently handle regulatory activities. Veterinary surgeons are the only cadre of workers with legal authority to prescribe antibiotics but these constitute a small proportion of the people who actually prescribe. Others who use antibiotics in practice include paraveterinarians, farm managers and farmers. The delivery of animal health services in the country is jointly undertaken by the public and the private sector.

As far as veterinary diagnostic services are concerned, there are 16 veterinary diagnostic laboratories in the country of which only three are able to carry out antimicrobial susceptibility tests. Even at these facilities, there are often shortages of media and reagents and there are not enough qualified technical staff to perform these tests. Treatment with antibiotics is often done without laboratory evaluation for the need to use particular antibiotics. Therefore, there is a great need to improve both human and infrastructure capacity for a more effective antibiotic management programme in agriculture. Veterinary professionals are regulated under the Veterinary Surgeons Act 1958.

Although the MAAIF is aware that antimicrobial resistance and its consequences are likely to be a major public health concern, the ministry does not monitor or publish information about antimicrobial resistance trends in the country as there is no dedicated programme for surveillance and monitoring. However, there are provisions for infection control through vector control, vaccination, disease treatment and regulation of animal movement especially at international borders which may indirectly contribute to the prevention of ABR.

3.4.3 Financing in the animal sector

At less than 2% of the national budget, animal sector financing is judged to be inadequate. From a Position Paper on the Agriculture, Animal Industry and Fisheries (MAAIF), Sector 2013/2014 (CSBAG, 2013), in the three consecutive financial years 2011/2012, 2012/2013 and 2013/2014, budgetary allocations to MAAIF were 42.258, 80.904 and 83.563 billions of UGX, respectively. Other funds applicable to animal industry activities were provided through the National Agricultural Advisory Services (NAADS), the National Agricultural Research Organisation (NARO) and the National Animal Genetic Resource Centre (NAGRC). It has not been possible to establish how much of this other funding goes towards the acquisition of antibiotics in the animal sector.

IV BURDEN OF DISEASE

4.1 Burden of human disease in Uganda

4.1.1 Inpatient mortality

According to the Ministry of Health Annual Health Sector Performance Report for the Financial Year 2012/2013, of the diseases due to infections, malaria continued to be the leading cause of inpatient mortality for all age groups. This was followed by pneumonia, especially among children under five years of age. Of the top 10 leading causes of death among hospitalised patients indicated in Table 6 below, bacterial infections accounted for about 20%.

Table 6: Causes of hospital-based mortality for all ages in 2012/13 (expressed as %)

	Condition	Percentage
1	Malaria	21
2	Pneumonia	12
3	Anaemia	11
4	Perinatal conditions (newborns 0–seven days)	6
5	Other types of meningitis	3
6	Other tuberculosis	2
7	Injuries – (trauma due to other causes)	3
8	Injuries – (road traffic accidents)	2
9	Tuberculosis (new smear positive cases)	2
10	Septicemia	3
11	All others	37
	Total	100

Source: Ministry of Health Sector Performance Report Financial Year 2012/2013 (MoH, 2013)

Bacterial infections among children under five years of age were responsible for approximately 25% of deaths in the same period (Table 7).

Table 7: Causes of inpatient mortality in children under five years of age in 2013

	Condition	Percentage
1	Malaria	31
2	Pneumonia	12
3	Anaemia	12
4	Perinatal (0-7 days) conditions	9
5	Neonatal septicemia	5
6	Acute diarrhoea	3
7	Septicemia	3
8	Respiratory infections	2
9	Severe malnutrition	2
10	Perinatal (8-28 days) conditions	2
11	All others	20
	Total	**100**

Source: Ministry of Health Sector Performance Report Financial Year 2012/2013 (MoH, 2013)

4.1.2 Hospital inpatient morbidity

Bacterial infections were responsible for a 37 % of hospitalised patients as is shown in Table 8 below. It should be noted that a portion of the upper respiratory tract infections, such as tonsillitis and most of the skin, eye and ENT conditions, as well as a considerable fraction of the "others" are caused by bacteria. In addition, numerous injuries become infected with bacteria, and all these add up to the proportion of bacterial infections in hospitalised patients.

Table 8: Top eleven causes of hospital morbidity

	Condition	Percentage
1.	Malaria	37
2	Upper respiratory infections - colds and coughs	29
3	Intestinal worms	6
4	Skin diseases	3
5	**Acute diarrhoea**	**3**
6	Eye conditions	3
7	**Urinary Tract Infections**	**3**
8	**Pneumonia**	**2**
9	E.N.T conditions	2
10	Injuries	2
11	All others	11
Total		100

Source: Ministry of Health Sector Performance Report Financial Year 2012/2013 (MoH, 2013)

4.1.3 Leading bacterial infections

4.1.3.1 Pneumonias

Pneumonia may predominantly involve the bronchi, in which case it is referred to as bronchopneumonia and is largely encountered in children and the elderly. If it involves the alveoli and brings about consolidation of a lung lobe, it is referred to as lobar pneumonia. Lobar pneumonia is most common in young adults. Pneumonia is predominantly acquired by droplet infection and from the perspective of epidemiology, may be community acquired or hospital acquired. According to Nantanda et al. (2008)**,** *Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenzae* are the most common bacterial causes of severe pneumonia in children under five years of age in Uganda.

Other causes of community acquired pneumonia include *Mycoplasma pneumoniae* and, especially in the case of developing countries such as Uganda, *Mycobacterium tuberculosis*. The most common causes of hospital-acquired pneumonia include enteric Gram-negative organisms such as *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Patients with HIV/AIDS have an added burden of pneumonia caused by opportunistic organisms such as *Pneumocystis jaroveci* and *M. tuberculosis* (Levison, 2001)**.**

4.1.3.2 Bacterial meningitis

Meningococcal meningitis is uncommon in Uganda except in the northern parts of the country, where it occurs mostly in the dry seasons. When it occurs, it tends to affect all age groups. In most of the country bacterial meningitis is mainly a paediatric problem, and before the introduction of vaccines against *H. influenzae* type b and *S. pneumoniae*, it used to be mostly caused by these two organisms as well as by staphylococci, streptococci and Gram-negative bacilli (Iriso, Ocakacon, Acayo, Mawanda, & Kisayke, 2008; Kiwanuka & Mwanga, 2001). Adult meningitis is mostly caused by *S. pneumoniae* as well as by *M. tuberculosis* (Mpairwe, 1972), but since the onset of HIV and AIDS, *Cryptococcus neoformans* has assumed a greater role (Aberg & Powderly, 2006). In recent times, the prevalence of *H. influenzae* type b meningitis has been reduced to almost zero following the introduction of the Hib vaccine (Iriso et al., 2008; Lewis et al., 2008)**.**

4.1.3.3 Septicaemia

Septicaemia may be caused by a wide range of organisms including bacteria and fungi. The most common bacteria in this condition, among Gram-positive species, include *S. aureus*, enterococci, *S. pneumoniae* and other streptococci as well as coagulase-negative staphylococci. The leading causes among Gram-negative bacteria are Enterobacteriaceae and *H. influenzae* (Munford, 2001)**.**

In populations where HIV/AIDS is highly prevalent, the causes of bacterial infections may be accordingly modified. A study on this condition involving predominantly HIV infected patients recruited from Mulago National Referral/Teaching Hospital as well as

from Masaka Regional Referral Hospital was conducted between July and November 2006 (Jacob et al., 2009). Blood from 381 patients was cultured and the organisms isolated were five *Cryptococcus neoformans* strains and 43 bacterial isolates of which non-typhoidal salmonellae were 47%, *S. aureus* 28%, *S. pneumoniae* 14%, *E. coli* 9% and *Proteus* species 2%.

In this study, 58% of the bacterial isolates (excluding mycobacteria) were Gram-negative. Mycobacterial isolates were found in 22% of 249 patients who were investigated. Ninety-five percent (95%) of the *Salmonella* isolates were resistant to chloramphenicol and co-trimoxazole but no *S. aureus* isolate was resistant to oxacillin. Unfortunately, the complete susceptibility pattern of the isolated bacteria was not given.

Blood cultures from the Department of Medical Microbiology, Makerere College of Health Sciences between August 2012 and July 2013 (Kajumbula, 2014b) yielded 187 isolates made up as follows: coagulase-negative staphylococci 27%, *S. aureus* 18%, *Klebsiella* species 10%, *E. coli* 8%, unidentified Enterobacteriaceae 8%, *Enterococcus* species 6%, *Salmonella* species 5%, *Acinetobacter* species 5%, *S. pneumoniae* 4% and *Pseudomonas* species 3%. Together, other isolates – *S. viridans*, yeasts, coryneforms and moulds – constituted 6%. Gram-negatives were 39% and Gram-positives were 55%. The large number of coagulase negative staphylococci in this study is atypical for this condition and may reflect poor specimen collection technique leading to gross contamination.

It should be noted that between 60 and 100% of these isolates were resistant to most of the antimicrobials tested including ampicillin, cefuroxime, Augmentin, ceftriaxone, ceftazidime, co-trimoxazole, chloramphenicol, ciprofloxacin and tetracycline. Fewer than 5% of isolates were resistant to gentamicin and the newer, more expensive antibiotics piperacillin-tazobactam, imipenem, meropenem and amikacin.

In an effort to describe the incidence and aetiology of septicaemia, antimicrobial drug resistance in HIV-infected and uninfected individuals, and the impact of antiretroviral therapy (ART) on septicaemia in rural Uganda between 1996-2007, Mayanja *et al.* (2010) found that the overall septicaemia incidence (per 1,000 person-years) was 32.4 (95%CI 26.2-40.6) but was only 2.6 (95%CI 1.3-6.2) in HIV-negative patients and 67.1 (95%CI 53.4-85.4) in HIV-positive patients not on ART. Among those on ART, the overall incidence was 71.5 (95%CI 47.1-114.3), although it was 121.4 (95%CI 77.9-200.4) in the first year on ART and 37.4 (95%CI 18.9-85.2) in the subsequent period. Septicaemia incidence was significantly associated with lower CD4 counts. The commonest isolates were *S. pneumoniae* (n = 68) and Non-typhi salmonellae (n = 42). Most *S. pneumoniae* isolates were susceptible to ceftriaxone and erythromycin, while resistance to co-trimoxazole and penicillin was common. All non-Typhi *Salmonella* isolates were susceptible to ciprofloxacin, but resistance to co-trimoxazole and chloramphenicol was common.

4.1.3.4 Acute diarrhoea

It has been previously noted that acute diarrhoea is caused by microbial infections in 90% of cases (Ahlquist & Camilleri, 2001). The causative agents are mainly transmitted from case to case by the faecal-oral route, largely through contaminated water or food. In infective diarrhoea, the causative agents range from viruses such as the Rotavirus to protozoa like *Entamoeba histolytica.* The causative agents, on the basis of the pathophysiology, include toxin producers such as certain strains of *S. aureus* as well as *Clostridium perfringens*; enterotoxin producers such as *Vibrio cholerae* and certain strains of *E. coli;* cytotoxin producers such as *Clostridium difficile*; and invasive organisms such as salmonellae and *Campylobacter* species. Then there are dysenteric types of diarrhoea caused by such bacteria as the shigellae and entero-invasive *E. coli*. Fortunately, in the majority of cases, diarrhoea is self-limiting or can be successfully treated by rehydration alone. Antibiotics are necessary in relatively few cases but are especially needed in the category of dysenteric diarrhoea, where their use minimises the likelihood of renal failure that may complicate dysentery. However, not much has been documented relating to dysenteric diarrhoea in Uganda; for this reason the relative importance of the various causative agents in the country is not known.

In an attempt to establish the proportion of children infected with *Campylobacter* species among children with acute diarrhoea at Mulago Hospital, Mshana, Joloba, Kakooza, and Kaddu-Mulindwa (2009) conducted a cross-sectional study from July to October 2005 involving 226 children with acute diarrhoea. This study found that *Campylobacter* species were isolated in 21 (9%) of 226 stool specimens analysed. *Campylobacter jejuni* 17 (81%), *Campylobacter lari* 2 (10%), *Campylobacter coli* 1 (5%) and *Campylobacter jejuni/coli* 1 (5%). All *Campylobacter* isolates were sensitive to erythromycin, and 20% had intermediate resistance to ampicillin.

4.1.3.5 Respiratory infections

The commonest causes of upper respiratory infections are viruses such as rhinovirus and coronaviruses. However, in Uganda this condition was found to be mainly caused by respiratory syncytial virus (RSV) and the *Parainfluenza* viruses (Sobeslavsky et al., 1977). Up to 15% of acute pharyngitis may be caused by bacteria, most commonly *S. pyogenes.* Other bacterial causes of upper respiratory infections include *H. influenzae*, *Corynebacterium diphtheriae* and *Neisseria gonorrhoeae* (Durand & Joseph, 2001).

4.1.3.6 Urinary tract infections (UTIs)

UTIs are more common in women by virtue of the close proximity of their urethral and anal orifices. Epidemiologically, UTIs are classified into community-acquired and hospital-acquired varieties. In both cases, the leading causes of infections are enteric organisms, especially *E. coli*, which is responsible for 80% of cases (Stamm, 2001). Other Gram-negatives include *Proteus* and *Klebsiella* species. The proportion of Gram-negatives increases in hospital-acquired UTIs. Among the Gram-positives the commonest include

coagulase negative staphylococci especially *S. saprophyticus* as well as *Enterococcus* species. The most commonly used antimicrobial for treatment of UTIs in Uganda is co-trimoxazole or ciprofloxacin (MoH, 2014b).

4.2 Burden of disease in animals

Livestock diseases are the most significant single constraint to development of the livestock industry in Uganda (MAAIF, 2005). These diseases vary in terms of national distribution and seasonality. Their relative importance determines their grouping into different categories such as notifiable animal diseases, transboundary animal diseases and zoonotic diseases. The major animal diseases in Uganda include: foot and mouth disease (FMD), contagious bovine pleuropneumonia (CBPP), tick-borne diseases, especially east coast fever (ECF), as well as others such as lumpy skin disease (LSD), newcastle disease (ND) and african swine fever (ASF). These diseases are highly contagious and have the potential to spread very rapidly across borders causing serious economic losses (Bayiyana, Ekere, & Mugisha, 2012).

4.2.1 Contagious bovine pleuralpneumonia (CBPP)

CBPP is a highly infectious, acute, sub-acute or chronic disease primarily of cattle affecting the lungs and occasionally the joints. It is caused by *Mycoplasma mycoides* (Tambi, Maina, & Ndi, 2006). CBPP is endemic in Uganda and it is an economically important disease where morbidity may reach 100% and mortality over 50% (Tambi et al., 2006). Uganda has had several outbreaks, including one in Nakasongola District reported by (Baluka, Ocaido, & Mugisha, 2014), where they recorded an average mortality rate of 1% in large herds and 3% in small herds and mainly affecting cows.

4.2.2 Clinical and subclinical mastitis

Clinical mastitis (CM) and subclinical mastitis (SCM) are conditions of common occurrence among dairy cattle in Uganda and elsewhere in the world (Abrahmsen, Persson, Kanyima, & Bage, 2014). CM differs from SCM in that the infection is not limited to the milk within the mammary ducts but involves the tissues of the mammary gland as well. The affected animal often has systemic signs of illness such as fever and inflammation of the affected mammary gland. It may lead to loss of appetite and cause wasting or death in the animal.

In SCM on the other hand, the infecting organisms are confined to the milk within the duct system of the mammary gland. A variety of microorganisms are involved in the causation of both conditions. Coagulase-negative staphylococci as well as streptococci are the main causes of SCM while *S. aureus*, enteric organisms such as *E. coli* and even *Klebsiella* and *Pseudomonas* species are the main causes of CM in Uganda (Abrahmsen et al., 2014; Björk, 2013; Bjork et al., 2014; Byarugaba, Nakavuma, Vaarst, & Laker, 2008; Kasozi, Tingiira, & Vudriko, 2014).

4.2.3 Theileriosis (East Coast fever)

Tick-borne diseases (TBDs) contribute to about 30% of calf mortality in Uganda. Of these, ECF is the most important comprising 79%. ECF is caused by *Theirelia parva*, a protozoan parasite transmitted by *Rhipicaphalus appendiculatus* ticks. All cattle in Uganda, an estimated population of 11.4 million, are at a risk of contracting ECF, and the disease is more severe in exotic and crossbred cattle than local cattle (Ikwap K et al., 2012).

ECF is a very important disease due to its economic impact on the livestock industry. According to Muhanguzi et al. (2014), the overall prevalence of *Theirelia parva* in Tororo District, eastern Uganda between September and December 2011 was 5% (n=2,658) with herd level prevalence ranging between 0% to 21%.

Ocaido et al. (2005) established the disease problems of cattle in Serere, Soroti District. Their study indicated that the major diseases were ECF, anaplasmosis, tick-borne diseases, trypanosomiasis, FMD, CBPP and brucellosis. Calves were mainly affected by ECF and helminths, while adult cattle were greatly affected by anaplasmosis. ELISA tests revealed that the prevalence of ECF antibodies was 63%. Also, a high mean prevalence of trypanosome infection (14.8±2%) was observed. All the three common trypanosome species were prevalent: *Trypanosoma vivax* (7%), *T. brucei* (4%) *and T. congolense* (1%). In addition, the prevalence of brucellosis was found to be 16%.

4.2.4 Poultry diseases in Uganda

According to Ojok (1993) and the Livestock Service Project (1989), only six diseases were known to occur in poultry in Uganda**.** These were Newcastle disease (NCD), fowl pox, Mareks' disease, fowl typhoid, fowl cholera and coccidiosis. However, a number of other poultry diseases were diagnosed in the Department of Veterinary Pathology, Makerere University, including viral, bacterial, protozoan, chlamydial, fungal and helminthes, among others. Among these, NCD, fowl typhoid, Pullorum disease, fowl cholera, collibacillosis and coccidiosis were the most common, causing the greatest economic loss to the industry.

4.2.5 Pig diseases in Uganda

According to Nsadha (2013)dNote>**,** diseases of pigs are not well studied in Uganda and information about their prevalence in the country is very sparse. African swine fever (ASF) is the most important disease, causing outbreaks in almost all pig rearing areas of the country and resulting in high mortalities. Between 2003 and 2007, several outbreaks were reported in many districts including Lira, Rakai, Mukono, Kasese, Soroti, Tororo, Nakasongola, Gulu, Nakapiripit and Kotido (Auditor_General, 2009)**.** Parasite infections are very common and many pig flocks suffer from mange, lice and at times jiggers.

Other pig diseases include mastitis, metritis and agalactia (MMA), piglet anaemia, foot and mouth disease, swine erysipelas, ectoparasites (MAAIF, 2011) and cysticercosis (Nsadha, 2013**)**, which is zoonotic.

V ANTIBIOTIC USE AND SUPPLY

5.1 Quantity, source and quality of antibiotics

5.1.1 Quantity

It was not possible to establish the quantities of the various antibiotics imported or manufactured in Uganda over the last 20 years because records are not easily collated and accessible.

5.1.2 Source of antibiotics

In one study, Foster, Sosa, Najjuka, and Mwenya (2011) established that the majority of amoxicillin (55%) and ciprofloxacin (73%) products came from India while most of co-trimoxazole (54%) products were manufactured in Uganda or Kenya.

Uganda has no research programme specifically established for the development of antimicrobial agents. However, there is a Natural Chemotherapeutics Research Institute (NCRI) established by the UNHRO Act of Parliament in 2009. The NCRI is mandated to carry out research on natural products (plants, animal parts and minerals) and on the use of traditional methods in the management of human disease. To date, it has identified 53 useful medicinal plants upon which phytochemical analyses have been carried out. At least one herbal product, "Jena", has been found to contain potent antibacterial properties against *E. coli* and *S. aureus* and was more effective on promoting healing of wounds in experimental rats than neomycin cream (Ogwang et al., 2011)**.** There are no more than a few companies that package a limited range of antibiotics.

5.1.3 Quality

Quality testing on the 270 capsules or tablets of amoxicillin, ciprofloxacin and co-trimoxazole by Foster et al. (2011) indicated that the majority (94%) of these were of acceptable quality. However, Nayyar, Breman, Newton, and Herrington (2012) reported on the rampancy of substandard and counterfeit anti-malarials and other drugs in Southeast Asia and Sub-Saharan Africa. On June 25, 2012, the National Drug Authority (NDA) suspended medicines manufactured by an Indian company, Flamingo Pharmaceuticals Limited, for low standards of manufacturing practice. Half of these medicines were antibiotics.

On August 21, 2012, in the *New Vision* newspaper, Steven Ssendagire wrote an article entitled, "Suspension of Indian poor quality medicines is necessary but not sufficient" (Ssendagire, 2012). As if to affirm contents of this article, on 8 February 2013, the *Red Pepper* newspaper reported on findings of the NDA that some pharmacists in the country were still selling antibiotics and anti-malarials of the banned Indian pharmaceutical firm, Flamingo (Admin, 2013).

While there is evidence that the NDA is exerting effort towards maintaining the quality of antibiotics imported into the country, it was not possible to establish whether the NDA has all the resources required to fully contain the entire problem of substandard antibiotics imported into the country from the many sources in Asia, the Middle East, Europe and elsewhere. Indeed, there was a common belief among the people interviewed that a significant portion of drugs imported into the country is substandard.

5.2 Antibiotic use in agriculture

All of the different antibiotics used in the treatment of human disease in Uganda are also used for a variety of reasons in agriculture. The agriculture ministry is the authority for monitoring and controlling the use of these drugs, as pointed out in Section 2.4.2, but it does not have adequate manpower to efficiently perform this task. Although veterinary surgeons are the only cadre of workers legally allowed to prescribe and administer antibiotics, in practice anybody, including inadequately trained workers, such as farm managers, veterinary assistants, animal husbandry officers or untrained farmers, have access to and can administer antibiotics without the supervision of veterinary doctors.

5.2.1 Use of antibiotics in poultry

Antibiotics are used in chicken feeds, and unfortunately their use is not always correct. For instance, from December 2002 to March 2003, (Sasanya, Ogwal Okeng, Ejobi, & Muganwa, 2005) studied the possible role played by knowledge, attitudes and practices in the levels of sulphonamide residues in chicken eggs among 60 poultry farmers in and around Kampala. It was found that nearly all (98%) of the eggs sampled had detectable levels of the sulphonamides and almost all came from farmers who applied antimicrobials in feeds or water.

Fifty one (85%) of the respondents knew of the need to respect the withdrawal periods for antimicrobial agents including sulphonamides. Nevertheless, 95% of the farmers did not comply with the stipulated withdrawal periods before selling or eating the eggs. Half of respondents considered economic loss they would face if they observed the withdrawal period as the reason for not complying.

The authors note that this state of affairs is a result of the absence of good veterinary practice in Kampala and its surroundings. They lamented the absence of a chemical-risk management programme in MAAIF and the National Drug Authority. They noted that the farm-to-table supervision of food safety recommended by FAO has not been implemented in Uganda as the enabling policies and regulatory framework have not been put in place.

5.2.2 Antibiotic use in aquaculture

In aquaculture the situation is different. Information from the Aquaculture Research and Development Centre, which is charged with developing technologies and generating information through research for improved fish production, indicates that antibiotics are

not used for any therapeutic purpose in aquaculture. Their use is confined to research and is under strict control. When pond infection is suspected, general disinfectants such as formalin or copper sulphate are used to disinfect ponds.

5.2.3 Antibiotic use in veterinary practice

In contrast, antibiotics are frequently used in veterinary practice for various purposes such as treatment of infectious diseases, prophylaxis and as additives in animal feeds. Tetracycline and penicillin are the most common antibiotics used, although several others such as fluoroquinolones are also used.

Unfortunately, antibiotics are quite often used without proper evaluation of the need to use them. This is because there are very limited veterinary diagnostic services in the country and even fewer laboratories have the capacity to carry out microbiological analyses. The few available are limited to academic institutions, especially the College of Veterinary Medicine, Makerere University.

High levels of ABR have been observed in veterinary practice. In some cases this is observed through treatment failures in the field. In addition, a number of studies have reported a high prevalence of resistant pathogens in animals. For example, a methicillin resistance prevalence rate of 64% was found by Kalule et al. (2014) among 85 *S. aureus* strains isolated from the noses of pigs and vervet monkeys in Luweero and Wakiso districts of central Uganda. Ninety percent (90%) of these isolates were also resistant to co-trimoxazole and multiple drug resistance (mostly to methicillin-erythromycin-co-trimoxazole) was encountered among 73% of the isolates. In the study by (Kalule et al., 2014; Mahero, Byarugaba, Doetkott, Olet, & Khaitsa, 2013) on 14 *Salmonella* isolates resistance to sulfisoxazole, chloramphenicol, tetracycline co-trimoxazole, amoxicillin, and nalidixic acid was expressed by between 50 and 83% of the isolates.

Several factors are implicated in the high ABR levels in veterinary practice: unapproved use of medicine - especially non-compliance with the regulatory framework of drugs to be sold over the counter, irrational use of antibiotics, handling and administration of antibiotics by non-professional personnel, non-professional conduct of pharmacists and pharmacists taking on the role of medical or veterinary doctors. It is thus suggested that one of the approaches for prevention and control of the emergence of resistant organisms is to ensure prudent use of antimicrobials at all levels of veterinary practice.

5.2.3.1 Antibiotic residues in milk and meat products

Reference has already been made in section 4.2.1 of this report to a finding by Sasanya et al. (2005) of detectable levels of sulphonamides in 98% of eggs destined for the market or the table. In addition, Sasanya, Ejobi, Enyaru, Olila, and Ssengoye (2008) in an undated study demonstrated that 13% of 384 milk samples obtained at milk cooling centres in Mbarara and Masaka districts and 18% of 453 edible bovine tissue samples collected from abattoirs or

slaughter slabs in the same districts had violable levels of penicillin as set by the European Union (EMA, 2010). Ninety-six percent of the cattle farmers or their farm managers did not adhere to regulations relating to withdrawal periods after treatment of animals with antibiotics and only 14% were aware of the dangers associated with exposing consumers to cattle products with offending levels of antibiotics.

5.2.4 Antibiotic use in wildlife

Information from the Uganda Wildlife Education Centre, Entebbe and from the Mountain Gorilla Conservation Project at the College of Veterinary Medicine, Makerere University indicates that antibiotics are being used at the Uganda Wildlife Education Centre, Entebbe, for various purposes including treatment of sick animals and infection control after surgery. The concerned personnel, however, are very strict about the sources of the antibiotics they use. The extent of use and sources of drugs differ according to whether the wildlife activity is limited to the zoo or to the game parks, but the key determinant in all cases is quality. The drug sources include: pharmaceutical agents of veterinary drug manufacturers such as Coopers and Norbrook, veterinary pharmacies, Joint Medical Store, and international sources like Kyron Pharmaceuticals of South Africa and the USA. In some projects, however, antibiotics from local pharmacies are used.

A broad range of antibiotics is being used in wildlife and these include fluoroquinolones, tetracyclines, trimethoprim, sulphonamides and cephalosporins. It is important to note that all of these are also used in the medical field to treat various human infections. However, proper evaluation is always made prior to administration of antibiotics, based on recommendations from studies carried out in collaboration with the Wildlife Animal Resource Management Department, CoVAB - Makerere University, where culture and sensitivity tests are done from time to time, especially at the Mountain Gorilla Veterinary Project Laboratory. All of this is always done with proper involvement of veterinary doctors who also administer the drugs to animals. We believe that for these reasons, antimicrobial resistance is reported to be low in wildlife, especially in game parks.

Nevertheless, there are growing concerns that humans in close proximity to wild animals are transmitting antibiotic resistant organisms to those animals. It is feared, for example, that antimicrobial resistance is being transferred to animals in zoos from the meat they are fed on, which is obtained from open markets where it is often contaminated with antibiotic-resistant organisms (Svanström, 2014). Moreover, it has been reported that chimpanzee communities in Kibaale District and some gorilla communities in Bwindi national park acquired antibiotic resistant strains of *E. coli* from game park rangers and the local human populations, respectively (Goldberg, Rwego, Wheeler, Estoff, & Chapman, 2007; Rwego, Isabirye-Basuta, Gillespie, & Goldberg, 2008). More recently, it has been reported that some communities of Vervet monkeys in Wakiso and Luweero districts have acquired high prevalence rates of methicillin-resistant *S. aureus* carriage in their noses from contact with humans with whom they share the habitat (Kalule et al., 2014).

On measures to control antimicrobial resistance, it was suggested that at all times practitioners should avoid irrational use of antibiotics including, but not limited to, under-dosing, weight underestimation, use of antibiotics in feeds and over the counter sale of antibiotics. Market place pharmacovigillance and post-market surveillance should be instituted or stepped up to remove counterfeit or sub-standard products. It was also recommended that prescription and administration of antibiotics should strictly be limited to qualified staff. It was further proposed that isolated microbes and sensitivity testing should form the basis of antibiotic prescription.

Finally, it was recommended that in order to minimise weaknesses in the veterinary drug regulations, more veterinary surgeons should get involved in NDA activities, especially in enforcement and quality assurance.

5.3 The practice of antibiotic prescription

5.3.1 Over-the-counter prescriptions in community pharmacies

In a study by Mukonzo et al. (2013), carried out during November 2011 and January 2012 on 72 drug outlets in Uganda including 62 community pharmacies, it was found that at community pharmacies, 41% of all antibiotic sales were over-the-counter, i.e., without a prescription. Over-the-counter antibiotic dispensing was also associated with under-dosing. This took place in spite of pharmacy supervision by qualified, knowledgeable and licensed pharmacists. Inefficiency in enforcement of regulations was cited as the main cause of over-the-counter dispensing. The antibiotic-seeking clientele is encouraged by the knowledge that enforcement of regulations is weak.

5.3.2 Inappropriate prescription (or withholding) of antibiotics in malaria patients

Batwala, Magnussen, and Nuwaha (2011) studied the influence of laboratory diagnosis of malaria by microscopy or by Rapid Diagnostic Test (RDT) on antibiotic prescription among patients with fever. The study was conducted in 15 health centres on 52,117 patients from March 2010 to July 2011. They found that a prescription of antibiotics was given to patients with febrile illness in 42% of 16,971 who had had no laboratory test for malaria and to 26% and 18% among those who tested positive for malaria by RDT or by microscopy, respectively.

In contrast, of those who tested negative by RDT or by microscopy, 61% and 39%, respectively, had antibiotics prescribed. From these findings, the authors concluded that testing positive for malaria in a patient reduced the likelihood of antibiotic prescription for that patient, while testing negative increased the likelihood of antibiotic prescription. The overall effect on antibiotic use from this analysis was, however, not clear.

The authors further observed that the age of the febrile patient influences the likelihood of having an antibiotic prescribed. Children under five years were more likely to have antibiotics prescribed (63%) than older patients (39%).

Between January and September 2011, Means et al. (2014) studied correlates of inappropriate antibiotic management of patients with confirmed malaria in 36 health centres in various parts of the country. Using the *Uganda Clinical Guidelines* as the point of reference, they found that 90% of 45,491 such patients did not have clinical indications for antibiotic therapy and yet, inappropriately, 42% of them had antibiotic prescriptions made for them. A number of factors were found that led to this error, but one that is relevant to this report was that most of the inappropriate prescribers had the shortest periods of professional training - clinical officers and nurses – as compared to medical practitioners.

Ten percent of 45,491 patients with malaria also had clinical indications for the administration of antibiotics. In 11% of these patients, antibiotics were not prescribed. In this instance, prescribers with least professional training periods were the ones who tended to get it right, while medical doctors tended to get it wrong. Overall, 39% of the patients with malaria were inappropriately treated by unnecessary prescription or withholding of antibiotics.

It was further observed that on days when antimalarials were out of stock, prescribers tended to prescribe antibiotics unnecessarily as if they were under compulsion to prescribe something.

These authors also observed that the prescription of antibiotics was more common for children under five years as compared to those above five.

Conclusions from the above two studies

- Fever of unresolved etiology enhances the rate of antibiotic prescription
- Professionals who underwent a shorter period of professional training (e.g., clinical officers) were found to prescribe antibiotics inappropriately
- Professionals who underwent longer periods of professional training (e.g., medical doctors) tended to withhold antibiotic prescription where indicated, and this may have something to do with the esteem that medical practitioners hold for the *Uganda Clinical Guidelines* advice on use of antibiotics (*vide infra* 4.4.3)
- Non-availability of antimalarials was associated with higher prescription rates for antibiotics
- Malaria in a child inclines the prescriber to a higher rate of antibiotic prescription

In the livestock industry, any febrile condition, such as ECF, anaplasmosis, babesiosis or cowdriosis, may be treated with antibiotics even though, as with malaria, they are not bacterial infections.

5.3.3 Polypharmacy

In this report, we use the term "polypharmacy" as the practice of prescribing or taking more than one antibiotic where only one would suffice (other definitions specify four or more drugs, but we are using the term more broadly).

Polypharmacy is quite common in Uganda, although not much published information about its extent and magnitude is available. In some situations, polypharmacy may be unavoidable, for example, as a stopgap measure in the treatment of septicemia, it is sensible after collecting appropriate specimens to start treatment immediately with a combination of gentamicin and cloxacillin or chloramphenicol as recommended in the *Uganda Clinical Guidelines***.** This is because culture and sensitivity testing take a long time while the patient requires immediate treatment. However, as soon as the definitive laboratory diagnosis and antibiotic sensitivity pattern of the infecting organism is known, polypharmacy should be discontinued.

Polypharmacy is a detrimental practice when used routinely due to a lack of information on sensitivity patterns of prevailing pathogens or as a measure of circumventing microbiological investigations or of making additional profit by selling more drugs. Some reasons as to why polypharmacy is common in Uganda:

- There are inadequate laboratories capable of isolating and investigating sensitivity patterns of pathogens
- In private practice, polypharmacy is used deliberately by some practitioners to enable them sell a larger volume of their antibiotic stocks and make more money

In a study by Ogwal-Okeng, Obua, Waako, Aupont, and Ross-Degnan (2004) on prescribing of antibiotics for acute respiratory tract infections, which are most commonly caused by viruses, in 119 private clinics and in 10 public health units in Kampala, Masaka and Jinja, polypharmacy was encountered in both the public and private sectors, with some prescriptions containing up to three antibiotics. Newer and more expensive ones were more commonly prescribed in the private sector.

The Pharmaceutical Society of Uganda in their report on the Consultative Meeting on the Medical Representatives Training Programme held on the 4th of May 2012 at Hotel Africana noted that medical representatives who promote drug sales for pharmaceutical companies, many of whom have no medical or pharmaceutical training, had a hand in the propagation of the habit.

5.4 Determinants of specific antibiotic prescriptions in health facilities

5.4.1 The Uganda Clinical Guidelines

Besides information gathered from teachers and text books during the course of their training, many prescribers rely on the *Uganda Clinical Guidelines* (MoH, 2014b). This is published by the MoH. The 2012 edition states that, "It is designed to provide updated, practical and useful information for both upper and lower level health facilities on the diagnosis and management of common conditions present in Uganda". It was first published in 2003 and revised in 2010 and 2012. In its various relevant sections, it attempts to give updated advice on antibiotic use. It also gives advice on numerous other conditions.

In a study on prescription practice in Mulago National Referral and Teaching Hospital, Knaapen (2012/2013) found that out of 182 prescriptions for patients with suspected bloodstream infections in the departments of pediatrics, medicine and surgery, compliance with the *Uganda Clinical Guidelines* (MoH, 2014b) as to the nature of the prescribed antibiotic was observed in about half (50%) of the treated patients. Among these patients for whom a correct antibiotic had been prescribed, the prescription was wrong on dosage in 19%, wrong on duration in 73% and wrong on frequency in 37%. It was only with regard to route of antibiotic administration that nearly all prescribers (97%) were correct as far as the guidelines are concerned. In the majority of instances, the prescriptions were empirical and often depended on the availability of the drugs. Ceftriaxone was the most commonly prescribed antibiotic in this group of patients.

Some prescriptions lacked clarity: in 7% duration of antibiotic use was not stated, in 6% no frequency was indicated on the prescription and in 3% no dosage was stated. In more than 50%, the prescription was changed in the course of hospitalisation, but in 51% of the cases where the change was effected, the reason for this change was not documented. In only one case was antibiotic resistance recorded as the reason for the change. On average, each patient was prescribed 1.39 antibiotics, with a range of between one and three per prescription.

The study further revealed that the *Uganda Clinical Guidelines* (MoH, 2014b) were hardly used; in fact, it would appear that many specialists in this teaching hospital ignored the guidelines. It is possible that this decision to ignore originates from the fact that the guidelines do not state the source of information upon which the advice is based. This interpretation might also explain why medical practitioners "erred" by withholding antibiotic prescriptions when, according to the guidelines, they were indicated, as observed in the Means et al. (2014) malaria study. It is not surprising, therefore, that in the treatment of septicaemia in the Mulago and Masaka study (Jacob et al., 2009), 52 different empiric regimens of antibiotic combinations were used.

5.5 Inadequacy of microbiology laboratory services

5.5.1 National laboratory structure

The national health laboratory services within Uganda are diverse and they mirror the health services levels, from the most basic Health Centre Levels III and IV, through general hospital and regional referral hospital laboratories to national reference laboratories.

At the national level are the specialised laboratories serving as national referral centres of excellence, including the Central Public Health Laboratory (CPHL), the National Tuberculosis Reference Laboratory (NTRL), the Infectious Diseases Institute (IDI), the National STI/STD Reference Laboratory, the Uganda Virus Research Institute (UVRI), the Joint Clinical Research Centre (JCRC) and the Uganda Blood Transfusion Services (UBTS).

At the next level, there are laboratory services at Regional Referral Hospitals. Most districts have a general hospital; in districts where there is no general hospital a Health Centre IV takes on this responsibility. Some districts also have additional hospitals, as well as four to five Health Centre IVs and five to ten Health Centre IIIs.

In addition to the laboratories under the public health system there are private laboratories at hospitals and health centres run by the non-profit sector such as Nsambya, Mengo, Kibuli, Rubaga and Lacor hospitals; and at private-for-profit hospitals such as Kampala International, Mayanja Memorial, Mbarara Community, Gulu Independent and others. There are many laboratories in private clinics as well as private stand-alone laboratories. In addition to the above, there are also laboratories associated with medical and laboratory training institutions, such as the Department of Medical Microbiology in the School of Biomedical Sciences at Makerere University.

Many of the facilities that were built some decades ago are dilapidated and in need of renovation or upgrading to meet current recommended infrastructural standards. Many lower level facilities have been upgraded to HC-III and IV level in terms of services delivered, but for some, their infrastructural capacity has not been improved. There is widespread lack of reliable sources of utilities such as water and power, and many laboratories lack effective mechanisms for safe waste disposal and infection control (MoH, 2009).

5.5.2 Human resources

Many laboratories do not meet the recommended staffing norms and instead resort to employing unqualified personnel referred to as laboratory attendants and microscopists. These cadres have no formal technical training and are not recognised or registered by the Allied Health Professionals Council. There is widespread dissatisfaction amongst laboratory practitioners with complaints of low pay; lack of respect and recognition by other health care practitioners, poor working conditions and lack career progression and professional development. All these cause low morale, which further compromises the quality of services delivered.

The number of highly specialised practitioners such as pathologists is still very low. Even so, there are limited positions at an appropriate level to absorb highly qualified practitioners. With all the above challenges, many laboratory professionals are leaving the country for better opportunities, further worsening the human resources crisis in the country's health sector (MoH, 2009).

5.5.3 Equipment and supplies

Laboratory supplies and reagents are procured through the Joint Medical Store, National Medical Stores and other sources. Generally, the higher-level facilities are relatively better equipped than lower-level facilities. The non-government sector facilities are usually better equipped and better stocked with reagents and supplies, probably due to multiple supply channels. But for the most part, inventory and procurement systems are too are weak and poorly coordinated to ensure a non-interrupted supply. Many experience regular stock-outs of essential reagents, limiting their ability to carry out basic tests (MoH, 2009).

Many government-aided laboratories lack basic equipment such as microscopes and sterilisers. Some equipment, including some that comes through donations, does not meet required standards owing to lack of an effective system that would ensure compliance to standards before procurement. Equipment in some facilities either lacks skilled users or is not adequately maintained, thus leading to waste of resources. This is usually due to lack of inclusion of maintenance agreements in purchase contracts and the lack of training programs for users in the use and basic maintenance of the equipment (MoH, 2009).

The Alliance for the Prudent Use of Antibiotics APUA (2011) carried out a study in Uganda and Zambia and produced a report in which 29 laboratories in Uganda were surveyed to examine their capacity to reliably provide clinical diagnostics, perform antibiotic sensitivity testing and transmit the data to be used by policy makers for clinical management and decision making. The following aspects of these laboratories were examined: the ability of laboratories to detect pathogens and perform sensitivity testing; availability of a system for quality control; availability of mechanisms for dissemination of laboratory/surveillance data; availability of a system for collection, analysis and transmission of the data to be used for antibiotic management decisions; ability of laboratories to deliver accurate results; and availability and use of the WHONET software for antimicrobial resistance surveillance.

Most surveyed laboratories had qualified staff with diplomas and degrees in their respective fields. Staff training on biosafety, isolation and characterisation of microorganisms, and quality control assurance was generally good in most laboratories, and records of laboratory consumables and tests performed were also well maintained in both countries. However, overall, in both countries, laboratory capacity to conduct sensitivity testing was poor, and only a few facilities were able to provide routine clinical diagnostics and sensitivity testing. The majority of hospital laboratories are not conducting any sensitivity testing and the demand from both clinicians and patients for obtaining cultures from patients seems to be low, because laboratory diagnosis of enteric and acute respiratory pathogens was not a priority.

Table 10 below provides assessment of the laboratories, based on their performance on the survey.

Those laboratories listed under Level I had almost no infrastructure for laboratory diagnosis of the most common acute enteric and respiratory pathogens. These laboratories also showed inadequate staff training in aspects of antibiotic susceptibility testing, lack of authenticated standard operating procedure manuals, lack of equipment and unsatisfactory maintenance of available equipment, unsatisfactory quality assurance and lack of quality reagents and kits used for AST. Even though there was an expectation that some regional and missionary hospitals would do better in terms of the surveyed aspects, this was not always the case. Three hospitals designated as regional referral hospitals (Lira, Masaka, and Arua) in Uganda had low scores, while mission hospitals and some other referral hospitals were better performing.

Laboratories listed under Level II had an average performance in terms of staffing, equipment availability and reagent availability, staff training in diagnosis and antibiotic resistance testing. A relatively small investment could upgrade these laboratories to perform laboratory diagnosis of enteric and respiratory pathogens and the antibiotic susceptibility testing of these pathogens.

Table 9: Assessment scores of Ugandan Microbiology Laboratories

Level I: Score Range 0-49%	Level II: Score Range 50%-74%	Level III : Score Range >75%
Kibuli Hospital	Soroti Hospital	Mbarara Regional Referral Hospital *
Kisubi Hospital	Kuluva Hospital	Kitovu Hospital *
Lira Regional Referral	Masaka Regional Referral Hospital	Mulago National Referral Hospital *
Cure Hospital	Arua Regional Referral hospital	Mengo Hospital *
Jinja Hospital	Lacor Hospital	Mbale Hospital*
	Kiwoko Hospital	International Hospital Kampala *
	Kagando Hospital	Butabika Regional Referral Hospital
	Nsambya Hospital	
	Kitovu Hospital	
	Tororo Hospital	
	Entebbe Hospital	
Kibuli Hospital		
	Gulu Independent Hospital	
	Rubaga Hospital	

**denotes a hospital carrying out antimicrobial sensitivity testing which could be targeted for improvement .*

Source: APUA (2011)

In both countries, there were a limited number of laboratories under Level III that are currently conducting AST, and which with minimal additional investment in equipment, supplies, and training could be improved and strengthened to form a small nucleus of a data collection network. Such data could be used to monitor treatment effectiveness from various locations around each country. Most laboratories also lacked proper networking, and most data from the laboratories was not used to inform policy or to design interventions. Most clinicians were either not aware of, or ignored the potential benefits of using laboratory diagnosis of acute respiratory and enteric pathogens. Despite having or knowing the benefits of using the WHONET software, only two laboratories in Uganda were using it.

One other major issue facing laboratories in both countries was the supply and distribution of laboratory consumables by the National Medical Stores and other commercial suppliers due to irregular demands for laboratory consumables. There are no standard budgets for laboratories in general, and since the supplies required for susceptibility testing are consumables that require continuous resupply, there should be a budget dedicated to this

For the most part, laboratory strengthening efforts have focused on malaria, HIV, and tuberculosis, with little done to improve the diagnosis of pneumonia and other bacterial infections.

Laboratories with the capacity to carry out microbiological investigations including antibiotic sensitivity testing for routine diagnostic work are found in only 8 public hospitals in Uganda. These are too few for a country with a population of over 34 million. Laboratories with similar capacity but which do not engage in routine diagnostic work are found in the Colleges of Health Sciences at Makerere and Mbarara and in the College of Veterinary Medicine, Animal Resources and Biosecurity (CoVAB) at Makerere, as well as at the Central Public Health Laboratory (CPHL) in Kampala. However, although laboratories at CoVAB and at the CPHL also do this type of work, they are constrained in terms of equipment and personnel. There are not enough medical microbiologist specialists because of poor conditions of service in government institutions. This leaves much of the work to be done by technicians who are not adequately trained. For reasons that are not clear, not as many laboratory technologists specialise in medical microbiology as in biochemistry, for example.

Currently, within health facilities under the MoH, the capacity to carry out medical microbiology work is said to be fairly well developed in only six of the 14 Regional Referral Hospitals and in the only National Referral Hospitals at Mulago and Butabika, both in the capital city. The six referral hospitals are those of Arua, Lacor, Mbale, Mbarara, Kabale and Naguru. Hoima and Fort Portal hospitals in the western region of the country are in the process of being upgraded for this purpose.

An attempt to spread the services of these six laboratories to cover the whole country was initiated in 2011 but is facing the challenge of specimen transportation. It is important to

note that each of the regional referral hospitals serve between 10-20 districts. The workload per hospital is, therefore, enormous. A number of faith-based hospitals are said to have good microbiology laboratory services; these include Kagando in Kasese, Kuluva in West Nile, Lacor and St. Joseph's hospitals. Not much is known about privately owned laboratories. Relatively speaking, the discipline of medical microbiology is best developed in the central region of the country leaving most of the rural areas poorly served.

Even among referral facilities there are challenges of competency of staff. For instance, at Mulago National Referral / Teaching Hospital and at Masaka Regional Referral Hospital, Jacob et al. (2009) perceived that services were poor quality and researchers had to hire the services of private laboratories for blood cultures. This speaks volumes about the quality of hospital laboratories not only at the level of regional hospitals but even at the level of the National Referral and Teaching Hospital where most of Uganda's doctors are trained.

Furthermore, it becomes understandable why only 13 of the 154 patients suspected to have septicaemia in the Knaapen (2012/2013) study had blood cultures done. It also explains why, of the 13 blood cultures, results were available to the clinicians in only three instances; and why, of these three, only one gave an ASR.

The challenges faced by the Mulago Hospital microbiology laboratory are further demonstrated by the fact that at the time of the Mukonzo et al. (2013) study on antibiotic dispensing in Uganda, the laboratory was equipped to perform sensitivity tests on only two of the six most commonly dispensed antibiotics reported in their study. Lack of competence in government hospital laboratories also explains why it is that almost all the papers cited in this report have come from the College of Health Sciences, CoVAB of Makerere University, Mbarara University of Sciences and Technology or St. Mary's Hospital Lacor, which is a missionary hospital. Hardly any of the publications cited in this report emanate from work undertaken in government hospital laboratories. There are only two papers on work carried out in the Mulago Hospital medical microbiology laboratory: Arya and Phillips (1970) and Mpairwe (1972), and these were written over 40 years ago.

Microbiology laboratories in public health institutions in Uganda are currently limited to employing no higher than diploma holders, although training institutions are producing degree holders. This limitation should be lifted, as the diploma holders are not sufficiently trained to handle microbiological investigations with the desired standard of competence that includes isolating organisms and determining their antibiotic sensitivities. It has not been possible to determine the number of private laboratories with the capacity to undertake microbiology studies in this country, nor to assess the quality of their work.

5.6 Lack of information

Lack of laboratory capacity invariably leads to a lack of knowledge about antibiotic susceptibility patterns of the pathogens; and lack of knowledge leads to prescriptions being largely empirical. Lack or inadequacy of information permits the continued prescription

of antibiotics that have long ceased to be effective as a result of acquired resistance of pathogens. This has the effect of sustaining antibiotic pressure on the pathogens, which in turn maintains or accelerates antimicrobial resistance. One of the consequences of lack of information is the practice of polypharmacy.

5.7 Patient influence on prescribers

While no published studies on patient influence on prescribers in Uganda were identified, it is widely believed that paying patients influence their health service providers to prescribe antibiotics more than is necessary.

5.8 Accelerators of antibiotic resistance

Many publications, for example Okeke, Lamikanra, and Edelman (1999), Byarugaba (2004), A Sosa, Najjuka, and Mwenya (2011) and A Sosa et al. (2010), have been written about the drivers of antibiotic resistance in developing countries. The term "*accelerators*" rather than "*drivers*" is probably a better choice because, according to present day knowledge, acquired antibiotic resistance is an inevitable consequence of antibiotic use. In the case of antibiotics, the organisms against which antibiotics work develop or acquire resistance to them. It is the rate at which antibiotics lose effectiveness that can and should be controlled for the benefit of mankind. The rate at which they get blunted depends on how they are used. The manner in which they are used depends on a mutually enhancing interplay of availability (or relative lack thereof) of three important factors:

- Economic power,
- Knowledge, and
- Information.

5.8.1 Lack of adequate economic power

As pointed out in Section 2.2, Uganda is the poorest of the East African countries and is likely to remain so for some time to come. Poor nutrition and overcrowded conditions result in increased levels of respiratory infections; and limited access to clean water contributes to higher rates of diarrhoeal diseases. Because of the relatively small number of hospitals, most are overcrowded and practices such as the sharing of beds or admission of floor cases increases the rate of hospital-acquired infections, antibiotic usage and potentially contributes to increased antibiotic resistance. Health facilities are poorly equipped and lack staff. The lack of high quality laboratories limits hospital capacity to isolate and test for antibiotic susceptibility of pathogens. Newer and more efficacious antibiotics are unaffordable for most patients. Because of the inadequacy of laboratory facilities, healthcare providers largely depend on empirical prescriptions. In short, poverty contributes to the antibiotic resistance burden through a number of routes.

One of the most challenging consequences of poverty is the presence of corruption and the misuse of public resources. According to a report (Transparency, 2012) posted on 30 August 2012, Uganda is the most corrupt nation among the East African countries, followed by Tanzania, Kenya, Burundi and Rwanda. The areas singled out where corruption was most rife included the health sector. Inadequacy of political will to fight corruption and poor remuneration of civil servants were cited as factors hampering efforts to combat corruption in Uganda. Corruption interferes with the enforcement of regulations and in conjunction with a lack of knowledge on the part of the public and some professionals, it leads to over-the-counter access to antibiotics and self-medication.

5.8.2 Lack of knowledge

The majority of Ugandans know that antibiotics cure within hours, days or, at the latest, weeks. Public perception is that antibiotics, or any antibiotic, can cure any fever, headache or almost any physical ailment such as pain. As far as public knowledge goes, there is an antibiotic for every malady. The vast majority of the public does not know how antibiotics work and, least of all that resistance against antibiotics develops.

Health professionals, including medical practitioners, dental surgeons, veterinary surgeons, clinical officers, nurses, and midwives, may also lack knowledge of the drivers of antibiotic resistance. In a recent publication (Kamulegeya, William, & Rwenyonyi, 2011) on an undated study carried out on 140 dental health-care givers, of whom 53 % were public health dental officers and 47% dental surgeons, knowledge on indications for culture and sensitivity testing was inadequate in 40% of respondents while in 26% it was totally absent. Nearly all (99%) could not state the right guidelines in deciding which effective antibiotics to prescribe.

It is likely that similar gaps in knowledge exist in all of the cadres of health professionals permitted by law to prescribe antibiotics, although no studies have been found on this topic in their case. Besides the legally authorised prescribers, there are others who prescribe illegally and in whom appropriate knowledge may even be lower. These include pharmacists, operators of drug shops, herbalists, untrained practitioners, and self-medicating patients as well as those in the agricultural sector including farm managers, veterinary assistants, animal husbandry officers, farmers and manufacturers of animal feeds, all of whom prescribe antibiotics and may administer them.

5.8.3 Discrepancy between knowledge and practice

Discrepancy between knowledge and practice is commonly encountered in many situations in human conduct including antibiotic use. It is one thing to know what to do, and another to do it. Many poultry farmers in the Sasanya et al. (2005) study were aware of the need and importance of observing the withdrawal period after the use of antibiotics in their birds prior to sale of eggs to the market, but chose not to. Among 721 students at Makerere University, Kampala, studied by Nambatya et al. (2011), of those who knew that it was

incorrect not to finish a prescribed course of antibiotics, 74% of those taking health science courses and 62% of those taking other courses of study reported that they did not complete their respective courses of antibiotics prescribed during their last bouts of infections. In the study on self-medication carried out by Ocan, Bbosa, Waako, Ogwal-Okeng, and Obua (2014) and Ocan, Bwanga, et al. (2014), a high proportion (76%) of respondents were aware of a number of disadvantages of self-medication, such as taking of the wrong medicine for the illness at hand, resulting in the waste of money (42%), promotion of drug resistance (33%) and masking of symptoms of underlying disease (16%). Possession of this knowledge, however, did not prevent them from engaging in self-medication. Many patients also practice self-medication.

5.8.4 Self-medication

Self-medication does away with what, to many, is the unnecessary or unaffordable burden of having to spend time and money receiving medical care. Patients may think they know how to self-medicate from having read about treatment from an insert of a previously prescribed medicine or from the internet. In poor countries, self-medicating saves the client the burden of the medical consultation fee.

It is no wonder, therefore, that self-medication is practiced even in developed countries such as the United Kingdom (McNulty, Boyle, Nichols, Clappison, and Davey (2006) and Italy (Napolitano, Izzo, Di Giuseppe, & Angelillo, 2013).

In Uganda, according to Nambatya et al. (2011), antibiotic self-medication was practiced among 65% of 721 sample students at Makerere University, Kampala. It was more prevalent (85%) among students taking courses in the College of Health Sciences as compared to other students (63%). The most common antibiotics used as single drugs in self-medication were amoxicillin, by 21% of the respondents, metronidazole by 8% and co-trimoxazole by 6%.

In a study carried out in northern Uganda in November and December, 2012 (Ocan, Bbosa, et al., 2014; Ocan, Bwanga, et al., 2014) it was shown that self-medication was practised by 76% of 313 respondents. In this study it was also observed that the most commonly self-prescribed antibiotics were similar to those observed by Nambatya et al. (2011) in the study cited above.

In the study by Odongo, Anywar, Luryamamoi, and Odongo (2013), 72% of 69 patients who had taken antibiotics before coming to the hospital with urinary tract infections had done so through self-medication.

5.8.5 Lack of an official policy on antimicrobial resistance surveillance and monitoring

The MoH is aware that the level of antimicrobial resistance in the country is high and is increasing further, but there are no national provisions for monitoring this trend apart from

those that monitor resistance to antiretrovirals, antimalarials and first line anti-TB drugs (isoniazid, rifampicin, ethambutol and pyrazinamide). Monitoring for these drugs is carried out by the AIDS Control Programme, the Malaria Control Programme and the National TB and Leprosy Programme, respectively. The results of this monitoring constitute the basis for the recommendations to health practitioners contained in the *Uganda Clinical Guidelines* in the management of those conditions.

An opinion was expressed in the MoH that controlling the problem of escalating antimicrobial resistance will require effectively regulating prescribers, minimising importation of substandard antimicrobials, controlling self-medication and minimising activities of unlicensed practitioners (Amandua, 2014). However, no concrete mechanisms were indicated as to how these would be implemented.

5.8.6 Dormancy of some legal provisions on antibiotic usage

There are two statutory bodies in Uganda that are mandated to handle issues related to drugs. These bodies are the National Drug Authority (NDA) and the National Medical Stores (NMS).

5.8.6.1 National Drug Policy

a) Policy Provisions

The national drug policy, as outlined in the NDA Statute 1993, aims, amongst other things, to:

- Ensure that essential, safe, efficacious and cost-effective drugs are made available to the entire population of Uganda to provide satisfactory health care;
- Make a continuous review of the needs, knowledge and resources of essential drugs;
- Promote the rational use of drugs both in the public and private sector; and
- Provide systematic public information and professional training and retraining of health workers.

In Part III, which deals with control of the drug supply, the NDA Act stipulates that there shall be a national list of essential drugs which shall be revised from time to time.

In the Second Schedule, the Act places antibiotics in Group I of Class B drugs or controlled drugs. In Section 20 of this Act, the need for prescription for classified drugs is defined as follows:

- A pharmacist or licensed person shall not supply a class A or class B Group I drug unless it is under prescription reasonably believed by the person supplying the drug to be valid; and

- A prescription shall be valid only if it is in indelible writing, dated and signed with the usual signature of a registered medical practitioner, dentist or veterinary surgeon.

b) Functionality of the provisions of the NDA Act

Uganda has an appropriate regulatory framework for proper acquisition, evaluation of quality, equitable distribution and prescription of antimicrobials.

Further, it was noted that the NDA takes measures to monitor illegal dealers in antimicrobials through licensing, regular inspection and skip testing of medicine samples picked from these outlets. It was also noted that NDA is strict on "compliance to current good manufacturing practices".

There is evidence that the NDA is making an effort to ensure that poor quality antibiotics are weeded from the country. For example, on June 25, 2012, the National Drug Authority suspended medicines manufactured by an Indian company, Flamingo Pharmaceuticals Limited, for low standards of manufacturing practice. Fifty percent of these were antibiotics (Ssendagire, 2012).

The NDA regulates medicines imported into the country. Regulations for registration of medicines & import control are available and are being implemented. It is only possible to import medicine into the country after obtaining a verification certificate which is only secured after submitting a proforma invoice reflecting the quantity and price of the medicines.

While there is evidence that the National Drug Authority is exerting effort towards maintaining quality of antibiotics imported into the country, it was not possible to establish whether the NDA has all the resources required to fully contain the entire problem of substandard antibiotics and/or other drugs imported into the country from the sources in Asia, the Middle East, Europe and elsewhere.

5.8.7 Illegal prescribers

According to the Second Schedule in the NDA Act, the only legally qualified prescribers of antibiotics are registered medical practitioners, dentists and veterinary surgeons. However, information from the Ministry of Health indicates that this list now includes clinical officers and midwives.

Nonetheless, it is common knowledge that others can and do prescribe antibiotics in spite of the law. These include pharmacists and other operators of community pharmacies under whose charge over-the-counter dispensing and self-prescription of antibiotics takes place (Mukonzo et al., 2013). It also includes farm managers, veterinary assistants, animal husbandry officers, farmers as well as animal feed makers who act without supervision of veterinary surgeons.

VI ANTIBIOTIC RESISTANCE IN UGANDA

6.1 Antibiotic Resistance

The story of the development of modern antimicrobial agents, starting with the discovery of Prontosil, by Paul Domagk in 1935 from which sulphonamides were developed, followed by the introduction of penicillin in 1940 developed by Howard Walter Florey and Ernst Boris Chain from the discoveries of Alexander Fleming in 1929, has been told time and again. Absence of records makes it impossible to pinpoint when antibiotics were first introduced into Uganda or the sequence of their introduction. An elderly Ugandan medical practitioner who was born before antibiotics were clinically used anywhere in the world (Mpairwe, 2014) recalled that the first antibacterial agents to be introduced into the country were the sulphonamides. Sulphathiazole was introduced in the late 1940s and was shortly followed by other sulphonamides of which the most important was sulphadimidine.

In subsequent years other antibacterial agents were introduced, mainly to address the emerging bacterial resistance to earlier agents as shown in Table 11 below.

Table 10: Approximate year of introduction of different antibiotics into Uganda

Antibiotic agent	Estimated year of first use in Uganda	Major impact of the antibiotics
Sulphonamides	Late 1940s	Prevalence of tropical ulcers and gonococcal urethral strictures went down; yaws eliminated.
penicillin G streptomycin	Late 1940s or early 1950s	
chloramphenicol, tetracycline, neomycin, nitrofurantoin, metronidazole	Mid 1950s	Reduction of mortality due to enteric fevers, septicaemias and UTIs.
ampicillin, co-trimoxazole erythromycin, gentamicin	1960s	
Tobramycin rifampicin	1980s	Management of gonorrhea and tuberculosis, which had grown resistant to earlier drugs.
cephalosporins, fluoroquinolones	1990s	Management of bacterial resistance to earlier drugs.
vancomycin, oleandomycin, imipenem, linezolid, teicoplanin daptomycin and other newer antibiotics	2000s	

Source: Authors

Summary:

Uganda, like the rest of the world, has introduced successive generations of antibiotics at different times since the 1940s, mainly to deal with declining efficacy in preceding generations of antibiotics due to increasing microbial resistance in the course of their use.

Antibiotics, in conjunction with antimalarials, contributed significantly in bringing about the rise of the Ugandan population from 4 million to nearly 35 million in the last seven decades.

6.2 Resistance of *Streptococcus pneumoniae*

A study of 115 nasopharyngeal isolates of *S. pneumoniae* from children who were attending hospital for immunisation or routine checkups, during the months of June and July 1995, aged one week to three years (Joloba, Bajaksouzian, Palavecino, Whalen, & Jacobs, 2001) revealed that 84% were resistant to co-trimoxazole. Resistance to tetracycline was expressed by 29% and to chloramphenicol by 10%, while 84% had intermediate resistance to penicillin. However, all isolates were susceptible to rifampicin, erythromycin, cefotaxime and clindamycin.

In a study conducted between December 2001 and May 2002 by Kateete, Kajumbula, Kaddu-Mulindwa, and Ssevviri (2012), all of 27 *S. pneumoniae* isolates from throats of 81 children with the sickle cell disease in Mulago National Referral Hospital were resistant to penicillin and 96% were resistant to co-trimoxazole. Resistance to other tested antibiotics - chloramphenicol, erythromycin, rifampicin, ceftriaxone and pefloxacin - was less than 15 %.

Among 30 Mulago Hospital *S. pneumoniae* meningeal isolates from pediatric cases between 2001 and 2006 studied by Kisakye et al. (2009), all isolates were susceptible to cefotaxime and 3% were resistant to chloramphenicol. Intermediate resistance was expressed by 83% to penicillin and by 30% to amoxicillin. The findings in these papers are summarised in Table 12.

Table 11: Percentage of antibiotic resistance of S. pneumoniae between 1995 and 2006

Antibiotic	Joloba M.L. (2001) work done in 1995 (n=115)	Kateete D.P. *et al.* (2012) work done in 2001/2002 (n=27)	Kisakye A. *et al.* (2009) work done in 2001/06 (n=30)
Penicillin	83.5*	100	83*
Co-trimoxazole	83.5	96	
Tetracycline	28.7		
Chloramphenicol	10.4	3	3
Amoxicillin			30*
Rifampicin	0	0	
Erythromycin	0	3	
Ceftriaxone		0	
Cefotaxime	0		0
Clindamycin	0		
Pefloxacin		0	

**intermediate resistance Source: Authors*

Summary

Prevalence of resistance of *S. pneumoniae* to older antibiotics penicillin and co-trimoxazole is high, between 83 and 100%, even though resistance may be partial in the case of penicillin. Prevalence of resistance to newer antibiotics such as rifampicin, erythromycin and cefotaxime is low and lies between 0 and 3%. Despite being an older antibiotic, chloramphenicol is still fairly effective against *S. pneumoniae,* with resistance to it expressed by between 3 and 11% of isolates.

6.3 Resistance of *Staphylococcus aureus* and other Staphylococci

In a study (Mpairwe, 1997) carried out at Naguru Medical Laboratory (a private laboratory in Kampala) between July and December 1996 on between 90 and 448 isolates of *S. aureus* from septic lesions in major hospitals in Kampala and Entebbe in the central region of Uganda, resistance to the various antibiotics tested was as indicated in Table 12 below:

Table 12: Resistance pattern of S. aureus isolates from various lesions

Antibiotic tested	No. of isolates tested	% Resistant
Penicillin G	434	93
Ampicillin	355	90
Tetracycline	397	57
Co-trimoxazole	309	40
Erythromycin	443	12
Streptomycin	425	10
Flucloxacillin	388	7
Gentamicin	448	4
Fucidin	413	4
Chloramphenicol	396	4
Ceftazidime	199	2
Cefuroxime	218	2
Augmentin	398	1
Ciprofloxacin	90	0
Pefloxacin	143	0

Source: (Mpairwe, 1997)

The prevalence of resistant *S. aureus* against the four most commonly used antibiotics, penicillin G, ampicillin, tetracycline and co-trimoxazole, was between 40% and 93%.

A subsequent study (Mpairwe, 1998) compared the sensitivity of isolates in the above study with that of isolates from rural hospitals lying between 40 and 300 kilometres from Kampala, namely Gombe, Kalisizo, Itojo, Kamuli and Kitagata to penicillin G, ampicillin, tetracycline and co-trimoxazole. It was found that among isolates in rural health units, prevalence of resistance tended to be lower by between 10% and 20% than it had been found for Kampala and Entebbe isolates except for tetracycline resistance to Gram-positives and penicillin G against Gram-negatives, where there was no difference between the rural and urban isolates.

Five to seven years later, Anguzu and Olila (2007), in a study on isolates from septic wounds of 94 patients in Jinja Regional Referral Hospital in eastern Uganda, conducted between February and April 2003, found the prevalence of *S. aureus* resistance was as follows: to gentamicin 13%, to ciprofloxacin 31%, to erythromycin 56% and to ampicillin 97%.

Another six to seven years later, Kateete et al. (2011) studied the antibiotic sensitivity pattern of 41 *S. aureus* isolates from 13 patients in two burns units as well as from 13 health workers and 15 environmental sites in Mulago Hospital, Kampala, isolated between November, 2009 and February, 2010. All (100%) of them were MRSA and 63% were multiple drug resistant, mostly to beta lactams, co-trimoxazole and tetracycline. Resistance to co-trimoxazole was expressed by 93% of patients, 68% of health workers and 66% of environment isolates,

respectively. Prevalence of resistance to erythromycin was 29%, to gentamicin 20% and to chloramphenicol 20%. All the isolates were sensitive to vancomycin.

In a study conducted during an unstated period but published in 2011, Kitara et al. (2011) isolated 66 strains of *S. aureus* from a total of 122 inpatients and outpatients with various pyogenic closed and open lesions in Lacor Hospital, Gulu District, northern Uganda. Their resistance to the eight antibiotics tested was as follows: to ampicillin 75%, co-trimoxazole 50%, tetracycline 45%, chloramphenicol 34%, erythromycin 8%, ciprofloxacin 2%, methicillin 2% and gentamicin 0%.

In a study of 9 *S. aureus* isolates from urine by Mwaka, Mayanja-Kizza, Kigonya, and Kaddu-Mulindwa (2011), the resistance pattern was found to be: to nitrofurantoin 0%, amoxiclav 0%, cefuroxime 6%, gentamicin 32%, ciprofloxacin 32%, ampicillin 42.%, nalidixic acid 53% and co-trimoxazole 65%.

In a more recent study (Iramiot et al., 2014) carried out between June 2012 and June 2013 at Mbarara University of Science and Technology in western Uganda, 300 isolates of *S. aureus* were obtained from diverse clinical specimens. The prevalence of resistance to various antibiotics was: to co-trimoxazole 70%, imipenem 16%, fucidic acid 4% and to clindamycin 0.01%. The only antibiotics in this study against which *S. aureus* isolates were not resistant at all were vancomycin and linezolid.

A methicillin resistance prevalence rate of 64% was found by Kalule et al. (2014) among 85 *S. aureus* strains isolated from the noses of pigs and vervet monkeys in Luweero and Wakiso districts of central Uganda. They also found resistance rates of 90% to co-trimoxazole, 38% to erythromycin, 12% to clindamycin and 2% to gentamicin. Multiple drug resistance (mostly to methicillin-erythromycin-co-trimoxazole) was encountered among 73% of the isolates.

Kajumbula (2014b) compiled data from the routine laboratory of Makerere University College of Health Sciences. From one of his histograms, resistance of the 33 strains of *S. aureus* he analyzed was expressed approximately as follows: to co-trimoxazole 98%, to tetracycline 78%, to erythromycin 70%, to ciprofloxacin 50%, to oxacillin 48%, to chloramphenicol 40%, to clindamycin 40%, to gentamicin 30% and to vancomycin 4%.

Ssennoga (2014) analysed 100 *S. aureus* isolates from archived materials in the Department of Medical Microbiology, College of Health Sciences of Makerere University collected from May 2014 to August 2014. Of these, 90 isolates were from community specimens and 10 from hospital sourced specimens. Among hospital isolates, the prevalence of resistance to tetracycline, erythromycin, daptomycin and ciprofloxacin was between 40% and 100% while resistance to gentamicin, clindamycin, vancomycin and linezolid was between 0% and 20%. Among community isolates, prevalence of resistance to daptomycin, erythromycin

and tetracycline was between 40% and 60%, while resistance to gentamicin, clindamycin, vancomycin and linezolid was below 20%.

Furthermore, Bazira et al. (2014) analyzed results from 36,080 various clinical specimens cultured at Mbarara Regional Referral Hospital microbiology laboratory in the 10 year period from 2003 to 2012. From these specimens, a total of 7,744 isolates were obtained, of which 48% were *S. aureus*. Over 80% of the *S. aureus* isolates expressed resistance to penicillin, tetracycline and co-trimoxazole. Between 25 and 80% expressed resistance to amoxicillin, cloxacillin, chloramphenicol and erythromycin. Among the tested antibiotics it was only against gentamicin and ceftriaxone that resistance was expressed by 25% or less of the isolates. They observed that since 2010, there has been a noticeable decrease of S. *aureus* resistance against penicillin and amoxicillin. They attributed this to the recent trend of clinicians preferring to prescribe ceftriaxone and gentamicin, to which resistance of *S. aureus* has risen since 2010.

6.3.1 Antimicrobial resistance of staphylococcal isolates in bovine mastitis

The pattern of antibiotic resistance of staphylococcal isolates from bovine mastitis (clinical and subclinical) isolated by Byarugaba et al. (2008) at the beginning of the last decade in the Jinja area is indicated in the following table [Modified from (Byarugaba et al., 2008)].

Table 13: Antimicrobial resistance of staphylococcal isolates from milk in subclinical mastitis

Antibiotic	N(91)	% Resistant
Penicillin	79	87
Tetracycline	70	77
Erythromycin	63	69
Ampicillin	54	59
Amoxicillin	37	41
Oxacillin	27	30
Co-trimoxazole	15	17
Gentamicin	3	3

Source: (Byarugaba et al., 2008)

Between February 2010 and end of March 2011, non-coagulase staphylococci and other organisms displaying high levels of resistance to antibiotics were found by Kateete et al. (2013) in a study on isolates from 97 milk samples from cows with clinical mastitis and from nasal swabs of 31 Kampala herdsmen. Of the 58 Gram-positive isolates from the milk, one was *S. aureus* and 20 were staphylococci of other species. There were 16 enterococci, 13 streptococci and eight cocci of other genera. There were 24 isolates of Gram-negative bacilli, 12 of which were *E. coli.*

From the nasal swabs of the 31 milkmen, 24 isolates were made and all were Gram-positives - 11 were staphylococci and four were *S. aureus,* while seven were other species of *Staphylococcus*. There were eight enterococci and five organisms of other species.

All of the 21 bovine staphylococcal isolates were resistant to penicillin G and ampicillin. However, all were sensitive to gentamicin as well as to the relatively newer antibiotics - daptomycin, ciprofloxacin, mupirocin, moxifloxacin and linezolid. The one *S. aureus* isolate was also sensitive to methicillin.

Of the coagulase negative staphylococcal isolates, 57% were methicillin resistant and a similar percentage were resistant to cefoxitin. The prevalence of resistance among these staphylococci was: to amoxicillin-clavulanate 52%, tetracycline 33% and to co-trimoxazole 29%.

Resistance to rifampicin was expressed by 10% of the bovine staphylococci. Two staphylococcal isolates were multi-drug resistant to vancomycin, methicillin and rifampicin.

All the 11 human staphylococcal isolates from milkmen were resistant to penicillin G and ampicillin. Three were resistant to ciprofloxacin as well. All 11 were susceptible to gentamicin and rifampicin as well as the newer antibiotics - daptomycin, mupirocin, moxifloxacin and linezolid.

Four of these were resistant to co-trimoxazole and tetracycline but were sensitive to cefoxitin and methicillin. Seven (64%) of the human coagulase negative Staphylococci were multi-drug resistant - to amoxicillin-clavulanate, tetracycline, cefoxitin and methicillin. Vancomycin resistance was expressed by only one staphylococcal isolate.

Between August and November 2012, Kasozi et al. (2014) isolated 163 organisms from milk in cows with SCM in the Kiboga area. Over sixty percent (64%) of these were CNS. Twenty-seven (17%) were *S. aureus*, 9.2 streptococci, 6% *Corynebacterium* species and 4% coliforms. Of the 27 *S. aureus* strains, 100% were resistant to penicillin, 85% to neomycin, 71% to tetracycline, 43% to streptomycin and 29% to gentamicin. Surprisingly, none was resistant to co-trimoxazole.

6.3.2 Methicillin-resistant *Staphylococcus aureus* (MRSA)

In a study of surgical site infections carried out between February and May 2007 on 188 patients in Mulago National Referral Hospital by Ojulong et al. (2008), 32% of 54 isolates of *S. aureus* were MRSA. Kitara et al. (2011) found MRSA prevalence to be 2% among 66 *S. aureus* strains isolated in Lacor Hospital, Gulu. In a study by Seni, Bwanga, et al. (2013) carried out at Mulago hospital, 38% of 64 isolates of *S. aureus* from 314 patients investigated during September 2011 to April 2012 were found to be MRSA. In addition, the

Iramiot et al. (2014) study at Mbarara University of Science and Technology showed that of the 114 *S. aureus* isolates, 38% were methicillin resistant. Kalule et al. (2014) reported a MRSA prevalence of 64% among 85 pigs and vervet monkeys in Wakiso and Luweero districts and 48% prevalence rate or resistance to oxacillin in the Kajumbula (2014a) series of 33 isolates at Mulago.

Table 14 presents a summary of the findings from the above cited publications about the sensitivity patterns of *S. aureus* isolates from pyogenic lesions and other sites in various places and at different times in the last 18 years in Uganda.

Table 14: Documented resistance pattern of S. aureus isolates

Antibiotic Tested	% resistant *S. aureus* isolates in different studies										
	Mpairwe (1997)Kampala - Entebbe	Anguzu and Olila (2007) Jinja	Kateete et al. (2011) Mulago	Mwaka et al. (2011)	Kitara et al. (2011) Lacor, northern Uganda	Iramiot et al. (2014) Mbarara, western Uganda	Kalule et al. (2014)Luweero/ Wakiso , central Uganda	Kajumbula (2014a) Microbiol. MUCHS	Ssennoga (2014) hospital	Ssennoga (2014) community	Kasozi et al. (2014)
Penicillin G	93.3							95			100
Ampicillin	89.6	97		42.1	75						
Tetracycline	57.2				45.3			78	50	48.9	71.4
Co-trimoxazole	39.5		93	64.7	50	70.18	90	95			0
Erythromycin	12.4	56.2	29		7.8		38	72	100	61.1	
Streptomycin	10.4										42.6
Flucloxacillin	7.2										
Gentamicin	4.2	12.5	20	31.6	0		2	24	20	16.7	28.6
Fucidin	3.6					4.39					
Chloramphenicol	3.5		20		34.4			40			
Nitrofurantoin				0							
Ceftazidime	2										
Amoxiclav				0							
Cefuroxime	1.8			5.6							
Augmentin	1										
Nalidixic Acid				52.6							
Ciprofloxacin	0	31.3		31.6	1.6			48	40	17.8	
Pefloxacin	0										
Methicillin		25	100		1.6	38					
Oxacillin								56			
Imipenem						15.79					
Clindamycin						0.01	12	38	10	2.2	
Vancomycin			0			0		4	0	0	
Linezolid						0			0	0	
Daptomycin									70	41	
Neomycin											85

Source: Authors

Summary of resistance patterns of *S. aureus*

Although various investigators tested susceptibilities of *S. aureus* from various sources using unequal sets of antibiotics, and although the majority of the studies were carried out in Kampala at different times and possibly using different methods, the following generalisations can be drawn for the entire period of 18 years. It is important to note that there is a high likelihood that the high prevalence of MRSA reported in these studies is due to the differences in the methodologies for sampling and MRSA screening that could have been used by the different investigators.

1. Resistance to penicillin G, ampicillin, tetracycline and co-trimoxazole was 40-100%.
2. Prevalence of resistance to erythromycin is currently 8-72%.
3. Resistance to ciprofloxacin is 2-48%.
4. Gentamicin resistance is up to 30%.
5. Resistance to fucidin is still below 5%.
6. Resistance to vancomycin is less than 5%.
7. With the exception of co-trimoxazole and chloramphenicol, prevalence of resistance for rural isolates tends to be lower than that for urban isolates.
8. Prevalence of methicillin resistance is 25-40%, although it may be lower than 2% in some rural areas and as high as 100% in some wards of certain urban hospitals, possibly due to clonal spread.
9. Gentamicin or chloramphenicol is the most effective of the relatively low priced antibiotics.

6.4 Resistance of Neisseria gonorrhoeae

Not much has been published about the resistance pattern of *N. gonorrhoeae* in Uganda.

In a study carried out on 237 male students of Makerere University (Arya & Phillips, 1970) that presented to the sickbay with urethritis from March to December 1968, a diagnosis of gonococcal urethritis was made in 242 instances. Eighty percent (80%) of the isolates showed diminished sensitivity to penicillin, which was almost always associated with diminished sensitivity to tetracycline and complete resistance to streptomycin. Nevertheless, 2-2.45 mega units of penicillin or 4-5g of tetracycline cured 94% of the patients.

In a study of 151 *N. gonorrhoeae* isolates from patients attending St. Mary's Hospital, Lacor, in northern Uganda, from January 2007 to December 2011 (Amito Florence, Otim, Okongo, Ogwang, & Greco, 2012), the prevalence of resistance to antibiotics was found

to be: to ampicillin 23%, ciprofloxacin 23%, erythromycin 17%, tetracycline 17%, to chloramphenicol 16%, gentamicin 6% and cefotaxime 2%. While prevalence of gonococcal resistance to other antibiotics tested was more or less stable throughout the five year period of this study, the prevalence of resistance to ciprofloxacin rose steadily from 5% at the beginning of the study to 23% at the end.

On the other hand, a study (Vandepitte et al., 2014) on 148 *N. gonorrhoeae* strains isolated from sex workers in Kampala revealed resistance of the organism to tetracycline in 97%, to ciprofloxacin in 83%, to penicillin in 68%, to azithromycin in 3% and to cefixime in 0.7%. However, all isolates were susceptible to ceftriaxone and spectinomycin.

The only two drugs to which *N. gonorrhoeae* is not known to be resistant in Uganda are ceftriaxone and spectinomycin.

6.5 Resistance of enterococci

In the Mpairwe (1997) study, the resistance pattern of enterococci *S. faecalis,* indicated that the percentage of resistance was highest, as expected, against streptomycin (75%), followed by co-trimoxazole (62%), while no strains were resistant to pefloxacin or ciprofloxacin. Resistance to augmentin, fucidin, ampicillin, penicillin G and chloramphenicol lay between 3% and 23%. Other details are indicated in Table 15 below.

Byarugaba, Kisame, and Olet (2011) investigated antibiotic resistance in 387 enterococcal isolates from faecal samples of various food animals collected over a six-month period in 2008. The antibiotics tested were gentamicin, erythromycin, tetracycline, chloramphenicol, ciprofloxacin, co-trimoxazole, penicillin G and ampicillin. Resistance was expressed by between 35% and 65% of the isolates to all antibiotics except against penicillin G and ampicillin, to which resistance was expressed by 22% and 14%, respectively. Multi-drug resistance, sometimes of up to seven antibiotics, was expressed by 60% of the isolates.

In a study of bacterial isolates from 97 milk samples from cows with clinical mastitis and from nasal swabs of 31 herdsmen, carried out between February 2010 and March 2011 (Kateete et al., 2013), the prevalence of resistance among the 16 enterococci isolates of bovine origin was as follows: to tetracycline 31%, vancomycin 19%, teicoplanin 13%, erythromycin 19%, daptomycin 6% and ciprofloxacin 6%; all were susceptible to ampicillin. Thirteen percent (13%) of the eight enterococci from humans were resistant to erythromycin but all the eight were susceptible to ampicillin, daptomycin, teicoplanin, vancomycin and moxifloxacin.

Of 100 enterococcal isolates from stool, urine, sputum, blood, ear swabs and pus from patients in Mulago Hospital between November 2011 and April 2012, Kigozi (2012) found that 40% were resistant to ampicillin, 41% expressed high level resistance to streptomycin and 36% expressed high level resistance to gentamicin. Over thirty percent (33%) expressed full resistance to vancomycin. Nearly half (48%) were fully resistant to ciprofloxacin.

Among the 53 isolates with intermediate or full resistance to vancomycin, co-resistance with streptomycin was expressed by 43%; 32% with gentamicin and 51% with ampicillin. Among 40 isolates with resistance to ampicillin, 53% exhibited co-resistance to streptomycin, 45% to gentamicin and 83% to ciprofloxacin. Of the 77 isolates with intermediate or full resistance to ciprofloxacin, 35% had co-resistance with gentamicin and 39% with streptomycin.

In a study by Seni, Najjuka, et al. (2013), out of 23 enterococci isolates from Surgical Site Infections, only one (4%) was resistant to vancomycin.

Table 15 summarizes the resistance pattern of enterococci in papers published in the years 1996-2012.

Table 15: Antibiotic resistance pattern of enterococci

Antibiotic	**Mpairwe (1997)** isolates collected in 1996	**Byarugaba et al. (2011)** isolates collected 2008	**Kateete et al. (2013)** isolates collected between 2010 and 2011		**Kigozi (2012)** isolates collected in 2011	**Mwaka et al. (2011)** isolation dates not stated	Seni, Najjuka, et al. (2013) isolates collected 2011 - 2012
	Human n=(17 – 73)	**Various animals n=387**	**Bovine n=16**	**Human n=8**	**Human n=100**	**Human Urinary n=8**	**Human n=23**
Ciprofloxacin	0.0	37.6	6		48	87.5	
Pefloxacin	0.0						
Nalidixic Acid						100	
Augmentin	3.0						
Fucidin	5.9						
Ampicillin	7.9	14	0	0	40	12.5	
Penicillin G	17.6	22					
Chloramphenicol	23.3	37.6					
Erythromycin	23.9	60.5	19	13			
Gentamicin	27.4	63.4			36*	62.5	
Cefuroxime	42.6					100	
FluCloxacillin	50.9						
Tetracycline	56.9	46.8	31				
Ceftazidime	59.2						
Co-trimoxazole	61.7	36.4				71.4	
Streptomycin	75.0				41*		
Nitrofurantoin						0	
Amoxiclav						0	
Vancomycin			19	0	33		4.4
Teicoplanin			13	0			
Daptomycin			6	0			
Moxifloxacin				0			

*high-level resistance **Source: Authors**

Summary: Publications on enterococcal resistance are too staggered in character to yield a dependable basis for generalisation, but the trend is that prevalence of resistance has gone up over the last 15 years. Resistance to ciprofloxacin appears to have risen sharply from 0% in 1996 to over 80% in 2011 (assuming the (Mwaka et al., 2011) date of publication was close to that of his study).

6.6 Antibacterial resistance of *Salmonella* Typhi and non-typhoidal salmonellae

In an unpublished study at Naguru Medical Laboratory between May 1995 and November 2000 (Mpairwe, 2000), the resistance pattern of *Salmonella* isolates from clinical specimens (including *Salmonella* Typhi) was found to be as indicated in Table 16:

Table 16: Resistance pattern of Salmonella isolates

Antibiotic	No. of isolates tested	% resistant
Co-trimoxazole	48	79
Ampicillin	46	63
Tetracycline	60	45
Chloramphenicol	65	2
Gentamicin	46	0
Pefloxacin	12	0
Norfloxacin	15	0

Source: (Mpairwe, 2000)

A study by Mahero et al. (2013) was carried out on *Salmonella* isolates obtained from clinical cases during the period from 2003 to 2008 from 72 areas around Uganda. Some isolates were from humans and some from cattle. The isolates were archived samples and were acquired from the Department of Microbiology, Faculty of Veterinary Medicine, Makerere University but their areas of origin in Uganda were not stated.

The susceptibility of the isolates was tested against amikacin, amoxicillin/clavulanic acid, ampicillin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline and co-trimoxazole

The isolates exhibited high prevalence rates of resistance to sulfisoxazole (86%), trimethoprim (76%), chloramphenicol (74%), streptomycin (67%), ampicillin (67%) and tetracycline (57%). The lowest rates of resistance among isolates (17%) were observed against kanamycin, ceftriaxone and amikacin among cattle isolates and all human isolates were completely sensitive to amikacin.

Resistance was slightly (1 to 3 times) more prevalent among human isolates for older antibiotics, except ampicillin, than it was in cattle isolates, but it was slightly higher in cattle

isolates than it was among human isolates for newer antibiotics. Nearly twenty percent (17%) of cattle isolates were resistant to amikacin but not a single human isolate was resistant to amikacin, while 24% of cattle isolates in Uganda were resistant to ampicillin as opposed to 16% of human isolates. These features are shown in Table 17.

Table 17: Resistance patterns of human and bovine Salmonella in Uganda

Antibiotic	Percentage of resistance in Ugandan isolates	
	Human (n=58)	Cattle (n=14)
Sulfizoxazole	92.9	*83.3*
Streptomycin	77.2	*36.4*
Chloramphenicol	81.0	*50.0*
Tetracycline	65.4	*58.3*
Ampicillin	*16.1*	23.7
Co-trimoxazole	85.7	*63.6*
Amoxiclav	73.7	*50.0*
Gentamicin	44.2	*25.0*
Kanamycin	49.0	*16.7*
Nalidixic Acid	*44.9*	72.7
Ceftiofur	*28.6*	41.7
Cefoxitin	*8.8*	25.0
Ceftriaxone	*14.8*	16.7
Ciprofloxacin	*14.3*	27.3
Amikacin	*0.0*	16.7

Source: Mahero et al. (2013)

In a collaborative study by Makerere University workers in the departments of microbiology of the faculties of veterinary and human medicine, between July 2007 and July 2009 (Bosco, Kaddu-Mulindwa, & Asiimwe, 2012), drug susceptibility patterns of 92 *Salmonella* isolates were determined. Fifty-eight of these were from human clinical specimens and were obtained from Mbale (eastern Uganda), Lacor (northern Uganda), as well as from Mulago and Entebbe hospitals (central Uganda). Thirty four (34) isolates were from foods of animal origin - beef, pork, milk and poultry products. The susceptibility of the isolates was tested against tetracycline, ampicillin, chloramphenicol, nalidixic acid, co-trimoxazole, ciprofloxacin and ceftriaxone.

Slightly more than eighty percent of the human isolates were resistant to co-trimoxazole as about the same level as those derived from the foods. Fifty four percent (54%) of human and animal isolates were multi-drug resistant. Resistance to ciprofloxacin was found in less than 10% of both the human and food isolates. Only 2% were susceptible to all the seven antibiotics tested. Fifty-five percent were resistant to one of the three commonly used antibiotics in the treatment of Salmonellosis at that time - chloramphenicol, nalidixic acid and ciprofloxacin - and 1% were resistant to all the three. Table 18 below shows the resistance patterns of the isolates they studied.

Table 18: Resistance pattern of Salmonella isolates in the collaborative study

Antibiotic	Percentages of resistant isolates*	
	Among human clinical specimen isolates: n=58	Among foods of animal origin isolates: n=34
Tetracycline	59	64
Chloramphenicol	58	59
Ampicillin	40	72
Co-trimoxazole	82	85
Nalidixic Acid	18	28
Ciprofloxacin	2	5
Ceftriaxone	4	8

**in this Table, percentage figures have been estimated from the histogram in the original paper Source: (Bosco et al., 2012)*

The prevalence of resistance in isolates originating from foods of animal origin tended to be higher than that among isolates from human clinical specimens. This was especially true for ampicillin and nalidixic acid, although it may have not been statistically significant for other antibiotics.

All the drugs used in the treatment of human Salmonellosis are commonly used in veterinary practice, some in animal feeds. The authors blamed indiscriminate use of antibiotics in animals in Uganda by farmers who use very high doses of antibiotics to treat their animals without veterinary guidance, which exerts heavy selective pressure on organisms in the treated animals, for the escalating levels of microbial antibacterial resistance. They cited the example of Salmonellosis in chickens being frequently treated with 20% tetracycline.

Following on this study, an outbreak of typhoid beset Kasese and Bundibugyo districts in western Uganda in the years 2009–2011 (Walters et al., 2014). Eighteen (18) of the *S.* Typhi isolates in this outbreak were tested for sensitivity to amoxicillin/clavulanic acid, ampicillin, ceftriaxone, chloramphenicol, ciprofloxacin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline and co-trimoxazole.

Fifteen isolates (83%) were MDR to ampicillin, chloramphenicol, co-trimoxazole, sulfisoxazole, streptomycin and tetracycline. A single isolate was resistant to nalidixic acid and had reduced sensitivity to ciprofloxacin, although it was fully sensitive to other antibiotics tested. Two isolates were sensitive to all the above tested antibiotics.

Comment on this outbreak: Given that, in this outbreak, there was no uniform sensitivity pattern of isolates to the various antibiotics tested, it is hard to believe that these isolates were descended from a common ancestor within the period of this epidemic. What is likely to have happened is that the organisms originated in a faecal collecting system – and this is not uncommon in Uganda (Kwiringira, Atekyereza, Niwagaba, & Gunther, 2014) – from where they infected the community. Their sensitivity patterns, therefore, most likely mirrored that of *S.* Typhi strains among carriers within the community and possibly the surrounding areas as well. If this interpretation is correct, the fact that 83% of them were MDR to six antibiotics, including two of the most commonly used against typhoid in the country, chloramphenicol and co-trimoxazole, is a matter of concern for the entire country. In this outbreak, the most commonly used antibiotic was ciprofloxacin but unfortunately the study did not give the percentage of the tested strains that were sensitive to this antibiotic nor was the report on sensitivity testing on the 18 isolates tested given in full.

In a study (Ikwap et al., 2014) carried out during 2011 and 2012 in Gulu and Soroti districts in northern and eastern Uganda, respectively, the antibiotic resistance pattern of 53 various species of Salmonellae isolates from faecal samples from piglets and weaners in different herds and homesteads was as follows: no isolate was resistant to ciprofloxacin, nalidixic acid, cefotaxime, ceftazidime or gentamicin. To kanamycin, resistance was expressed by 2% of the isolates, to tetracycline 4%, to ampicillin 4%, chloramphenicol 6%, trimethoprim 13%, streptomycin 15% and sulphamethoxazole 43%.

Table 19 summarizes the resistance patterns of *Salmonella* isolates in the various studies in the last 19 years (1995-2015).

Table 19: Percentage of resistance of *Salmonella* isolates in the various studies in the last 19 years

Antibiotic tested	Mpairwe Y. (unpublished data) 1995 - 2000 (n=12- 65)	Mahero M. *et al.* (2013), (human isolates n=58)	Mahero M.*et al.* (2013), (cattle isolates n=14)	Kalule J.B. *et al.*(2012), 2007/09 human isolates(n=58)	Kalule J.B. *et al.*(2012), 2007/09 animal foods isolates (n=34)	Ikwap K. *et al.* (2014) 2011/12 (n=53)
Co-trimoxazole	79	85.7	63.6	82	85	
Ampicillin	63	16.1	23.7	40	72	3.8
Tetracycline	45	65.4	58.3	59	64	3.8
Chloramphenicol	2	81	50	58	59	5.7
Gentamicin	0	44.2	25			0
Pefloxacin	0					
Ciprofloxacin		14.3	27.3	2	5	0
Norfloxacin	0					
Sulfisoxazole		92.9	83.3			
Streptomycin		77.2	36.4			15.1
Amoxiclav		73.7	50			
Kanamycin		49	16.7			1.9
Nalidixic Acid		44.9	72.7	18	28	0
Ceftiofur		28.6	41.7			
Cefoxitin		8.8	25			
Ceftriaxone		14.8	16.7			
Amikacin		0	16.7	4	8	
Cefotaxime						0
Ceftazidime						0
Sulphamethoxazole						43.4
Trimethoprim						13.2

Source: Author Summary of resistance pattern of Salmonella species isolates in the period 1995 to 2014

Summary of resistance pattern of Salmonella species isolates in the period 1995 to 2014

1. Resistance to co-trimoxazole, ampicillin, tetracycline and chloramphenicol was expressed by between 50 and 85% of isolates.
2. Resistance to amikacin and ceftriaxone was expressed by less than 20% of isolates.
3. The low prevalence rate of resistance in the Ikwap et al. (2014) study is an exception most probably related to the rural locality of the study animals, and a period of armed insurgency which preceded that study and which might have minimised the inflow of antibiotics to that area.

6.7 Resistance pattern of *Shigella*

Not much has been documented about the antibiotic susceptibility patterns of *Shigella* in Uganda. The resistance of *Shigella* isolates at Naguru Medical Laboratory for the period 1995 to 2000 (Mpairwe, 2000) were as shown in Table 20.

Table 20: Antibiotic resistance patterns of Shigella isolates at Naguru Medical Laboratory

Antibiotic	Various *Shigella* isolates	
	No. tested	% resistant
Co-trimoxazole	35	83
Ampicillin	33	76
Tetracycline	44	75
Chloramphenicol	50	36
Gentamicin	33	6
Pefloxacin	16	0
Norfloxacin	15	0

Source: (Mpairwe, 2000)

During this period, Kajumbula (2014a) found the resistance pattern of 59 *Shigella* strains isolated in Mulago in 1997 to be as shownin Table 21.

Table 21: Antibiotic resistance patterns of Shigella isolates at Mulago Hospital

Antibiotic	% resistant
Tetracycline	98
Co-trimoxazole	93
Ampicillin	92
Chloramphenicol	88
Nalidixic Acid	2
Gentamicin	0
Ciprofloxacin	0

Source: Kajumbula (2014a)

Of the 24 *Shigella* strains studied by Legros, Ochola, Lwanga, and Guma (1998) in Mbarara district in southwestern Uganda, 100% were resistant to co-trimoxazole, 67% to ampicillin and 8% to nalidixic acid, but no isolate was resistant to ciprofloxacin or norfloxacin.

In a more recent study, Atwiine (2007) obtained 45 *Shigella* isolates from stool specimens of 160 patients with dysentery in eight widely separated districts of Uganda in June 2007. Susceptibility tests carried out against five antibiotic agents recommended by WHO for use in Shigellosis showed that all isolates were fully sensitive to ciprofloxacin. However, 2% were resistant to nalidixic acid, 80% to chloramphenicol, 89% to ampicillin and 100% to co-trimoxazole.

Summary of resistance patterns in *Shigella* 1995-2007

All of these studies, conducted between 1995 and 2007, indicate that the resistance of *Shigella* isolates in varying parts of the country is high to several drugs – between 36 and 100% to chloramphenicol, ampicillin and co-trimoxazole, but remained lower – between 0 and < 3% (in three of the four studies) – to quinolones. The last study, however, was carried out eight years ago and the current situation is not known.

6.8 Resistance of *Escherichia coli*

E. coli is the most common cause of urinary tract infections (UTIs), and also causes many other conditions including dysentery, neonatal sepsis, neonatal meningitis, intra-abdominal infections such as peritonitis and liver abscesses, as well as wound sepsis. In a study on isolates from UTIs at Rubaga Hospital, Kampala, (Kyabaggu, Ejobi, & Olila, 2007) the prevalence of resistance among 13 *E. coli* isolates ranged between 23% and 92% against the six antibiotics tested – amoxicillin, co-trimoxazole, erythromycin, nalidixic acid, ciprofloxacin and nitrofurantoin.

Andabati and Byamugisha (2010) investigated the resistance patterns of 15 *E. coli* isolates from expectant mothers attending antenatal clinics in Mulago Hospital with asymptomatic bacteriuria between May 2009 and December 2009. Resistance to amoxicillin was expressed by 60%, to co-trimoxazole by 58%, to erythromycin by 57%, to nitrofurantoin by 50%, to ampicillin by 48%, to gentamicin by 44%, to Augmentin by 15% and to ceftriaxone by 0%.

To characterise AmpC beta-lactamases among *Enterobacteriaceae* isolates from clinical samples at Mbarara Regional Referral Hospital, using 293 *Enterobacteriaceae* isolates recovered from clinical specimens that included blood, urine, stool and aspirates, Nakaye et al. (2014) determined the production of AmpC beta-lactamase using the disc placement method for cefoxitin at a break point of <18mm, and the determination of the common AmpC plasmid mediated genes was determined by multiplex PCR. Plasmid mediated AmpC phenotype was confirmed in 107 of the 293 (37%) cefoxitin resistant isolates, with 30 isolates having more than one gene coding for resistance. The most common source that harbored AmpC beta-lactamases was urine, and *E. coli* was the most common AmpC producer (60%). Nakaye et al. (2014) showed that the prevalence of AmpC beta-lactamase at Mbarara Regional Referral Hospital was high (40%), with EBC genes as the most common genotype among *Enterobacteriaceae*, while urine and *E. coli* were the most common source and organism, respectively, that harboured AmpC beta-lactamases.

In the Byarugaba et al. (2011) study, resistance of 441 *E. coli* isolates from faecal samples of various food animals were tested against 13 antibiotics, namely: gentamicin, erythromycin, tetracycline, chloramphenicol, ciprofloxacin, co-trimoxazole, ampicillin, streptomycin, amoxicillin, cephalothin, nalidixic acid, aztreonam and meropenem. To seven of these, namely: ciprofloxacin, gentamicin, aztreonam, chloramphenicol, nalidixic acid, cephalothin, and amoxicillin, resistance was expressed by between 7% and 31% of the isolates. Against the rest, resistance was expressed by between 50% and 96% of the isolates. No isolate was resistant to meropenem. Multi-drug resistance, sometimes to up to nine or more antibiotics, was expressed by 78% of the isolates. In a study by Kyeyune (2011) on 188 isolates of *E. coli* from faecal samples obtained from 200 live broiler chicken samples in three divisions of Kampala City, namely: Kawempe, Makindye and Nakawa, during January and February 2011, resistance to tetracycline was found in 91%, to ampicillin in 88%, to co-trimoxazole in 85%, to gentamicin in 55%, to chloramphenicol in 49% and to ciprofloxacin in 31%. These findings are summarised in Table 22.

Table 22: Antibiotic resistance patterns of Escherichia coli in Uganda between 2007 and 2011

Antibiotic	Kyabaggu et al 2007 (human isolates)	Andabati/ Byamugisha 2010 (human isolates)	Byarugaba et al 2011 (animal isolates)	Kyeyune 2011 (chicken isolates)
Tetracycline			61	91
Chloramphenicol			16.5	49
Amoxicillin	92.3		31	
Ampicillin		48	55.3	88
Co-trimoxazole	83.3	58	50	85
Gentamicin		44	6.9	55
Nitrofurantoin	30.8	50		
Erythromycin	76.9	57	96	
Ciprofloxacin	23.1		6.5	31
Augmentin		15		
Ceftriaxone		0		
Nalidixic Acid	69.2		16.7	
Ciprofloxacin	23.1			
Penicillin G				
Streptomycin			49.7	
Cephalothin			30.3	
Aztreonam			8.8	
Meropenem			0	

Source: Author

In summary, the data on *E. coli* are inadequate to make generalisations although on the whole, resistance to most of the tested antibiotics was expressed by over 40% of the isolates.

6.9 Extended spectrum beta-lactamase (ESBL) producers

In a study conducted at Mbarara Regional Referral Hospital in the months of June and August 2012 by Acaku, Freddie, Yap, and Joel (2013), a total of 484 isolates of Gram-negative bacilli from a variety of clinical specimens were screened for ESBL. Of these, 51% were ESBL producers by genetic screening and only 30% were so by phenotypic assessment. The commonest ESBL producers were *E. coli* (34%), *Klebsiella* species (13%) and *Salmonella* species (10%).

The ESBL producers had their sensitivity pattern to other antibiotics determined for the following antibiotics: gentamicin, ampicillin, nitrofurantoin, ciprofloxacin, chloramphenicol, co-trimoxazole, ticarcillin, imipenem and nalidixic acid.

Resistance to nitrofurantoin was expressed by 34% and to ampicillin by 96%, while for the other antibiotics tested resistance lay between these two percentage extremes, except resistance to imipenem, which was expressed by none of the isolates.

In the study by Nakiwala (2013), the prevalence of ESBL producers among 47 *E. coli* isolates from diverse specimens in Mulago Hospital during January to May 2013 was 28%. It was 54% among 41 *K. pneumoniae* isolates and 75% among 12 isolates of the Proteus species.

A study by Ainembabazi (2014) on 42 isolates each of *E. coli* and *K. pneumoniae* that were ESBL producers indicated that chlorhexidine is still an effective antiseptic and works optimally against these pathogens in concentrations between 195 ug/ml and 250 ug/ml.

Kateregga, Kantume, Atuhaire, Lubowa, and Ndukui (2015) found out that 47 % of the 245 samples had Enterobacteriaceae isolates in samples from patients in various wards of Mulago Hospital. Of these isolates 62 % were ESBL producers while 38 % were of non-ESBL phenotype. E. coli was the most isolated organism (53.9 %), followed by K. pneumoniae (28.7 %). Majority of Enterobacteriaceae organisms were isolated from urine samples, followed by pus samples and of these 64.9 % and 47.4 % were ESBL-producers respectively. K pneumoniae had the highest percentage of ESBL producers (72.7 %). There was a higher percentage of isolates showing resistance to ceftazidime (73 %) compared to cefotaxime (57.5 %). All Enterobacter cloacae isolates showed resistance to ceftazidime.

Summary of resistance patterns in ESBL producers

Not many papers were encountered on this topic. The few available suggest that ESBL producers range between 10 to 75% of the isolates among Gram-negative organisms. Their resistance to other antibiotics available in Uganda lies between 34% and 96%, except to imipenem to which they are still fully susceptible. However, this conclusion was derived from one study, which suggests that more studies on this topic are desperately needed.

6.10 Resistance patterns of bacterial isolates from the urinary tract

The resistance patterns of bacterial isolates from patients with urinary tract infections seen at Naguru Medical Laboratory (NAMELA) between 1995 and 2005 (Mpairwe, 2005) are presented in Table 23 below. Unfortunately the identities of the organisms were not available.

Table 23: Resistance patterns of urinary tract isolates at NAMELA (1995-2005)

ANTIBIOTIC	Yr 1995 – 1997		Yr 1998 – 2000		Yr 2001 – 2005	
	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant
Norfloxacin	34	0	66	12	115	22
Ciprofloxacin	-	-	-	-	71	24
Nitrofurantoin	80	5	78	4	-	-
Cefuroxime	34	6	-	-	28	43
Gentamicin	53	13	-	-	-	-
Ceftazidime	30	17	72	38	106	54
Co-amoxiclav	30	60	73	62	100	59
Ampicillin	88	78	76	72	70	67
Co-trimoxazole	86	92	19	79	80	54

Source: (Mpairwe, 2005)

Of between 55 and 58 isolates from 40 patients with significant bacteriuria studied by Mwaka et al. (2011) from 399 midstream urine samples of non-pregnant women in Mulago Hospital in a period that was not stated, 58% were *E. coli* and 23% were *S. aureus*. Enterococci were 15% and *K. pneumoniae* 5%. Resistance of these pathogens was expressed by 80% of the isolates to co-trimoxazole, 60% to ampicillin, 52% to nalidixic acid, 40% to ciprofloxacin, 39% to gentamicin, 35% to amoxiclav, 11% to cefuroxime and 2% to nitrofurantoin.

In the study by Odongo et al. (2013), from 339 patients with symptoms of urinary tract infection over a three-month period (June to August, 2011), 82 uropathogens were isolated. Of these, 46% were staphylococcal species, 39% *E. coli,* 7% *Enterococcus faecalis*, 5% *Klebsiella pneumoniae* and 2% *Proteus mirabilis*. In this study, the highest prevalence of resistance was expressed against co-trimoxazole (72%) and the lowest against gentamicin (15%). Table 24 below indicates the details of the resistance patterns of the isolated uropathogens.

Table 24: Percentage resistance of urinary tract isolates

Antibiotic	Mpairwe (2005).			Mwaka et al. (2011). Not all symptomatic of UTI Mulago n = 55 - 58	Odongo et al. (2013) during 2011 Symptomatic UTI northern Uganda n = 82
	During 1995 – 1997 Symptomatic UTI Central Uganda n = 30 – 88	During 1998 – 2000 Symptomatic UTI Central Uganda n = 19 – 78	During 2001 – 2005 Symptomatic UTI Central Uganda n = 28 – 115		
Norfloxacin	0	12	22		
Ciprofloxacin			24	40.4	29.2
Nitrofurantoin	5	4		1.7	48.8
Cefuroxime	6		43	10.5	
Gentamicin	13		-	38.6	14.6
Ceftazidime	17	38	54		
Co-amoxiclav	60	62	59	34.5	28.0
Ampicillin	78	72	67	60.3	
Co-trimoxazole	92	79	54	80	72.2
Nalidixic Acid				51.7	52.4
Amoxicillin					51.2
Cephalexin					41.5
Levofloxacin					23.2
Azithromycin					34.1
Oxacillin					22.2*
Imipenem					
Tetracycline					

**Tested against nine strains of S. aureus included in the study. Source: Author*

Summary of resistance patterns of urinary tract isolates 1996 to 2010

Prevalence of resistance to norfloxacin and possibly ciprofloxacin rose from 0% to between 40% and 60% currently. For cefuroxime, resistance rose from 6% to 40% in the first ten years, but dropped to about 10% as of now. Prevalence for ceftazidime resistance rose from 17% to 54% in the first 10 years but declined to about 35% currently, while to amoxiclav resistance remained constant at about 60% for the initial 10 years and then dropped to about 35% in central Uganda. To ampicillin it continued to decline from 78% to possibly 60% currently, while to co-trimoxazole resistance dropped from 92% to 54% in the first 10 years, but rose again to about 80% in the central region of Uganda.

6.11 Surgical site infections

Findings of a study on resistance patterns of bacterial isolates from surgical wounds in obstetrics and gynecology and surgical wards in major hospitals in Kampala and Entebbe between July and December 1996 (Mpairwe, 1997) are shown in Table 25.

Table 25: Resistance patterns of bacterial isolates from surgical wounds in major hospitals in Kampala and Entebbe between July and December 1996

Antibiotic tested	No. of isolates tested (% resistant)
Penicillin G	262 (88)
Ampicillin	237 (76)
Co-trimoxazole	223 (70)
FluCloxacillin	222 (69)
Tetracycline	257 (67)
Fucidin	272 (65)
Erythromycin	272 (56)
Streptomycin	255 (49)
Chloramphenicol	253 (41)
Gentamicin	281 (22)
Augmentin	259 (20)
Cefuroxime	108 (15)
Ceftazidime	104 (11)
Ciprofloxacin	53 (2)
Pefloxacin	81 (0)

Source: (Mpairwe, 1997)

In this study, 30% of antibiotic prescriptions (penicillin G and ampicillin) used to treat these infections had resistance expressed by between 76 and 88% of the bacterial isolates.

In another study carried out in various obstetrics and gynecology, general surgery and orthopedic wards of Mulago Hospital between September 2011 and April 2012, Seni, Najjuka, et al. (2013) isolated 216 aerobic organisms from a total of 314 patients with surgical site infections. Gram-negative isolates constituted 68% of the isolates. The predominant bacterial flora among Gram-negatives were: *E. coli,* which accounted for 24% of all isolates, and *S. aureus,* which accounted for 21%.

The isolates were tested against antibiotics drawn from a list of 20, depending on whether they were Gram-positive or Gram-negative. Nearly eighty percent (79%) of *E. coli*, 92% of *Klebsiella* species and 74% of other *Enterobacteriaceae* were phenotypically ESBL producers. On average, more than 75% of *Enterobacteriaceae* were phenotypically ESBL producers.

All 12 *P. aeruginosa* isolates were sensitive to colistin, but 4% of the 52 isolates of *Acinetobacter* species were resistant to this drug. The 64 isolates of *S. aureus* were all sensitive to vancomycin. Enterococcal resistance to vancomycin was encountered in one out of the 23 (4%) isolates.

Nearly 40% (38%) of the *S. aureus* isolates were MRSA. Multiple drug resistance was encountered among 78% of all isolates. Nearly eighty percent (79%) of the Gram-negatives, as contrasted to only 21% of Gram-positives, were MDR organisms. In Table 26, the percentage range of resistant isolates against 17 of the tested antibiotics are presented.

Table 26: Percentage ranges of resistant isolates from infected surgical sites in Mulago Hospital against tested antibiotics 2011 – 2012

Antibiotic	% Resistant isolates	
	Gram-negative	Gram-positive
Ampicillin	97.1 –100	30_a – 100_b
Amoxiclav	90.3 – 100	N.T
Co-trimoxazole	86.1 – 100	80.0 – 89.1
Tetracycline	65.4 – 100	42.2 – 74
Erythromycin	N.T	46.9 – 65.2
Chloramphenicol	41.7 – 71.8	15.6 – 37.5
Gentamicin	54.2_c – 88.5	18.8 – 50
Ciprofloxacin	47.1_c – 77	29.7 – 60.9
Ceftriaxone	67.6 – 92.3	N.T
Ceftazidime	61.8_d – 90.4	N.T
Cefepime	38.2_c – 87.2	N.T
Piperacillin	66.7 – 100	N.T
Piperacillin-tazobactam	16.7 – 53.8	N.T
Clindamycin	N.T	40.6 – 62.5
Amikacin	0.0 – 32.7	N.T
Vancomycin	N.T	0.0 – 4.4_e
Imipenem	0.0 – 3.9_f	N.T

Source: Seni, Najjuka, et al. (2013)

$_a$against enterococci; $_b$against *S. aureus*; N.T. = not tested; $_c$except against *P. aeruginosa* where only 16.7% were resistant; $_d$except against *P. aeruginosa* where only 25% were resistant; $_e$the 4.4% resistance was expressed only by enterococci; $_f$the 3.9% resistance was expressed by *Acinetobacter* species isolates only.

Basing on these findings, the authors appealed for improvements in antibiotic stewardship as well as for an investigation into the possibility of clonal spread of resistant strains in the hospital.

Summary on surgical site infections

Not many papers on surgical site infections were encountered. Of the two included, resistance was lowest to imipenem, at less than 4% of the isolates. Resistance to the majority of the antibiotics tested varied between 60% and 100%.

6.12 Carbapenem-resistant *Enterobacteriaceae* (CREs)

Resistance to imipenem was expressed by less than 4% of Gram-negatives in the Seni, Najjuka, et al. (2013) publication cited above. Imipenem is a member of the carbapenem group of antibiotics that are considered to constitute the last line of therapeutic efficacy in the treatment of multiple resistant ESBL producers. However, in another study (Ampaire, Katawera, Nyehangane, Yap, & Bazira, 2014), out of 183 MDR Enterobacteriaceae strains from clinical specimens investigated at Mbarara Regional Referral Hospital between September 2013 and June 2014, 13% and 31% were phenotypically and genotypically resistant to carbapenems, respectively. It is not clear what proportion of these isolates were from the community or were from a single organism spreading clonally in the hospital. Whatever the case might have been, these findings are a cause for concern with regard to the management of ESBL producers in Uganda.

6.13 Transmission of antibiotic resistant microbes from man to wild animals

There is a tendency for wild animals to acquire gut organisms from humans with whom they may be sharing their habitat. This was demonstrated in the study by Rwego et al. (2008), where gorilla populations sharing habitats with humans in the Bwindi Forest area were found to harbour *E. coli* strains that were genetically more closely related to those from the people and their livestock than strains from gorillas that did not share habitats with people. It was further found that 35% of human *E. coli* isolates, 27% of isolates from domestic animals and 17% of isolates from gorillas were resistant to at least one antibiotic used by the humans in the area, even though gorillas were not known to have ever been given treatment with those antibiotics.

Similar findings regarding the transmission of *E. coli* strains, including those that were antibiotic resistant, from park rangers to chimpanzees, were reported in an earlier study in Kibaale (Goldberg et al., 2007).

In a study by (Kalule et al. (2014)), carried out between February 2012 and September 2013, eighty free-range domestic pigs and 15 vervet monkeys interfacing with humans in Luweero and Wakiso districts had their anterior nares swabbed. *S. aureus* was isolated from 88% of the 80 pigs and from 100% of the 15 monkeys. Sixty-three (63%) of the pig isolates and 67% of the monkey isolates were MRSA and 90% of the 87 strains from both pigs and vervet monkeys were resistant to co-trimoxazole. As vervet monkeys were not receiving antibiotics, their antibiotic resistant *S. aureus* must have come from humans or from pigs treated with those antibiotics.

VII CONCLUSION

1. The vast majority of people in Uganda are not aware about the problem of bacterial resistance to antibiotics. The problem of antibiotic resistance is known to the MoH but is considered to be a matter of relative insignificance except in the case of tuberculosis, AIDS and malaria.
2. Surveillance for antibiotic resistance is not routinely performed in Uganda. Individual efforts to highlight the problem of antimicrobial resistance have been isolated, uncoordinated and largely ignored.
3. Published information about antibiotic resistance is limited and fragmented in time and location. Resistance has not been investigated consistently to the same antibiotics or to the same clinical conditions over a long period of time. This minimises the ability of clinicians to appreciate the worsening trends of resistance and diminishing efficacy of antibiotics in the country. The available information is not collated. Consequently, it is rarely circulated to relevant professionals and its influence on clinical practice is minimal. Because information is not available to most clinicians, the prescription of antibiotics in the country is largely empirical and a matter of trial and error.
4. There are some discernable trends in resistance patterns. Over the years, microbial resistance to antibiotics has been increasing. In some places and against certain pathogens, prevalence of resistance to penicillin G and co-trimoxazole is approaching or already at 100%, and that of many others is following closely. The highest prevalence of resistance is among Gram-negative bacilli and *S. aureus,* amongst which methicillin resistance is important.
5. The antibiotics available in Uganda against which the prevalence of *S. aureus* resistance is not yet known to be above 50% are vancomycin, gentamicin, clindamycin, imipenem and linezolid. But the cost of these relatively newer antibiotics is much higher than that of the older antibiotics. Consequently, the affordability of effective antibiotics is a problem for the country.
6. The number of laboratories capable of isolating pathogens from clinical specimens and performing antibiotic sensitivity on them are too few and are largely absent in government hospitals. The medical laboratory at Mulago National Referral and Teaching Hospital is also seriously lacking in this capacity.
7. The laws regulating antibiotic use are fairly adequate but they are not effectively enforced. Antibiotics can be accessed without a prescription from community pharmacies and drug shops, often unnecessarily and in sub-optimal quantities. Self-medication is common.
8. Many individual members of the health professions that may legally prescribe antibiotics are aware of antimicrobial resistance but do not know the ideal way to address it. Faced with this problem they frequently resort to polypharmacy. A special

form of polypharmacy is actually officially sanctioned; in the syndromic treatment of a urethral discharge, for example, it is recommended to use ciprofloxacin in combination with doxycycline or erythromycin combined with co-trimoxazole.

9. Recommendations about antibiotic use in the *Uganda Clinical Guidelines* are not based on research that is generally respected or appreciated by prescribers. Consequently, the guidelines are largely ignored or not sought after, especially by senior clinicians.
10. Although they are not legally sanctioned, the practice of antibiotic self-medication and over-the-counter dispensing of antibiotics by pharmacists are common.
11. Knowledge about antibiotic use among professionals is limited. Even where it exists, professionals do not always act in accordance with it. Dispensing of antibiotics without prescription in pharmacies manned or supervised by pharmacists is a case in point.
12. The profit motive often adversely influences prescription, especially among private practitioners and dispensing pharmacists.
13. While antibiotic resistance is lower among wild animals, there is a growing concern that wild animals are being colonised with antibiotic resistant strains from humans who interface with those animals. Transmission of resistant strains to zoo animals may originate from meat used to feed those animals bought from slaughter-houses of domestic farm animals.
14. The increasing trend in antibiotic resistance is being driven by irrational use of antibiotics including;

    a) Self-medication with uncontrolled over-the-counter access of antibiotics;
    b) Continued use of antibiotics to which a large proportion of pathogens have developed resistance;
    c) Failure of patients to complete their courses of prescribed antibiotics;
    d) Involvement of non-qualified prescribers;
    e) Misuse of antibiotics; for example, their use in the treatment of uninvestigated fevers;
    f) Inadequacy of competent laboratories to isolate and test pathogens for antibiotic susceptibility;
    g) Prevalence of empirical prescription;
    h) Antibiotic polypharmacy; and
    i) Use of antibiotics in animal feeds.

VIII RECOMMENDATIONS

Based on the findings of this analysis, GARP-Uganda recommends as a priority:
The creation and realization of a national strategy for containment of antibiotic resistance that safeguards antibiotic effectiveness while ensuring access to antibiotics for all when needed.

The achievement of this goal will require collaboration with a diverse set of stakeholders from all sectors. Though the specific content for such a strategy will need to be developed based on patterns of resistance and other contextual factors, six major areas have been identified for action at the national level:

1. **Reduce the need for antibiotics through public health measures**

   Improve vaccination coverage and access to clean water, sewage systems and a safe food supply to reduce the burden of infectious diseases, bacterial and other, which may be treated with antibiotics.

2. **Improve hospital infection control and antibiotic stewardship**

   Prevent the spread of infections in hospitals by improving hand hygiene and improve antibiotic prescribing practices within hospitals through stewardship programs and surveillance.

3. **Rationalize antibiotic use in the community**

   Reduce the prescription of antibiotics for coughs and colds that are not caused by bacteria and cannot be treated by antibiotics, and ensure that access to quality medications is balanced with correct treatment practices.

4. **Reduce antibiotic use in agriculture**

   Eliminate the use of antibiotics as growth promoters, which do not benefit animal health, and reduce their sub-theraputic use for disease prevention.

5. **Educate health professionals, policy makers and the public on sustainable antibiotic use**

   Provide and update guidelines and curricula, develop awareness campaigns, policy briefs and new research to identify and communicate best practices in antibiotic use.

6. **Ensure political commitment to meet the threat of antibiotic resistance**

   Bring together stakeholders from human and animal health, government, academia, agriculture, the private and other sectors to develop actionable policies based on local resistance patterns.

While the realization of such a plan may take several years, GARP-Uganda will spearhead the process by conducting research to fill information gaps and convening stakeholders to foster collaboration.

(a) GARP-Uganda will continue to focus on creating more and sharing the evidence to support policies aimed at containing the problem of antimicrobial resistance working with all stakeholders across all relevant sectors and with all partners globally. In particular, UNAS will Support policies to create awareness about the problem of antibiotic resistance among all Ugandans;

(b) Support the proposed a plan for monitoring antibiotic resistance in Uganda;

(c) Support the revision and use of the clinical treatment guidelines

(d) Support the plan for monitoring antibiotic use and dispensing patterns at different levels of the healthcare system;

(e) Develop a national research agenda by creating a mechanism for soliciting and funding projects, based on an objective and open review of proposals;

(f) Seek and engage in national, regional and international collaboration for purposes of enhancing capacity and sharing knowledge and experiences;

(g) Report regularly to the MoH, the MAAIF and the population at large on the status of antibiotic resistance and related issues

(h) Develop policy papers to influence treatment and prescription patterns.

IX SELECTION CRITERIA FOR EVIDENCE INCLUSION AND LIMITATIONS OF THE REPORT

- Many papers on antimicrobial resistance on archived materials which lacked archival history were excluded;
- One paper whose methodology suggested the possibility of deliberate falsification of results was turned down;
- Many papers had incomplete information and sometimes contained errors. For example, in a number of papers, figures in the text differed from those in the tables. In such cases it was assumed that figures in tables were the correct ones;
- A number of papers did not state the period in which the work they were reporting on was done. In this case, we regarded the year of publication to be the year of the work;
- This report is based on relatively few studies because of paucity of relevant publication;
- The few studies were almost always uncoordinated in time, location and spectra of antibiotics tested;
- The studies differed in specimens investigated and in hosts from which isolates were obtained;
- The culture media, identification procedures as well as antibiotic concentrations in the test discs must have differed in some of these studies;
- Professional skills and experience of those who carried out the studies differed; and
- A further limitation was failure of target respondents in the various departments to respond at all or to respond in time.

It is important to note that the summaries on the respective resistance patterns made were based on relatively few studies, all of which suffered the effects of the limitations highlighted above. This needs to be borne in mind when appraising the conclusions arrived at.

REFERENCES

Aberg, A. J., & Powderly, G. W. (2006). Cryptococcosis and HIV. *Insite: Comprehensive, up-to-date information on HIV/AIDS treatment, prevention, and policy from the University of California San Francisco.* Retrieved 12th February, 2015, from http://hivinsite.ucsf.edu/InSite?page=kb-00&doc=kb-05-02-05

Abrahmsen, M., Persson, Y., Kanyima, B. M., & Bage, R. (2014). Prevalence of subclinical mastitis in dairy farms in urban and peri-urban areas of Kampala, Uganda. *Trop Anim Health Prod, 46*(1), 99-105. doi: 10.1007/s11250-013-0455-7

Acaku, M., Freddie, B., Yap, B., & Joel, B. (2013). Prevalence and Genotypic Characterization of Extended- Spectrum Beta-Lactamases Produced by Gram Negative Bacilli at a Tertiary Care Hospital in Rural South Western Uganda *British Microbiology Research Journal, 4*(12), 1541-1550. doi: 10.9734/BMRJ/2014/9792

Admin. (2013, February 8, 2013). Pharmacists Nabbed With Banned, Expired Drugs, *Red Pepper*. Retrieved from http://www.redpepper.co.ug/pharmacists-nabbed-with-banned-expired-drugs/

Ahlquist, D. A., & Camilleri, M. (2001). *Diarrhoea and Constipation in Harrison's Principles of Internal Medicine* (15th ed.). NY: McGraw-Hill.

Ainembabazi, P. (2014). *The effect of Chlorhexidine gluconate on Gram negative Multi-drug Resistant Bacteria that produce Extended Spectrum Beta Lactamases in Mulago Hospital* (Bachelors Degree in Biomedical Laboratory Technology of Makerere University), Makerere University.

Amandua, J. (2014). Control of antimicrobial resistance, Ministry of Health. In Y. Mpairwe (Ed.), *Global Antibiotic Resistance Partnership*.

Amito Florence, P., Otim, F., Okongo, F., Ogwang, M., & Greco, D. (2012). The prevalence and antibiotics susceptibility pattern of Neisseria gonorrhoeae in patients attending OPD clinics at St. Mary's Hospital Lacor Uganda. *J Prev Med Hyg, 53*(4), 186-189.

Ampaire, M. L., Katawera, V., Nyehangane, D., Yap, B. I., & Bazira, J. (2014). Epidemiology of Carbapenem resistance among multi-drug resistant Enterobacteriaceae. *British Microbiology Research Journal, 8*(2), 418-423 doi: 10.9734/BMRJ/2015/17055

Andabati, G., & Byamugisha, J. (2010). Microbial aetiology and sensitivity of asymptomatic bacteriuria among ante-natal mothers in Mulago hospital, Uganda. *African Health Sciences, 10*(4), 349-352.

Anguzu, J. R., & Olila, D. (2007). Drug sensitivity patterns of bacterial isolates from septic post-operative wounds in a regional referral hospital in Uganda. *Afr Health Sci, 7*(3), 148-154. doi: 10.5555/afhs.2007.7.3.148

APUA. (2011). Global Health Final Report (pp. 1-19). Boston: Alliance for the Prudent Use of Antibiotics

Arya, O. P., & Phillips, I. (1970). Antibiotic sensitivity of gonococci and treatment of gonorrhoea in Uganda. *Br J Vener Dis, 46*(2), 149-152.

Atwiine, A. K. (2007). *Determination of Circulating Shigella Serotypes and their antimicrobial Susceptibility Patterns in selected Districts of Uganda.* (Bachelor of Biomedical Laboratory Technology), Makerere University, Kampala.

Auditor_General. (2009). Value for money audit report on the prevention and control of livestock diseases. Office of the auditor general. (T. D. o. L. H. a. Entomology, Trans.): Ministry of Agriculture Animal Industry and Fisheries.

Baluka, S. A., Ocaido, M., & Mugisha, A. (2014). Prevalence and economic importance of Foot and Mouth disease, and Contagious Bovine Pleuropneumonia Outbreaks in cattle in Isingiro and Nakasongola Districts of Uganda. *Discourse Journal of Agriculture and Food Sciences, 2*(4), 107-117.

Batwala, V., Magnussen, P., & Nuwaha, F. (2011). Antibiotic use among patients with febrile illness in a low malaria endemicity setting in Uganda. *Malar J, 10*(1), 1-8. doi: 10.1186/1475-2875-10-377

Bayiyana, I., Ekere, W., & Mugisha, J. (2012). *Economic analysis of transboundary animal disease control in Ntungamo and Rakai districts in Uganda*. Paper presented at the RUFORUM Third Biennial Conference, Entebbe. http://repository.ruforum.org/sites/default/files/Bayiyana%2C%20I.%20et%20al..pdf

Bazira, J., Yap, B. I., Sempa, J., , I., Jacobs, Nanjebe, D., Sewankambo, N., & Nakanjako, D. (2014). Trends in Antimicrobial Resistance of Staphylococcus aureus Isolated from Clinical Samples at Mbarara Regional Referral Hospital in Rural Uganda. *British Microbiology Research Journal, 4*(10).

Björk, S. (2013). Clinical and subclinical mastitis in dairy cattle in Kampala, Uganda. Second cycle, A2E. Uppsala: SLU, Dept. of Clinical Sciences *(VH) > Dept. of Clinical Sciences, 2013:65*.

Bjork, S., Bage, R., Kanyima, B., Andre, S., Nassuna-Musoke, M., Owiny, D., & Persson, Y. (2014). Characterization of coagulase negative staphylococci from cases of subclinical mastitis in dairy cattle in Kampala, Uganda. *Irish Veterinary Journal, 67*(1), 12.

Bosco, K. J., Kaddu-Mulindwa, D. H., & Asiimwe, B. B. (2012). Antimicrobial Drug Resistance and Plasmid Profiles of <i>Salmonella</i> Isolates from Humans and Foods of Animal Origin in Uganda. *Advances in Infectious Diseases, Vol.02No.04*, 5. doi: 10.4236/aid.2012.24025

Byarugaba, D. K. (2004). Antimicrobial resistance in developing countries and responsible risk factors. *Int J Antimicrob Agents, 24*(2), 105-110. doi: 10.1016/j.ijantimicag.2004.02.015

Byarugaba, D. K., Kisame, R., & Olet, S. (2011). Multi-drug resistance in commensal bacteria of food of animal origin in Uganda. *Afr. J. Microbiol. Res, 5*(12), 1539-1548. doi: 10.5897/AJMR11.202

Byarugaba, D. K., Nakavuma, J. L., Vaarst, M., & Laker, C. (2008). Mastitis occurrence and constraints to mastitis control in smallholder dairy farming systems in Uganda. *Livestock Research for Rural Development, 20*(5).

CDC. (2014). Global Health Security Agenda: GHSA Antimicrobial Resistance Action Package (GHSA Action Package Prevent-1). Retrieved 8 July 2015, 2015, from http://www.cdc.gov/globalhealth/security/actionpackages/antimicrobial_resistance.htm

CIA. (2014, June 20, 2014). CIA World Factbook, Africa, Uganda. Retrieved 3rd December 2014, 2014, from https://www.cia.gov/library/publications/the-world-factbook/geos/ug.html

CSBAG. (2013). Position Paper on the Agriculture, Animal Industry and fisheries (MAAIF), Sector 2013/14 (pp. 1-6). Kampala: CIVIL SOCIETY BUDGET ADVOCACY GROUP.

Durand, M., & Joseph, M. (2001). *Infections of the Upper Respiratory Tact in Principles of Internal Medicine* (15 ed.). N.Y: McGraw-Hill,.

EMA. (2010). Maximum residue limit assessment reports. *Penicillins: Summary report - Committee for Veterinary Medicinal Products.* Retrieved 10 April 2015, from http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500015568&mid=WC0b01ac058006488e

Foster, S. D., Sosa, A., Najjuka, C. F., & Mwenya, D. (2011). Drivers of antibiotic resistance in Uganda and Zambia, Presentation to the Global Health Council. Washington DC: Alliance for the Prudent Use of Antibiotics.

Goldberg, G. T. R., Rwego, I. B., Wheeler, E., Estoff, E. L., & Chapman, C. A. (2007). Patterns of gastrointestinal bacterial exchange between chimpanzees and humans involved in research and tourism in western Uganda. *Biological Conservation, 135*, 511 – 517.

Ikwap K, M, K., Kato CD, Nanteza A, Tumwine G, Saimo M, & ., K. J. (2012). Enhancing East Coast Fever vaccine delivery and marketing systems in uganda.

Ikwap, K., Erume, J., Owiny, D. O., Nasinyama, G. W., Melin, L., Bengtsson, B., . . . Jacobson, M. (2014). Salmonella species in piglets and weaners from Uganda: prevalence, antimicrobial resistance and herd-level risk factors. *Prev Vet Med, 115*(1-2), 39-47. doi: 10.1016/j.prevetmed.2014.03.009

Iramiot, J. S., Bwanga, F., Herbert, I., Martha, N., Mwambi, B., & Joel, B. (2014). Prevalence and Antibiotic Susceptibility Patterns of Clinical Isolates of Methicillin-Resistant Staphylococcus aureus in a Tertiary Care Hospital in Western Uganda. *British Microbiology Research Journal, 4*(10), 1168-1177 doi: 10.9734/BMRJ/2014/9909

Iriso, R., Ocakacon, R., Acayo, J. A., Mawanda, M. A., & Kisayke, A. (2008). Bacterial meningitis following introduction of Hib conjugate vaccine in northern Uganda. *Ann Trop Paediatr, 28*(3), 211-216. doi: 10.1179/146532808X335660

Jacob, S. T., Moore, C. C., Banura, P., Pinkerton, R., Meya, D., Opendi, P., . . . Promoting Resource-Limited Interventions for Sepsis Management in Uganda Study, G. (2009). Severe sepsis in two Ugandan hospitals: a prospective observational study of management and outcomes in a predominantly HIV-1 infected population. *PLoS One, 4*(11), e7782. doi: 10.1371/journal.pone.0007782

Joloba, M. L., Bajaksouzian, S., Palavecino, E., Whalen, C., & Jacobs, M. R. (2001). High prevalence of carriage of antibiotic-resistant Streptococcus pneumoniae in children in Kampala Uganda. *Int J Antimicrob Agents, 17*(5), 395-400.

Kajumbula, H. (2014a). Antimicrobial Resistance (T. D. o. M. Microbiology, Trans.): Makerere University College of Health Science.

Kajumbula, H. (2014b). Routine findings (M. laboratory, Trans.): Microbiology Makerere University College of Health Sciences.

Kalule, J. B., Sendawula, S. P., Wamala, S., Nabukenya, I., Atimnedi, P., Ndumu, D., & Kaboyo, W. (2014). Methicillin Resistant Staphylococcus aureus in Free-ranging Domestic Pigs and Vervet Monkeys at the Human-Animal Interface in Luwero and Wakiso districts, Uganda: Using vervet monkeys for Sentinel surveillance of MRSA in Domestic animals and Man. Kampala: Makerere University.

Kamulegeya, A., William, B., & Rwenyonyi, C. M. (2011). Knowledge and Antibiotics Prescription Pattern among Ugandan Oral Health Care Providers: A Cross-sectional Survey. *Journal of Dental Research, Dental Clinics, Dental Prospects, 5*(2), 61-66. doi: 10.5681/joddd.2011.013

Kasozi, K., Tingiira, J., & Vudriko, P. (2014). High Prevalence of Subclinical Mastitis and Multidrug Resistant Staphylococcus aureus Are a Threat to Dairy Cattle Production in Kiboga District (Uganda). *Open Journal of Veterinary Medicine, 4*, 35-43. doi: 10.4236/ojvm.2014.44005

Kateete, D. P., Kabugo, U., Baluku, H., Nyakarahuka, L., Kyobe, S., Okee, M., . . . Joloba, M. L. (2013). Prevalence and antimicrobial susceptibility patterns of bacteria from milkmen and cows with clinical mastitis in and around Kampala, Uganda. *PLoS One, 8*(5), e63413. doi: 10.1371/journal.pone.0063413

Kateete, D. P., Kajumbula, H., Kaddu-Mulindwa, D. H., & Ssevviri, A. K. (2012). Nasopharyngeal carriage rate of Streptococcus pneumoniae in Ugandan children with sickle cell disease. *BMC Res Notes, 5*, 28. doi: 10.1186/1756-0500-5-28

Kateete, D. P., Namazzi, S., Okee, M., Okeng, A., Baluku, H., Musisi, N. L., . . . Najjuka, F. C. (2011). High prevalence of methicillin resistant Staphylococcus aureus in the surgical units of Mulago hospital in Kampala, Uganda. *BMC Res Notes, 4*, 326. doi: 10.1186/1756-0500-4-326

Kateregga, J. N., Kantume, R., Atuhaire, C., Lubowa, M. N., & Ndukui, J. G. (2015). Phenotypic expression and prevalence of ESBL-producing Enterobacteriaceae in samples collected from patients in various wards of Mulago Hospital, Uganda. *BMC Pharmacology & Toxicology, 16,* 14. doi: 10.1186/s40360-015-0013-1

Kigozi, E. (2012). *Enterococci Species Occurrence and their Levels of Resistance to commonly used Drugs:*. (Bachelors Degree in Biomedical Laboratory Technology), Makerere Unviersity, Makerere.

Kisakye, A., Makumbi, I., Nansera, D., Lewis, R., Braka, F., Wobudeya, E., . . . Gessner, B. D. (2009). Surveillance for Streptococcus pneumoniae meningitis in children aged <5 years: implications for immunization in Uganda. *Clin Infect Dis, 48 Suppl 2*, S153-161. doi: 10.1086/596495

Kitara, L. D., Anywar, A. D., Acullu, D., Odongo-Aginya, E., Aloyo, J., & Fendu, M. (2011). Antibiotic susceptibility of Staphylococcus aureus in suppurative lesions in Lacor Hospital, Uganda. *Afr Health Sci, 11 Suppl 1*, S34-39.

Kiwanuka, J. P., & Mwanga, J. (2001). Childhood bacterial meningitis in Mbarara Hospital, Uganda: antimicrobial susceptibility and outcome of treatment. *Afr Health Sci, 1*(1), 9-11.

Knaapen, J. (2012/2013). An insight into antibiotic prescription practice at Mulago Hospital, Uganda. In N. Florence & O. L. Astrid (Eds.): FHML- Medicin Maastricht University

Makerere University.

Kwiringira, J., Atekyereza, P., Niwagaba, C., & Gunther, I. (2014). Descending the sanitation ladder in urban Uganda: evidence from Kampala Slums. *BMC Public Health, 14*, 624. doi: 10.1186/1471-2458-14-624

Kyabaggu, D., Ejobi, F., & Olila, D. (2007). The sensitivities to first-line antibiotic therapy of the common urinary tract bacterial infections detected in urine samples at a hospital in metropolitan Kampala (Uganda). *Afr Health Sci, 7*(4), 214-222.

Kyeyune, P. (2011). *Antibiotic Resistance Patterns of Escherichia coli isolated from fecal Matter of healthy broiler Chicken reared under dip liter System from selected Divisions of Kampala District.* (Bachelors Degree in Biomedical Laboratory Technology), Makerere University.

Legros, D., Ochola, D., Lwanga, N., & Guma, G. (1998). Antibiotic sensitivity of endemic Shigella in Mbarara, Uganda. *East Afr Med J, 75*(3), 160-161.

Levison, M. E. (2001). *Pneumonia, Including Necrotizing Pulmonary Infection (Lung Abscess) in Harrison's Principles of Internal Medicine* (15 ed.). Hill N.Y: McGraw.

Lewis, R. F., Kisakye, A., Gessner, B. D., Duku, C., Odipio, J. B., Iriso, R., . . . Kekitiinwa, A. (2008). Action for child survival: elimination of Haemophilus influenzae type b meningitis in Uganda. *Bull World Health Organ, 86*(4), 292-301.

MAAIF. (2005). National Livestock Productivity Improvement Project: Baseline Survey Report, A Benchmark for Measuring Project Impact: Ministry of Agriculture, Animal Industry and Fisheries.

MAAIF. (2007). Sector Strategic Plan for Statistics 2007-2011 (pp. 1-40). Entebbe: Ministry of Agriculture, Animal Industry and Fisheries.

MAAIF. (2011). *Guide on pig production*. Uganda.

MAAIF. (2015). Policy, Planning and Support Services Retrieved 16th February 2015, 2015, from http://www.agriculture.go.ug/Directorates

MAAIF, & UBOS. (2010). THE NATIONAL LIVESTOCK CENSUS REPORT 2008. Kampala: Ministry of Agriculture, Animal Industry & Fisheries.

Mahero, M., Byarugaba, D., Doetkott, D., Olet, S., & Khaitsa, M. (2013). Antimicrobial Resistance and Presence of Class 1 Integrons in Salmonella Serovars Isolated from Clinical Cases of Animals and Humans in North Dakota and Uganda. *Clin Microbial, 2*(128). doi: 10.4172/2327-5073.1000128

Mayanja, B. N., Todd, J., Hughes, P., Van der Paal, L., Mugisha, J. O., Atuhumuza, E., . . . Grosskurth, H. (2010). Septicaemia in a population-based HIV clinical cohort in rural Uganda, 1996–2007: incidence, aetiology, antimicrobial drug resistance and impact of antiretroviral therapy. *Tropical Medicine & International Health, 15*(6), 697-705. doi: 10.1111/j.1365-3156.2010.02528.x

McNulty, C. A., Boyle, P., Nichols, T., Clappison, D. P., & Davey, P. (2006). Antimicrobial drugs in the home, United Kingdom. *Emerg Infect Dis, 12*(10), 1523-1526. doi: 10.3201/eid1210.051471

Means, A. R., Weaver, M. R., Burnett, S. M., Mbonye, M. K., Naikoba, S., & McClelland, R. S. (2014). Correlates of inappropriate prescribing of antibiotics to patients with malaria in Uganda. *PLoS One, 9*(2), e90179. doi: 10.1371/journal.pone.0090179

MoH. (2009). Uganda National Health Laboratory Services Policy (A. H. P. Council, Trans.) (pp. 1-21). Kampala: Ministry of Health.

MoH. (2013). Annual Health Sector Performance Report Financial Year 2012 / 2013 (pp. 1-186). Kampala: Ministry of Health.

MoH. (2014a). Annual Health Sector Performance Report Financial Year 2013/2014 (pp. 1-217). Kampala: Ministry of Health.

MoH. (2014b). *Uganda Clinical Guideline 2012* (Vol. 2014). Kampala: Ministry of Health.

Mpairwe, Y. (1972). *Bacterial Meningitis Medicine in a Tropical Environment*. Hutt, London: Hutt.

Mpairwe, Y. (1997). A report on Antibiotic Sensitivity of Isolates in pyogenic Lesions in Kampala and Entebbe in July-December, 1996: National Drug Authority.

Mpairwe, Y. (1998). A comparison of Sensitivity Patterns of pyogenic Isolates from some up-country Hospitals with that in the Kampala-Entebbe Area to Penicillin G, Ampicillin, Tetracycline and Cotrimoxazole. Kampala: National Drug Authoriy.

Mpairwe, Y. (2000). Resistance Pattern of Shigella Isolates at Naguru Medical Laboratory, Kampala (1995 and 2000) Naguru Medical Laboratory, Kampala.

Mpairwe, Y. (2005). *Resistance Pattern of Urinary Tract Isolates at NAMELA between 1995 and 2005*. Paper presented at the Uganda Private Medical Practitioners' Association CME Seminar Kampala.

Mpairwe, Y. (2014). [Personal Communication].

Mshana, S. E., Joloba, M., Kakooza, A., & Kaddu-Mulindwa, D. (2009). Campylobacter spp among Children with acute diarrhea attending Mulago hospital in Kampala - Uganda. *African Health Sciences, 9*(3), 201-205.

Muhanguzi, D., Picozzi, K., Hatendorf, J., Thrusfield, M., Welburn, S. C., Kabasa, J. D., & Waiswa, C. (2014). Prevalence and spatial distribution of Theileria parva in cattle under crop-livestock farming systems in Tororo District, Eastern Uganda. *Parasit Vectors, 7*, 91. doi: 10.1186/1756-3305-7-91

Mukonzo, J. K., Namuwenge, P. M., Okure, G., Mwesige, B., Namusisi, O. K., & Mukanga, D. (2013). Over-the-counter suboptimal dispensing of antibiotics in Uganda. *J Multidiscip Healthc, 6*, 303-310. doi: 10.2147/JMDH.S49075

Munford, R. S. (2001). *Sepsis and Septic Shock in Harrison's Principles of Internal Medicine* (15 ed.). N.Y: McGraw-Hill.

Mwaka, A. D., Mayanja-Kizza, H., Kigonya, E., & Kaddu-Mulindwa, D. (2011). Bacteriuria among adult non-pregnant women attending Mulago hospital assessment centre in Uganda. *Afr Health Sci, 11*(2), 182-189.

Nakaye, M., Bwanga, F., Itabangi, H., Iramiot, J. S., Mwambi, B., & Bazira, J. (2014). AmpC-BETA Lactamases among Enterobacteriaceae Isolated at a Tertiary Hospital, South Western Uganda. *British Biotechnology Journal, 4*(9), 1026-1036 doi: 10.9734/BBJ/2014/10570

Nakiwala, D. (2013). *Performance of Cefepime-Clavulanic acid in the Detection of Extended Spectrum Beta Lactamases* (Bachelor of Biomedical Laboratory Technology), Makerere University, Makerere University.

Nambatya, J. L., Nyairo, S., Bironse, M., Kacwiya, S., Musigunzi, N., & Kamulegeya, A. (2011). Antibiotic use knowledge and behavior at a Ugandan university. *International Journal of Infection Control, 7*(4), 1-7. doi: 10.3396/ijic.v7i4.7968

Nantanda, R., Hildenwall, H., Peterson, S., Kaddu-Mulindwa, D., Kalyesubula, I., & Tumwine, J. K. (2008). Bacterial aetiology and outcome in children with severe pneumonia in Uganda. *Ann Trop Paediatr, 28*(4), 253-260. doi: 10.1179/146532808X375404

Napolitano, F., Izzo, M. T., Di Giuseppe, G., & Angelillo, I. F. (2013). Public knowledge, attitudes, and experience regarding the use of antibiotics in Italy. *PLoS One, 8*(12), e84177. doi: 10.1371/journal.pone.0084177

Nayyar, G. M., Breman, J. G., Newton, P. N., & Herrington, J. (2012). Poor-quality antimalarial drugs in southeast Asia and sub-Saharan Africa. *Lancet Infect Dis, 12*(6), 488-496. doi: 10.1016/S1473-3099(12)70064-6

Nsadha, Z. (2013). Porcine diseases of economic and public health importance in Uganda: Review of successes and failures in disease control and interventions (pp. 1-26): ILRI.

Ocaido, M., Otim, C. P., Okuna, N. M., Erume, J., Ssekitto, C., Wafula, R. Z. O., . . . Monrad, J. (2005). Socio-economic and livestock disease survey of agro-pastoral communities in Serere County, Soroti District, Uganda. *Livestock Research for Rural Development, 17*.

Ocan, M., Bbosa, G. S., Waako, P., Ogwal-Okeng, J., & Obua, C. (2014). Factors predicting home storage of medicines in Northern Uganda. *BMC Public Health, 14*, 650. doi: 10.1186/1471-2458-14-650

Ocan, M., Bwanga, F., Bbosa, G. S., Bagenda, D., Waako, P., Ogwal-Okeng, J., & Obua, C. (2014). Patterns and predictors of self-medication in northern Uganda. *PLoS One, 9*(3), e92323. doi: 10.1371/journal.pone.0092323

Odongo, C. O., Anywar, D. A., Luryamamoi, K., & Odongo, P. (2013). Antibiograms from community-acquired uropathogens in Gulu, northern Uganda--a cross-sectional study. *BMC Infect Dis, 13*, 193. doi: 10.1186/1471-2334-13-193

Ogwal-Okeng, J., Obua, C., Waako, P., Aupont, O., & Ross-Degnan, D. (2004). A comparison of prescribing practices between public and private sector physicians in Uganda. *East Afr Med J, Feb;Suppl*, S12-16.

Ogwang, P. E., Nyafuono, J., Agwaya, M., Omujal, F., Tumusiime, H. R., & Kyakulaga, A. H. (2011). Preclinical efficacy and safety of herbal formulation for management of wounds. *Afr Health Sci, 11*(3), 524-529.

Ojok, L. (1993). Disease as important factor affecting increased poultry production in Uganda. *Trop. Landwirk., 94*, 7-44.

Ojulong, J., Mwambu, T., Jolobo, M., Agwu, A., Bwanga, F., Najjuka, C., & Kaddu-Mulindwa, D. (2008). Prevalence of Methicillin resistant Staphylococcus aureus (MRSA) among isolates from surgical site infections in Mulago hospital- Kampala, Uganda. *The Internet Journal of Infectious Diseases, 7*(2).

Okeke, I. N., Lamikanra, A., & Edelman, R. (1999). Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. *Emerg Infect Dis, 5*(1), 18-27. doi: 10.3201/eid0501.990103

Rwego, I. B., Isabirye-Basuta, G., Gillespie, T. R., & Goldberg, T. L. (2008). Gastrointestinal Bacterial Transmission among Humans, Mountain Gorillas, and Livestock in Bwindi Impenetrable National Park, Uganda

Transmisión de Bacterias Gastrointestinales entre Humanos, Gorilas de Montaña y Ganado en el Parque Nacional Bwindi Impenetrable, Uganda. *Conservation Biology, 22*(6), 1600-1607. doi: 10.1111/j.1523-1739.2008.01018.x

Sasanya, J. J., Ejobi, F., Enyaru, J., Olila, D., & Ssengoye, G. (2008). Public Health Perspectives of Penicillin G Residues in Cow Milk and Edible Bovine Tissues Collected from Mbarara and Masaka Districts, Uganda. *African Journal of Animal and Biomedical Sciences, 3*(35-40).

Sasanya, J. J., Ogwal Okeng, J. W., Ejobi, F., & Muganwa, M. (2005). Use of sulfonamides in layers in Kampala district, Uganda and sulfonamide residues in commercial eggs. *African Health Sciences, 5*(1), 33-39.

Seni, J., Bwanga, F., Najjuka, C. F., Makobore, P., Okee, M., Mshana, S. E., . . . Kateete, D. P. (2013). Molecular characterization of Staphylococcus aureus from patients with surgical site infections at Mulago Hospital in Kampala, Uganda. *PLoS One, 8*(6), e66153. doi: 10.1371/journal.pone.0066153

Seni, J., Najjuka, C. F., Kateete, D. P., Makobore, P., Joloba, M. L., Kajumbula, H., . . . Bwanga, F. (2013). Antimicrobial resistance in hospitalized surgical patients: a silently emerging public health concern in Uganda. *BMC Res Notes, 6*, 298. doi: 10.1186/1756-0500-6-298

Sobeslavsky, O., Sebikari, S. R., Harland, P. S., Skrtic, N., Fayinka, O. A., & Soneji, A. D. (1977). The viral etiology of acute respiratory infections in children in Uganda. *Bull World Health Organ, 55*(5), 625-631.

Sosa, A., Byarugaba, D., Amabile-Cuevas, C. F., Hsueh, P.-R., Kariuki, S., & Okeke, I. N. (2010). *Antimicrobial Resistance in Developing Countries*. New York: Springer.

Sosa, A., Najjuka, C. F., & Mwenya, D. (2011). Drivers of antibiotic resistance in Uganda and Zambia Presentation to Global Health Council, Washington, DC,. In D. F. Susan (Ed.): Alliance for the Prudent Use of Antibiotics.

Ssendagire, S. (2012). Suspending importation of Indian poor quality medicines is necessary but not sufficient, *New Vision*. Retrieved from http://www.newvision.co.ug/mobile/Detail.aspx?NewsID=634362&CatID=4

Ssennoga, A. (2014). *Assessement of drug susceptibility patterns of methicillin resistant Staphylococcus aureus on archived samples within Mulago National Referral and Teaching Hospital.* (Bachelor of Biomedical Laboratory Technology), Makerere University, Kampala.

Stamm, W. E. (2001). *Urinary Tract Infections and Pyelonephritis in Harrison's Principles of Internal Medicine* (15 ed.). N.Y: McGraw-Hill

Svanström, P. (2014). *Pathogens and antibiotic resistant bacteria in abattoir waste and animals.* (Veterinary Medicine), Upsalla, Uppsala.

Tambi, N. E., Maina, W. O., & Ndi, C. (2006). An estimation of the economic impact of contagious bovine pleuropneumonia in Africa. *Rev Sci Tech, 25*(3), 999-1011.

Transparency, I. (2012, 30 August 2012). Uganda tops East Africa in corruption. Retrieved 12 September 2014, 2014, from http://www.transparency.org/news/pressrelease/uganda_tops_east_africa_in_corruption

UBOS. (2014). National Population and Housing census 2014 Provisional Result. In R. Edition (Ed.), (Vol. NOVEMBER 2014, pp. 1-73). Kampala: UGANDA BUREAU OF STATISTICS.

Vandepitte, J., Hughes, P., Matovu, G., Bukenya, J., Grosskurth, H., & Lewis, D. A. (2014). High Prevalence of Ciprofloxacin-Resistant Gonorrhea Among Female Sex Workers in Kampala, Uganda (2008–2009). *Sexually Transmitted Diseases, 41*(4), 233-237. doi: 10.1097/olq.0000000000000099

Walters, M. S., Routh, J., Mikoleit, M., Kadivane, S., Ouma, C., Mubiru, D., . . . Mintz, E. (2014). Shifts in Geographic Distribution and Antimicrobial Resistance during a Prolonged Typhoid Fever Outbreak — Bundibugyo and Kasese Districts, Uganda, 2009–2011. *PLoS Negl Trop Dis, 8*(3), e2726. doi: 10.1371/journal.pntd.0002726

WHO. (2015). Antimicrobial resistance: Draft global action plan on antimicrobial resistance (Vol. SIXTY-EIGHTH WORLD HEALTH ASSEMBLY, pp. 1-19). Geneva: World Health Organisation

Wolfgang, F. (2012). The East African ride to Middle Income. from http://blogs.worldbank.org/africacan/the-east-african-ride-to-middle-income

APPENDIX

UNAS COUNCIL

Nelson K. Sewankambo Prof.	President
Patrick R. Rubaihayo Prof.	Vice-President
Edward K. Kirumira Prof.	Treasurer
Justin Epelu-Opio Prof.	Secretary General
David Bakibinga Prof.	Member
Elly N. Sabiiti Prof.	Member
Fredrick I.B. Kayanja Prof.	Member
John R. S. Tabuti Prof.	Member
Julius Y.K. Zake Prof.	Member
Livingstone S. Luboobi Prof.	Member
Mary J.N. Okwakol Prof.	Member
Celia Nalwadda MS.	Ex-Officio / Caretaker Executive Secretary

GARP-UGANDA WORKING GROUP

Prof. Denis K. Byarugaba (Chair). Associate Professor of Microbiology at Makerere University, College of Veterinary Medicine, Animal Resources and Biosecurity.

Donna A. Kusemererwa (Co-Chair). Pharmacist. Private Consultant.

Aziz A. Maij. Pharmacist, Senior Programme Associate for the Sustainable Drug Seller Initiative (SDSI) Project, Management Sciences for Health.

Charles B. Rwabukwali. Professor of Medical Anthropology, Department of Sociology, Makerere University.

Connie Cleona Kyarisiima. Lecturer, Department of Agricultural Production, College of Agricultural and Environmental Sciences, Makerere University.

Eric Wobudeya. MD. Consultant Pediatrician, Mulago National Referral Hospital, Investigator, MU-JHU Research Collaboration.

Florence Najjuka. MD. Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University.

Frederick Byarugaba. Professor of Microbiology, Head of Microbiology Department, Mbarara University of Science and Technology.

George Mukiibi-Muka. Senior Principal Research Officer, National Agriculture Research Organisation.

Henry Wamala Kakande. MD. Deputy Chief of Party, Management Sciences for Health, STRIDES.

Michael Romeo Mutyaba. Pharmacist, Drug Assessment and Research Officer, National Drug Authority.

Morries Seru. Principal Pharmacist, Ministry of Health.

Richard Odoi Adome. Professor of Pharmacy, School of Health Sciences, College of Health Sciences, Makerere University.

Victoria Katawera. Medical Microbiologist, MSF-Epicentre Mbarara Research Base, Mbarara University of Science and Technology.

GARP SECRETARIAT: Center for Disease Dynamics, Economics & Policy (CDDEP)

Hellen Gelband, GARP Global Coordinator, Associate Director, CDDEP.
Ramanan Laxminarayan, Director, CDDEP.

Sciences for Prosperity

Uganda National Academy of Sciences
A4 Lincoln House Makerere University
P.O. Box 23911, Kampala, Uganda
Tel: +256-414-533 044
Fax: +256-414-533 044
E-mail: unas@unas.or.ug
www.ugandanationalacademy.org

ISBN 978-9-9704241-0-8