ANTIBIOTIC PRESCRIBING PATTERNS AT RIFT VALLEY PROVINCIAL GENERAL HOSPITAL: A POINT PREVALENCE SURVEY

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DEDICATION

To the Almighty God who gave me the strength to do all things and was faithful to complete the good work He had begun.

To my loving and supportive parents, Mr. & Mrs. Momanyi, I am because you are.

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Abstract

Background: Antibiotics are commonly prescribed drugs globally but most of their use is irrational. This causes wastage of scarce health care resources, poses increased risk of adverse drug reactions, emergence of resistance and poor treatment outcomes. There is scarce published local data on patterns of antibiotic prescribing in Kenya and hence the impetus for the present study.

Study Objective: To describe the antibiotic prescribing patterns among the patients admitted to Rift Valley Provincial General Hospital in Kenya.

Methods: This was a cross-sectional study. A total of 179 participants were recruited from all inpatient departments through stratified proportionate random sampling. All admitted patients on oral or parenteral antibiotic therapy were eligible. Data was abstracted from the patients' medical records into predesigned structured forms. This data included socio-demographic characteristics of patients, the name and regimen of antibiotic, diagnosis, ward or department type and adherence to the prescribing guidelines. The raw data was coded, entered into Microsoft excel version 2010 to create a database and then exported to STATA version 13 for analysis. Prevalence of antibiotic use was determined using proportions. Data was presented in frequency tables and figures for important variables. Associations between predictor variables such as socio-demographic factors and outcome variables such as the type of antibiotics, prevalence of use, guideline compliance and rational prescribing were determined using Chi square. Stepwise backward binary logistic regression was done to determine the independent predictors of rational antibiotic prescribing and guideline compliance. Statistical significance was set at 95% confidence level and values with $p \leq 0.05$ were considered statistically significant.

Results: The prevalence of antibiotic prescribing at Rift Valley Provincial General Hospital was 54.7%. Among the department/ward type, the highest prevalence of antibiotic prescribing was found in critical care unit and isolation ward, both at 100%. Obstetrics and gynecology department had the least prevalence at 20.8%. Penicillins (46.9%) followed by cephalosporins (44.7%) were the most prescribed antibiotic classes.

Benzylpenicillin (52.0%) was the most prescribed penicillin while ceftriaxone (91.0%) was the most prescribed cephalosporin. There was rational prescribing in 33.9% (n=121) of all the 357 antibiotic encounters. The use of an antibiotic for prophylaxis or treatment of a neonatal infection was 5 times more likely to be rational as compared to other antibiotic uses (COR=5.84, 95% CI=2.05-16.64, p=0.001). Compliance to prescribing according to the guidelines was observed in 45.8% (n=82) of the study population. There was a negative association between age and compliance to guideline such that the prevalence of guideline compliance declined as participants' age increased (COR=0.67, 95% CI=0.54-0.84, p<0.001). Antibiotic prescribing among the neonates was 4 times more likely to be in accordance to the established guidelines as compared to adults (COR=0.23, 95% CI= 0.08 – 0.69, p=0.009).

Conclusion: There was a high prevalence of irrational antibiotic prescribing and low compliance to local and international guidelines at Rift Valley Provincial General Hospital.

Recommendations: Prescribers should be encouraged to improve on their antibiotic prescribing habits by following the treatment guidelines. Further research is, however, necessary to find out the patients, prescribers and hospital contextual factors that may be impacting on poor antibiotic prescribing habits as well non-adherence to treatment protocols.

Abbreviations & Acronyms

ARPEC	Antibiotic Resistance and Prescribing in European Children
BRICS	Brazil, Russia, India, China South Africa
ECDC-PPS	European Centre for Disease Prevention and Control Point Prevalence Survey
EML	Essential Medicines List
ESAC	European Surveillance of Antimicrobial Consumption
GARP	Global Antibiotic Resistance Partnership
GLOBAL-PPS	Global Point Prevalence Survey of Antimicrobial Consumption and Resistance
ICU	Intensive Care Unit
INN	International Non-proprietary Name
KEML	Kenya Essential Medicines List
KEMSA	Kenya Medical Supplies Agency
KNH	Kenyatta National Hospital
LMICs	Low and Middle Income Countries
MDR-TB	Multi Drug Resistant Tuberculosis
MRSA	Methicillin Resistant Staphylococcus Aureus
RVPGH	Rift Valley Provincial General Hospital
PPS	Point Prevalence Surveys
STGs	Standard Treatment Guidelines
TB	Tuberculosis
WHO	World Health Organization
WHA	World Health Assembly
XDR-TB	Extensively Drug Resistant Tuberculosis

Operational Definition of Terms

Antibiotics	Medicines used to prevent and treat bacterial infections
Rational use of an antibiotic	Prescribing of the correct choice of antibiotic only where it is necessary, at the correct dose, frequency, duration and route of administration
Irrational use of an antibiotic	Injudicious use of an antibiotic to treat non bacterial infections and use of incorrect drug, dose, frequency, duration or route of administration
Guideline compliance	Adherence to the facility based, national or international treatment guidelines for a specific medical condition as regards to the choice of antibiotic, dose, frequency, duration and route of administration

CHAPTER ONE: INTRODUCTION

1.1 Background

1.1.1 Prevalence of Antibiotic use

Antibiotics form part of the most frequently prescribed therapeutic class of drugs. Studies show that more than 1 out of 3 hospitalized patients receives an antibiotic (1). Over the period between 2000 to 2010, global antibiotic consumption increased by 36% (2) with Brazil, Russia, India, China and South Africa accounting for 76% of this increase. Australia and New Zealand had the highest antibiotic consumption per person. The largest absolute increase in consumption during this period was observed for broad spectrum penicillins, cephalosporins and fluoroquinolones (2). There was also an increase in consumption of two last resort antibiotics – carbapenems (45%) and polymixins (13%) (2). The first global point prevalence survey was able to establish the over use of second line antibiotics such as vancomycin in North America and meropenem in Asia and North America (1). Ceftriaxone was found to be the most frequently used antibiotic worldwide (1). In Kenya, penicillins were found to be the most frequently prescribed class of antibiotics followed by tetracyclines in the period between 1997 to 2001 (3). The prevalence of outpatient antibiotic prescribing was found to be 77% in public health facilities and 68% in faith based organizations (4).

1.1.2 Rational and Irrational use of antibiotics

The rational use of medicines requires that patients receive appropriate medications according to their clinical needs, in the right dose, for an adequate duration and at the lowest cost to them and the community (5). Rational use of antibiotics therefore involves using the appropriate drug based on clinical findings together with laboratory support. It also involves using the right dose, frequency, duration and route of administration (6) at a cost that the patient can afford. Irrational use of medicines is a global problem (5).

The WHO estimates that over half of all medicines worldwide are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly (5). In Africa, it is estimated that up to two thirds of antibiotics are used irrationally (7). The irrational use of medicines involves the use of too many medicines (poly-pharmacy), inappropriate use of antimicrobials such as inadequate dosage, duration or use of

antibiotics for non-bacterial infections, overuse of injections where oral route would be sufficient, among others (5). Irrational use of antibiotics results in wastage of scarce health care resources, increased risk of adverse drug reactions, possible emergence of resistance and poor outcomes (8).

1.1.3 Guidelines on use of antibiotics

There are several important considerations when prescribing antibiotics. It is important to first establish whether an antibiotic is necessary. This is because many of the infections in general practice are of viral origin and thus antibiotics will not work (6). When choosing an appropriate antibiotic, the etiological agent, patient factors and pharmacokinetic and pharmacodynamic properties of the drug must be considered (5,8). The choice of the regimen in terms of the dose, route, frequency and duration should also be considered (6). In addition, the cost of the medicines is an important factor. Identifying opportunities to switch to narrow-spectrum, cost-effective oral agents for the shortest duration necessary is important (9). The prescriber should also take into consideration the potential adverse reactions of the antibiotic and possible drug- drug or drug – food interactions (9). These principles ensure that antibiotics are used in a responsible manner that benefits individuals and the community.

1.1.4 Targets for potential improvement in the use of antibiotics

At the hospital level, WHO recommended that each facility drafts its own hospital antibiotics policy. This should be in line with the national policy except for a few changes as warranted by the local antimicrobial resistance profiles (10). The policy should be based on the spectrum of antibiotic activity, pharmacokinetics/pharmacodynamics profile of the medicines, adverse effects, potential to select resistance, cost and special needs of individual patient groups (10). It should also set the levels for prescribing antibiotics specifically first line antibiotics, second line, reserve antibiotics and restricted choice antibiotics (10). There should be surveys on antibiotic consumption in order to quantify antibiotic use and establish resistance patterns. The findings should be disseminated to the prescribers in order to improve antibiotic prescribing. Promoting use of diagnostic tools to guide antibiotic use is another useful approach (11). The study therefore sought

to assess the use of antibiotics in a level 5 hospital in Kenya in order to identify targets for potential improvement.

1.2 Problem Statement

It is estimated that half of all medicines in Africa are used irrationally including up to two thirds of antibiotics (7). Studies show that both public health facilities and retail pharmacies in Kenya prescribe and dispense antibiotics that are not indicated for particular infections and they provide insufficient regimens of correct drug choices (12). In a study conducted by the Ministry of Health in 2003, only 4 out of 10 public health facilities prescribed antibiotics according to national treatment guidelines in at least 90% of the time (13). Previous findings at Kenyatta National Hospital in 2000 showed that prolonged (73%) and sometimes unjustified use (42%) of antibiotics in the neonatal unit were contributory factors of increased antibiotic resistance in hospital acquired infections (14). About a third of all monthly admissions to the unit were given antibiotics and nearly half of those patients were not investigated with a laboratory evaluation or confirmation of drug susceptibility (14). Another study found that drug sensitivity discs were not always available at the KNH laboratory and thus patients often received antibiotics assumed to be effective (15). Anecdotal reports at Rift Valley Provincial General Hospital (RVPGH) indicated irrational use of antibiotics particularly in the internal medicine department where selection of antibiotics was based on drug availability. The frequency of the dose, duration and route of administration of the antibiotics were often not optimal. There was also inadequate use of laboratory support in terms of culture and sensitivity to guide the choice of antibiotics. This study therefore sought to describe and document the prevalence of use and prescribing patterns at the facility in order to establish whether there was rational or irrational use of antibiotics then identify potential areas of improvement in order to promote rational use. This would help in curbing antibiotic resistance that has been shown to arise directly from the irrational use of antibiotics.

1.3 Research Questions

1. What are the antibiotic prescribing patterns at the Rift Valley Provincial General Hospital?
2. Is the prescribing of antibiotics at the Rift Valley Provincial General Hospital rational or irrational?
3. Is there compliance with existing guidelines in antibiotics prescribing at the Rift Valley Provincial General Hospital?

1.4 Study Objectives

1.4.1 General Objective

To describe the antibiotic prescribing patterns in Rift Valley Provincial General Hospital

1.4.2 Specific Objectives

1. To estimate the prevalence of antibiotic prescribing in Rift Valley Provincial General Hospital
2. To find out whether antibiotics are used rationally or irrationally in Rift Valley Provincial General Hospital
3. To determine the compliance of antibiotic prescribing at Rift Valley Provincial General Hospital with existing guidelines

1.5 Study Significance

There is need for coordinated efforts on rational antibiotic use in order to counter the acceleration of antibiotic resistance. WHO requires that all countries develop national action plans on antibiotic resistance (16). Kenya drafted its national policy on the prevention and containment of antibiotic resistance(17). The Ministry of Health formulated a National Action Plan that has 5 strategic objectives that address the emergence of antibiotic resistance (18). Strategic objective number 4 aimed at the optimization of antibiotic use and thus required baseline data on the use of the antibiotics in various facilities around the country. The study thus formed part of the baseline survey of antibiotic use in a level 5 facility. This helped to fill a knowledge gap as previously there was no study on antibiotic utilization patterns in a level 5 facility in Kenya. The study findings also enabled the identification of gaps for quality improvement in the

prescribing and use of antibiotics at RVPGH. The gaps identified would also guide the development of various interventional programs to promote rational antibiotic use at the facility. One of the expected products of the study is an antimicrobial stewardship committee that would oversee the implementation of the various quality interventions.

The study also formed part of the first national point prevalence surveys of antibiotic consumption in the country. This provided baseline data that could be compared with subsequent point prevalence studies in order to determine the effectiveness of various interventions aimed at improving antibiotics use.

The study is useful to healthcare personnel in promoting rational antibiotic use. Previous studies have shown that feedback of reliable reports to clinicians on antimicrobial use and resistance patterns helps to improve antimicrobial use (19). It also benefits the patients who will receive appropriate antibiotics in the correct dosages, frequency, route and duration and proper medication counseling on rational antibiotics use.

1.6. Conceptual Framework

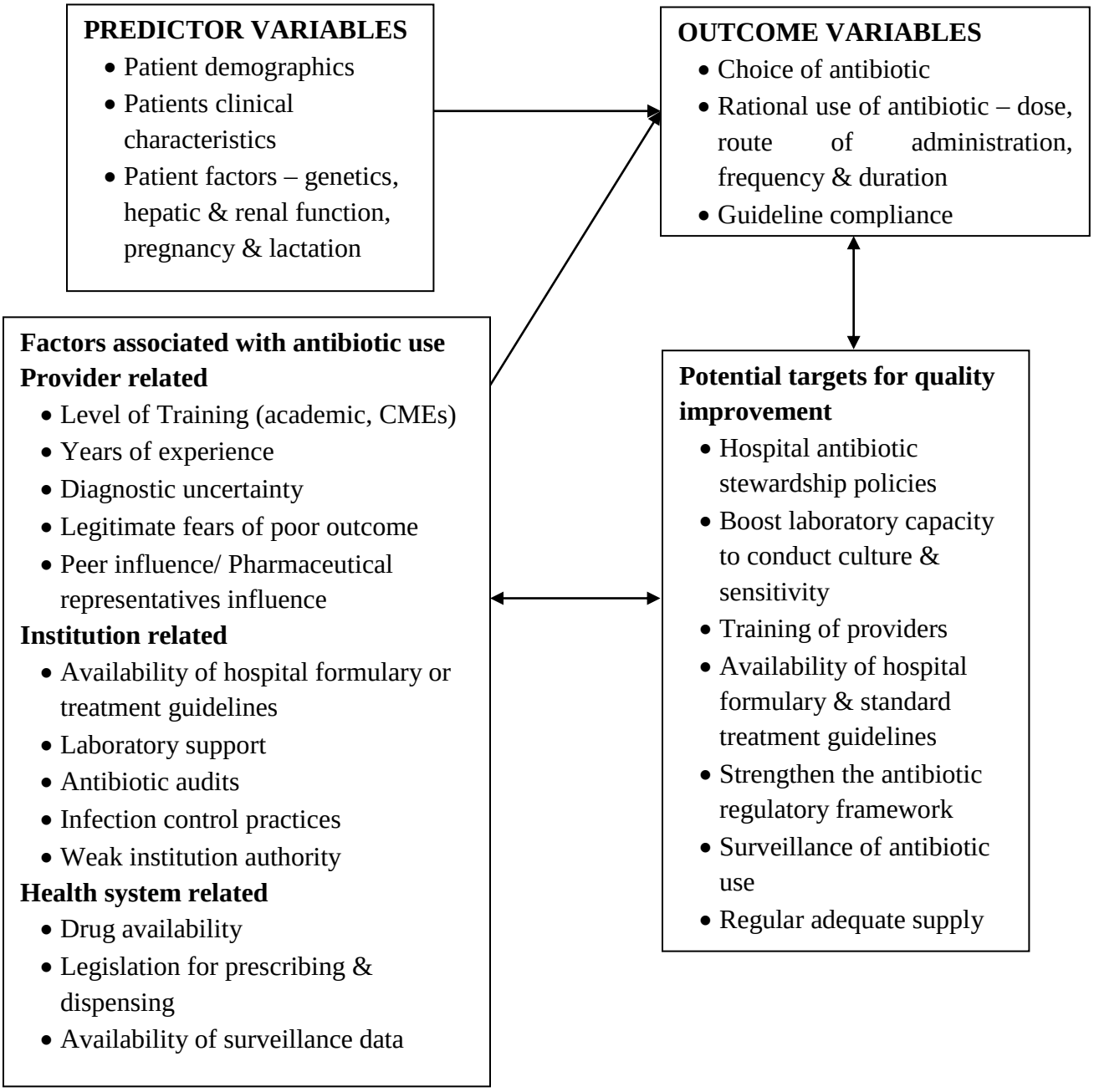


Figure 1: Conceptual Framework

CHAPTER TWO: LITERATURE REVIEW

2.1 Global, Regional and Local Antibiotic Consumption

Antibiotics are one of the most widely used therapeutic class of drugs globally (9). Antibiotics are medicines used to prevent and treat bacterial infections (20). The discovery of antibiotics revolutionized the history of medicine in that they saved many lives and contributed to the control of infectious diseases that were responsible for majority of the morbidity and mortality for most of human existence (21). Infectious diseases remain a big challenge particularly in developing countries where antibiotics have had remarkable benefits (12). However, the gains are now seriously jeopardized by the emergence of antibiotic resistance where the microbes have become resistant to the most commonly available and effective first line agents (12). It has been shown that antibiotic use drives the development of antibiotic resistance (22). Antibiotic prescriptions vary significantly between continents and countries as shown by 1 out of 2 hospitalized patients receiving antibiotics in Africa and Asia while 1 out of 3 patients in Europe is on an antibiotic (1). The variation in volumes and patterns of antibiotic consumption is among the factors that contribute to variations in antibiotic resistance across countries (2).

Global antibiotic consumption is on the rise with most of this increase occurring in low and middle income countries (23). In the most comprehensive analysis to date on global antibiotic consumption conducted in the period 2000 to 2010 in 71 countries, the total antibiotic consumption increased by 36% from approximately 50 billion to 70 billion standard units (2). The five "BRICS" nations – Brazil, Russia, India, China and South Africa - accounted for 76% of this increase. Two major trends have been shown to be responsible for the global rise in antibiotic consumption. They are linked to the rising household income such that many households can afford antibiotics. Moreover, with higher incomes, households can afford animal protein diet leading to increased demand for animal products. To meet this demand, livestock farming has been intensified where sub therapeutic doses of antibiotics are used to promote animal growth (22,21). According to the global antibiotic consumption analysis, India consumes the largest volume of antibiotics followed by China (2). The per capita antibiotic consumption was generally higher in high income countries with Australia and New Zealand having the highest

antibiotic consumption per person (2). In majority of the countries studied, about 20% of the antibiotics were used in the hospital and health care facilities while 80% were used in the community, either prescribed by health care providers or purchased directly by the consumers without prescription (25). The study found that, in many countries, at all economic levels, clinicians had incentives to overuse antibiotics (2,20).

By antibiotics class, about 60% of the global antibiotic consumption in 2010 consisted of cephalosporins and broad spectrum penicillins, increasing by 41% from 2000 (2). These are among the oldest antibiotics and are still the first line agents thus forming the primary treatment for common infections worldwide (2). The class with the greatest increase in consumption in the period 2000 to 2010 was monobactams with more than 20 fold increase. This was followed by the glycopeptides that includes vancomycin. There was also increased consumption of two last resort classes - carbapenems (45%) and polymixins (13%). In majority of the countries, there was seasonal variation in antibiotic consumption. This increased during the winter flu season, heavy rains and monsoons or very hot weather when the incidence of infectious diseases peaked (2).

The prevalence of antibiotic use in Germany was 25.5% in 2011. This was higher than in 1994 where it was 17.7%(26). Surgery had the highest antibiotic use (29.8%) followed by the internal medicine department (28.1%). Half of all patients in the intensive care units (ICU) were on an antibiotic. The most frequently prescribed class of antibiotics was the second generation cephalosporins (14.6%) with Cefuroxime as the most frequently used agent. This class was followed by fluoroquinolones (14%) then penicillin with a beta lactamase inhibitor (12.6%) and third generation cephalosporins (10.6%) (26).

In Nigeria, the prevalence of antibiotic use was 55.9%. Of those on antibiotics, 61.9% received combination therapy. The highest proportion of antibiotic use was among persons less than 12 years (58.9%) (27). Similar findings were reported in Egypt where the most significant use of antibiotics was found to be in persons less than 12 years and in ICU patients (28). According to the study, the overall prevalence of antibiotic use in

Egypt was 59%. The third generation cephalosporins was the most frequently prescribed class of antibiotics (28) as compared to penicillins in Nigeria(27).

In a national report on antibiotic use in Kenya for the period 1997 to 2001, penicillins were the most frequently prescribed class of antibiotics followed by tetracyclines (3). Cotrimoxazole consumption increased from 1997 to 1999 due to its growing prophylactic use against opportunistic infections in the HIV infected population (3). Fluoroquinolone use increased 18 fold during 1997 to 1998 following the release of generics into the market. Aminoglycoside consumption increased steadily after 1999 with gentamicin accounting for 75% of the mean annual amount (3). During the study, the use of first generation cephalosporins was higher than that of second and third generation (3). Macrolide use remained stable after 1999 while the popularity of rifampicin grew due to the new TB combination regimen and increased treatment of TB as an opportunistic infection in the HIV infected population (12). In 2003, an assessment of the pharmaceutical situation in Kenya showed that the percentage of patients prescribed one or more antibiotics in public health facilities was 73% (13). This was consistent with another health facility survey in 2009 that reported a prevalence of 77% in public health facilities and 68% in faith based facilities. This indicated very high antibiotic prescribing compared to the reference of 30% (4).

2.2 Rational and irrational use of antibiotics

There are several phases that comprise the rational prescribing of an antibiotic. These include the perception of the need of an antibiotic, choice of the antibiotic, choice of the regimen, timing of initiation of the antibiotic and monitoring the efficacy of the drug (6). It is estimated that 20-50% of total antibiotic use is inappropriate or irrational. Inappropriate use is the unnecessary use of antibiotics for instance to treat viral infections or the sub-optimal use of antibiotics for responsive conditions. It also includes the unnecessary use of broad spectrum antibiotics, incorrect dose or duration, inappropriate route of administration or poor patient adherence to prescribed treatment (29).

A myriad of evidence indicates inappropriate antibiotic use in the hospital and health care facility setting. For instance, the rate of inappropriate antibiotic prescribing in Nepal ranges from 10-42% (30). Furthermore, in Vietnam, one third of the hospital antibiotic prescriptions were found to be inappropriate. These were found particularly in the surgical wards, obstetrics and gynecology departments and in the national hospital (31).

Several studies have revealed over use of antibiotics in several countries. In Germany, it was reported that there was an increase in the use of the new medicines against methicillin resistant *staphylococcus aureus* (MRSA) without an increase in the incidence or prevalence of MRSA infections (26). A study in Nigeria found that 96.7% of inpatients and 50.3% of outpatients received at least one antibacterial drug. Only 4.2% of this antibiotic prescribing was supported by susceptibility testing (32). The situation in Kenya is not very different as shown by a study done in the neonatal unit of Kenyatta National Hospital showed that prolonged (73%) and unjustified (42%) use of antibiotics were some of the factors that led to increased antibiotic resistance in hospital acquired infections (14). In this unit, 50% of the patients admitted were put on antibiotics while only half of those were investigated with laboratory evaluation of sepsis or confirmation of drug susceptibility (14). In another study done in the intensive care unit of KNH, it was established that only 26% of the patients were on appropriate antibiotic treatment (15). Drug sensitivity discs were not always available in the hospital laboratory and thus patients only received antibiotics presumed to be effective (15).

Rational use of medicines involves the use of several key documents to guide the procurement, prescribing and dispensing of antibiotics. These documents include standard treatment guidelines (STGs), essential medicines list (EML) and hospital formularies. In Kenya, it was found that majority of these important documents were not available to the health care professionals. The national EML, facility specific formulary or model WHO medicine list were found in 41.7% of the government facilities while STGs were found in 38.9% of these facilities (4). It should be noted that the availability of the guidelines do not necessarily indicate adherence. For instance, a survey conducted in Kenya by the Ministry of Health found that only 4 in 10 public healthcare facilities

prescribed according to the national treatment guidelines, at least 90 percent of the time (13). Similarly, a general assessment of inpatient paediatric care in all district hospitals found poor adherence to national or international treatment guidelines. For instance, prescribed doses per kilogram body weight of the three most frequently prescribed parenteral antibiotics (penicillin, gentamicin and chloramphenicol) showed significant variation. There was evidence of overdosing of chloramphenicol and under dosing of gentamicin in respiratory tract infections (33).

In certain hospitals, broad spectrum antibiotics were administered even where a specific pathogen had been identified (22). As these drugs are effective against a wide range of microbes, they may contribute to the development and spread of resistant strains of many non-target organisms(22). In a study done in the United States of America in the period 2009 and 2010, it was shown that broad spectrum antibiotics were prescribed to inpatients even where clinical signs of infection were not present and that the treatment remained unchanged even after negative culture results (34).

Health care providers play an important role in promoting the inappropriate use of antibiotics. This occurs principally by prescribing antibiotics for non-bacterial infections such as malaria, diarrhea, influenza and uncomplicated viral upper respiratory tract infections (22). For instance in Nigeria, malaria accounted for 23.7% of all antibiotic prescriptions (27). One study investigated the antibiotic recommendations for common infections by various health care providers (physicians, nurses, pharmacists and pharmacy clerks) and these were compared with the Kenya national clinical guidelines for concordance. Seven case scenarios depicting throat infections caused by *Streptococcus*, acute otitis media, bronchitis, cystitis, common cold, *Shigella* dysentery and malaria were used (12). The health providers recommended antibiotic treatment at 67% of the time for acute bronchitis and 48% of the time for common colds neither of which are indicated for antibiotic use by the national guidelines. In 28% of the cases of acute otitis media and 58% of the cases of *Streptococcus* throat infections, drug choices were inappropriate. The drug choices for dysentery and cystitis were almost always incorrect (12). Inappropriate prescribing is most common for acute respiratory tract

infections and enteric diseases for which demand for treatment is high (12). In district hospitals, about 71% of the antibiotics prescribed for pneumonia were for very severe cases while only 16% of recorded admissions fit into this category (33). Diarrhea rarely requires antibiotic treatment. The WHO and Kenya national guidelines clearly stipulate that young children should be treated with Oral Rehydration Salts (ORS) for most types of diarrhea (12). However, antibiotics remain a popular choice for empiric therapy in Kenya as more than half of the cases of diarrhea were given one or more antibiotics (13). In health clinics, antibiotics were prescribed in 67% of the visits for diarrhea in 2006 (35) while fewer than 3 in 10 primary health care providers used ORS for management of diarrhea in at least 90% of the cases (13). In another health survey in Kenya, it was found that all cases of upper respiratory tract infections were prescribed antibiotics (13). This deviates from guideline recommendations that stipulates symptomatic treatment of the cough with linctus or home remedy, adequate intake of fluids, use of antipyretics in case of fever but no use of antibiotics unless a bacterial cause is established (4). In Germany, it was found that anti-pseudomonas antibiotics (piperacillin with a beta lactamase inhibitor and carbapenems) were prescribed for community acquired pneumonia in about 20% of the cases. This is injudicious practice as *Pseudomonas* species does not normally play a role in the pathogenesis of community acquired pneumonia (26).

Inappropriate antibiotic use has also been reported in surgical prophylaxis. Use of antibiotics before surgery is the evidence based standard. However, it has been shown that antibiotics are used post-surgery in many low and middle income countries (22). The administration of antibiotic prophylaxis after surgery has been associated with increased risk of surgical site infections. Seven times more antibiotics are used post-surgery than before surgery thus increasing cost and contributing to the potential for antibiotic resistance (36). Even where antibiotics are administered before surgery for prophylaxis, the dose or duration may be sub-optimal. In India, 19-86% of patients received inappropriate antibiotic prophylaxis (37). In Germany, surgical prophylaxis was prolonged (> 1 day) in 70% of the cases (26). In Nigeria, clinicians had several misconceptions regarding surgical prophylaxis. They believed that prolonging the duration of antibiotic prophylaxis and use of broad spectrum agents reduced the risk of

surgical site infections and other nosocomial infections (27). The study found that a large proportion of patients received antibiotics for medical prophylaxis with no justification of a medically accepted indication for prophylaxis. It was common practice for patients to receive antibiotics during their hospital stay in order to reduce the incidence of nosocomial infections (25). This was preferred over infection control practices.

It is important to accurately establish the need for antibiotics in a patient. This is because not all infections are caused by bacteria. A majority of infections in clinical practice are caused by viruses and antibiotics will not be effective. Even where a bacterial cause is established, an antibiotic may not always be necessary as many bacterial infections resolve spontaneously (6).

2.3 Antibiotic prescribing guidelines

When choosing an antibiotic, there are three main factors that should be considered. These include the aetiological agent, patient factors and the drug itself (6). The accurate determination of the causative agent is dependent on a combination of clinical acumen and laboratory support. Even where a bacteriology report is available, it is necessary to interpret the report as bacterial isolates from culture specimens may represent normal flora, colonisers or contaminants rather than true pathogens (6). Sensitivity results when available are at best only a guide to treatment. This is because they have some inherent limitations such as showing susceptibility of organism to an antibiotic that is not able to reach the site of infection or some organisms carry enzymes that, when expressed in vivo, can inactivate antimicrobial agents to which the organism shows in vitro susceptibility (9).

There are various patient factors to consider when selecting an antibiotic. Age is important as the very young and the very old tend to be more prone to the adverse effects of the antibiotics. Thoughtful selection and dose modifications are necessary in patients with hepatic or renal impairment (6). There are some antibiotics that cause severe toxic reactions in patients with certain genetic abnormalities for instance sulphonamides in patients with glucose-6-phosphate dehydrogenase deficiency. Antibiotics should, where possible, be avoided in pregnancy and when it is necessary to use them, beta lactam and

macrolides are probably the safest. A history of allergy to antibiotics should always be sought before administration (6).

The inherent characteristics of the specific antibiotic should also guide the appropriate selection. The prescriber should have adequate knowledge of the pharmacokinetic properties of the drug. Antibiotics vary in their ability to be absorbed orally or to cross the blood brain barrier and these factors will affect their routes of administration. The ability of the antibiotic to achieve therapeutic concentrations at the site of infection is also an important consideration that guides the choice of an appropriate agent. It is also necessary to know when to choose a bactericidal or bacteriostatic agent. Bactericidal agents are preferred over bacteriostatic ones in the case of serious infections such as endocarditis and meningitis to achieve rapid cure (9). Single agent antibiotics are preferred, however, combinations are considered in situations where synergistic action is desired and where critically ill patients require empiric therapy before microbiological etiology and/or antimicrobial susceptibility can be established (9). In addition, they can be used to extend the antimicrobial spectrum beyond that achieved by use of a single agent for the treatment of polymicrobial infections and to prevent emergence of resistance by using 2 or more agents with different mechanisms of resistance. In this case, the chance of a mutant strain being resistant to both antimicrobial agents is much lower than it being resistant to either one (9). The prescriber should also be aware of potential drug-drug interactions as many antibiotics can interact with other drugs. The drugs themselves also carry the risk of severe adverse effects that should be taken into consideration, for instance, sulphonamides are likely to cause severe skin reactions. Patient compliance to medication is an important factor when choosing antibiotics. The cost of the antibiotic is also of major concern. In calculating costs it is perhaps more reasonable to take into account the total cost of treatment rather than just the actual cost of antibiotic per dose (6).

The prescriber should review relevant clinical guidelines when determining the dose regimen and duration. The choice of antibiotic and regimen should also be guided by current best practice evidence. Whether the route of administration should be oral or

parenteral would depend on whether the patient is able to take oral treatment reliably. In critically ill patients, the parenteral route is preferred (9).

The appropriate timing of initiation of an antibiotic should be guided by the urgency of the situation. In critically ill patients, antibiotics should be started empirically immediately after or concurrently with the collection of diagnostic specimens (9). In more stable patients, antibiotics should be deliberately withheld until adequate specimens have been collected and submitted to the microbiology laboratory. This is because the drugs can suppress bacterial growth and thus make it difficult to arrive at an accurate diagnosis (9).

A routine early review of the patient's response about 3 days after commencing antibiotic treatment, is important to ensure that the patient is receiving appropriate treatment. After review the doctor will have to decide whether to continue with the present regimen, increase the level of treatment by for instance, increasing the dose or switching to a broader spectrum antibiotic, decrease the level of treatment or stopping the antibiotic if the infection has resolved or the objective of treatment has been achieved (6). Monitoring serum concentrations for antibiotics is useful for medications that have a fairly narrow therapeutic index (9).

Antibiotics can also be used for prophylaxis in several scenarios such as in surgical prophylaxis and in immunocompromised patients. Antibiotic prophylaxis can also be used to prevent transmission of communicable pathogens to susceptible contacts for instance ciprofloxacin can be given to close contacts of a patient with meningitis caused by *Neisseria meningitides.* Prophylaxis can be done before dental and other invasive procedures in patients susceptible to bacterial endocarditis. It can also be given in patients with traumatic injuries with a high probability of infectious complications such as in certain types of animal bites (36) and after penetrating brain injury (9). In surgical prophylaxis, antibiotics are used to reduce the incidence of postoperative surgical site infections. The antibiotic should cover the most likely organisms and be present in the tissues when the initial incision is made. Adequate serum concentrations should also be

maintained during the procedure. The duration of prophylaxis for surgical site infection should not exceed twenty four hours in most cases (39).

2.4 Challenges in the use of Antibiotics

Antibiotic consumption has increased worldwide but limited access to these medicines is a bigger challenge. Poor access to antibiotics is responsible for more deaths than antibiotic resistance (38). Over a million children die each year due to untreated pneumonia and sepsis (39). An estimated 169,760 deaths in India and 49,407 deaths in Nigeria could have been prevented through timely access to effective antibiotics (38).

Antibiotics are easily accessible over the counter in many parts of the world. In India, regulations that control over the counter sale of antibiotics are poorly enforced (38). In Kenya, antibiotics are available from a wide range of providers including family members and friends, physicians, health care workers, pharmacists and pharmacy clerks (12). There is a lot of self-medication with regards to antibiotics. It has been shown that where patients felt confident about the efficacy of an antibiotic previously prescribed to them, they preferred to visit a retail pharmacy to self-medicate or stock up on drugs for repeat conditions in the future (12).

Retail pharmacies, frequently operating without a license were shown to be preferred by patients because of accessibility, lack of consultation fees, shorter waiting times and willingness to negotiate treatment regimens to meet the financial needs of the clients (40). Studies show that more than a third of Nairobi residents use retail pharmacies as the first site for outpatient care (42,41). Antibiotics are available without prescription in more than 70% of pharmacies in Kenya (43).

The above shortcomings in the use of antibiotics in Kenya are as a result of weak pharmaceutical management and inadequate regulation that lead to the proliferation of unlicensed pharmacies, over the counter sale of prescription-only medicines and indiscriminate use of antibiotics in health care facilities (12). In addition, lack of adequate diagnostics and quality laboratory facilities promotes empiric prescribing of antibiotics to

treat non bacterial infections where the etiological agent cannot be established or different conditions manifest with similar symptoms (12). This irrational use of antibiotics in Kenya has culminated in the rising rate of antimicrobial resistance in the country (12). Antimicrobial resistance is a global public health threat because simple and curable infections could once again kill in the post antibiotic era that the world is heading to if the current rise in resistance is not reversed (18). Few novel antibiotics have been discovered in the last three decades and these do not match the rate of development of resistance (44). There is therefore an urgent need to preserve the currently available drugs (44).

2.5 Antibiotic resistance and its consequences

Antibiotic resistance presents a serious challenge especially in Sub Saharan Africa where the range of antibiotics is already limited. This therefore means that the resistance will lead to a near total loss of treatment choices for many severe infections (12). Antibiotic resistance occurs where bacteria adapt and grow in the presence of antibiotics (45).

When microbes become resistant to medicines, the options for treating the diseases they cause are reduced. The direct consequences include longer illnesses, increased mortality, prolonged stays in hospital, loss of protection for patients undergoing operations and other medical procedures, and increased costs (45). The indirect impact of antibiotic resistance has many public health consequences with wide implications for instance on development (45). It is a drain on the global economy with economic losses due to reduced productivity caused by sickness (of both human beings and animals) and higher costs of treatment (45). Antibiotic resistance occurs naturally overtime usually through genetic changes (46) however there are certain factors that accelerate this process. These include inappropriate use of medicines through suboptimum dose and/or duration, low quality medicines that achieve sub-therapeutic levels in the body, wrong prescription and poor infection prevention and control (46,47). The development of antibiotic resistance is also driven by widespread use of antibiotics in livestock to promote growth and prevent illness (46).

The World Health Organization (46) has documented the prevalence of antibiotic resistance in various parts of the world. *Klebsiella pneumoniae* has shown resistance to carbapenems, the last resort treatment in all regions of the world. *Escherichia coli* has developed resistance to fluoroquinolones, the most widely used agent in different parts of the world. *Neisseria gonorrhea* has shown resistance to the third generation cephalosporins, the last resort treatment in at least 10 countries that include Australia, Austria, Canada, France, Japan, Norway, Slovenia, South Africa, Sweden and the United Kingdom of Great Britain and Northern Ireland. The prevalence of MRSA is widespread and patients infected with the organism are estimated to be 64% more likely to die than those with a non-resistant form of the infection (46). *Enterobacteriaceae* which are resistant to carbapenems have also shown resistance to colistin, the last resort treatment in several countries and regions. This makes infections caused by such bacteria untreatable (48).

WHO estimates that, in 2014, there were about 480 000 new cases of multidrug-resistant tuberculosis (MDR-TB), a form of tuberculosis that is resistant to the two most powerful anti-tuberculosis medicines Isoniazid and Rifampicin (46). MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB (46). There is also the emergence of a more dangerous threat, the extensively drug resistant tuberculosis, a type that is resistant to at least 4 of the core anti-TB drugs (46). It has been identified in 105 countries where an estimated 9.7% of people with MDR-TB have XDR-TB (46). Kenya is not spared from the threat of antibiotic resistance, in fact, it is worsening (12).

Studies have shown high rates of resistance for respiratory, enteric and hospital acquired infections within the country (12). For instance, 25% of *Streptococcus pneumonia* isolates in Nairobi were resistant to penicillins in the mid 1980s and by 2003, 43% were resistant (48). In 2003, *Shigella* isolates were highly resistant to ampicillin (85%), cotrimoxazole (94%), chloramphenicol (91%) and tetracycline (100%) (12).

2.6 Factors affecting antibiotic prescribing pattern

2.6.1 Patient factors

Age is an important demographic factor that influences antibiotic prescribing. The extremes of age are more prone to the adverse effects of the antibiotics. Neonates have immature liver and renal functions which affect their ability to metabolise or excrete antibiotics. Antibiotics and their metabolites may adversely affect growing tissues and organs in children. For instance tetracycline chelates calcium ions and gets incorporated into teeth, cartilage and bone resulting in discoloration of both the primary and permanent dentitions (49). Elderly patients are more likely to suffer from nephrotoxicity and allergic reactions. Broad spectrum antibiotics should be used cautiously in women of child bearing age who are on contraceptives as they can cause contraception failure. If they must be used, an additional mode of contraception must be sought.

The renal and hepatic function of patients must be considered as these are the principal organs responsible for elimination of drugs from the body (9). In most cases concern is with dose reduction to prevent accumulation and toxicity in patients with reduced renal or hepatic function. However, sometimes doses might need to be increased to avoid under dosing patients with rapid renal elimination or those with rapid hepatic metabolism due to enzyme induction by concomitant use of drugs such as rifampin or phenytoin (9).

Genetic variation is an important patient factor. Genetic susceptibility to the adverse effects of some antimicrobial agents has been demonstrated and is occasionally significant enough to warrant testing for such variability before administration of the drugs (9). An example is in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, which can result in hemolysis in individuals when exposed to antimicrobial agents, such as dapsone, primaquine, and nitrofurantoin (9).

Pregnancy and lactation present a unique situation as many antibiotics are not routinely recommended. This is due to the risk posed to the mother and the fetus/infant. Human studies on safety of many antimicrobial agents in pregnancy and lactation are limited, and hence these agents should be prescribed with caution. Penicillins, cephalosporins and

macrolides that have historically been the most commonly used antimicrobial agents are considered safe in pregnancy (9).

Other patient factors that are useful when prescribing an antibiotic include establishment of a history of allergy or intolerance to a particular drug and a history of recent antibiotic use where the likelihood of resistance towards that particular agent is high and thus an alternative agent should be considered (9). The clinical presentation of the patient and findings on clinical examination are key determinants in the diagnosis and hence influence antibiotic prescribing. While this may be justifiable in most cases, certain clinical features of disease may inappropriately influence clinician treatment choices. For instance, the presence of purulent nasal discharge is more likely to result in a physician prescribing an antibiotic for a patient with acute bronchitis (50). However, this may not be necessary as purulent nasal discharge does not adequately differentiate viral from bacterial etiology (51). The socio economic status of the patient also influences antibiotic prescribing. In a study done in New Delhi, the general practitioners reported that they were more likely to prescribe an antibiotic for patients from poor backgrounds due to inadequate sanitation thus increased risk of bacterial infections (52).

2.6.2 Provider related factors that influence antibiotic prescribing

Training is an important provider related variable. Inadequate clinical training may play a role in the irrational use of antibiotics where the clinicians may prescribe antibiotics for non-bacterial infections such as malaria, acute diarrhea, influenza, uncomplicated viral infections among others (20). In addition, in-practice training on rational use of medicines positively influences the prescribing of antibiotics. This was established by a study in Scotland that compared antibiotic prescribing between training and non-training practices. It was found that antibiotic prescribing in training practices was more conservative. This was postulated to be due to the participation in a series of training as part of staff development exercises that promote rational prescribing and appropriate use of medicines (53).

Uncertainty in the diagnosis is among the factors cited by many studies that influence antibiotic prescribing. Many doctors in India reported that it was a challenge to distinguish, at an early stage whether an infection was bacterial or viral particularly for diarrhea and upper respiratory tract infections (52). Medical tests were not routinely requested as most patients did not want to be tested in case of a day's fever or could not afford to take these tests due to lack of time or money. For this reason, doctors prescribed antibiotics just in case it was a bacterial infection (52). In a study on antibiotic prescribing among trainee medical registrars in Australia, the participants reported a lack of clinical and diagnostic experience as among the factors promoting antibiotic prescribing. This uncertainty among the trainee doctors caused a tendency to 'play it safe' thus leading to increased antibiotic prescriptions just in case they missed something (54). Uncertainty in diagnosis is a common problem especially in Kenya where there is weak laboratory and diagnostic support. This leads to an overprovision of antibiotics and heavy reliance on broad spectrum antibiotics (12).

Studies also indicate that legitimate fear of worse outcomes in case of not prescribing an antibiotic pushes doctors to give their patients these medications even where their conditions do not necessarily warrant antibiotic use. According to the doctors, they prescribed antibiotics as a preventive measure in case of an infection (52,12). A study in Western Kenya highlights this issue where due to overlap in clinical presentation between malaria and respiratory illness, penicillin was given as a safeguard treatment for possible pneumonia in more than a fifth of children with a sole diagnosis of malaria (55).

Influence from pharmaceutical representatives was also cited as another provider related factor influencing the prescribing pattern of antibiotics. Doctors reported that they prescribed newer antibiotics on the recommendations by the representatives who presented them with skewed studies in favour of the medicines they wanted to market(52,12).

Prescribers and dispensers report that the demand by clients is an important factor for prescribing of antibiotics. In a survey of Oral Rehydration Solution (ORS) use in Kenya, the majority of the caregivers reported that they preferred antibiotics for the management of childhood diarrhea while the drug providers stated that the clients' demand for antibiotics influenced their prescription decisions (56). Doctors in India were of the same opinion where they reported that some patients demanded 'strong' medicines. Some who had previous antibiotic prescriptions asked to be given these drugs again. Educated patients went a step further to name the antibiotics they wanted (52). Doctors often succumb to the patient demands and expectations for antibiotic prescriptions (52). Dosages are also given according to the client demand. This was shown by a study in Kibera where about 94% of the chemists were willing to sell smaller doses of antibiotics for STI management at the request of the patients (12).

Financial incentives from the sale of unnecessary or newer second line drugs is another provider related factor affecting the prescribing pattern of antibiotics. Anecdotal reports indicate that some pharmacies have commercial contracts or are physician owned. The clinicians therefore derive direct financial benefits from the prescription and sale of antibiotics (12).

The ORS study found an association between higher drug prices and treatment recommendations such that antibiotics were recommended more by the dispensers compared to ORS for childhood diarrhea as the former had higher profit margins (12). In India, doctors in the private sector reported that they preferred to prescribe antibiotics in order to satisfy and retain their patients rather than employ a watch and wait policy that would make them lose their clients in case the patients went to different physicians. Many of them prescribed those brands of antibiotics with higher profit margins or at times gave antibiotics when they were not indicated in order to boost profits (52). It is reported that hospital clinicians in Kenya have different prescribing standards depending on their status as hospital staff or consultants and the resultant amount of revenue that they bring to the institution (12).

2.6.3 Institutional factors that affect antibiotic prescribing

Institutional factors that influence the prescribing pattern of antibiotics include availability of hospital formulary or standard treatment guidelines, availability of laboratory and other diagnostic support, presence of antibiotic audits, overcrowding and lack of thorough infection control practices.

Availability of national and/or hospital treatment guidelines highly influence the prescribing pattern of antibiotics. Doctors find guidelines easy to use and helpful in guiding and justifying prescribing decisions. Medical registrars in Australia felt that guidelines helped them keep abreast of changes and maintain up to date information. Failure to adhere to guidelines was considered suboptimal practice by majority of them (54).

Institutional laboratory and diagnostic capacity are important factors in assisting clinicians to reach a definitive diagnosis and thus avoid empiric therapy. They therefore influence antibiotic prescribing. Overcrowding particularly in government health facilities leads to an increased clinician to patient ratio. The clinicians therefore have little time to study a patient's case, do a proper physical examination or educate patients. In order to save time, doctors simply prescribe antibiotics without looking at the rationality of prescribing them (52).

Failure to implement and follow infection control practices by health institutions drive irrational use of antibiotics. This occurs partly due to reliance on antibiotics as a low cost prophylactic alternative in high risk hospital departments such as surgical wards, ICU and neonatal unit. Where patients bear the cost of prophylactic antibiotic use, the hospital is further encouraged not to finance infection control practices (12).

2.6.4 Health system factors that affect antibiotic prescribing

Health system related factors such as the presence and implementation of legislation on prescribing and dispensing, availability of surveillance data on antibiotic susceptibility patterns and availability of drugs also influence antibiotic prescribing pattern.

Absence of surveillance data on local causes of infections and prevailing antibiotic susceptibility patterns complicates empirical diagnosis and treatment. This promotes irrational use of antibiotics particularly the broad spectrum agents. Therefore, a better understanding of antibiotic susceptibility patterns in the region could inform empiric treatment and thus reduce injudicious use of broad spectrum agents. This will preserve the utility of available medicines (12).

The presence and enforcement of legislation on the use of antibiotics will promote rational use of antibiotics. In Kenya, there are few regulatory bodies that oversee antibiotic prescribing practices by health care workers. A study in Kibera found that only a few of the private health facilities and retail pharmacies had official licenses from authorized agencies (57).

The drug availability status also affects antibiotic prescribing. The ability of a prescriber to provide correct treatment may be limited by the absence of indicated medications. For example, in Thika district hospital, the Kenya Medical Supplies Agency (KEMSA) only supplied 6 out of the 13 injectable antibiotics listed by the Kenya Essential Medicines List (KEML) as vital antibiotics. In addition, the quantities supplied were inadequate to meet the patient demands leading to stock outs (12). Anecdotal reports in Kenya reveal that public facilities purchase second line antibiotics pushed by private distributors when government supplies run dry (12). This promotes irrational use. On the flip side, overstocked and near expiry drugs in health facilities in India promoted irrational antibiotic prescribing. One study showed that in a drive to clear the stock, antibiotics were prescribed even where they were not indicated (52).

2.7 Identified targets for potential improvement in the use of antibiotics

The management of antibiotic resistance requires interdependent action in three areas that include conservation, access and innovation (22). Conservation of antibiotics to limit the development of resistant microbes and thus ensuring continued efficacy of the drugs is an important strategy. This should occur simultaneously with efforts to promote increased access for those who really need them. In addition, encouraging antibiotic research and

development to produce new drugs into the pipeline will be equally important (22). The World Health Assembly (WHA), in May 2015, endorsed the Global Action Plan on Antimicrobial Resistance that requires all countries to adopt national antimicrobial resistance strategies within two years (45). Several countries such as the United States of America, the European Union, South East Asian WHO countries and South Africa have taken up the challenge (20). Kenya has not been left behind and is it has already drafted a national policy on prevention and containment of antimicrobial resistance (18). According to the WHO, the national antibiotic policy should address the following important issues: enforcement of existing laws to prevent non-prescription, over-the-counter sale of antibiotics; preparation of national guidelines on antibiotics use and the adaptation of these guidelines institutionally at the facility level; monitoring of antibiotic consumption in order to estimate national consumption of antibiotics; establishment of a national antimicrobial resistance surveillance system that is coordinated with international systems; establishment and implementation of national and hospital based infection control programs, availability of educational programs on rational antibiotic use for both health care providers and the public and provision of financial resources by the government and other stakeholders (10).

GARP, in working with several countries to establish the capacity and methods for developing antibiotic resistance policies identified six strategies will contribute to slowing antibiotic resistance and maintaining effectiveness of current drugs (20). These include: reducing the need for antibiotics through improved water, sanitation and vaccination; improved hospital infection control and antibiotic stewardship; promotion of incentives that encourage antibiotic stewardship in hospitals, communities and in agriculture; reduce and eventually phase out sub-therapeutic use of antibiotics in agriculture; educate health professionals, policy makers and the public on rational antibiotic use; ensure political commitment to meet the threat of antibiotic resistance (20).

WHO recommends that each facility should draft its own hospital antibiotics policy in line with the national antibiotics policy except for a few changes as warranted by the

local antimicrobial resistance profiles (10). The policy should be based on the spectrum of antibiotic activity; pharmacokinetics/pharmacodynamics profile of the medicines; adverse effects; potential to select resistance; cost and special needs of individual patient groups (10). It should also set the levels for prescribing antibiotics specifically first line medicines, second line, reserve antibiotics and restricted choice antibiotics (10). There should be surveys on antibiotic consumption in order to quantify antibiotic use and establish resistance patterns. The findings should be disseminated to the prescribers in order to improve antibiotic prescribing. Promoting use of diagnostic tools to guide antibiotic use is another useful approach (11). Increasing access to vaccines against bacterial infections has been shown to reduce the need for antibiotics worldwide and thus avert selection pressure. These include the pneumococcus and *Haemophilus influenza* type b vaccines (38).

2.8 Knowledge gaps identified

The most comprehensive analysis to date on global antibiotic consumption was conducted in 71 countries with the biggest data gaps being in Sub Saharan Africa and Asia (21). The literature has revealed that there was only one comprehensive study done in Kenya on the overall use of antimicrobials. This was done over 15 years ago for a 5year period – from 1997 to 2001. There are no recent studies to document the changes in antibiotic use over time. This study will therefore help to fill a data gap by providing current information on the prevalence of antibiotic use in a level 5 facility in Kenya, one of the sub Saharan countries. It has been shown that lack of data in relation to the quality and quantity of antibiotic prescribing is one of the key barriers in the successful development or implementation of antimicrobial stewardship programs worldwide (59).

A health survey conducted in the country in 2009 by the Ministry of Health was able to estimate the prevalence of antibiotic use in the country (4). The study was however conducted among outpatient encounters. This study will be able to fill the data gap by looking at the prevalence of antibiotic use among hospitalized patients. There are limited published studies on point prevalence surveys of antibiotic use in any hospital in Kenya.

CHAPTER THREE: METHODOLOGY

3.1 Research Design

This was a cross sectional study and more specifically a point prevalence survey. The study aimed at obtaining the prevalence of antibiotic prescribing, establishing whether there was rational or irrational prescribing and adherence to guidelines in a level 5 facility at a specific point in time. The study formed part of an initiative of the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (**GLOBAL-PPS**). The PPS has been shown to be a practical surveillance tool for providing information about antibiotic use and for assessing the effects of antibiotic stewardship interventions (25).

3.2 Location of the Study

The study was conducted at the Rift Valley Provincial General Hospital, the fourth largest government referral hospital in the country. The hospital has a bed capacity of about 500. This facility was chosen for the study due to the anecdotal reports of irrational antibiotic use. These reports required scientific documentation and identification of potential targets for quality improvement so that the patients at the facility would benefit from rational antibiotic use.

RVPGH was started as a military hospital in 1906 (60). It serves about 3.6 million people in South Rift Valley plus patients coming as far as Western, Nyanza, North Rift Valley and Central parts of Kenya (60). RVPGH has 15 general wards and sophisticated facilities such as CT scan and MRI. The hospital hosts both undergraduate and postgraduate training programs. It is an accredited training centre for part one of the Membership of the College of Surgeons of East, Central and Southern Africa (MCS COSESCA) in general and orthopedic surgery (60). It is also the training centre for Egerton University medical school and the Kenya Medical Training Centre (KMTC). It is located in Nakuru town, the headquarter of Nakuru County, about 160 km from Nairobi. The county covers an area of 7496.5 square kilometers (61) and is home to 1,603,325 people (male – 50.2% and female – 49.8%), according to the 2009 National Census.

The RVPGH inpatient department has paediatric, adult medical, surgical, ICU, orthopedic and obstetric wards. All the departments were included in the study. This was necessary in order to identify the pattern of antibiotic use in the various departments and to identify the specific sites with irrational use. Specific targets for quality improvement in antibiotic use suited for those areas were then identified.

3.3 Target population

This comprised of all patients admitted at the RVPGH who were on systemic antibiotics. The survey was conducted on all inpatient departments within the hospital.

3.4 Inclusion and Exclusion Criteria

3.4.1 Inclusion Criteria

The medical records of inpatients on systemic antibiotics as at 8AM of the day of the survey of a particular ward were reviewed for the purposes of the study. Where an antibiotic was prescribed after 8 AM for instance, during the ward round or when results became available, this was not included.

All inpatient wards (units/departments) within the hospital were included. New born healthy children in the maternity ward were included. This ward was encoded as NMW.

The patients on the following systemic antibiotics were included in the study: antibacterials for systemic use (J01), drugs for treatment of tuberculosis (J04A), antibiotics used as intestinal anti-infectives (A07AA) and anti-protozoals used as antibacterial agents such as nitroimidazole derivatives (P01AB). The codes were derived from the WHO Anatomical Therapeutic Chemical classification system (WHO ATC). This is a system where the active medicinal substances are divided into different groups according to the anatomical system they act and their pharmacological, therapeutic and chemical properties (62).

3.4.2 Exclusion Criteria

Outpatients and daytime admissions for ambulatory patients for procedures such as endoscopy or renal dialysis were excluded from the study. Patients admitted and started

on systemic antibiotics after 8 AM on the day of the survey were excluded. Antibiotics for topical use were also excluded from the survey.

3.5 Sampling

3.5.1 Sample Size Estimation

The sample size was calculated using the Fischer formula(64):

$$n = \frac{Z^2 P\,(1 - P)}{d^2}$$

Where n was the sample size, Z was the statistic for the level of confidence, P was the expected prevalence and d was the allowable error.

Z was set at 1.96 for the desired confidence interval of 95%. From literature, P was estimated to be 73%. This was from a survey of the pharmaceutical situation in Kenya conducted by the Ministry of Health in 2003 that showed the prevalence of antibiotic prescribing to be 73% (13). The allowable error was 5% as the expected prevalence was between 10% and 90% (64).

$$n = \frac{1.96^2\ 0.73(1 - 0.73)}{0.05^2}$$

$$n = 302.8 \sim 303 \text{ patients}$$

The RVPGH had a finite population of patients who were likely to be on antibiotics. This was determined by multiplying the total bed capacity of the hospital by the prevalence of antibiotic use at the hospital as elicited by the Ministry of Health (13).

Adjusting for a finite population, the expected sample size (n) was calculated as shown below:

$$n = \frac{n0 * N}{n0 + (N - 1)}$$

Where N was the finite population size and n0 was the expected sample size as determined by the Fischer equation above.

The RVPGH had an inpatient bed capacity of about 532. Of these, about 73% were expected to be on antibiotics according to the study by the Ministry of Health (13). The finite population of patients at RVPGH expected to be antibiotics was determined by:

$$N = 0.73 \times 532 = 388.36 \sim 389 \text{ patients}$$

Therefore:

$$n = \frac{303 \times 389}{303 + (389 - 1)}$$

$$n = 170.32 \sim 171 \text{ patients}$$

A 10% over estimation of the sample size was provided to cater for non-response or missing data,

$$n = \frac{170.32}{0.9}$$

$$n = 189.24 \sim 190 \text{ patients}$$

The study was able to attain a 94.2% sample size (n=179). This was due to the fact that the hospital bed occupancy was at 88.9% (n=473). There were also challenges in getting all the required patient files and treatment sheets as some had been taken to other various departments such as the x-ray, finance or pharmacy department for medication dispensing.

3.5.2 Sampling Technique

Stratified proportionate random sampling technique was used. A proportionate sample was obtained from each department as shown below. On the day of the survey of a particular ward, the medical records of all inpatients on systemic antibiotics were obtained. Their file numbers were entered into Microsoft Excel version 2010. The computer was then commanded to give a random sample of the files that were to be studied.

Table 1: Proportionate sampling of the RVPGH according to bed capacity

Department (Specific Ward Numbers)	Bed capacity	Proportion	No of patients sampled
Paediatric Medical Ward (2,6)	70	$^{70}/_{509} \times 190$	32
Mixed Wards (14,15, Isolation, Eye)	99	$^{99}/_{509} \times 190$	21
Adult Medical Ward (5,11,12)	105	$^{105}/_{509} \times 190$	58
Adult Surgical Ward (1,7,10,13)	129	$^{129}/_{509} \times 190$	53
New Born Unit	11	$^{11}/_{509} \times 190$	5
Intensive Care Unit	9	$^{9}/_{509} \times 190$	4
Obstetrics and gynecology (Mat,3,4)	86	$^{86}/_{509} \times 190$	17
Total	509	$^{509}/_{509} \times 190$	190

3.6 Participants Recruitment

The sample population was obtained from all patients who were admitted in a particular ward and were on systemic antibiotics at the beginning of the day of the survey. A random sample was obtained from the sampling software. There was no direct engagement of these patients. Relevant information was collected from the medical records of only those patients who were on a systemic antibiotic at the beginning of the survey of the particular ward.

On the day of the survey of a particular department, the medical records of all the admitted patients who were on systemic antibiotics were obtained. Their hospital identification numbers were manually entered into the computer software which was then commanded to select a random number of files that were studied.

3.7 Research Instruments

Two data collection forms were used. One was for the ward/department while the other was for the patient details. The patient form was filled for only those patients on systemic antibiotics. It contained details such as the patient demographics, the antibiotic name, dose, frequency and route of administration. The form as shown in appendix 2 also contained the patient diagnosis, the type of indication and the reason given in the notes, whether there was guideline compliance or not, the type of treatment whether empiric or targeted and whether treatment was based on biomarker data.

The ward form in appendix 1 contained details such as the ward name and department type, total number of eligible patients and total number of beds in the ward.

3.8 Pilot Study

A pilot study was conducted in one inpatient ward at the RVPGH. This department was randomly selected by the computer via Microsoft Excel version 2010. During this study, the ward form and patient forms were pre-tested. The data obtained was then critically assessed for completeness and ability to accurately capture the study objectives.

3.9 Study Validity

Validity refers to how well a test or research instrument measures what it is supposed to measure (65). This was achieved by piloting the research instruments under the same conditions and using the same procedures as in the main study. The data obtained was analysed using descriptive and inferential statistics to determine whether they meet the study objectives. The pretesting helped to identify internal inconsistencies in the research instrument that were likely to introduce measurement bias. Other possible threats to internal validity included information bias. This was avoided by a rigorous prior training of the research assistants on the research instruments and the data collection technique. Objective records were used to collect data rather than relying on the study participants' recall. Measurement bias was avoided by thorough pretesting of the research instruments.

3.10 Study Reliability

Reliability is a measure of how consistent the results from the test or research instrument are (63). The internal consistency of the data collection forms were described using the Cronbach's alpha. This test describes the extent to which all items in a research instrument measure the same concept and therefore it measures the strength of inter-relatedness of items within the instrument. The value of alpha was found to be 0.90.This confirmed the reliability of the study instrument because the acceptable value of alpha ranges from between 0.7 and 0.9 (66).

3.11 Data collection technique

Data collection was performed using two paper forms: a department/ward form and a patient form. The source of information for completing the patient data collection tool was from a review of the medical records. Details such as patient demographics, comorbidities, antibiotic treatment including the name, dose, frequency, duration and route of administration were obtained from the medical records. The records were also reviewed as to whether the indication for the antibiotic had been documented

All inpatient wards participated in the study. Each ward was surveyed only once on a single day. The departments were grouped into paediatric, neonatal and adult departments as shown below.

Table 2: Classification of the hospital departments

Paediatric departments	PMW (Paediatric Medical Ward) HO-PMW (Haematology-Oncology PMW) T-PMW (Transplant (BMT/Solid) PMW) PSW (Paediatric Surgical Ward) PICU (Paediatric Intensive Care Unit)
Neonatal departments	NMW (Neonatal Medical Ward) NICU (Neonatal Intensive Care Unit
Adult departments	AMW (Adult Medical Ward) HO-AMW(Haematology-Oncology AMW) T-AMW (Transplant (BMT/solid) AMW) P-AMW (Pneumology AMW) OBGYN (Obstetrics and Gynecology) ASW (Adult Surgical Ward) AICU (Adult Intensive Care Unit)
Mixed Department	Ward with both adult and paediatric patients

3.12 Data Management

Data was recorded as anonymous by employing a study number for each of the participants. This data was coded then entered into Microsoft Excel version 2010. The data was then validated for completeness and correctness. The electronic data was password protected and accessible to only the principal investigator. The hard copies were stored in a locked cabinet accessible only to the principal investigator.

3.13 Study Variables

Independent Variables

These included the patient demographics such as age, sex, diagnosis, comorbidities and the type of department they were admitted in.

Dependent Variables

They comprised of the type of antibiotic chosen, indication, dose, route of administration, frequency and duration of treatment.

3.14 Data Analysis

In the calculation of overall prevalence of antibiotic use, denominator data was composed of the total number of admitted patients while the numerator was the total number of admitted patients on systemic antibiotics at the beginning of the day in the ward surveyed. The prevalence of antibiotic use in the various departments was also calculated. The most frequent class and type of antibiotics were determined and the prevalence calculated. This information was presented in the form of tables and graphs.

Associations between independent variables such as socio-demographic factors and outcome variables such as the type of antibiotics prescribed were determined using Chi square. Logistic regression was used to measure the relationship between the outcome variables such as rational antibiotic prescribing and the predictor variables such as patient diagnosis, age and sex. It was also used to measure the relationship between guideline compliance and the patient characteristics such as age, sex and diagnosis. Statistical significance was set at 95% confidence level. In order to assess whether there was rational prescribing of antibiotics, various indicators were reviewed. These included appropriate choice of antibiotic, correct dose, correct frequency, correct duration and appropriate route of administration. Other indicators of quality antibiotic prescribing such as inclusion of the reason for antibiotic in the notes, generic prescribing and targeted versus empiric prescribing were also evaluated. Guideline compliance was also assessed based on several indicators. These included adherence to the choice of antibiotic, dose, route, frequency and duration with regards to the diagnosis.

3.15 Logistical and Ethical Considerations

Ethical approval was obtained from the KNH-UON Ethics committee reference number P36/01/2017. Further approval was obtained from the hospital administration of the RVPGH before commencement of the study. Confidentiality of the data was highly regarded. A study number was allocated to each participant that made them anonymous. The hardcopy records were kept under lock and key while the electronic records were password protected accessible only to the principal investigator. During the survey in the various hospital departments, discussions or personal judgement of the appropriateness of antibiotic prescribing was not entertained to avoid the ward staff feeling evaluated at an individual level.

CHAPTER FOUR: RESULTS

4.1 Sociodemographic characteristics of the study population

The study was conducted among 179 patients. The median age of the study population was 25.3 years (IQR = 4 - 38). The adults (20-59 years) formed the largest proportion (93, 52%) of age category followed by neonates (23, 12.9%). There were more females (99, 55.3%) than males (44.6%). The adult surgical ward (53, 29.6%) and the adult medical ward (41, 22.9%) had the largest proportion of patients in the study population (Table 3).

Table 3: Sociodemographic characteristics

Age Category	n	%
Neonates (1-30days)	23	12.9
Children (1-23months)	18	10.1
Children (2-12years)	19	10.6
Adolescents (13-19years)	9	5.0
Adults (20-59years)	93	**52.0**
Elderly (60years and above)	17	9.5
Sex		
Male	80	44.7
Female	99	**55.3**
Department		
Paediatric Medical Ward	32	17.9
Neonatal Medical Ward	15	8.4
Adult Medical Ward	41	22.9
Adult Surgical Ward	53	**29.6**
Obstetrics & Gynecology	17	9.5
Intensive Care Unit	4	2.2
MIXED*	17	9.5

*Mixed – all those departments that have both adults and paediatrics in the same ward namely isolation ward, ear nose and throat surgical ward, one general surgical ward and eye ward

4.2 Clinical Characteristics of the Study Population

4.2.1 Use of Antibiotics in Hospital

A larger proportion of antibiotic prescribing was for treatment (135, 75.4%) as compared to prophylaxis (52, 29.0%). The respiratory system was the anatomical site with largest proportion of antibiotics prescribed for treatment (44, 24.6%) followed by the skin, soft

tissue, bone and joint infections (22, 12.3%). For prophylactic use, obstetric or gynecological surgery was highest (18, 10.1%) followed by skin, soft tissue, bone and joints anatomical sites (16, 8.9%).

Table 4: Use of Antibiotics in the Hospital

Type of infection	Prophylaxis (N=52)* n (%)	Treatment (N=135)* n (%)	Total N=179* n (%)
Respiratory	1 (0.6)	**44 (24.6)**	**45 (25.1)**
SSTBJ	**16 (8.9)**	**22 (12.3)**	**38 (21.2)**
OBGY/GUM	**18(10.1)**	11 (6.2)	**29 (16.2)**
Neonatal	0 (0.0)	**18 (10.1)**	18 (10.1)
Central Nervous System	4 (2.2)	10(5.6)	14 (7.8)
Gastrointestinal	**5 (2.8)**	8 (4.5)	13 (7.3)
No defined site	0 (0.0)	12 (6.7)	12 (6.7)
Urinary Tract	0 (0.0)	6 (3.4)	6 (3.4)
Eye	4 (2.3)	1(0.6)	5 (2.8)
Ear nose & throat	4 (2.3)	0 (0.0)	4 (2.2)
Unknown	0 (0.0)	2 (1.1)	2 (1.1)
Cardiovascular system	0(0.0)	1 (0.6)	1 (0.6)

*Some patients had more than one diagnosis

Key:-

SSTBJ – Skin, soft tissue, bone and joint infections

OBGY/GUM – Obstetrics & Gynecology & Male Genito-Urinary infections

4.2.2 Co-morbidities

The majority of the study population on antibiotics had no comorbidities (96, 53.6%). Among those with comorbidities, the most prevalent was HIV (15, 8.4%) followed by diabetes mellitus (12, 6.7%) and low birth weight (12, 6.7%). Each of the comorbidities classified under 'Other' had one patient each in the population. These included rickets, psychosis, nephrotic syndrome, kwashiorkor, cerebral palsy, eclampsia, goitre, gastritis, Gullaine Barre Syndrome, Gastrointestinal ulcers, ascites and adenoid hypertrophy (Figure 2).

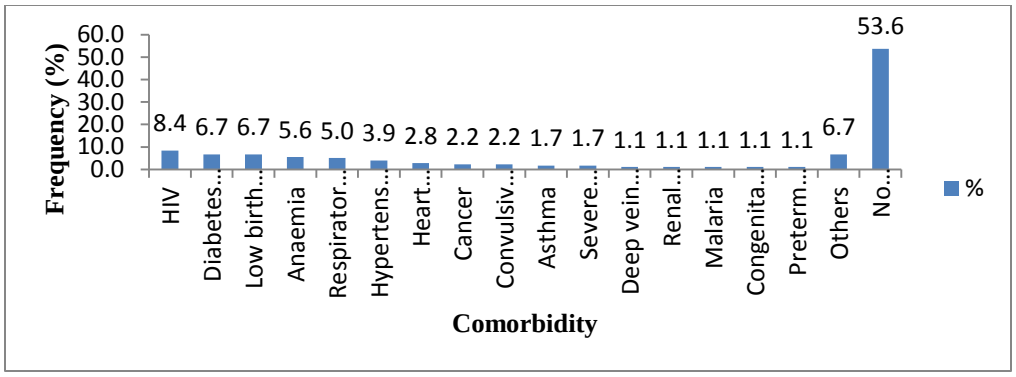
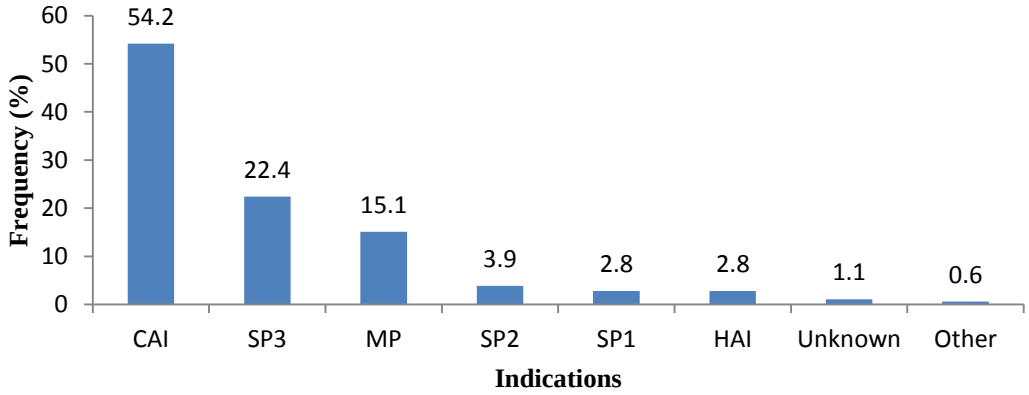


Figure 2: Prevalence of comorbidities in the study population

4.2.3. Indications

Figure 3: Indications for antibiotic use



The most frequent indication for antibiotic use was for community acquired infections (97, 54.2%) followed by prolonged surgical prophylaxis (40, 22.4%) then medical prophylaxis (27, 15.1%). Other indications comprised other pharmacological uses besides treatment or prophylaxis of infections. For instance, erythromycin could be used as a motility agent (Figure 3).

Key:-

CAI – Community acquired infection

SP1 – single dose surgical prophylaxis

SP2 – one day surgical prophylaxis

SP3 – surgical prophylaxis > 1 day

MP – Medical Prophylaxis

HAI – Hospital acquired infection

4.3 Prevalence of Antibiotic Prescribing

4.3.1 Overall prevalence of antibiotic prescribing

The overall prevalence of antibiotic prescribing at RVPGH was 54.7%. The ICU (100.0%) and the isolation ward (100.0%) classified under the mixed department had the highest prevalence of antibiotic prescribing (100.0%) followed by the new born unit (93.7%) and the paediatric medical ward (57, 84.2%). The obstetrics and gynecology department had the least prevalence of antibiotic prescribing (20.8%) (Table 5).

Table 5: Overall prevalence of Antibiotic Prescribing

Department type	Total No. of Pts on Abs	Total No. of Admitted Pts	Prevalence
Adult Surgical Ward	90	157	57.3
Paediatric Medical Ward	48	57	84.2
Obstetrics & Gynaecology	16	77	20.8
Adult Medical Ward	67	109	61.5
Mixed	19	53	35.8
Intensive Care Unit	4	4	100.0
Neonatal Medical Ward	15	16	93.7
TOTAL	**259**	**473**	**54.7**

4.3.2 Prevalence of antibiotic classes

The penicillin class of antibiotics (84, 46.9%) had the highest proportion of prescribing followed by the cephalosporins (80, 44.7%) and aminoglycosides (47, 26.3%). The furadantoins had the least proportion of antibiotic prescribing (1, 0.6%) (Figure 4).

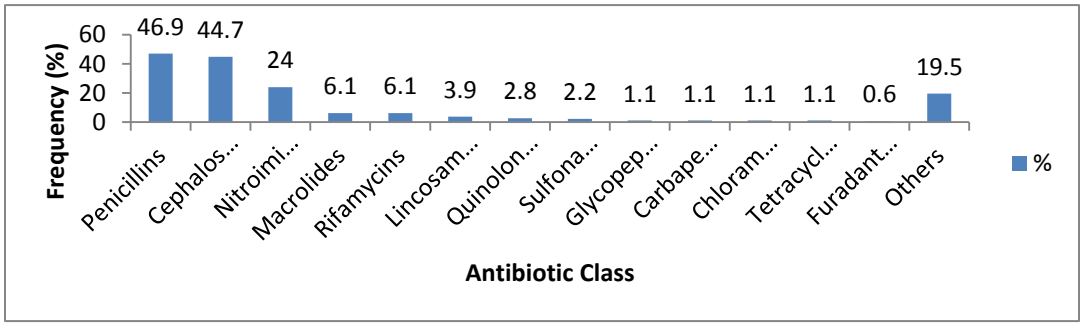


Figure 4: Prevalence of Antibiotic prescribing by class

4.3.3 Prevalence of specific antibiotics prescribed

Ceftriaxone had the highest proportion of use (71, 39.7%) followed by benzyl penicillin (52, 29.0%) then metronidazole (45, 25.1%). Prothionamide (1, 0.6%), cycloserine (1, 0.6%), nitrofurantoin (1, 0.6%), clarithromycin (1, 0.6%) and levofloxacin (1, 0.6%) all had the least proportion of prescribing (Table 6).

Table 6: Prevalence of specific antibiotics prescribed

	Specific antibiotics	n	%
Cephalosporins	Ceftriaxone	71	**39.7**
	Ceftazidime	7	3.9
Penicillins	Benzyl penicillin	52	**29.0**
	Flucloxacillin	20	11.2
	Ampicillin/cloxacillin	14	7.8
	Amoxicillin/ clavulanic acid	10	5.6
	Amoxicillin	4	2.2
Nitroimidazole derivatives	Metronidazole	45	**25.1**
Aminoglycosides	Gentamicin	40	22.3
	Amikacin	7	3.9
Rifamycins	Rifampicin	11	6.1
Macrolides	Erythromycin	10	5.6
	Clarithromycin	1	**0.6**
Lincosamides	Clindamycin	7	3.9
Sulfonamides	Cotrimoxazole	5	2.8
Chloramphenicol	Chloramphenicol	3	1.7
Quinolones	Ciprofloxacin	3	1.7
	Levofloxacin	1	**0.6**
Tetracyclines	Doxycycline	2	1.1
Carbapenems	Meropenem	2	1.1
Glycopeptides	Vancomycin	2	1.1
Furadantoins	Nitrofurantoin	1	**0.6**
Others	Ethambutol	12	6.7
	Pyrazinamide	12	6.7
	Isoniazid	11	6.1
	Capreomycin	2	1.1
	Cycloserine	1	**0.6**
	Prothionamide	1	**0.6**

4.3.4 Association between age and antibiotic class

Chi square was used to find the association between the antibiotic class and the age category in order to establish whether the age of a patient influenced the choice of

antibiotics prescribed. There was a statistically significant relationship between the prescribing of aminoglycosides (p<0.001), nitroimidazole derivatives (p=0.002) and glycopeptide (0.004) classes of antibiotics and the age category. Aminoglycosides were the most frequently prescribed class among the neonates (1-30days) (16, 8.9%), nitroimidazole derivatives were frequently prescribed among the adults (20-59years) (33, 18.4%) while glycopeptides were most commonly prescribed among the children (2-12 years) (2, 1.1) (Table 7).

Table 7: Relationship between prescribed classes of antibiotics and participants' age category

Antibiotic Class	1-30days n (%)	1-23months n (%)	2-12years n (%)	13-19years n (%)	20-59years n (%)	≥60years n (%)	P Value
Aminoglycosides	16 (8.9)	8 (4.5)	8 (4.5)	2 (1.1)	12 (6.7)	1 (0.6)	**<0.001**
Cephalosporins	7 (3.9)	9 (5.0)	5 (2.8)	5 (2.8)	44 (24.6)	10 (5.6	0.240
Penicillins	16 (8.9)	8 (4.5)	11(6.1)	4 (2.2)	41 (22.9)	4 (2.2)	0.082
Macrolides	0 (0.0)	1 (0.6)	3 (1.7)	0 (0.0)	7 (3.9)	0 (0.0)	0.253
Quinolones	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	1 (0.6)	0.645
Nitroimidazole derivatives	1(0.6)	1 (0.6)	1 (0.6)	2 (1.1)	33 (18.4)	5 (2.8)	**0.002**
Carbapenems	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.169
Sulfonamides	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	0 (0.0)	0.581
Glycopeptides	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	**0.004**
Chloramphenicol	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)	0.867
Lincosamide	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	3 (1.7)	2 (1.1)	0.340
Tetracyclines	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)	0.867
Furadantoins	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0.968
Rifamycins	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	9 (5.0)	1 (0.6)	0.373
Isoniazid	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	9 (5.0)	1 (0.6)	0.373
Pyrazinamide	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	9 (5.0)	2 (1.1)	0.335
Ethambutol	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	9 (5.0)	1 (0.6)	0.373
Others	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0.088

4.3.5 Association between age and specific antibiotics

Chi square test was used to find the association between the specific antibiotics prescribed and the age category. This was done in order to identify whether age influenced the choice of specific antibiotics. The prescribing of amikacin (p=0.027), gentamicin (p<0.001), ceftriaxone (p=0.004), ceftazidime (p=0.003), metronidazole (p=0.001), ampicillin/cloxacillin (p=0.015), benzyl penicillin (p<0.001) and vancomycin (p=0.004) were significantly associated with age category. Ceftazidime (5, 2.8%) and gentamicin (15, 8.4%) were commonly prescribed among the neonates (1-30days) while amikacin (3, 1.7%) and vancomycin (2, 1.1%) were frequently prescribed among the children (2-12years).

Metronidazole (35, 19.5%), ampicillin/cloxacillin (14, 7.8%), benzylpenicillin (18, 10.0%) and ceftriaxone (37, 20.7%) were commonly prescribed among the adults (20-59years) (Table 8).

Table 8: Relationship between the specific antibiotics prescribed and the participants' age category

Antibiotic	1-30days	1-23months	2-12years		13-19years		20-59years		≥60years		P Value
	n (%)	n (%)	n	(%)	n	(%)	n	(%)	n	(%)	
Amikacin	1 (0.6)	2 (1.1)	3	(1.7)	0	(0.0)	1	(0.6)	0	(0.0)	**0.027**
Amoxicillin	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	3	(1.7)	0	(0.0)	0.727
Amoxicillin/ clavulanic acid	0 (0.0)	0 (0.0)	2	(1.1)	0	(0.0)	7	(3.9)	1	(0.6)	0.479
Ampicillin/ cloxacillin	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	14	(7.8)	0	(0.0)	**0.015**
Benzyl penicillin	16 (8.9)	6 (3.3)	7	(3.9)	2	(1.1)	18	(10.0)	3	(1.7)	**<0.001**
Capreomycin	0 (0.0)	1 (0.6)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)	0.139
Ceftazidime	5 (2.8)	1 (0.6)	1	(0.6)	1	(0.6)	1	(0.6)	0	(0.0)	**0.003**
Ceftriaxone	2 (1.1)	8 (4.5)	4	(2.2)	6	(3.3)	37	(20.7)	10	(5.6)	**0.004**
Chloramphenicol	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	3	(1.7)	0	(0.0)	0.727
Ciprofloxacin	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	3	(1.7)	0	(0.0)	0.727
Clindamycin	1 (0.6)	0 (0.0)	0	(0.0)	1	(0.6)	3	(1.7)	2	(1.1)	0.340
Clarithromycin	0 (0.0)	0 (0.0)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0.132
Cotrimoxazole	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	5	(2.8)	0	(0.0)	0.446
Cycloserine	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)	0.088
Doxycycline	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	2	(1.1)	0	(0.0)	0.867
Erythromycin	0 (0.0)	1 (0.6)	2	(1.1)	2	(1.1)	6	(3.3)	0	(0.0)	0.521
Ethambutol	0 (0.0)	1 (0.6)	0	(0.0)	1	(0.6)	10	(5.6)	1	(0.6)	0.291
Flucloxacillin	0 (0.0)	1 (0.6)	2	(1.1)	0	(0.0)	14	(7.8)	1	(0.6)	0.263
Gentamicin	15 (8.4)	6 (3.3)	5	(2.8)	1	(0.6)	12	(6.7)	1	(0.6)	**<0.001**
Isoniazid	0 (0.0)	1 (0.6)	0	(0.0)	0	(0.0)	9	(5.0)	1	(0.6)	0.373
Levofloxacin	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)	0.088
Meropenem	0 (0.0)	1 (0.6)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0.169
Metronidazole	1 (0.6)	1 (0.6)	1	(0.6)	2	(1.1)	35	(19.5)	5	(2.8)	**0.001**
Nitrofurantoin	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	1	(0.6)	0	(0.0)	0.968
Prothionamide	0 (0.0)	0 (0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)	0.088
Pyrazinamide	0 (0.0)	1 (0.6)	0	(0.0)	0	(0.0)	9	(5.0)	2	(1.1)	0.335
Rifampicin	0 (0.0)	1 (0.6)	0	(0.0)	0	(0.0)	9	(5.0)	1	(0.6)	0.373
Vancomycin	0 (0.0)	0(0.0)	2	(1.1)	0	(0.0)	0	(0.0)	0	(0.0)	**0.004**

4.3.6 Association between Department and Antibiotic Class

Chi square test was also used to find the variation and association between the antibiotic class and the specific departments in order to understand how the department influenced the choice of antibiotics. There was a statistically significant association between the prescribing of several classes of antibiotics and the department type. Aminoglycosides were commonly prescribed in the paediatric medical wards ($p<0.001$). Macrolides

(p=0.002), nitroimidazole derivatives (p=0.002) and antituberculosis agents such as rifamycins (p<0.001), isoniazid (p<0.001), ethambutol (p<0.001) and pyrazinamide (p<0.001) were most frequently prescribed in the adult medical wards. Penicillins (p=0.002) were commonly prescribed in the adult surgical wards. Tetracyclines were prescribed mostly in the Obgyn departments (P=0.004). Carbapenems were commonly prescribed in the ICU and paediatric medical wards (p=0.002) (Table 9).

Table 9: Variation of antibiotic prescribing by classes across the various departments

	PMW	NMW	AMW	ASW	ICU	OBGY	MIXED	P Value
Antibiotic Class	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Aminoglycosides	17 (9.5)	13 (7.3)	6 (3.3)	8 (4.5)	2 (1.1)	1 (0.6)	0 (0.0)	**<0.001**
Cephalosporins	16 (8.9)	2 (1.1)	19(10.6)	29 (16.2)	2 (1.1)	7 (3.9)	5 (2.8)	0.114
Penicillins	16 (8.9)	13 (7.3)	13 (7.3)	27 (15.1)	0 (0.0)	5 (2.79)	10 (5.6)	**0.002**
Macrolides	0 (0.0)	0 (0.0)	4 (2.2)	0 (0.0)	0 (0.0)	3 (1.7)	4 (2.2)	**0.002**
Quinolones	0 (0.0)	0 (0.0)	2 (1.1)	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	0.758
Nitroimidazole	2 (1.1)	1 (0.6)	10 (5.6)	2 (1.1)	0 (0.0)	7 (3.9)	2 (1.1)	**0.002**
Carbapenems	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	**0.002**
Sulfonamides	1(0.6)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.287
Glycopeptides	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0.409
Chloramphenicol	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0.480
Lincosamide	1 (0.6)	0 (0.0)	0 (0.0)	6 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.071
Tetracycli	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)	**0.004**
Furadantoins	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	**<0.001**
Rifamycins	2 (1.1)	0 (0.0)	9 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**<0.001**
Isoniazid	2 (1.1)	0 (0.0)	9 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**<0.001**
Pyrazinamide	2 (1.1)	0 (0.0)	10 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**<0.001**
Ethambutol	2 (1.1)	0(0.0)	9 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0(0.0)	**<0.001**
Others	0 (0.0)	0(0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.759

Key:-
PMW – Paediatric Medical Ward
NMW – Neonatal Medical Ward
AMW – Adult Medical Ward
ASW – Adult Surgical Ward
OBGYN – Obstetrics & Gynecology
ICU – Intensive Care Unit
Mixed – All those departments that have both adults and paediatrics in the same ward

4.3.7 Antibiotic prescribing by Indication

The pattern of antibiotic prescribing varied with the patient indications. The penicillin class of antibiotics was the most commonly used across the various indications. For community acquired infections, cephalosporins (47, 24.1%) were the most frequently prescribed class followed by penicillins (33, 16.9%) then aminoglycosides (23, 11.8%). Penicillins were the most frequently prescribed for management of postoperative surgical site infections (2, 50%) and other hospital acquired infections (3, 60%). The penicillins were also the most prescribed agents for medical prophylaxis (17, 30.4%). Cephalosporins and penicillins were the classes of antibiotics frequently used for surgical prophylaxis. Cephalosporins were frequently prescribed as a single dose in surgical prophylaxis (3, 42.9%) with ceftriaxone being the main antibiotic (3, 100%). Penicillins were also the most prevalent antibiotic for surgical prophylaxis that lasted one day (6, 50%) and for more than a day (23, 32.4%) (Figure 5).

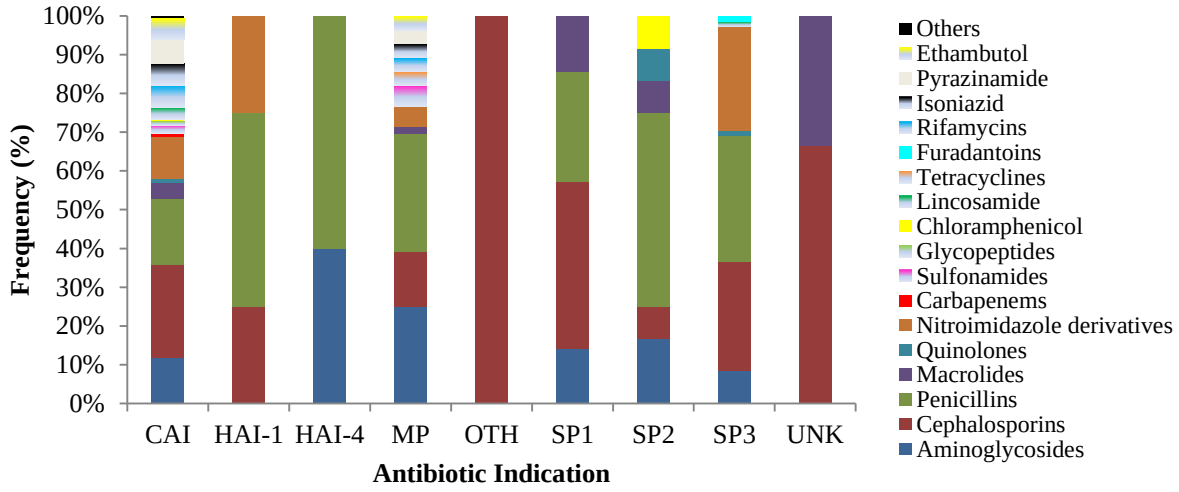


Figure 5: Antibiotic prescribing by indication

Key:
CAI – Community acquired infection
SP1 – single dose surgical prophylaxis
SP2 – one day surgical prophylaxis
SP3 – surgical prophylaxis > 1 day
MP – Medical Prophylaxis
HAI-1– Post operative surgical site infection
HAI-4 – Other hospital acquired infection
OTH – Other indication besides prophylaxis or treatment of infection
UNK – Completely unknown indication

4.3.8 Antibiotic prescribing according to anatomical site infections

The pattern of antibiotic prescribing also varied across the various anatomical sites of infection. The respiratory system (113, 43.0%) was the anatomic site with the highest prevalence of antibiotic use followed by the skin, soft tissue, bone and joint infections (37, 14.1%) and neonatal conditions (34, 12.9%). The most commonly prescribed antibiotic classes for respiratory infections were aminoglycosides (22, 19.5%) and penicillins (21, 18.6%). For the SSTBJ infections, cephalosporins (14, 37.8%) and penicillins (10, 27.0%) were commonly prescribed. For neonatal infections, aminoglycosides (14, 41.2%) and penicillins (14, 41.2%) were commonly prescribed (Figure 6).

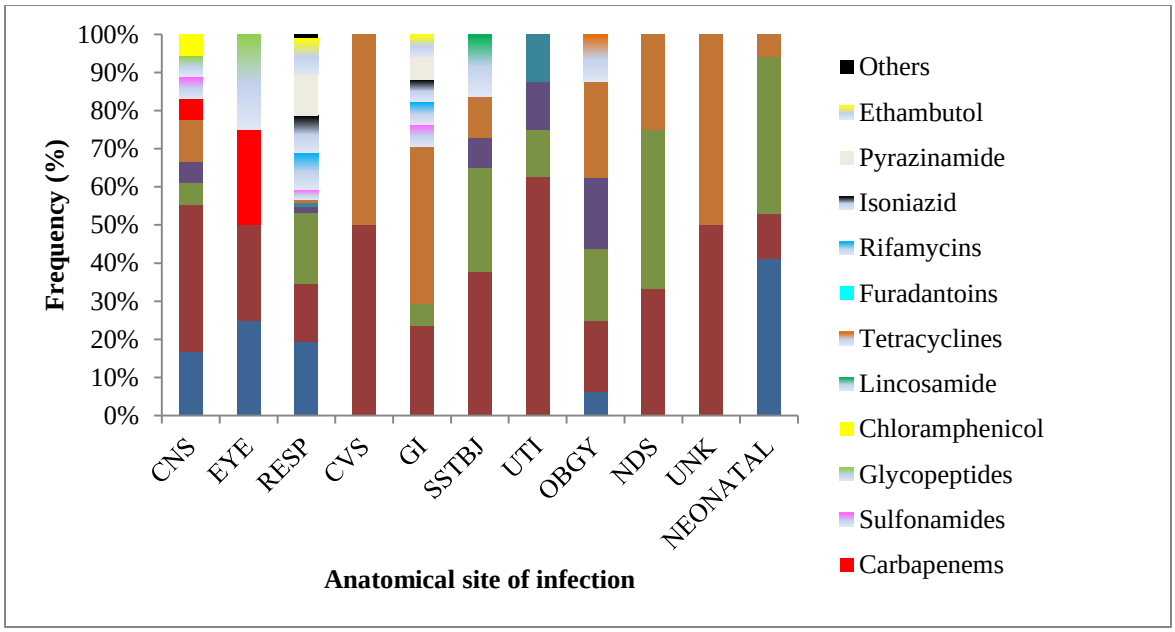


Figure 6: Pattern of antibiotic use for treatment of infections

Key:
SSTBJ – Skin, soft tissue, bone and joint infections
OBGY/GUM – Obstetrics & Gynecology & Male Genito-Urinary infections
NDS – No defined site
UTI – Urinary Tract Infection
ENT – Ear, nose and throat infections
UNK – Completely unknown indication
CVS – Cardiovascular system infections
CNS – Central Nervous System infections

4.3.9 Number of Antibiotics Prescribed

The number of antibiotics that were prescribed per patient is shown in Figure 7. Less than half of the patients were on a single antibiotic (74, 41.3%). Majority (105,58.7%) of the patients were on combination therapy with 17.9% (n=32) of the population having 3 or more antibiotics.

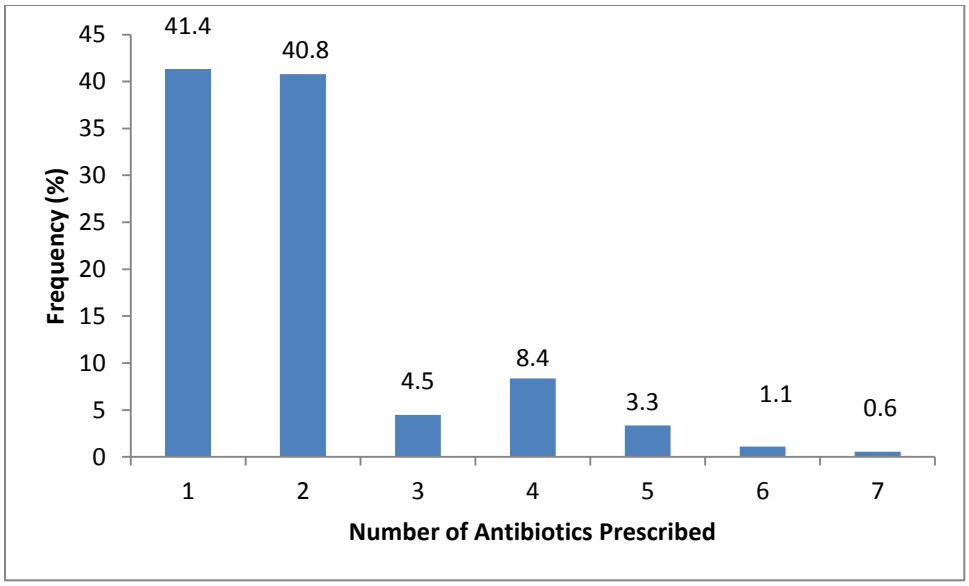


Figure 7: Number of antibiotics prescribed

4.3.10 Antibiotic combinations

The most prevalent antibiotic combinations were aminoglycosides and penicillins (20.7%) followed by cephalosporins and nitroimidazole derivatives (13.4%) then penicillins and nitroimidazole derivatives (9.5%). Other combinations comprised of those with only one patient each in the population. These included aminoglycoside combinations with quinolones, carbapenems, sulphonamides or glycopeptides. It also included cephalosporin combinations with quinolones, carbapenems and furadantoins (Figure 8).

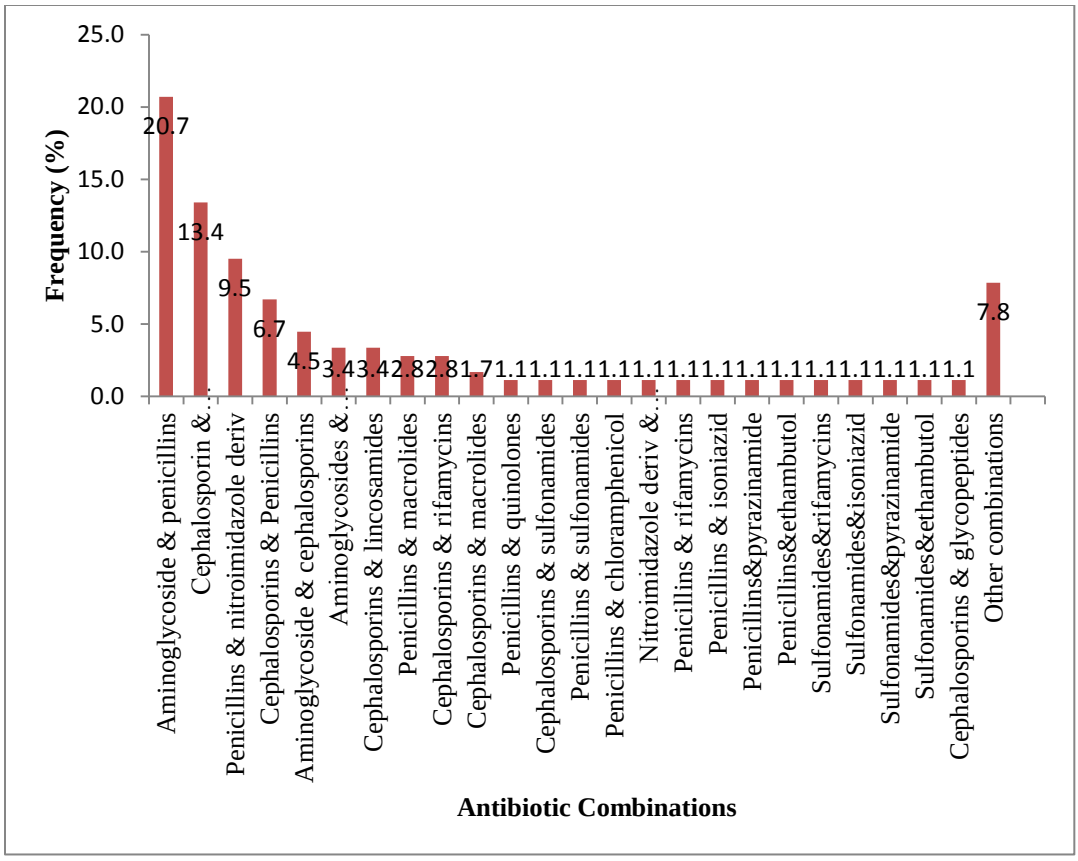


Figure 8: Prevalence of antibiotic combinations

There were also unusual combinations where agents from the same or different classes but with similar spectrum of activity were prescribed. For instance, Amoxicillin/clavulanic acid and ampicillin/cloxacillin, were prescribed together in 4 (2.2%) patients. Amoxicillin and Benzylpenicillin were prescribed together in 1 (0.6%) patient, Amoxicillin/clavulanic acid and Benzylpenicillin in 2 (1.1%) patients while Ampicillin/cloxacillin and Benzylpenicillin in 5 (2.8%) patients as shown in Figure 9.

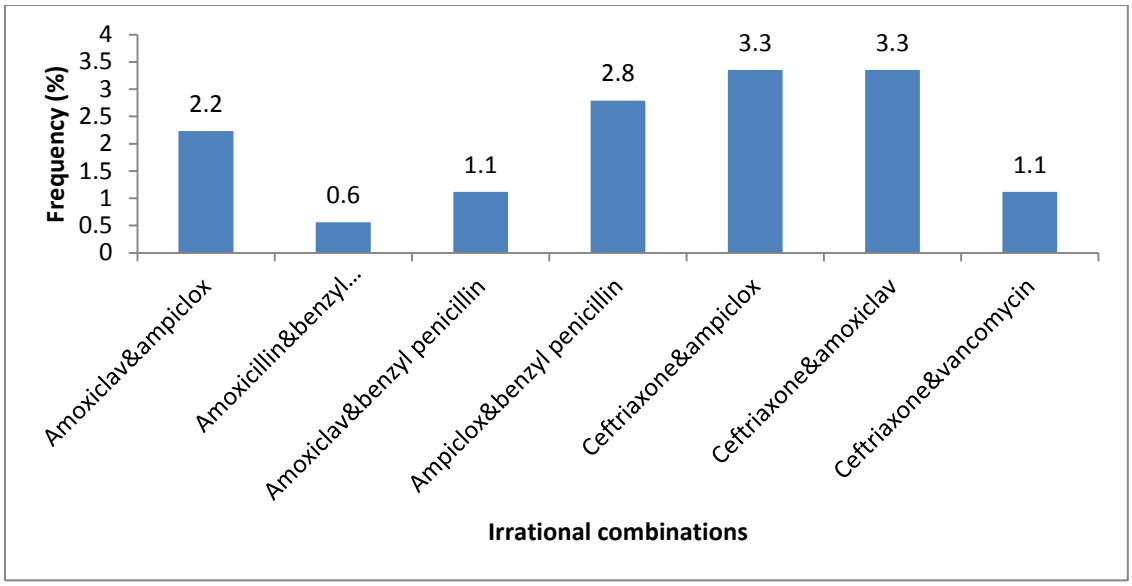


Figure 9: Prevalence of irrational antibiotic combinations

4.4 Quality Indicators of antibiotic prescribing

The study investigated the quality indicators for antibiotic prescribing. These included: documentation of the reason for antibiotics in the notes, generic prescribing and empiric versus targeted prescribing.

4.4.1 Documentation of antibiotic indication in notes

The reason for the antibiotic prescription was documented in 37.3% (n=133) of all the antibiotics prescribed. Clarithromycin, levofloxacin and the anti-tuberculosis medicines – isoniazid, cycloserine and prothionamide had the reason for their use documented all the time. Ampicillin cloxacillin, doxycycline, nitrofurantoin and vancomycin did not have the reason documented at any one encounter (Table 10).

Table 10: Prevalence of documentation of Indication in notes

Reason in notes	No n (%)		Yes n (%)		Total (100%)
Amikacin	2	(28.6)	5	(71.4)	7
Amoxicillin	2	(50.0)	2	(50.0)	4
Amoxicillin/ Clavulanic acid	9	(90.0)	1	(10.0)	10
Ampicillin/ cloxacillin	14	**(100.0)**	0	(0.0)	14
Benzyl penicillin	38	(73.1)	14	(26.9)	52
Capreomycin	1	(50.0)	1	(50.0)	2
Ceftazidime	2	(28.6)	5	(71.4)	7
Ceftriaxone	48	(67.6)	23	(32.4)	71
Chloramphenicol	2	(66.7)	1	(33.3)	3
Ciprofloxacin	2	(66.7)	1	(33.3)	3
Clindamycin	5	(71.4)	2	(28.6)	7
Clarithromycin	0	(0.0)	1	(100.0)	1
Cotrimoxazole	3	60.0)	2	(40.0)	5
Cycloserine	0	(0.0)	1	**(100.0)**	1
Doxycycline	2	**(100.0)**	0	(0.0)	2
Erythromycin	5	50.0	5	50.0	10
Ethambutol	2	16.7	10	83.3	12
Flucloxacillin	16	80.0	4	20.0	20
Gentamicin	30	75.0	10	25.0	40
Isoniazid	0	(0.0)	11	**(100.0)**	11
Levofloxacin	0	(0.0)	1	**(100.0)**	1
Meropenem	1	50.0	1	50.0	2
Metronidazole	35	77.8	10	22.2	45
Nitrofurantoin	1	**(100.0)**	0	(0.0)	1
Prothionamide	0	(0.0)	1	**(100.0)**	1
Pyrazinamide	1	8.3	11	91.7	12
Rifampicin	1	9.1	10	90.9	11
Vancomycin	2	**(100.0)**	0	(0.0)	2
Total	224	**62.7**	133	**37.3**	357

4.4.2 Generic Prescribing

The prevalence of generic prescribing was 62.5% (n= 223). There were some antibiotics that were always prescribed in their brand names. These included amoxicillin/clavulanic acid, ampicillin/cloxacillin and cotrimoxazole (Table 11).

Table 11: Prevalence of Generic Prescribing

Generic Prescribing	No n (%)		Yes n (%)		Total (100%)
Amikacin	1	14.3	6	85.7	7
Amoxicillin	2	50.0	2	50.0	4
Amoxiclav	10	**100.0**	0	0.0	10
Ampiclox	14	**100.0**	0	0.0	14
Benzyl penicillin	45	86.5	7	13.5	52
Capreomycin	0	0.0	2	**100.0**	2
Ceftazidime	0	0.0	7	**100.0**	7
Ceftriaxone	0	0.0	71	**100.0**	71
Chloramphenicol	1	33.3	2	66.7	3
Ciprofloxacin	0	0.0	3	**100.0**	3
Clindamycin	0	0.0	7	**100.0**	7
Clarithromycin	0	0.0	1	**100.0**	1
Cotrimoxazole	5	**100.0**	0	0.0	5
Cycloserine	0	0.0	1	**100.0**	1
Doxycycline	0	0.0	2	**100.0**	2
Erythromycin	0	0.0	10	**100.0**	10
Ethambutol	0	0.0	12	**100.0**	12
Flucloxacillin	18	90.0	2	10.0	20
Gentamicin	0	0.0	40	**100.0**	40
Isoniazid	0	0.0	11	**100.0**	11
Levofloxacin	0	0.0	1	**100.0**	1
Meropenem	0	0.0	2	**100.0**	2
Metronidazole	38	84.4	7	15.6	45
Nitrofurantoin	0	0.0	1	**100.0**	1
Prothionamide	0	0.0	1	**100.0**	1
Pyrazinamide	0	0.0	12	**100.0**	12
Rifampicin	0	0.0	11	**100.0**	11
Vancomycin	0	0.0	2	**100.0**	2
Total	134	**37.5**	223	**62.5**	357

4.4.3 Empiric versus targeted antibiotic prescribing

The prevalence of empiric prescribing was 82.6% (n=295) while that of targeted treatment was 17.4% (n=62). There were four agents that were always used for targeted therapy and these included clarithromycin and the antituberculosis medicines cycloserine, prothionamide and levofloxacin (Table 12).

Table 12: Prevalence of empiric versus targeted prescribing

Type of Treatment	Empiric prescribing n (%)		Targeted prescribing n (%)		Total no. of times prescribed N (100%)
Amikacin	5	71.4	2	28.6	7
Amoxicillin	4	**100.0**	0	0.0	4
Amoxiclav	10	**100.0**	0	0.0	10
Ampiclox	14	**100.0**	0	0.0	14
Benzyl penicillin	49	94.2	3	5.8	52
Capreomycin	1	50.0	1	50.0	2
Ceftazidime	7	**100.0**	0	0.0	7
Ceftriaxone	62	87.3	9	12.7	71
Chloramphenicol	3	**100.0**	0	0.0	3
Ciprofloxacin	3	**100.0**	0	0.0	3
Clindamycin	6	85.7	1	14.3	7
Clarithromycin	0	0.0	1	**100.0**	1
Cotrimoxazole	5	**100.0**	0	0.0	5
Cycloserine	0	0.0	1	**100.0**	1
Doxycycline	2	**100.0**	0	0.0	2
Erythromycin	10	**100.0**	0	0.0	10
Ethambutol	3	25.0	9	75.0	12
Flucloxacillin	19	95.0	1	5.0	20
Gentamicin	38	95.0	2	5.0	40
Isoniazid	4	36.4	7	63.6	11
Levofloxacin	0	0.0	1	**100.0**	1
Meropenem	1	50.0	1	50.0	2
Metronidazole	43	95.6	2	4.4	45
Nitrofurantoin	1	**100.0**	0	0.0	1
Prothionamide	0	0.0	1	**100.0**	1
Pyrazinamide	2	16.7	10	83.3	12
Rifampicin	2	18.2	9	81.8	11
Vancomycin	1	50.0	1	50.0	2
Total	295	**82.6**	62	**17.4**	357

4.5 Rational antibiotic prescribing

4.5.1 Evaluation of rational antibiotic prescribing

Rational antibiotic prescribing was evaluated based on five main indicators: appropriate choice, correct dose, correct frequency, duration and route of administration. These were assessed according to local and international guidelines. Prescribing was uncertain in the following circumstances: where the diagnosis was not specified in the patient records,

where the specific disease guidelines could not be found in any guideline or where the guidelines were available but did not clearly address the specific indicator. Each of the 5 indicators was summarized from Table 13 – 17 then the overall determination of whether the prescription was rational or not was provided in Table 18.

Out of the 357 antibiotic encounters, 82.3% (n=294) were appropriate choices for the specific diagnoses while 10.4% (n=37) were inappropriate choices for the various diagnosis (Table 13).

Table 13: Evaluation of choice of specific antibiotics

Specific Antibiotic	Incorrect n (%)		Correct n (%)		Uncertain n (%)		Total
Amikacin	1	(14.3)	6	(85.7)	0	(0.0)	7
Amoxicillin	1	(25.0)	2	(50.0)	1	(25.0)	4
Amoxicillin/ Clavulanic Acid	7	(70.0)	3	(30.0)	0	(0.0)	10
Ampicillin/ Cloxacillin	2	(14.3)	12	(85.7)	0	(0.0)	14
Benzyl penicillin	0	(0.0)	50	(96.1)	2	(3.8)	52
Capreomycin	1	(50.0)	1	(50.0)	0	(90.0)	2
Ceftazidime	0	(0.0)	7	(100.0)	0	(0.0)	7
Ceftriaxone	14	(19.7)	49	(69.0)	8	(11.3)	71
Chloramphenico	1	(33.3)	2	(66.7)	0	(0.0)	3
Ciprofloxacin	0	(0.0)	3	(100.0)	0	(0.0)	3
Clindamycin	0	(0.0)	2	(28.6)	5	(71.4)	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	1
Cotrimoxazole	1	(20.0)	4	(80.0)	0	(0.0)	5
Cycloserine	0	(0.0)	1	(100.0)	0	(0.0)	1
Doxycycline	0	(0.0)	2	(100.0)	0	(0.0)	2
Erythromycin	2	(20.0)	6	(60.0)	2	(20.0)	10
Ethambutol	0	(0.0)	12	(100.0)	0	(0.0)	12
Flucloxacillin	0	(0.0)	20	(100.0)	0	(0.0)	20
Gentamicin	2	(5.0)	37	(92.5)	1	(2.5)	40
Isoniazid	0	(0.0)	11	(100.0)	0	(0.0)	11
Levofloxacin	0	(0.0)	1	(100.0)	0	(0.0)	1
Meropenem	0	(0.0)	2	(100.0)	0	(0.0)	2
Metronidazole	5	(11.1)	33	(73.3)	7	(15.6)	45
Nitrofurantoin	0	(0.0)	1	(100.0)	0	(0.0)	1
Prothionamide	0	(0.0)	1	(100.0)	0	(0.0)	1
Pyrazinamide	0	(0.0)	12	(100.0)	0	(0.0)	12
Rifampicin	0	(0.0)	11	(100.0)	0	(0.0)	11
Vancomycin	0	(0.0)	2	(100.0)	0	(0.0)	2
TOTAL	**37**	**(10.4)**	**294**	**(82.3)**	**26**	**(7.3)**	**357**

Out of the 357 antibiotic encounters, 78.7% (n=281) had the correct doses prescribed according to the indication and diagnosis while 13.4% (n=48) had incorrect doses (Table 14).

Table 14: Evaluation of Dose of specific antibiotics

Specific Antibiotic	Incorrect n (%)		Correct n (%)		Uncertain n (%)		Missing n (%)		Total
Amikacin	2	(28.6)	4	(57.1)	1	(14.3)	0	(0.0)	7
Amoxicillin	0	(0.0)	4	(100.0)	0	(0.0)	4	(100.0)	4
Amoxicillin/ Clavulanic acid	5	(50.0)	5	(50.0)	0	(0.0)	0	(0.0)	10
Ampicillin/ Cloxacillin	0	(0.0)	14	(100.0)	0	(0.0)	0	(0.0)	14
Benzyl penicillin	10	(19.2)	40	(76.9)	2	(3.8)	0	(0.0)	52
Capreomycin	1	(50.0)	0	(0.0)	1	(50.0)	0	(0.0)	2
Ceftazidime	5	(71.4)	3	(42.9)	1	(14.3)	0	(90.0)	7
Ceftriaxone	3	(4.2)	63	(88.7)	5	(7.0)	0	(0.0)	71
Chloramphenico	1	(33.3)	2	(66.7)	0	(0.0)	0	(0.0)	3
Ciprofloxacin	1	(33.3)	2	(66.7)	0	(0.0)	0	(0.0)	3
Clindamycin	2	(28.6)	1	(14.3)	4	(57.1)	0	(0.0	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Cotrimoxazole	0	(0.0)	5	(100.0)	0	(0.0)	0	(0.0)	5
Cycloserine	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Doxycycline	0	(0.0)	2	(100.0)	0	(0.0)	0	(0.0)	2
Erythromycin	0	(0.0)	9	(90.0)	0	(0.0)	1	(10.0)	10
Ethambutol	2	(16.7)	10	(83.3)	0	(0.0)	0	(0.0)	12
Flucloxacillin	1	(5.0)	18	(90.0)	0	(0.0)	1	(5.0)	20
Gentamicin	8	(20.0)	25	(62.5)	7	(17.5)	0	(0.0)	40
Isoniazid	1	(9.1)	10	(90.9)	0	(0.0)	0	(0.0)	11
Levofloxacin	0	(0.0)	0	(0.0)	1	(100.0)	0	(0.0)	1
Meropenem	1	(50.0)	1	(50.0)	0	(0.0)	0	(0.0)	2
Metronidazole	3	(6.7)	40	(88.9)	1	(2.2)	1	(2.2)	45
Nitrofurantoin	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Prothionamide	0	(0.0)	0	(0.0)	1	(100.0)	0	(0.0)	1
Pyrazinamide	1	(8.3)	10	(83.3)	1	(8.3)	0	(0.0)	12
Rifampicin	1	(9.1)	10	(90.9)	0	(0.0)	0	(0.0)	11
Vancomycin	0	(0.0)	1	(50.0)	1	(50.0)	0	(0.0)	2
TOTAL	**48**	**(13.4)**	**281**	**(78.7)**	**26**	**(7.3)**	**8**	**(2.2)**	**357**

Of the 357 antibiotic encounters, 85.9% (n=307) had the correct frequency while 10.9% (n=39) had incorrect frequencies of administration. The frequency of administration was missing in 3.1% (11) of the antibiotics prescribed (Table 15).

Table 15: Evaluation of frequency of specific antibiotics

Specific Antibiotic	Incorrect n (%)		Correct n (%)		Missing n (%)		Total
Amikacin	1	(14.3)	6	(85.7)	0	(0.0)	7
Amoxicillin	0	(0.0)	4	(100.0)	0	(0.0)	4
Amoxicillin/ Clavulanic acid	5	(50.0)	5	(50.0)	0	(0.0)	10
Ampicillin/ Cloxacillin	0	(0.0)	14	(100.)	0	(0.0)	14
Benzyl penicillin	0	(0.0)	51	(98.1)	1	(1.9)	52
Capreomycin	1	(50.0)	1	(50.0)	0	(0.0)	2
Ceftazidime	5	(71.4)	1	(14.3)	1	(14.3	7
Ceftriaxone	13	(18.3)	53	(74.6)	5	(7.0)	71
Chloramphenicol	1	(33.3)	2	(66.7)	0	(0.0)	3
Ciprofloxacin	1	(33.3)	2	(66.7)	0	(0.0)	3
Clindamycin	0	(0.0)	7	(100.0)	0	(0.0)	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	1
Cotrimoxazole	1	(20.0)	4	(80.0)	0	(0.0)	5
Cycloserine	0	(0.0)	1	(100.0)	0	(0.0)	1
Doxycycline	0	(0.0)	2	(100.0)	0	(0.0)	2
Erythromycin	2	(20.0)	8	(80.0)	0	(0.0)	10
Ethambutol	1	(8.3)	11	(91.7)	0	(0.0)	12
Flucloxacillin	2	(0.0)	18	(90.0)	0	(0.0)	20
Gentamicin	2	(5.0)	37	(92.5)	1	(2.5)	40
Isoniazid	0	(0.0)	11	(100.0)	0	(0.0)	11
Levofloxacin	0	(0.0)	1	(100.0)	0	(0.0)	1
Meropenem	1	(50.0)	1	(50.0)	0	(0.0)	2
Metronidazole	1	(2.2)	42	(93.3)	2	(4.4)	45
Nitrofurantoin	0	(0.0)	0	(0.0)	1	(100.0)	1
Prothionamide	0	(0.0)	1	(100.0)	0	(0.0)	1
Pyrazinamide	2	(16.7)	10	(83.3)	0	(0.0)	12
Rifampicin	0	(0.0)	11	(100.0)	0	(0.0)	11
Vancomycin	0	(0.0)	2	(100.0)	0	(0.0)	2
TOTAL	**39**	**(10.9)**	**307**	**(85.9)**	**11**	**(3.1)**	**357**

Out of the 357 times that antibiotics were prescribed, 283 (79.3%) had the correct route of administration while 19 (5.3%) had incorrect route of administration. Those without the route of administration were 54 (15.1%) (Table 16).

Table 16: Evaluation of route of specific antibiotics

Specific Antibiotic	Incorrect n (%)		Correct n (%)		Uncertain n (%)		Missing n (%)		Total
Amikacin	3	(42.9)	3	(42.9)	0	(0.0)	1	(14.3)	7
Amoxicillin	0	(0.0)	4	(100.0)	0	(0.0)	0	(0.0)	4
Amoxicillin/ Clavulanic acid	2	(20.0)	5	(50.0)	0	(0.0)	3	(30.0)	10
Ampicillin/ Cloxacillin	0	(0.0)	2	(14.3)	0	(0.0)	12	(85.7)	14
Benzyl penicillin	0	(0.0)	50	(96.1)	0	(0.0)	2	(3.8)	52
Capreomycin	1	(50.0)	1	(50.0)	0	(0.0)	0	(0.0)	2
Ceftazidime	0	(0.0)	4	(57.1)	0	(0.0)	3	(42.9)	7
Ceftriaxone	2	(2.8)	66	(93.0)	0	(0.0)	3	(4.2)	71
Chloramphenico	0	(0.0)	3	(100.0)	0	(0.0)	0	(0.0)	3
Ciprofloxacin	0	(0.0)	2	(66.7)	0	(0.0)	1	(33.3)	3
Clindamycin	1	(14.3)	6	(85.7)	0	(0.0)	0	(0.0)	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Cotrimoxazole	0	(0.0)	5	(100.0)	0	(0.0)	0	(0.0)	5
Cycloserine	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Doxycycline	0	(0.0)	1	(50.0)	0	(0.0)	1	(50.0)	2
Erythromycin	2	(20.0)	6	(60.0)	0	(0.0)	2	(20.0)	10
Ethambutol	0	(0.0)	11	(91.7)	0	(0.0)	1	(8.3)	12
Flucloxacillin	5	(25.0)	11	(55.0)	0	(0.0)	4	(20.0)	20
Gentamicin	1	(2.5)	37	(92.5)	0	(0.0)	2	(5.0)	40
Isoniazid	0	(0.0)	10	(90.9)	0	(0.0)	1	(9.1)	11
Levofloxacin	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Meropenem	0	(0.0)	2	(100.0)	0	(0.0)	0	(0.0)	2
Metronidazole	2	(4.4)	30	(66.7)	1	(2.2)	12	(26.7)	45
Nitrofurantoin	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Prothionamide	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Pyrazinamide	0	(0.0)	10	(83.3)	0	(0.0)	2	(16.7)	12
Rifampicin	0	(0.0)	10	(90.9)	0	(0.0)	1	(9.1)	11
Vancomycin	0	(0.0)	2	(100.0)	0	(0.0)	0	(0.0)	2
TOTAL	**19**	**(5.3)**	**283**	**(79.3)**	**1**	**(0.3)**	**54**	**(15.1)**	**357**

Out of all the 357 antibiotic encounters, 80 (22.4%) had incorrect duration of use while 180 (50.4%) had the correct duration. This was evaluated based on various local and international guidelines. There was no duration of antibiotic use in 80 (22.4%) of the total antibiotics prescribed (Table 17).

Table 17: Duration of antibiotic use

Specific Antibiotic	Incorrect n (%)		Correct n (%)		Uncertain n (%)		Missing n (%)		Total
Amikacin	1	(0.1)	4	(57.1)	0	(0.0)	2	(28.6)	7
Amoxicillin	0	(0.0)	3	(75.0)	1	(25.0)	0	(0.0)	4
Amoxicillin/ Clavulanic acid	7	(70.0)	1	(10.0)	0	(0.0)	2	(20.0)	10
Ampicillin/Cloxacillin	14	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	14
Benzyl penicillin	5	(9.6)	33	(63.5)	0	(0.0)	14	(26.9)	52
Capreomycin	1	(50.0)	1	(50.0)	0	(0.0)	0	(0.0)	2
Ceftazidime	1	(14.3)	4	(57.1)	0	(0.0)	2	(28.6)	7
Ceftriaxone	11	(15.5)	37	(52.1)	7	(9.9)	16	(22.5)	71
Chloramphenicol	2	(66.7)	0	(0.0)	0	(0.0)	1	(33.3)	3
Ciprofloxacin	0	(0.0)	2	(66.6)	0	(0.0)	1	(33.3)	3
Clindamycin	1	(14.3)	0	(0.0)	3	(42.9)	3	(42.9)	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Cotrimoxazole	1	(20.0)	2	(40.0)	0	(0.0)	2	(40.0)	5
Cycloserine	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Doxycycline	1	(50.0)	0	(0.0)	0	(0.0)	1	(50.0)	2
Erythromycin	5	(50.0)	2	(20.0)	0	(0.0)	3	(30.0)	10
Ethambutol	2	(16.7)	7	(58.3)	1	(8.3)	2	(16.7)	12
Flucloxacillin	4	(20.0)	13	(65.0)	0	(0.0)	3	(15.0)	20
Gentamicin	5	(12.5)	28	(70.0)	0	(0.0)	7	(17.5)	40
Isoniazid	1	(9.1)	7	(63.6)	1	(9.1)	2	(18.2)	11
Levofloxacin	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Meropenem	0	(0.0)	0	(0.0)	0	(0.0)	2	(100.0)	2
Metronidazole	14	(31.1)	18	(40.0)	4	(8.9)	9	(20.0)	45
Nitrofurantoin	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1
Prothionamide	0	(0.0)	1	(100.0)	0	(0.0)	0	(0.0)	1
Pyrazinamide	2	(16.7)	8	(66.7)	0	(0.0)	2	(16.7)	12
Rifampicin	2	(18.2)	7	(63.6)	0	(0.0)	2	(18.2)	11
Vancomycin	0	(0.0)	0	(0.0)	0	(0.0)	2	(100.0)	2
TOTAL	**80**	**(22.4)**	**180**	**(50.4)**	**17**	**(4.8)**	**80**	**(22.4)**	**357**

Based on the above indicators of rational antibiotic prescribing, the prescription was then evaluated overall as to whether it was rational or not as shown in Table 18. A prescription was found to be rational if it met all the 5 indicators – correct choice, dose, duration, route and frequency of administration and irrational if it missed even one of the indicators. Out of the 357 antibiotics that were prescribed, 121 (33.9%) were rational. Out of the 179 patients that participated in the study, only 50 (27.9%) had a rational antibiotic prescription (Table 18).

Table 18: Rational prescribing of specific antibiotics

Rational prescribing	No n (%)		Yes n (%)		Uncertain n (%)		Total
Amikacin	5	(71.4)	2	(28.6)	0	(0.0)	7
Amoxicillin	2	(50.0)	1	(25.0)	1	(25.0)	4
Amoxicillin/ Clavulanic acid	10	(100.0)	0	(0.0)	0	(0.0)	10
Ampicillin/Cloxacillin	12	(85.7)	2	(14.3)	0	(0.0)	14
Benzyl penicillin	28	(53.8)	23	(44.2)	1	(1.9)	52
Capreomycin	1	(50.0)	1	(50.0)	0	(0.0)	2
Ceftazidime	6	(85.7)	1	(14.3)	0	(0.0)	7
Ceftriaxone	45	(63.4)	21	(29.6)	5	(7.0)	71
Chloramphenicol	3	(100.0)	0	(0.0)	0	(0.0)	3
Ciprofloxacin	2	(66.7)	1	(33.3)	0	(0.0)	3
Clindamycin	4	(57.1)	0	(0.0)	3	(42.9)	7
Clarithromycin	0	(0.0)	1	(100.0)	0	(0.0)	1
Cotrimoxazole	4	(80.0)	1	(20.0)	0	(0.0)	5
Cycloserine	0	(90.0)	1	(100.0)	0	(0.0)	1
Doxycycline	2	(100.0)	0	(0.0)	0	(0.0)	2
Erythromycin	9	(90.0)	1	(10.0)	0	(0.0)	10
Ethambutol	6	(50.0)	6	(50.0)	0	(0.0)	12
Flucloxacillin	13	(65.0)	7	(35.0)	0	(0.0)	20
Gentamicin	22	(55.0)	18	(45.0)	0	(0.0)	40
Isoniazid	5	(45.4)	6	(54.5)	0	(0.0)	11
Levofloxacin	0	(0.0)	1	(100.0)	0	(0.0)	1
Meropenem	2	(100.0)	0	(0.0)	0	(0.0)	2
Metronidazole	28	(62.2)	13	(28.9)	4	(8.9)	45
Nitrofurantoin	1	(100.0)	0	(0.0)	0	(0.0)	1
Prothionamide	0	(0.0)	1	(100.0)	0	(0.0)	1
Pyrazinamide	5	(41.7)	7	(58.3)	0	(0.0)	12
Rifampicin	5	(45.4)	6	(54.5)	0	(0.0)	11
Vancomycin	2	(100.0)	0	(0.0)	0	(0.0)	2
TOTAL	222	(62.2)	**121**	**(33.9)**	14	(3.9)	357

Was the prescription rational?	No n (%)	Yes n (%)	Uncertain n (%)
	117 (65.4)	**50.00 (27.9)**	**12 (6.7)**

4.5.2 Association between rational prescribing and sociodemographic patient characteristics

Chi square test was used to find the association between rational prescribing and probable predictors such as the patient age, sex, department and diagnosis.

Rational prescribing of antibiotics did not vary significantly with the age (p=0.179) or sex (p=0.396) of the patients. There was a significant association between rational

prescribing and the department (p<0.001). The highest proportion of rational prescribing was documented in the neonatal medical ward (80%, n=12) followed by the adult medical ward (41.5%, n=17) and paediatric medical ward (21.8%, n=9). The highest proportion of irrational use was documented in the ICU (100%, n=4) followed by the mixed departments (88.2%, n=15) and the adult surgical ward (75.5%, n=40) (Table 19).

Table 19: Relationship between rational prescribing of antibiotics and sociodemographic characteristics of the patient

Patient characteristics	Rational prescribing n (%)		Irrational prescribing n (%)		Uncertain n (%)		P value
Age							
1-30days	12	(6.7)	10	(5.6)	1	0.6	
1-23months	4	(2.2)	14	(7.8)	0	(0.0)	
2-12years	6	(3.3)	13	(7.3)	0	(0.0)	
13-19years	2	(1.1)	6	(3.3)	1	0.56	0.179
20-60years	20	(11.2)	65	(36.3)	8	4.5	
>60years	6	(3.3)	9	(5.0)	2	1.1	
Total	**50**	**(27.9)**	**117**	**(65.4)**	**12**	**6.7**	
Sex							
Male	26	(14.5)	48	(26.8)	6	3.3	
Female	24	(13.4)	69	(38.5)	6	3.3	0.396
Total	50	(27.9)	117	(65.4)	12	6.7	
Departments							
PMW	9	(28.1)	22	(68.7)	1	3.1	
NMW	12	(80.0)	3	(20.0)	0	(0.0)	
AMW	17	(41.5)	21	(51.2)	3	7.3	
ASW	8	(15.1)	40	(75.5)	5	9.4	**<0.001**
OBGYN	2	(11.8)	12	70.6)	3	17.6	
ICU	0	(0.0)	4	(100.0)	0	(0.0)	
MIXED	2	(11.8)	15	(88.2)	0	(0.0)	

4.5.3 Association between rational prescribing and patient clinical factors

The prescribing of antibiotics was significantly rational for neonatal conditions (p<0.001). However there was high prevalence of irrational prescribing in the prophylactic use of antibiotic in the gynaecological tract (p=0.013) and also in the treatment of gynecological or male urogenital infections (p=0.016) (Table 20)

Table 20: Relationship between rational prescribing of antibiotics and patient clinical factors

Antibiotic Indication	Rational Prescribing n (%)		Irrational Prescribing n (%)		Uncertain n (%)		P Value
Prophylaxis							
ProphCNS	0	(0.0)	3	(75.0)	1	(25.0)	0.198
Proph EYE	1	(25.0)	3	(75.0)	0	(0.0)	0.842
Proph ENT	0	(0.0)	4	(100.0)	0	(0.0)	0.338
Proph RESP	0	(0.0)	1	(100.0)	0	(0.0)	0.766
Proph GI	0	(0.0)	4	(80.0)	1	(20.0)	0.227
Proph SSTBJ	2	(12.5)	14	(87.5)	0	(0.0)	0.136
Proph OBGY/GUM	0	(0.0)	17	(94.4)	1	(5.6)	**0.016**
Treatment							
Central nervous system	2	(20.0)	8	(80.0)	0	(0.0)	0.523
Eye	0	(0.0)	1	(100.0)	0	(0.0)	0.766
Respiratory	12	(27.3)	32	(72.7)	0	(0.0)	0.111
Cardiovascular system	0	(0.0)	0	(0.0)	1	(100.0)	**0.001**
Gastrointestinal system	3	(37.5)	4	(50.0)	1	(12.5)	0.608
SSTBJ	9	(40.9)	9	(40.9)	4	(18.2)	**0.013**
Urinary tract Infections	4	(66.7)	2	(33.3)	0	(0.0)	0.094
OBGY/GUM	0	(0.0)	9	(81.8)	2	(18.2)	**0.048**
No defined site	6	(50.0)	5	(41.7)	1	(8.3)	0.183
Unknown	0	(0.0)	1	(50.0)	1	(50.0)	**0.043**
Neonatal	12	(66.7)	6	(33.3)	0	(0.0)	**<0.001**
Indications							
Community Acquired Infection	29	(29.9)	57	(58.8)	11	(11.3)	0.585
HAI-1	0	(0.0)	2	(100.0)	0	(0.0)	0.585
HAI-4	1	(33.3)	2	(66.7)	0	(0.0)	0.888
Medical Prophylaxis	15	(55.5)	12	(44.4)	0	(0.0)	**0.002**
Other	0	(0.0)	1	(100.0)	0	(0.0)	0.766
SP1	1	(20.0)	2	(40.0)	2	40.0	**0.010**
SP2	0	(0.0)	7	(100.0)	0	(0.0)	0.145
SP3	2	(5.0)	38	(95.0)	0	(0.0)	**<0.001**
Unknown	2	(100.0)	0	(0.0)	0	(0.0)	0.074

Key:-

SSTBJ – Skin, soft tissue, bone and joint

OBGY/GUM – Obstetrics & gynaecology and male genito-urinary system

SP1 – single dose surgical prophylaxis
SP2 – one day surgical prophylaxis
SP3 – surgical prophylaxis > 1 day
HAI -1 – Post operative surgical site infection
HAI-4 – Other hospital acquired infection

4.5.4. Variation of rational prescribing according to antibiotic class

In an attempt to establish whether there was variation in rational prescribing based on antibiotic class, chi square test was used to find an association between the class of antibiotics and rationality of prescribing as shown in Table 21. The aminoglycoside class of antibiotics had the highest proportion (38.0%) of rational prescribing across all the classes of antibiotics and this was statistically significant (p=0.032). This was followed by the penicillin class of antibiotics (33.3%) (p=0.048).

Table 21: Relationship between rational prescribing and antibiotic class

Class	Rational n (%)		Irrational n (%)		Uncertain n (%)		Total n (%)		P Value
Aminoglycosides	18	(38.0)	29	(61.7)	0	(0.0)	47	(100.0)	**0.032**
Cephalosporins	17	(21.2)	57	(71.2)	6	(7.5)	80	(100.0)	0.200
Penicillins	28	(33.3)	54	(64.3)	2	(2.4)	84	(100.0)	**0.048**
Macrolides	2	(18.2)	8	(72.7)	1	(9.1)	11	(100.0)	0.742
Quinolones	0	(0.0)	5	(100.0)	0	(0.0)	5	(100.0)	0.256
Nitroimidazole derivatives	9	(20.9)	29	(67.4)	5	(11.6)	43	(100.0)	0.215
Carbapenems	0	(0.0)	2	(100.0)	0	(0.0)	2	(100.0)	0.585
Sulfonamides	0	(0.0)	4	(100.0)	0	(0.0)	4	(100.0)	0.338
Glycopeptides	0	(0.0)	2	(100.0)	0	(0.0)	2	(100.0)	0.585
Chloramphenicol	0	(0.0)	2	(100.0)	0	(0.0)	2	(100.0)	0.585
Lincosamide	0	(0.0)	3	(42.9)	4	(57.1)	7	(100.0)	**<0.001**
Tetracyclines	0	(0.0)	2	(100.0)	0	(0.0)	2	(100.0)	0.585
Furadantoins	0	(0.0)	1	(100.0)	0	(0.0)	1	(100.0)	0.766
Rifamycins	3	(27.3)	8	(72.7)	0	(0.0)	11	(100.0)	0.642
Isoniazid	3	(27.3)	8	(72.7)	0	(0.0)	11	(100.0)	0.642
Pyrazinamide	3	(25.0)	9	(75.0)	0	(0.0)	12	(100.0)	0.581
Ethambutol	3	(27.3)	8	(72.7)	0	(0.0)	11	(100.0)	0.642
Others	0	(0.0)	1	(100.0)	0	(0.0)	1	(100.0)	0.766

4.5.5 Regression analysis for predictors of rational antibiotic prescribing

In order to understand the influence of the predictor variables on the outcome (rational prescribing), binary logistic regression was done. Since the output was required to be binary and in order to avoid bias, the uncertain values were dropped from the analysis. The odds ratio from univariate analysis and adjusted odds ratios from multivariate analysis were obtained as shown in Table 21 and 22. The odds of having a rational antibiotic prescription among children (1-23months) were 0.24 times the odds of a rational antibiotic prescription in neonates (1-30days). This means that there was a higher chance of rational antibiotic prescribing among the neonates as compared to children (1-23months) and this was significant (p=0.043). This was also true of the respective departments where the odds of having a rational antibiotic prescription in the neonatal medical ward were 9 times the odds in the paediatric medical ward (for children as from 1 month and above). This was significant (p=0.003). The same was also true of the diagnosis. The odds of rational antibiotic prescribing for any neonatal condition were 5 times higher than those of other conditions and this was found to be significant (p=0.001).

Neonates were also two times more likely to get a rational antibiotic prescription as compared to adults (20-59years) and this was significant (p=0.006).

The most powerful predictor of rational antibiotic prescribing was a diagnosis of a neonatal condition as shown in Table 21 as this had the lowest Akaike's Information Criterion value (AIC) and Bayesian Information Criterion value (BIC) of all predictor variables. There was a strong positive association between having a neonatal diagnosis and rational prescribing of antibiotics (Crude odds ratio: 5.84 (CI: 2.051 - 16.643)) and this was significant (p=0.001) (Table 21).

Table 22: Univariate binary logistic regression analysis for predictors of rational antibiotic prescribing

	Univariate Analysis			
Variable	COR (95% CI)	Pvalue	AIC	BIC
Age Category			205.0	211.3
Neonates (1-30days)	1			
Children (1-23months)	0.24 (0.059-0.958)	**0.043**		
Children (2-12years)	0.38 (0.107 - 1.384)	0.144		
Adolescents (13-19years)	0.28 (0.045 - 1.692)	0.165		
Adults (20-59years)	0.26 (0.096 - 0.681)	**0.006**		
Elderly (60years and above)	0.55 (0.147 – 2.102)	0.387		
Sex			206.1	212.4
Male	1			
Female	0.64 (0.330 - 1.250)	0.192		
Department			200.1	206.3
PMW	1			
NMW	9.78 (2.324 - 44.967)	**0.003**		
AMW	1.98 (0.673 - 4.871)	0.183		
ASW	0.49 (0.155 - 1.333)	0.270		
OBGYN	0.41 (0.064 - 1.800)	0.297		
MIXED	0.32 (0.051 - 1.398)	0.187		
ICU	1			
Diagnosis				
Proph Eye	0.77 (0.079 – 7.641)	0.828	207.8	214.0
Proph SSTBJ	0.31 (0.067 - 1.402)	0.128	204.9	211.1
CNS	0.57 (0.116 – 2.773)	0.484	207.3	213.5
Resp	0.84 (0.390 – 1.804)	0.653	207.6	213.9
GI	1.80 (0.388 – 8.370)	0.452	207.3	213.5
SSTBJ	2.63 (0.977 – 7.099)	0.056	204.3	210.5
UTI	5.00 (0.885 – 28.24)	0.068	204.3	210.5
NDS	3.05 (0.887 – 10.523)	0.077	204.8	211.0
Neonatal	5.84 (2.051 - 16.643)	**0.001**	**196.1**	**202.3**

Key:
AIC – Akaike's Information Criterion
BIC – Bayesian Information Criterion

The Parsimonius model of binary logistic regression was used to identify the four most powerful predictors of rational antibiotic prescribing. These were found to be a diagnosis of neonatal infection, a diagnosis of skin, soft tissue, bone or joint infections, a diagnosis of no defined site and the department type as shown in Table 23.

There was a strong positive association between a diagnosis of a neonatal infection and rational prescribing of antibiotics (Adjusted odds ratio: 5.992 (95% CI: 1.985 – 18.094)).

This was significant (p=0.001). There was also found to be a positive association between the diagnosis of a skin, soft tissue, bone or joint infection and rational prescribing of antibiotics (Adjusted odds ratio: (6.221 (95%CI: 2.053 – 18.847)) and this too was significant (p=0.001). The association between a no defined site diagnosis and rational prescribing was also found to be positive (Adjusted odds ratio: 5.540 (95% CI: 1.486 – 20.648)) and it was significant (p=0.011). There was a negative association between the department type and rational antibiotic prescribing (Adjusted odds ratio: 0.778 (95% CI: 0.640 – 0.945)). This too was significant (p=0.011).

Table 23: Parsimonius model of the most powerful predictors of rational prescribing

Variable	Adjusted Odds Ratio (95% Confidence Interval)	P Value
Neonatal infections	5.992 (1.985 – 18.094)	0.001
Skin, soft tissue, bone & joint infections	6.221 (2.053 – 18.847)	0.001
Department	0.778 (0.640 – 0.945)	0.011
No defined site	5.540 (1.486 – 20.648)	0.011

4.6 Guideline Compliance

The antibiotic prescriptions were compared with the available local and international guidelines in order to establish compliance. Compliance was assessed based on choice of antibiotic, dose, frequency, duration and route of administration. There was guideline compliance if all these parameters were consistent with the guideline recommendations. There were however scenarios where the guidelines were not available for the specific disease conditions, or did not clearly spell out all the parameters. There were also cases where the specific diagnosis was not specified in the records. These were labelled uncertain.

4.6.1 Guidelines used for assessment of compliance and availability of local guidelines

Various guidelines were used in assessing appropriateness of the antibiotics chosen, dose, route, frequency and duration of use. Priority was given to local guidelines and where these were not available, international guidelines such as the Infectious Disease Association of America were reviewed. The specific guidelines considered are shown in

Figure 10. Local guidelines were available in 66.5% (n=119) of the diagnoses as shown in Figure 11.

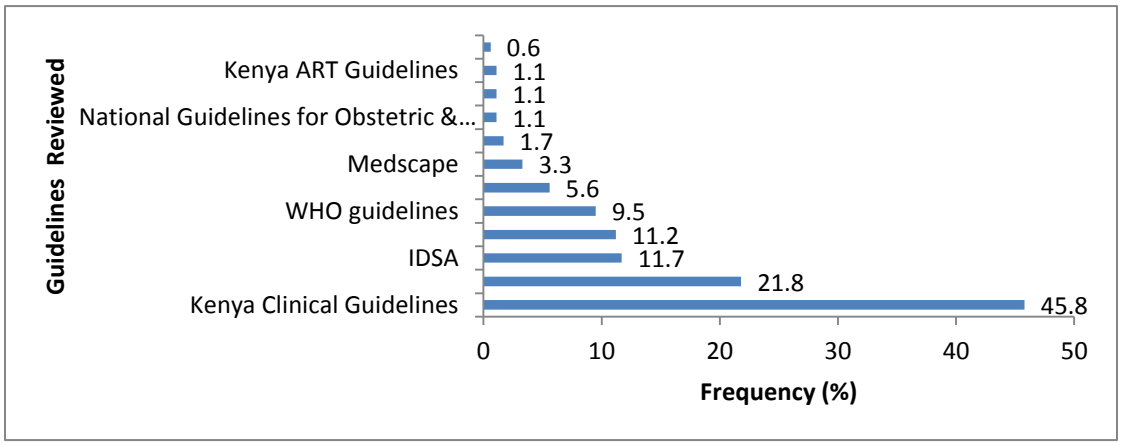


Figure 10: Specific Guidelines Reviewed

Key:
IDSA – Infectious Disease Society of America
BNF – British National Formulary
WHO – World Health Organisation
EASL – European Association for the Study of the Liver

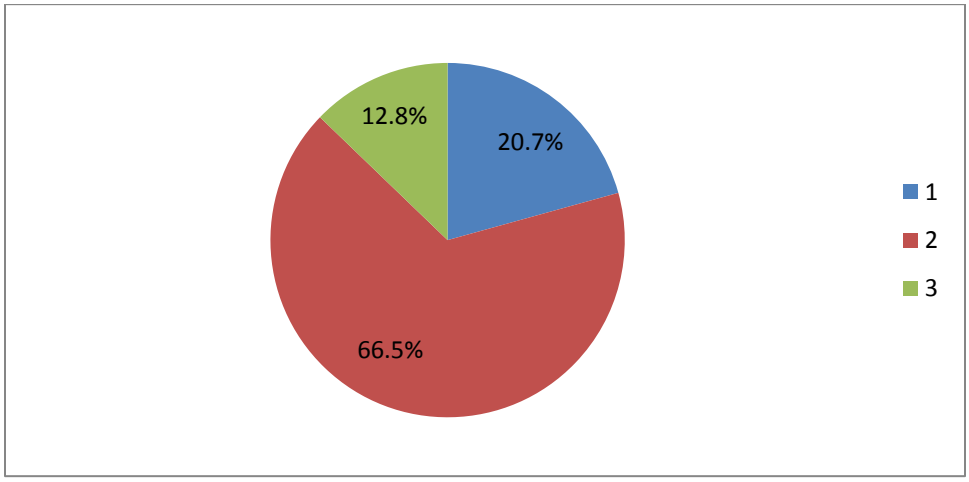


Figure 11: Existence of diagnoses in the local guidelines

Key:

1 – Local guidelines not available

2- Local guidelines available

3-Uncertain

4.6.2 Association between availability of local guidelines and patient diagnoses

Chi square was used to find the association between the specific patient diagnoses and availability of local guidelines. This was done in order to establish the gaps that exist in practice with regards to non-availability of guidelines for certain disease conditions. This is shown in Table 24. All the neonatal infections (100.0%) followed by respiratory infections (95.5%) had the highest proportion of availability of local guidelines and this was significant ($p=0.006$ and $p<0.001$ respectively). There was also significant availability of local guidelines for prophylactic use of antibiotics in obstetrics and gynecology (94.4% $p=0.026$).

There was significantly poor availability of local guidelines for the prophylactic use of antibiotics in the gastrointestinal ($p=0.004$) and skin, soft tissue, bone and joint anatomical sites ($p<0.001$).

Availability of local guidelines also varied among the indications for antibiotic use. All conditions under other hospital acquired infections (HAI-4) were present in the local guidelines. This was followed by medical prophylaxis where 81.5% of the conditions were captured in the local guidelines. Majority (73.2%) of the conditions under community acquired infections were present in the local guidelines and this was significant ($p=0.003$). There was equal distribution of conditions present in local guidelines and those absent under the surgical prophylaxis for a day or more and this was significant ($p=0.032$ and $p<0.001$) respectively.

Table 24: Availability of local guidelines across the various Indication and Diagnosis

Antibiotic Indication	Yes n (%)	No n (%)	Uncertain n (%)	Total (100%)	P value
Diagnosis					
Proph CNS	2 (50.0)	1 (25.0)	1 (25.00)	4	**0.001**
Proph Eye	0 (0.0)	1 (25.0)	3 (75.00)	4	**0.001**
Proph ENT	1 (25.0)	1 (25.00)	2 (50.00)	4	0.064
Proph Resp	0 (0.0)	1 ((100.0))	0 (0.00)	1	0.145
Proph GI	1 (20.0)	4 (80.00)	0 (0.00)	5	**0.004**
Proph SSTBJ	1 (6.2)	15 (93.75)	0 (0.00)	16	**<0.001**
Proph OBGY/GUM	17 (94.4)	0 (0.00)	1 (5.55)	18	**0.026**
CNS	8 (80.0)	2 (20.00)	0 (0.00)	10	0.437
Eye	1 ((100.0)	0 (0.00)	0 (0.00)	1	0.776
Resp	42 (95.4)	1 (2.27)	1 (2.27)	44	**<0.001**
CVS	0 (0.0)	0 (0.00)	1 ((100.0))	1	**0.033**
GI	7 (87.5)	0 (0.00)	1 (12.50)	8	0.318
SSTBJ	7 (30.4)	8 (34.78)	8 (34.78)	23	**0.001**
UTI	3 (50.0)	3 (50.00)	0 (0.00)	6	0.162
OBGY/GUM	7 (63.4)	1 (9.09)	3 (27.27)	11	0.263
NDS	8 (66.7)	2 (16.67)	2 (16.67)	12	0.884
UNK	0 (0.0)	0 (0.00)	2 (100)	2	**0.001**
Neonatal	18 (100.0)	0 (0.00)	0 (0.00)	18	**0.006**
Indications					
CAI	71 (73.2)	11 (11.34)	15 (15.46)	97	**0.003**
HAI-1	1 (50.0)	1 (50.00)	0 (0.00)	2	0.553
HAI-4	3 (100.0)	0 (0.00)	0 (0.00)	3	0.463
MP	22 (81.5)	4 (14.81)	1 (3.7))	27	0.159
OTH	0 (0.0)	1 (100)	0 (0.00)	1	0.145
SP1	1 (20.0)	2 (40.00)	2 (40.00)	5	0.062
SP2	2 (28.6)	2 (28.57)	3 (42.86)	7	**0.032**
SP3	19 (47.5)	19 (47.50)	2 (5.0)	40	**<0.001**
UNK	1 (50.0)	1 (50.00)	0 (0.00)	2	0.553

4.6.3 Overall Guideline compliance

Overall, there was guideline compliance (both local and international guidelines) in 45.8% (n=82) of the study population as shown in Figure 12. Of these, majority 82.9% (n=68) had locally available guidelines. There was a significant association between availability of local guidelines and guideline compliance (P<0.001) as shown in Table 25.

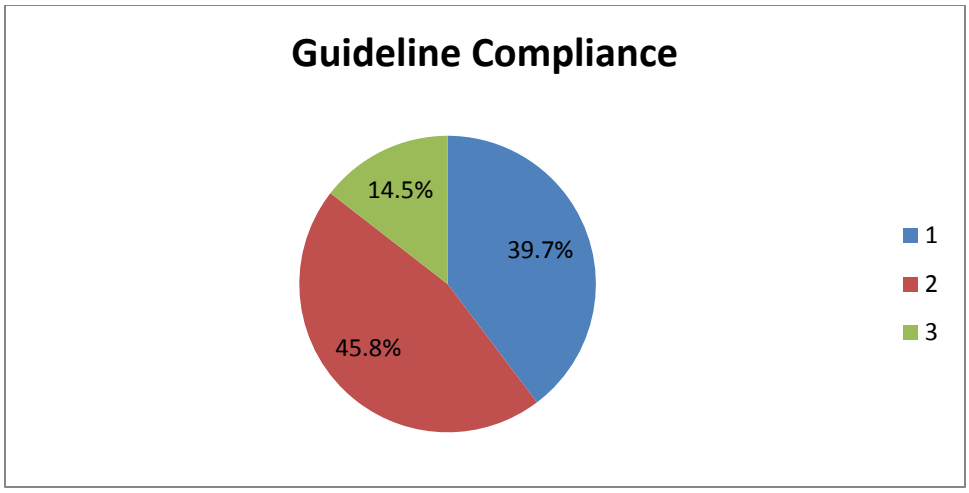


Figure 12: Guideline Compliance

Key:

1 – No compliance

2 – Guideline Compliance

3 – Uncertain

Table 25: Relationship between guideline compliance and availability of local guidelines

	Guideline Compliance			
	Yes n (%)	No n (%)	Uncertain n (%)	P - Value
Local guidelines available	68 (82.9)	50(70.4)	1(3.8)	<0.001
Local guidelines not available	13 (15.8)	21 (29.6)	3 (11.5)	
Uncertain	1 (1.2)	0 (0.0)	22 (84.6)	
Total	82 (100.0)	71 (100.0)	26 (100.0)	

4.6.4 Association between guideline compliance and patient sociodemographic characteristics

Chi square test was used to evaluate the association between guideline compliance and the various predictors such as the age, sex, department and diagnosis of the patient as shown in Table 26 and 27. There was a statistically significant association between age and guideline compliance. Of the total study population, the neonates (9.5%) followed by the children (1-23months) (6.7%) and those between 2-12 years (6.7%) had significantly high prevalence of guideline compliance ($p<0.001$). There was a statistically significantly poor prevalence of guideline compliance among the adolescents age category ($p<0.001$).

There was a higher prevalence of guideline compliance among the males (23.4%) compared to the females (22.3%). However this was not significant (P=0.092). There was a significantly high proportion of guideline compliance in the neonatal medical ward (93.3%) followed by the paediatric medical wards (68.8%) (p<0.001). There was significantly poor guideline compliance in the adult surgical wards (p<0.001) (Table 26).

Table 26: Guideline Compliance across patient sociodemographic characteristics

Patient Characteristics	Guideline compliance		Guideline non compliance		Uncertain		
Age	n (%)		n (%)		n (%)		P Value
1-30days	17	(9.5)	9	(5.0)	1	(0.6)	
1-23months	12	(6.7)	1	(0.6)	0	(0.0)	
2-12years	12	(6.7)	12	(6.7)	6	(3.4)	
13-19years	3	(1.7)	35	(19.6)	6	(3.4)	**<0.001**
20-60years	34	(1.0)	7	(3.9)	7	(3.9)	
>60years	4	(2.2)	7	(3.9)	6	(3.4)	
TOTAL	82	(27.8)	71	(39.7)	26	(14.5)	
Sex							
Male	42	(23.5)	31	(17.3)	7	(3.9)	
Female	40	(22.4)	40	(22.4)	19	(10.6)	0.092
TOTAL	82	(45.8)	71	(39.7)	26	(14.5)	
Departments							
PMW	22	(12.3)	9	(5.0)	1	(0.6)	
NMW	14	(7.8)	1	(0.6)	0	(0.0)	
AMW	23	(12.9)	12	(6.7)	6	(3.4)	**<0.001**
ASW	12	(6.7)	35	(19.6)	6	(3.4)	
OBGYN	3	(1.7)	7	(3.9)	7	(3.9)	
MIXED	8	(4.5)	7	(3.9)	6	(3.4)	

4.6.5 Association between guideline compliance and patient clinical factors

There was a significantly high proportion of guideline compliance among patients in whom antibiotics were used to treat respiratory infections (p<0.001) and neonatal infections (p=0.001). There was significantly poor guideline compliance in the prophylactic use of antibiotics for Obstetric and gynaecological conditions (p<0.001). Among the indications, there was significantly high guideline compliance among antibiotics used to treat community acquired infections (p=0.014) and for medical prophylaxis (p=0.001). There was significantly poor guideline compliance in prolonged surgical prophylaxis (p=0.001) (Table 27).

Table 27: Guideline compliance across patient diagnosis and indications

	Guideline compliance		Guideline non compliance		Uncertain		P Value
Patient Characteristic	n (%)		n (%)		n (%)		
Prophylaxis							
Proph CNS	0	(0.0)	3	(75.0)	1	(25.0)	0.176
Proph Eye	0	(0.0)	0	(0.0)	4	(100.0)	**<0.001**
Proph ENT	0	(0.0)	2	(50.0)	2	(50.0)	0.063
Proph Resp	0	(0.0)	1	(100.0)	0	(0.0)	0.465
Proph GI	1	(20.0)	3	(60.0)	1	(20.0)	0.499
Proph SSTBJ	7	(43.8)	9	(56.3)	0	(0.0)	0.151
Proph OBGY/GUM	0	(0.0)	17	(94.4)	1	(5.6)	**<0.001**
Treatment							
CNS	6	(60.0)	3	(30.0)	1	(10.0)	0.649
Eye	1	(100.0)	0	(0.0)	0	(0.0)	0.552
Resp	33	(75.0)	10	(22.7)	1	(2.3)	**<0.001**
CVS	0	(0.0)	0	(0.0)	1	(100.0)	0.052
GI	5	(62.5)	2	(25.0)	1	(12.5)	0.611
SSTBJ	11	(50.0)	5	(22.7)	6	(27.3)	0.095
UTI	2	(33.3)	4	(66.7)	0	(0.0)	0.324
OBGY/GUM	2	(18.2)	6	(54.5)	3	(27.3)	0.141
NDS	3	(25.0)	6	(50.0)	3	(25.0)	0.282
UNK	0	(0.0)	0	(0.0)	2	(100.0)	**0.003**
Neonatal	16	(88.9)	2	(11.1)	0	(0.0)	**0.001**
Indications							
CAI	51	(52.6)	29	(16.2)	17	(31.2)	**0.014**
HAI-1	2	(100.0)	0	(0.0)	0	(0.0)	0.302
HAI-4	3	(100.0)	0	(0.0)	0	(0.0)	0.165
MP	21	(77.8)	4	(14.8)	2	(7.4)	**0.001**
OTH	0	(0.0)	1	(100.0)	0	(0.0)	0.465
SP1	2	(40.0)	1	(20.0)	2	(20.0)	0.242
SP2	2	(28.6)	2	(28.6)	3	(42.9)	0.094
SP3	4	(10.0)	33	(82.5)	3	(7.5)	**<0.001**
UNK	2	(100.0)	0	(0.0)	0	(0.0)	0.302

4.6.6. Guideline compliance across the various antibiotic classes

There was a significantly high proportion of guideline compliance among the aminoglycosides ($p<0.001$), penicillins ($p=0.034$) and the tuberculosis medicines – rifamycins, isoniazid, pyrazinamide and ethambutol ($p<0.05$). There was significantly

high guideline non-compliance among the cephalosporins (p<0.001) and nitroimidazole derivatives (p=0.024) (Table 28).

Table 28: Guideline compliance across the various antibiotic classes

Antibiotic Class	Compliance n (%)		Noncompliance n (%)		Uncertain n (%)		Total N (100%)	P value
Aminoglycosides	34	(72.3)	12	(25.5)	1	(2.1)	47	**<0.001**
Cephalosporins	25	(31.2)	44	(55.0)	11	(13.7)	80	**<0.001**
Penicillins	47	(55.9)	28	(33.3)	9	(10.7)	84	**0.034**
Macrolides	8	(72.7)	2	(18.2)	1	(9.1)	11	0.178
Quinolones	1	(20.0)	3	(60.0)	1	(20.0)	5	0.499
Nitroimidazole derivatives	12	(27.9)	22	(51.2)	9	(20.9)	43	**0.024**
Carbapenems	1	(50.0)	1	(50.0)	0	(0.0)	2	0.837
Sulfonamides	4	(100.0)	0	(0.0)	0	(0.0)	4	0.089
Glycopeptides	1	(50.0)	0	(0.0)	1	(50.0)	2	0.278
Chloramphenicol	1	(50.0)	0	(0.0)	1	(50.0)	2	0.278
Lincosamide	0	(0.0)	2	(28.6)	5	(71.4)	7	**<0.001**
Tetracyclines	0	(0.0)	2	(100.0)	0	(0.0)	2	0.215
Furadantoins	0	(0.0)	1	(100.0)	0	(0.0)	1	0.465
Rifamycins	10	(90.9)	1	(9.1)	0	(0.0)	11	**0.008**
Isoniazid	10	(90.9)	1	(9.1)	0	(0.0)	11	**0.008**
Pyrazinamide	11	(91.7)	1	(8.3)	0	(0.0)	12	**0.004**
Ethambutol	10	(90.9)	1	(9.1)	0	(0.0)	11	**0.008**
Others	1	(100.0)	0	(0.0)	0	(0.0)	1	0.552

4.6.7 Logistic regression analysis for the predictors of guideline compliance

Binary logistic regression was carried out in order to determine the influence of the predictor variables on guideline compliance, the outcome variable. The uncertain values were dropped in order to make the output binary and to eliminate bias. The odds ratios, adjusted odds ratios from univariate and multivariate analysis respectively were as shown in Table 29 and 30.

Adults (20-59years) had 0.23 times the odds of neonates of being compliant to antibiotic guidelines. This means that neonates were significantly 4 times more likely to be compliant to guidelines compared to adults (p=0.009). The neonates were also 9 times more likely to be compliant to guidelines as compared to the elderly (>65 years) and this too was significant (p=0.006). There was negative association between age and guideline compliance such that an increase in age reduced the level of guideline compliance and this was significant (p<0.001). Age was found to be the most powerful predictor of

guideline compliance as it had the lowest AIC and BIC values. The department type also influenced guideline compliance. The adult surgical ward had 0.23 times the odds of the paediatric medical ward of being compliant to guidelines. This was significant (p<0.001). The obstetrics and gynaecology wards had 0.17 times the odds of paediatric medical ward being adherent to guidelines. This was significant (p=0.006) (Table 29).

Table 29: Univariate binary logistic regression analysis for predictors of Guideline compliance

	Univariable Analysis			
Variable	COR (95% CI)	Pvalue	AIC	BIC
Age Category	0.667 (0.537 – 0.829)	**<0.001**	**200.3**	**206.4**
Neonates (1-30days)	1			
Children (1-23months)	0.59 (0.145 - 2.380)	0.457		
Children (2-12years)	1.18 (0.235 – 5.891)	0.455		
Adolescents (13-19years)	0.22 (0.036 – 1.333)	0.042		
Adults (20-59years)	0.23 (0.078- 0 .694)	**0.009**		
Elderly (60years and above)	0.12 (0.025-0.543)	**0.006**		
Sex				
Male	1			
Female	0.74 (0.390-1.400)	0.350	214.4	220.5
Department			204.5	210.5
PMW	1			
NMW	5.73 (0.732-55.295)	0.093		
AMW	0.78 (0.220-1.531)	0.272		
ASW	0.14 (0.049-0.357)	**<0.0001**		
OBGYN	0.17 (0.023-0.417)	**0.029**		
MIXED	0.71 (0.088-0.888)	0.652		
ICU	0.14 (0.012 – 1.492)	0.103		
Diagnosis				
Proph GI	0.28 (0.031-2.620)	0.275	213.9	220.0
Proph SSTBJ	0.64 (0.324-2.568	0.407	214.6	220.7
CNS	1.79 (0.499-6.741)	0.423	214.6	220.7
Resp	4.11 (1.843 – 9.154)	0.001	201.8	207.9
GI	2.24 (0.471-8.784)	0.344	214.3	220.4
SSTBJ	2.04 (0.496-2.958)	0.206	213.6	219.7
UTI	0.42 (0.104-3.257)	0.324	214.3	220.3
OBGYN/GUM	0.27 (0.051-1.165)	0.117	212.4	218.5
NDS	0.41 (0.097-1.420)	0.222	213.7	219.8
Neonatal	8.36 (2.561-51.770)	**0.006**	203.6	209.7

Key:
AIC – Akaike's Information Criterion
BIC – Bayesian Information Criterion

The Parsimonius model of binary logistic regression was used to identify the four most powerful predictors of guideline compliance. These were found to be a diagnosis of neonatal conditions, respiratory conditions and skin, soft tissue, bone & joint infections. Age was also found to be another predictor as shown in Table 30.

Table 30: Parsimonius model of the most powerful predictors of guideline compliance

Variable	Adjusted Odds Ratio (95% Confidence Interval)	P Value
Neonatal infections	10.603 (1.671 – 67.280)	**0.012**
Age	0.837 (0.624 – 1.122)	0.234
Respiratory Infections	7.141 (2.950 – 17.287)	**<0.001**
Skin, soft tissue, bone & joint infections	5.606 (1.730 – 18.162)	**0.004**

There was a strong positive relationship between neonatal conditions and guideline compliance (Adjusted odds ratio:10.603 (CI:1.671 – 67.280)). This was significant (p=0.012). There was a strong positive relationship between respiratory infections and guideline compliance (Adjusted odds ratio: 7.141 (CI: 2.950 – 17.287)). This too was significant (p<0.001). The same applied to skin, soft tissue, bone & joint infections (Adjusted odds ratio: 5.606 (CI:1.730 – 18.162)). This was significant (p=0.004). There was a negative association between age and guideline compliance (Adjusted odds ratio: 0.837 (CI:0.624 – 1.122)). However this was not significant (p=0.234).

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Prevalence of Antibiotic Prescribing

A total of 473 patients were admitted at the RVPGH on the day of the survey. Of these, 259 were on antibiotics. This translated to a prevalence of 54.7%. The prevalence is comparable to that in Nigerian hospitals where it was found to be 55.9% (27), in a survey of hospitals in Egypt where it was 59% (28) and in China where it was found to be 56% (67). Therefore, one out of every two patients admitted at RVPGH was on an antibiotic. This prevalence was obviously high as compared to that in developed countries such as the UK where it was found to be 29% (68). In Netherlands, the prevalence of antibiotic use was 22.9% (69). The higher prevalence of antibiotic prescribing in hospitals in lower income countries could be due to the higher burden of infectious diseases compared to the developed countries. High income countries have lowered their burden of infections through aggressive enforcement of various public health measures such as improved sanitation, improved nutrition and chlorination of water. This is largely lacking in lower income countries where antibiotics are used to treat diseases emanating from failure to observe public health measures (40).

The ICU and the Isolation departments had the highest prevalence of antibiotic prescribing (100%). This concurs with a PPS in Egypt where the most significant use of antibiotics was among the ICU patients (28). The ICU also had the highest proportion of patients on antibiotics in a UK based PPS (68) and in a survey conducted in China (67). This could be due to the critical nature of the patients' illness and increased risk of acquiring infections. It is therefore common practice among clinicians to cover these patients with antibiotics to prevent them from hospital acquired infections (28) rather than strengthen their infection control practices. The Obstetrics and gynecology department (20.8%) had the least prevalence of antibiotic prescribing. This was contrary to findings in China where the medical wards (39%) had the least prevalence of antibiotic prescribing (67).

5.1.2 Patterns of Antibiotic Prescribing

A larger proportion (75.4%) of antibiotic prescribing was for treatment as compared to prophylactic use (29.0%). The respiratory system was the anatomical site with the largest proportion of antibiotics prescribed for treatment (24.6%) followed by the skin, soft tissue, bone and joint infections (12.3%). This finding concurred with a study in Egypt where the respiratory tract (39.2%), gastrointestinal tract(16%) and the skin, bone and joints (15.7%) accounted for the anatomical sites with the largest proportion of antibiotic use for treatment (28). Similar findings were documented in a UK based point prevalence survey where the respiratory tract (27.2%), skin, soft tissue, bone and joints (19%) and gastrointestinal tract (17.2%) accounted for the anatomical sites with the highest indications for antibiotic use (68). This could probably be due to the fact that these infections are influenced by environmental factors such as ventilation, hygiene, water and sanitation. The gynecological system had the highest proportion of prophylactic antibiotic use (10.1%) and this also concurred with the Egyptian PPS where the gynecologic tract accounted for 23.9% of prophylactic antibiotic use (28). This could be due to the frequent use of prophylactic antibiotics in caeserian section procedures that are conducted in large numbers at the study facility.

The most common indication for antibiotic use was for treatment of community acquired infections (54.2%) followed by surgical prophylaxis (29.1%). Hospital acquired infections accounted for 5 (2.8%) of antibiotic prescribing. This was comparable to that in Egypt where HAIs accounted for 11.3% of antibiotic prescribing (28) but very low as compared to France where 39.2% of the patients were treated for HAIs (46). The low prevalence of HAI in our study could probably be due to poor documentation of hospital acquired infections at RVPGH.

The use of penicillins was prevalent across the various indications. They were prescribed for CAIs (16.9%), medical prophylaxis (30.4%), postoperative surgical site infections (50%) and other hospital acquired infections. Cephalosporins were the most prescribed class for CAI (24.1%) with ceftriaxone being the specific antibiotic (91.3%). Ceftriaxone was also the most prescribed agent for single dose surgical prophylaxis (100%). Ceftriaxone is a broad spectrum agent that is used as a first-line agent in many bacterial

infections. This is likely to have serious implications on the development of antibiotic resistance (27). Guidelines on surgical antibiotic prophylaxis are against the use of broad spectrum first-line agents as this is associated with emergence of resistance strains (39).

Majority (76.9%, n=52) of the patients in RVPGH on surgical prophylaxis were on prolonged duration (>1 day). Only 9.6% (n=5) of the patients on surgical prophylaxis were on a single dose as per current guidelines (39). A similar finding was observed in Egypt where only 5.4% of the patients on surgical prophylaxis were on a single dose while 73.6% were prescribed antibiotics for more than 24 hours (28). The situation was not very different in developed nations such as the UK where 53% of patients on surgical prophylaxis were on prolonged duration. In France, prolonged surgical prophylaxis was 21% of the cases (46). This points out to the irrational use of antibiotics in surgical prophylaxis. Guidelines require that surgical antibiotic prophylaxis should only cover the peri-operative period. Therefore a single dose administered pre-operatively is sufficient unless the procedure is prolonged or there is excessive blood loss (70). Informal discussions with clinicians in a study conducted in Nigeria revealed that misconceptions such as prolonged duration of surgical prophylaxis and use of broad spectrum agents were commonly practiced in order to reduce the incidence of surgical site infections. It also arose that there was little clinician confidence in the hospital infection control practices (70). These are some of the reasons in addition to poor antimicrobial stewardship that contributed to irrational antibiotic prescribing in surgery at RVPGH. This forms one of the areas where quality interventions in improving rational antibiotic prescribing at RVPGH can be instituted as seen in Thika level 5 hospital where a quality improvement study on surgical antibiotic prophylaxis was conducted. Before the study, less than 2% of the surgical antibiotic prophylaxis was administered pre-operatively while 99% was administered postoperatively and for prolonged duration (36). A quality improvement intervention was formulated that entailed an antibiotics policy for surgical prophylaxis. There was a 98% adherence to the policy by week six of policy implementation (36). There was a significant reduction in the risk of superficial surgical site infections in both clean/clean-contaminated (RR 0.66; 95% CI: 0.49-0.91; p=0.01) and in contaminated/dirty surgery (RR 0.17; 95% CI: 0.04-0.74; p=0.005) (36).

The majority (58.7%) of the patients in the study population were on 2 or more antibiotics (combination therapy). A similar finding was observed in Nigeria where 61.9% (n=548) of the patients were on combination therapy (27). The number of antibiotics prescribed varied significantly with the department (p=0.004) such that there was a higher proportion of combination therapy among the medical wards (paediatric and adult) and adult surgical wards as compared to the ICU. This pointed out to irrational prescribing. There was prevalence of clinically unjustified antibiotic combinations. For instance, Amoxiclav and ampiclox were prescribed together in 4 (2.23%) patients. Amoxicillin and Benzylpenicillin were prescribed together in 1 (0.56%) patient, Amoxiclav and Benzylpenicillin in 2 (0.56%) patients while Ampiclox and Benzylpenicillin in 5 (2.79%) patients. The combination of 2 agents with similar spectrum of activity meant that there was selective gram positive over-eradication and possibility of superinfection with gram negative isolates. There was also potential for increased adverse drug effects. Patients treated for HAIs had a higher proportion of combination therapy as compared to those treated for CAIs (80% vs 60.8%). A similar finding was observed in French hospitals where HAIs were more likely to receive 2 or more antibiotics compared to CAIs (47.6% vs 34.4%) The most prescribed classes of antibiotics for HAIs were carbapenems (14.4%) and glycopeptides (14.4%). This differed from the situation in RVPGH where the most prescribed classes for HAIs were penicillins (5, 55.5%), aminoglycosides (2, 22.2%) cephalosporins (11.1%) and nitroimidazole derivatives (1,11.1%) (46).

Beta lactam antibiotics were the most frequently prescribed class of antibiotics at 92.7%. The penicillins were the most commonly used class (46.9%) followed by the cephalosporins (44.7%). This concurred with a previous study on antimicrobial use in Kenya over a 5 year period (1997-2001) where penicillins were the most widely used class of antibiotics at 67.5% (3). It also concurred with the findings on global antibiotic consumption in 2010 where penicillins and cephalosporins accounted for about 60% of the total antibiotic consumption (22). The prescribing of carbapenems was quite low (1.12%) and was limited to the ICU and paediatric wards. Overall, ceftriaxone was the most frequently prescribed antibiotic (39.7%) followed by benzylpenicillin (29.1%) and gentamicin (22.4%). This was similar to findings in Vietnam where cephalosporins

(70.2%), penicillins (21.6%) and aminoglycosides (18.9%) were the most prescribed agents (31). This differed from other countries such as the UK where penicillins with beta lactam inhibitors (24%) were the most prescribed followed by macrolides (15%), fluoroquinolones (11%) and third generation cephalosporins (10%) (19). In the USA, fluoroquinolones (14.1%) were the most prescribed antibiotics followed by glycopeptides (12.3%) and penicillin combinations (11%) (71). The differences in antibiotic prescribing may be attributed to regional variations in bacterial susceptibilities and resistance, prescription habits and levels of guideline implementation (67).

5.1.3 Rational use of antibiotics

It has been documented that up to two thirds of antibiotic use in Africa is irrational (7). This creates possibilities for the development of antibiotic resistance (72). Prevalence studies have been shown to be useful tools in assessing the appropriateness of antibiotic therapy and to identify determinants of inappropriate use (69). Rational antibiotic prescribing in this study was based on several indicators namely correct choice of antibiotic, appropriate dose, frequency, duration and route of administration. An antibiotic was considered to be rationally prescribed if it met all the above criteria and irrationally prescribed if it missed any one or more of the above criteria. There was rational prescribing in a third (33.9%, n=121) of all antibiotic encounters. This was way below the prevalence of appropriate antibiotic prescriptions in the USA that was found to be 69.8% (n=353) (73). This study was, however conducted on the outpatient department and may differ with the inpatient department. A study on inpatients in Netherlands found the prevalence of appropriate antimicrobial prescribing to be at 62.6% (n=587) (69). More specifically, an incorrect choice of antibiotic was made in 14.9% (n=140) of the antibiotics prescribed. This was comparable to RVPGH where in 10.4% (n=37) of the patients, an incorrect choice was made.

The aminoglycoside class of antibiotics had the highest proportion (38.3%) of rational prescribing across all the classes of antibiotics and this was significant (p=0.032). This was followed by the penicillin class of antibiotics (33.3%) and this too was significant (p=0.048). This was close to the findings in Netherlands where cephalosporins, aminoglycosides, metronidazole, meropenem and narrow spectrum penicillins were

significantly associated with more frequent appropriate use while co-amoxiclav and fluoroquinolones were significantly associated with inappropriate use (69).

Age was found to be a predictor of rational prescribing as neonates were two times more likely to have a rational antibiotic prescription as compared to adults (p=0.006). This concurred with a study in Netherlands where a younger age was significantly associated with more appropriate antibiotic use (p=0.007) (69). A diagnosis of a neonatal infection or antibiotic use for prophylaxis of newborn or maternal risk factors, was found to be the most powerful predictor of rational antibiotic prescribing (Adjusted Odds ratio= 5.992, 95% CI=1.985–18.094, p=0.001). This could be due to the delicate nature of newborns that makes the prescribers more cautious and attentive when prescribing antibiotics. This could also be due to the availability of the basic paediatric protocol that outlines how antibiotics should be used in the neonates for various conditions. Other powerful predictors of rational prescribing included a diagnosis of skin, soft tissue, bone and joint infections (Adjusted odds ratio= 6.221, 95% CI=2.053–18.847, p=0.001), a diagnosis of non-defined site such as sepsis (Adjusted odds ratio=5.540, 95% CI=1.486–20.648, p=0.011). This could be due to availability of guidelines for these conditions. The department type was also a powerful predictor of rational prescribing (Adjusted odds ratio=5.540, 95% CI=1.486–20.648, p=0.011). The ICU, mixed departments and adult surgical wards had the highest proportion of irrational prescribing while the neonatal and adult medical wards had the highest proportion of rational prescribing. The increased proportion of irrational prescribing among the surgical wards could be due to the poor compliance to the recommended duration of surgical prophylaxis and also inappropriate selection of broad spectrum agents for prophylaxis. This was supported by the fact that a significant proportion (94.4%) of prophylactic antibiotic use for obstetric and gynecological surgical cases were irrational (p=0.016). In addition, there was irrational prescribing of antibiotics for surgical prophylaxis and this was significant (p<0.001).

There was increased prevalence of irrational antibiotic use with increased number of antibiotics. This was however not significant (p=0.32). This could be due to the fact that increasing the number of antibiotics could be associated with increased likelihood of poor

selection of antibiotics, wrong doses or inappropriate frequencies, routes and duration of use.

5.1.4 Compliance to the Guidelines in Antibiotic Prescribing

Local guidelines were available in 68.5% of the antibiotic prescriptions reviewed. Neonatal and respiratory infections had the highest proportion of availability of local guidelines ($p=0.006$ and $p<0.001$ respectively). There was low availability of local guidelines for surgical prophylactic use of antibiotics in gastrointestinal, respiratory, skin, soft tissue, bone and joints. International guidelines were used where local guidelines were not available. Overall, guideline compliance to both local and international guidelines was 45.8%. This was quite low as compared to Namibia where compliance to the national standard treatment guidelines was 62% (74) and in the UK where guideline compliance was 62.8% of the sampled population (68). This could be due to low availability of these guidelines at the facilities for reference by the healthcare providers. An assessment conducted in 2008 found that key documents that promoted rational prescribing were not available to most health professionals (4). For instance, standard treatment guidelines were only available in 38.9% of government facilities (4).

The neonatal and paediatric medical wards had the highest compliance to guidelines. Univariate binary logistic regression showed a significant negative association between age and guideline compliance (COR=0.667, 95% CI=0.537 – 0.829, $p<0.001$). This was probably due to the readily available local paediatric guidelines that were promoted and widely distributed by the Ministry of Health as compared to the adult clinical guidelines. There was poor guideline compliance among the adult wards such that the adult surgical ward only had 25% compliance.

Multivariate analysis showed that the important predictors of guideline compliance were the use of antibiotics for prophylaxis or treatment of a neonatal infection (Adjusted odds ratio=5.992, 95% CI=1.985 – 18.094, p=0.001), treatment of skin, soft tissue, bone or joint infections (Adjusted odds ratio=6.221, 95% CI=2.053 – 18.847, p=0.001) and treatment of ‘no defined site’ such as sepsis or bacteremia (Adjusted odds ratio=5.540, 95% CI=1.486 – 20.648, p=0.011).

There was a significant relationship between availability of local guidelines and guideline compliance ($p<0.001$). Studies show that prescribers prefer local guidelines to international ones (75,76). This could be attributed to the fact that these take into account the local antimicrobial susceptibility patterns (74). It could also be influenced by their easy availability and a sense of ownership as compared to international guidelines which may be considered to be foreign practice by clinicians. There was significantly high guideline compliance among the TB medicines ($p<0.05$). This could be due to the availability of national TB guidelines that were rolled out by the National Tuberculosis and Lung disease program and adequate supervision of the same that promoted guideline compliance among the clinicians.

There was a significant relationship between guideline compliance and rational prescribing of antibiotics ($p<0.001$). This could be due to the fact that guideline compliance was based on similar indicators as rational prescribing namely appropriate choice of antibiotic, dose, frequency, route and duration of use.

5.1.5 Quality indicators for antibiotic prescribing

These are the performance indicators according to the ESAC whose amelioration is desired in order to improve patient outcomes. They include documentation of the reason for antibiotics in the patient notes, guideline compliance and switching from parenteral to oral route when the patient improves (68). This last one was not captured in the study, however other indicators such as generic prescribing and empiric versus targeted prescribing were incorporated.

The reasons for which antibiotics were prescribed, were recorded in 37.3% of all the antibiotic encounters. This differed from the UK where reason in notes was documented in 75% of the patient medical records (68).

Rational prescribing of medicines dictates the use of generic names, also known as international non-proprietary names (INN), when prescribing. This has been shown to lower health care costs as cheaper generic alternatives can be selected where they are available (77). Generic prescribing also safeguards patients from potential adverse drug events due to being prescribed the same molecule with different unrecognized brand

names. It also helps to minimize commercial influence on medical practice (77). Generic prescribing was documented in 62.5% of the total antibiotics prescribed. This was an improvement compared to the prevalence of generic prescribing in outpatient departments in government facilities that was 31.8% in the year 2008 (4).This could possibly be due to increased awareness and availability of official therapeutic documents such as the Kenya essential medicines list and the clinical guidelines where medicines are always stated by generic name (4).

Rational use of antibiotics encourages the use of diagnostic support when selecting the antibiotics. This can be through culture and sensitivity tests, microscopy among others. This is what is considered to be targeted treatment. Prescribing of antibiotics without diagnostic support but based on experience or local susceptibility patterns is empiric prescribing. Empiric prescribing accounted for 82.6% of the total antibiotic encounters while targeted treatment was recorded in 17.4%. A similar finding was observed in Namibia where only 23% of doctors commenced treatment after obtaining results from laboratory cultures while 91% of the prescribers reported doing laboratory cultures when empiric treatment failed (74). The high rates of empiric prescribing at RVPGH should be guided by local microbiology data so as to facilitate selection of effective antibiotics. Studies show that poor access to local antimicrobial susceptibility data causes prescribers to under-appreciate the prevalent levels of resistance and therefore opt for antibiotics with lower sensitivity (74). The prescribers are also likely to prefer broad spectrum agents over effective narrow spectrum agents (74). This drives irrational use of antibiotics and increased potential for development of resistance.

5.2 Study limitations

There were challenges in getting all the relevant participant medical records for review and therefore a 94% (n=179) response rate was achieved.

There patient diagnosis was not always specified in the medical records and in certain cases it was unknown. This therefore created challenges during the assessment of rationality of prescribing and guideline compliance.

In majority of the participants, the indication of an antibiotic whether it was for a community acquired infection, hospital acquired infection or surgical prophylaxis was

not clearly documented. In such instances, this was arrived at subjectively by the researcher.

Additionally, this was a point prevalence survey therefore what was occurring throughout the year may not be known.

5.3 Conclusion

The prevalence of antibiotic consumption at RVPGH was high as compared to the reference in hospitals in developed countries. The penicillins, cephalosporins and aminoglycosides were the most frequently prescribed classes of antibiotics. Ceftriaxone was the most prescribed antibiotic overall. The ICU, Isolation ward and the new born unit had the highest prevalence of antibiotic prescribing.

Rational prescribing was documented in only a third of all antibiotics prescribed. Of note, there was inappropriate prescribing in surgical prophylaxis with regards to the duration of prophylaxis. The ICU, mixed departments and the adult surgical wards had the highest prevalence of irrational antibiotic prescribing.

There was poor compliance to guidelines. Local guidelines were not available in a significant proportion of conditions. International guidelines were consulted in such scenarios.

5.4 Recommendations

5.4.1. Recommendations on Policy and Practice

There is need to lower the prevalence of antibiotic prescribing at RVPGH particularly in the ICU, isolation ward, neonatal unit and the paediatric medical wards. This can be through establishment of antibiotic protocols that clearly outline situations where an antibiotic is necessary and strengthening of the hospital infection control practices in order to reduce the need for prophylactic antibiotics against nosocomial infections. These activities can be initiated and coordinated by a hospital antimicrobial stewardship committee.

A quality intervention should be carried out in order to improve the prescribing of antibiotics for surgical prophylaxis. This should involve the clinicians, nurses and the patients and measures of accountability instituted in order to promote adherence to the guidelines.

There should be increased accessibility to local guidelines by the prescribers. Guidelines on prophylactic use of antibiotics against obstetric and gynecological, respiratory, skin, soft tissue, bone and joint infections should be made available.

There is a high incidence of empiric antibiotic prescribing at RVPGH. The hospital should promote continuous surveillance and dissemination of findings to the prescribers on antibiotic susceptibility and resistance profiles in order to guide selection of antibiotics.

5.4.2. Recommendations on Future Areas of Research

A multi-centre PPS should be conducted in various counties in order to generate data generalizable to the whole of Kenya

A study on prescriber knowledge, attitude and practices in order to understand the key factors that guide antibiotic prescribing at RVPGH

A study on patients, prescribers and hospital contextual factors that impact on poor prescribing practices as well as non-adherence to protocols

A follow up PPS should be conducted in order to establish the effect of the above recommendations on prevalence of antibiotic prescribing and various quality indicators.

APPENDICES

Appendix 1: Ward Form

Please fill in one form for each ward included in the PPS

Date of survey (dd/mm/year)	_____/_____/_____		
Person completing form (Auditor code)			
Hospital			
Ward Name			
Department Type: Place a tick against the type of department	Paediatric departments: PMW (Paediatric Medical Ward) HO-PMW (Haematology-Oncology PMW) T-PMW (Transplant (BMT/Solid) PMW) PSW (Paediatric Surgical Ward) PICU (Paediatric Intensive Care Unit) Neonatal departments: NMW (Neonatal Medical Ward) NICU (Neonatal Intensive Care Unit)	Adult departments: AMW (Adult Medical Ward) HO-AMW (Haematology-Oncology AMW) T-AMW (Transplant (BMT/solid) AMW) P-AMW (Pneumology AMW) ASW (Adult Surgical Ward) AICU ([Adult] Intensive Care Unit)	
Mixed Department	Yes	No	
Activity: Tick as appropriate. In case of mixed departments, tick all the encountered specialities	Medicine	Surgery	Intensive Care
Total number of eligible patients on the ward present at 8.00 am on day of PPS			
Total number of admitted patients on the ward present at 8:00 am on day of PPS			

Include only inpatients admitted before 08:00 hours on the day of the PPS.

Appendix 2: Global-PPS Patient Form

(Please fill in one form per patient on antimicrobial treatment/prophylaxis)

Ward Name/code	**Activity** [i] (M, S, IC)	**Patient Identifier** [ii]	**Survey Number** [iii]	**Patient Age**[iv]	**Weight** In kg, 2 decimals	**Gender** M or F

Antimicrobial Name[v]		**1.**		**2.**		**3.**		**4.**		**5.**	
Single Unit Dose [vi]	**Unit** (g, mg, or IU) [vii]										
Doses/ day[viii]	**Route** (P, O, R, I) [ix]										
Duration											
Diagnosis [x] (see appendix 3B)											
Comorbidities? (Y,N, Specify)											
Type of indication [xi] (see 3C)											
Reason in Notes (Yes or No) [xii]											
Guideline Compliance (Y, N, NA, NI) [xiii]											
Is a stop/review date											
Treatment (E: Empirical; T: Targeted)											
Treatment based on biomarker data (Yes or No) [xiv]											
If yes, on which biomarker [xv] (fill in: CRP, PCT or other)											
The next section is to be filled in only if the treatment choice is based on microbiology data (Treatment=targeted) AND the organism is one of the											
MRSA (Yes or No) [xvi]											
MRCoNS (Yes or No) [xvii]											
VRE (Yes or No) [xviii]											
ESBL-producing Enterobacteriaceae (Yes or No) [xix]											

[i] M: medicine (including Psychiatric cases, *etc.*), S: surgery (including orthopaedics, obstetrics and gynaecology, *etc.*), IC: intensive care

[ii] - A unique patient identifier that allows linkage to patient records at local level for more detailed audit. This unique identifier will not be included in the online database.

[iii] A unique non-identifiable number given by WebPPS for each patient entered in the database. Leave blank but note down the number after the patient data has been recorded in the online database. The number is displayed once (and only) after the patient data has been recorded in the online database.

[iv] If the patient is 2 years old or older, specify only the number of years, if between 1 and 23 months specify only the number of months, if less than 1 month specify the number of days.

[V] Insert generic name.

[vi] Numeric value for dose per administration in grams, milligrams or IU.

[vii] The unit for the dose (g, mg or IU)

[viii] if necessary provide fractions of doses: (e.g., every 16h = 1.5 doses per day, every 36h = 0.67 doses per day, every 48h = 0.5 doses per day)

[ix] Routes of administration are: Parenteral (P), Oral (O), Rectal (R), Inhalation (I).

[x] See diagnoses groups list (Appendix 3B)

[xi] See Indication codes (Appendix 3C)

[xii] A diagnosis / indication for treatment is recorded in the patient's documentation (treatment chart, notes, etc.) at the start of antibiotic treatment (Yes or No)

[xiii] Antibiotic choice (not route, dose, duration etc) in compliance with local guidelines (Y: Yes; N: No; NA: Not assessable because no local guidelines for the specific indication; NI: no information because indication is unknown)

[xiv] Treatment based on biomarker(Yes/No)

[xv] If treatment based on biomarker, specify which one: CRP (C-reactive protein), PCT (Procalcitonin) or Other (=lab-based culture and sensitivity result from a relevant clinical sample)

[xvi] Methicillin-resistant *Staphylococcus aureus* (MRSA)

[xvii] Methicillin-resistant coagulase negative staphylococci (MRCoNS)

[xviii] Vancomycin-resistant enterococci (VRE)

[xix] Bacteria, producing extended-spectrum beta-lactamases (ESBL)

[xx] Carbapenem-resistant *Enterobacteriaceae* (CRE) – enteric bacteria resistant to imipenem, meropenem or other carbapenems

[xxi] Nonfermenters: *Pseudomonas aeruginosa, Acinetobacter baumannii, Burkholderia spp., Stenotrophomonas maltophilia* [xxii] Carbapenem-resistant Nonfermenters (CR-NF) – nonfermenters resistant to imipenem, meropenem or other carbapenems

[xxiii] Multi-drug resistant (MDR) pathogens, others than the listed above.

Appendix 3A - Diagnostic codes (what the clinician aims at treating)

Appendix 3A - Diagnostic codes (what the clinician aims at treating)

Site	Codes	Examples
CNS	**Proph CNS**	Prophylaxis for CNS (neurosurgery, meningococcal)
	CNS	Infections of the **C**entral **N**ervous **S**ystem
EYE	**Proph EYE**	Prophylaxis for Eye operations
	EYE	Therapy for Eye infections e.g., Endophthalmitis
ENT	**Proph ENT**	Prophylaxis for **E**ar, **N**ose, **T**hroat (**Surgical or Medical**
	ENT	Therapy for **E**ar, **N**ose, **T**hroat infections including mouth, sinuses, larynx
RESP	**Proph RESP**	Pulmonary surgery, prophylaxis for **Resp**iratory pathogens
	LUNG	Lung abscess including aspergilloma
	URTI	**U**pper **R**espiratory **T**ract viral **I**nfections including influenza but not ENT
	Bron	Acute **Bron**chitis or exacerbations of chronic bronchitis
	Pneu	**Pneu**monia or LRTI (lower respiratory tract infections)
	TB	Pulmonary TB (Tuberculosis)
CVS	**Proph CVS**	**C**ardiac or **V**ascular Surgery, endocarditis prophylaxis
	CVS	**C**ardio**V**ascular **S**ystem infections: endocarditis, endovascular prosthesis or device
GI	**Proph GI**	Surgery of the **G**astro-**I**ntestinal tract, liver or biliary tree, GI prophylaxis in neutropaenic patients or hepatic failure
	GI	GI infections (salmonellosis, *Campylobacter*, parasitic, *C.difficile*, etc.)
	IA	**I**ntra•**A**bdominal sepsis including hepatobiliary, intra-abdominal abscess *etc*.
SSTBJ	**Proph BJ**	Prophylaxis for plastic or orthopaedic surgery (**B**one or **J**oint)
	SST	**S**kin and **S**oft Tissue: Cellulitis, wound including surgical site infection, deep soft tissue not involving bone e.g., infected pressure or diabetic ulcer,
	BJ	**B**one/**J**oint Infections: Septic arthritis (including prosthetic joint),
UTI	**Proph UTI**	Prophylaxis for urological surgery **(SP)** or recurrent **U**rinary **T**ract **I**nfection
	Cys	Lower UTI
	Pye	Upper UTI including catheter related urinary tract infection, pyelonephritis
GUOB	**Proph**	Prophylaxis for **OB**stetric or **GY**naecological surgery
	OBGY	**Ob**stetric/**Gy**naecological infections, **S**exual **T**ransmitted **D**iseases (**STD**) in
	GUM	**G**enito-**U**rinary **M**ales + Prostatitis, epididymo•orchitis, STD in men
No defined site (NDS)	**BAC**	Bacteraemia with no clear anatomic site and no shock
	SEPSIS	Sepsis, sepsis syndrome or septic shock with no clear anatomic site
	Malaria	
	PUO	**P**yrexia of **U**nknown **O**rigin - Fever syndrome with no identified source or site of infection
	PUO-HO	Fever syndrome in the non-neutropaenic **H**aematology–**O**ncology patient with no identified source of pathogen
	FN	**F**ever in the **N**eutropaenic patient
	LYMPH	Infection of the **lymph**atics as the primary source of infection e.g.suppurative lymphadenitis
	Other	Antibiotic prescribed with documentation for which there is no above
	MP-GEN	Drug is used as **M**edical **P**rophylaxis in **gen**eral, without targeting a specific site, e.g. antifungal prophylaxis during immunosuppression
	UNK	Completely **Unk**nown Indication

	PROK	Antimicrobial (e.g. erythromycin) prescribed for **Prok**inetic use
Neonatal	**MP-MAT**	Drug is used as **M**edical **P**rophylaxis for **MAT**ERNAL risk factors e.g. maternal prolonged rupture of membranes
	NEO-MP	Drug is used as **M**edical **P**rophylaxis for **NE**WBORN risk factors e.g. VLBW (Very Low Birth Weight) and IUGR (Intrauterine Growth

Appendix 3B - Type of Indication

CAI Community acquired infection	Symptoms started <48 hours from admission to hospital (or present on admission).		
HAI Healthcare-Associated Infection ➢ Symptoms start **≥48 hours after admission** to hospital	**HAI1** Post-operative surgical site infection (within: 30 days of surgery OR; 1 year after implant surgery)		
	HAI2 Intervention related infections including CR-BSI, VAP and C- UTI		
	HAI3 *C. difficile* associated diarrhoea (CDAD) (>48 h post-admission or <30 days after discharge from previous admission episode.		
	HAI4 Other hospital acquired infection (includes HAP, etc.)		
	HAI5 Infection present on admission from another hospital		
	HAI6 Infection present on admission from long-term care facility (LTCF) or Nursing Home*.		
SP Surgical prophylaxis	**SP1** Single dose	**SP2** one day	**SP3** >1 day
For **surgical patients**, administration of prophylactic antimicrobials **should be checked in the previous 24 hours** in order to encode the duration of prophylaxis as either one dose, one day (= multiple doses given within 24 hours) or >1 day.			
MP Medical prophylaxis	For example long term use to prevent UTI's or use of antifungals in patients undergoing chemotherapy or penicillin in asplenic patients *etc*.		
OTH Other	For example erythromycin as a motility agent (motilin agonist).		
UNK	Completely unknown indication		

Select 1 possibility for each reported antimicrobial

CR-BSI= Catheter related-Blood Stream Infection C-UTI= Catheter related-Urinary Tract Infection HAP=Hospital Acquired Pneumonia VAP=Ventilator Associated Pneumonia

* Long-term care facilities represent a heterogeneous group of healthcare facilities, with care ranging from social to medical care. These are places of collective living where care and accommodation is provided as a package by a public-agency, non-profit or private company (e.g. nursing homes, residential homes).

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