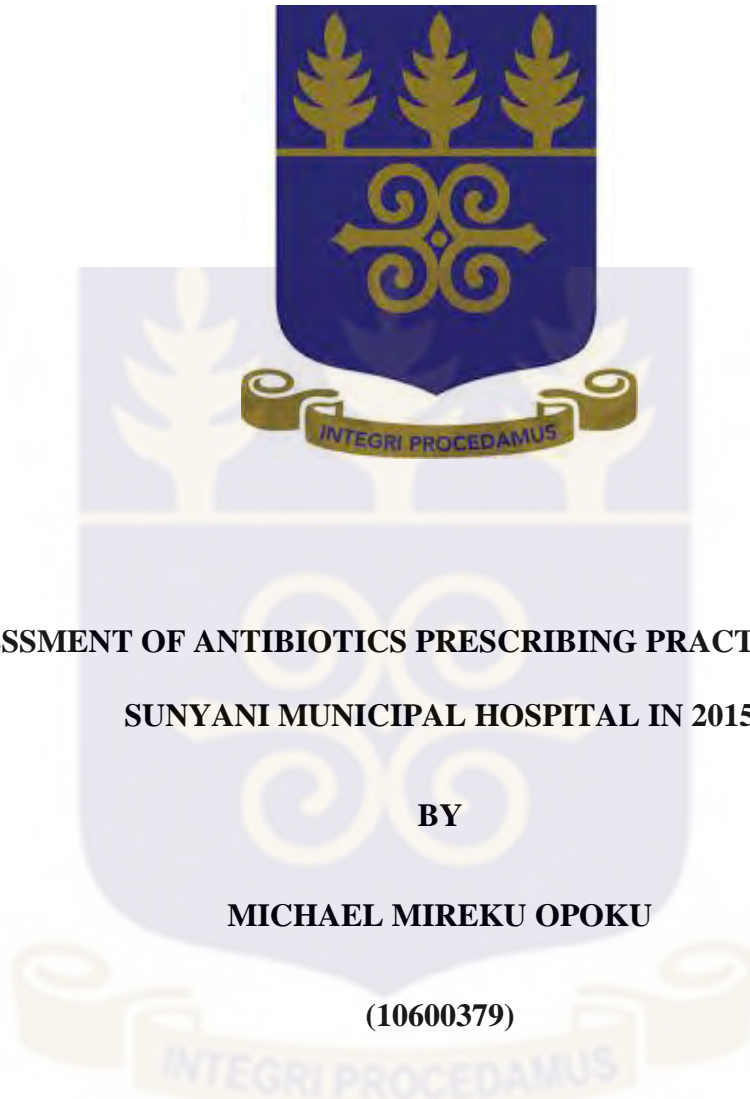


SCHOOL OF PUBLIC HEALTH

COLLEGE OF HEALTH SCIENCE

UNIVERSITY OF GHANA



**ASSESSMENT OF ANTIBIOTICS PRESCRIBING PRACTICES AT THE
SUNYANI MUNICIPAL HOSPITAL IN 2015**

BY

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(10600379)

**THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF GHANA,
LEGON IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE
AWARD OF MASTER OF PUBLIC HEALTH DEGREE**

JULY 2017

DECLARATION

I, Michael Mireku Opoku hereby declare that with the exception of cited literature, this dissertation is the result of my own original research and this has not been presented elsewhere either in part or in whole for the purposes of the award of another degree.

Michael Mireku Opoku

Student

Signature

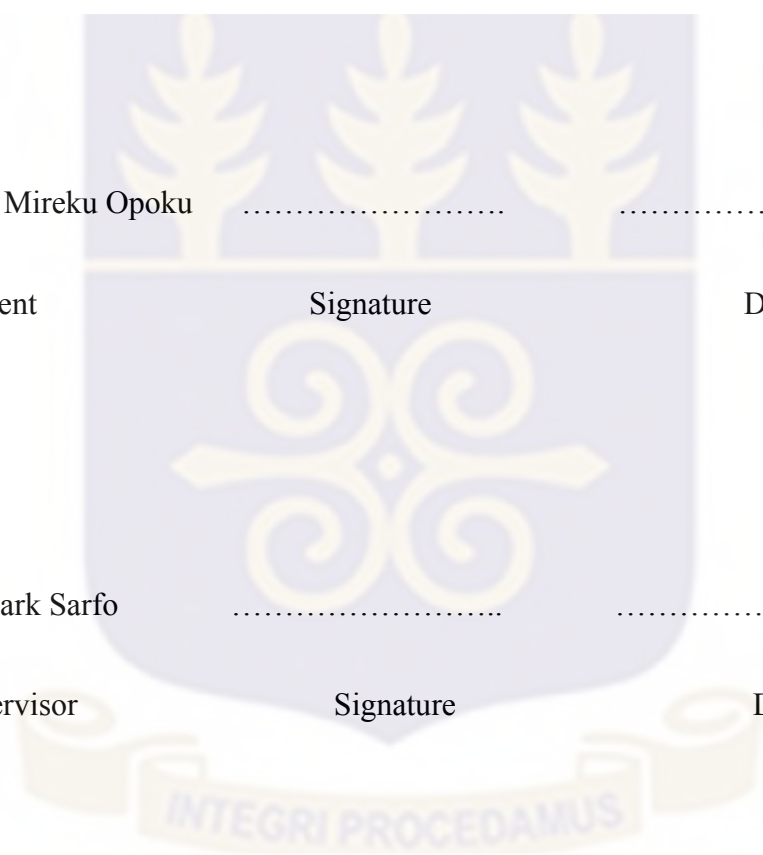
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Dr Bismark Sarfo

Supervisor

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DEDICATION

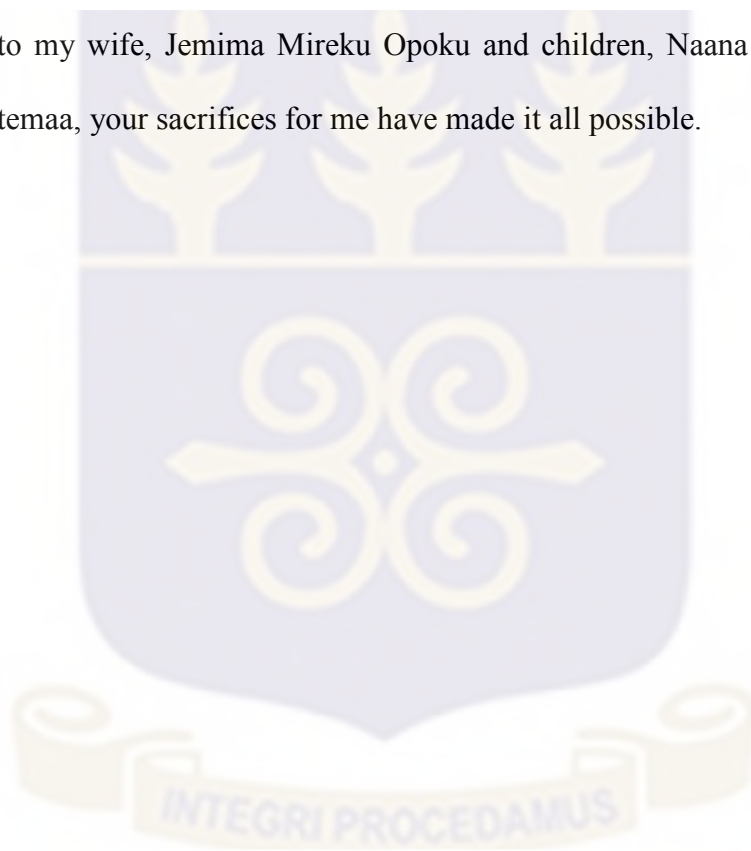
I dedicate this work to Mr and Mrs Kwaku Opoku-Agyekum of McCarthy Hills, Accra and Mr and Mrs Yaw Obeng-Agyemang of Trede, Kumasi for their encouragement, support and guidance over the years. My successes are yours also.



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Finally, to my wife, Jemima Mireku Opoku and children, Naana Serwaa and Nana Yaa Boatemaa, your sacrifices for me have made it all possible.



ABSTRACT

INTRODUCTION: High use of antibiotics is associated with the emergence and spread of antibiotic resistance. Global antibiotics consumption has increased in recent years with an even more significant increase coming from developing countries. The Ministry of Health in Ghana estimates that the median prevalence of antibiotic prescribing in health facilities is 44.3% against a standard of 30%. The quarterly prevalence of antibiotic prescribing at the Sunyani Municipal Hospital outpatient department ranged from 57% to 67.5% in 2015. The objective of this study was to assess antibiotics prescribing practices at Sunyani Municipal Hospital in order to identify clinical and administrative factors of concern that need to be addressed.

METHODS: A one year retrospective records review was designed for the assessment. Medical records of patients who were prescribed antibiotics upon their visit to the outpatient department from January to December, 2015 were reviewed and relevant data collected. The frequencies of prescribing antibiotics were recorded according to age, sex and diagnoses. Pearson's Chi square test was used to assess the association between prescribing of broad-spectrum antibiotics and age, sex and diagnoses. *T*-test analysis was used to assess how the prescribed doses of antibiotics compare with the WHO DDD as well as the difference between recommended and prescribed days of therapy. Multiple logistic regression was used to determine the strength of association between prescribing recommended antibiotics and diagnoses as well as prescribing broad-spectrum antibiotics and diagnoses.

RESULTS: The diagnosis most frequently treated with antibiotics was respiratory tract infection 25.9%. The proportion of broad-spectrum antibiotics prescribed was 48.2%. The average number of antibiotics per prescription was 1.20(SD=0.49). The

proportion of antibiotics prescribed singly was 83% (95% CI: 79.0 – 86.4%). The proportion of antibiotics that made up the drug utilization 90% was 31.6%. Amoxicillin/Clavulanic acid and cefuroxime accounted for approximately 50% by volume of all antibiotics used. The mean defined daily dose prescribed at the outpatient department was greater than 1 [t(449)=12.17, p<0.001]. The mean recommended days of therapy was significantly different from the mean prescribed days of therapy [t(500) = 2.54, p<0.01].

CONCLUSION: The use of combination therapy in the treatment of bacterial infections was low. The quality of prescribing assessed using the drug utilization 90% was high. Amoxicillin/Clavulanic acid and cefuroxime were overused. Broad-spectrum antibiotics were most likely to be prescribed for the treatment of urinary tract infections. Recommended antibiotics were least likely to be prescribed for the treatment of urinary tract infections. Prescribing of broad-spectrum antibiotics was higher than recommended. There was high non-recommended use of cefuroxime and the imidazoles. The prescribed doses are averagely higher than the WHO DDD. The prescribed duration of therapy was sub-optimal.



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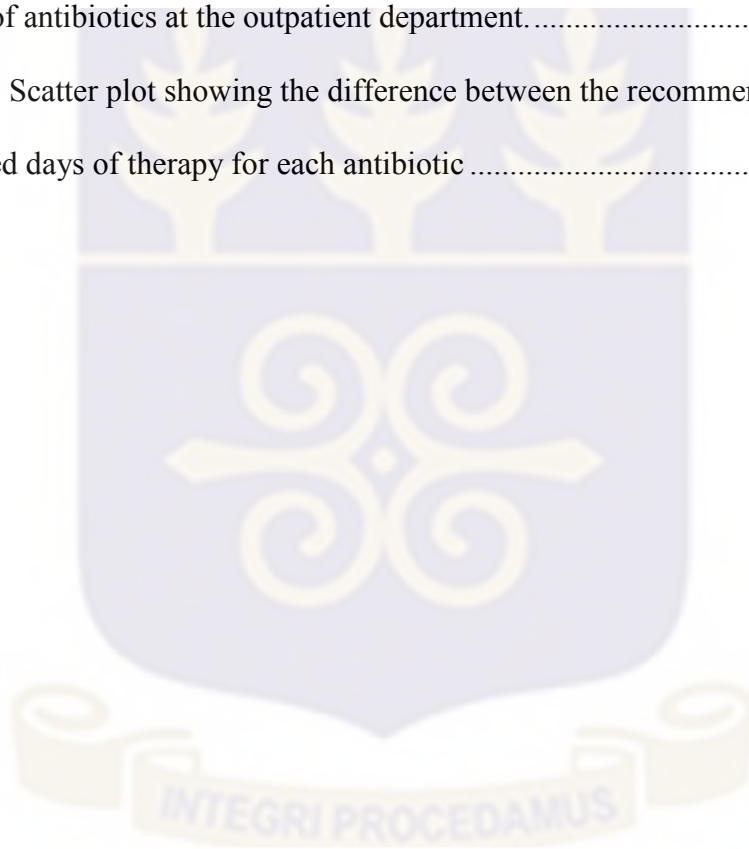
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LIST OF ABBREVIATIONS

ANC – Antenatal clinic

AMC – Amoxicillin/Clavulanic acid

AMX - Amoxicillin

ART – Antiretroviral therapy

ATC – Anatomical therapeutic chemical

CIP - Ciprofloxacin

CMX - Cefuroxime

DDD – Defined daily dose

DU90% – Drug utilization 90%

EML – Essential medicines list

FCC - Flucloxacillin

MD – Multiple Diagnoses

MTZ - Metronidazole

NBI – No bacterial Infection

NCM – Nordic council on medicines

PDD – Prescribed daily dose

PMTCT – Prevention of mother to child transmission

PNC – Postnatal clinic

RTI – Respiratory tract Infection

SI – Skin Infection

STG – Standard treatment guidelines

STI – Sexually transmitted Diseases

Urinary tract Infection

WHO – World health organization



CHAPTER ONE

INTRODUCTION

1.1 Background

The introduction of antibiotics for the management of infections from the 1940s has been one key intervention which has contributed to lowering morbidity and mortality of infectious diseases (Singh, Chowdhary, Bashir, Abbas, Zaffar, Farhat, & Singh., (2012). The World Health Organization (2005) estimates that over 11 million people die annually from infectious diseases and this in an era of relatively efficacious antibiotics. It is well established that the inappropriate use of antibiotics facilitates the emergence and dissemination of antibiotic resistance (WHO, 2015; Springer, 2010; Singh et al., 2012; Naaber, Ko, & Maimets, 2000; Aryanti & Hilbrand, 2002). It is alarming therefore, to note that global consumption of antibiotics has gone up by 36%, with 76% of this proportion contributed by developing countries (Boeckel, Gandra, Ashok, Caudron, Grenfell, Levin, & Laxminarayan, 2014). Further complicating this situation is the fact that 40% to 50% of antibiotics prescribed may not be needed (Esposito, Esposito, & Leone, 2012 ; Samore, 2003).

A point prevalence survey of some hospitals in Europe showed that 30.1% of patients received antibiotics upon hospitalization with 48.4% of them being treated for community-acquired infections, 30% for hospital-acquired infections, 15% for preoperative prophylaxis and 6.7% for medical prophylaxis (Ansari, Erntell, Goossens, & Davey, 2009). In Lesotho, a study of the antibiotics prescribing patterns in six hospitals showed that averagely 37.6% of patients on admission were given antibiotics, an improvement on previous statistics. In this study, however, adherence to the essential medicines list was 79% on average and compliance with standard

treatment guidelines ranged from 28.3% to 59.2% (Ntšekhe & Tjipura, 2011). The need to monitor antibiotic prescribing and use is important for a number of reasons, not least, the need to identify patterns to guide interventions.

The World Health Organization's global surveillance of antimicrobial resistance shows as high proportions as 95% resistance against third generation cephalosporins and 98% against fluoroquinolones in *Escherichia coli*, a common disease causing pathogen (WHO, 2014). According to this report, 8% to 77% resistance has been reported against third generation cephalosporins by *Klebsiella pneumoniae*, in some African countries. A study by Obeng-Nkrumah, Twum-Danso, Krogfelt, & Newman (2013) at the Korle Bu Teaching hospital in Accra Ghana found high resistance against regularly used antibiotics. According to the authors, resistance by *Enterobacteriaceae* was 82% to tetracycline, 73% to cotrimoxazole and 75% to chloramphenicol. At this rapid rate of emergence of antibiotic resistance it is a possibility that the unpleasant experience of high infectious diseases morbidity and mortality which was before the antibiotic era could become a reality again (Singh et al., 2012).

Olofsson & Cars (2007) identify the following factors as important for the enhancement of emergence of antibiotic resistance: accessing antibiotics without a prescription, prescribing an antibiotic when there is no clinical need for it, choosing an antibiotic when it is not clinically indicated for the treatment of a particular infection, and choosing a smaller or higher dose, frequency of administration and duration of therapy than is required to treat a particular infection. Varley, Sule & Absalom (2009) identified four main factors at the heart of antibiotic resistance emergence: using antibiotics more frequently than is required, using broad-spectrum

antibiotics inappropriately, using an inappropriate dose or duration of treatment, and patient defaulting on treatment.

Antibiotic resistance is of concern because of its implications for higher morbidity, longer duration of stay in hospitals and increasing costs of infectious disease management on individuals and the health system at large (Mannan, Shohel, Rajia, Mahmud, Kabir, & Hasan, 2014). In response to antibiotic resistance prescribers have adopted the practice of switching their clients to more efficacious second and third line options (WHO, 2005). This practice leads subsequently to fewer alternatives from which to choose and also increases the likelihood of the spread of antibiotic resistance against otherwise effective antibiotics. Most of these alternatives are broad-spectrum antibiotics and they have been found to enhance the development of healthcare-associated infections and relatively higher rate of emergence of antibiotic resistance (Rao, Cooper, & Wade, 2011). Additionally, they are more costly economically and tend to have higher side effect profiles, further compounding the substantive challenge of treating the infections. The general increase in antibiotic consumption and the sharp rise in the use of broad-spectrum antibiotics are key issues of public health concern globally (WHO, 2015; Boeckel et al., 2014; Springer, 2010; Singh et al., 2012).

One other consequence of high antibiotic use is that it enhances the overgrowth of disease causing microorganisms due to suppressive effects of antibiotics on the protective normal flora (WHO, 2015; Thompson, 2009).

In Ghana, the establishment of the National Health Insurance Scheme has increased utilization of hospitals (Yawson, Nimo, & Biritwum, 2013). Increased utilization of hospitals by extension means increased access to medicines including antibiotics. In

addition to the increased need for antibiotic use is the reportedly high number of infectious diseases recorded by health facilities. Another concern is the fact that most infections are treated empirically rather than based on bacteriological evidence (Thompson, 2009). Surveys have shown that many people believe that antibiotics are effective against infections like common cold, influenza, fever and diarrhoea caused by viruses.

According to the Health facilities survey in Ghana by the Ministry Of Health (2009) the national median percentage of patients prescribed antibiotics in public health facilities is 43.3% (IQR: 39.3% to 50.8%). This study concludes based on this proportion that antibiotic prescribing is unacceptably high and the situation is worsening since the previous study conducted in 2002.

1.2 Problem statement

Rational use of medicines indicator studies at the Sunyani Municipal Hospital in the course of the year 2015 showed that antibiotic prescribing was high (Sunyani Municipal Hospital, 2015). It ranged from 57% in the first quarter to 67.5% in the fourth quarter. Comparing these with the national standard of 30%, antibiotic prescribing was 90% to 125% in excess of acceptable levels. According to the annual report, 38.7% instead of 100% of medicines were prescribed by their generic names further suggesting that prescribing practices were at variance with standards.

Despite these statistics, antibiotics' prescribing remains inadequately characterized. The prescribing practices on the bases of spectrum selection, antibiotic classes, the daily strength prescribed and duration of therapy are unknown. One key strategy identified to be useful in implementing successful antibiotic stewardship programmes is the development and adherence to treatment guidelines (Lee, Cho, Jeong, & Lee,

2013). The standard treatment guideline (STG) serves this purpose in Ghana. The level of adherence to the recommendations of Standard Treatment Guidelines as regards antibiotic choice, combination of antibiotics for treating common diseases and duration of therapy is unknown. Also, the specific choice of antibiotics prescribed based on age, sex and diagnoses are not known. With these gaps in knowledge remaining the optimal use of antibiotics cannot be assured.

The purpose of this study was to provide an assessment of antibiotics prescribing practices at the Sunyani Municipal Hospital in order to identify clinical and administrative factors of concern that need to be addressed.

1.3 Justification of the study

Health facilities in Ghana routinely use the percentage of patient encounters with antibiotics prescribed as the main and often the only indicator for the assessment of rational use of antibiotics. As useful as this indicator may be, it does not provide a comprehensive description of the use, misuse or abuse of antibiotics and as such leaves several questions unanswered. Truter (2008) argues that inappropriate and expensive prescribing is unavoidable since prescribing of antibiotics is not always necessarily based on patient needs or bacteriological evidence. It is necessary therefore to quantitatively describe the dosage, duration of treatment, frequency and variability in the prescribing of antibiotics.

One of the five strategic objectives of the WHO identified for the global action plan on antimicrobial resistance is the optimal use of antimicrobial medicines in humans and animals (WHO, 2015a). To optimize use, there is the need to assess, monitor and evaluate current usage and to appropriately target interventions in situations of misuse and overuse (WHO, 2015b). It is important to monitor antibiotic use in order to

recognize unmet needs so that interventions to improve practice can be appropriately designed (WHO, 2011). The need for developing countries like Ghana to take action against the occurrence and spread of antibiotic resistance cannot be overemphasized as the problem is higher in such countries than in the developed countries where studies abound (Springer, 2010).

A key step to controlling antibiotic use is to routinely provide objective consumption information to prescribers and policy makers to facilitate clear definition of acceptable limits (Hutchinson et al., 2004).

Antibiotic resistance is an inevitable problem. The more microorganisms are exposed to antibiotics, the more resistance emerges. Rationalizing and managing prescribing practices of antibiotics is one way that the process can be slowed (WHO, 2009; Lee et al., 2013).

1.4 Conceptual framework

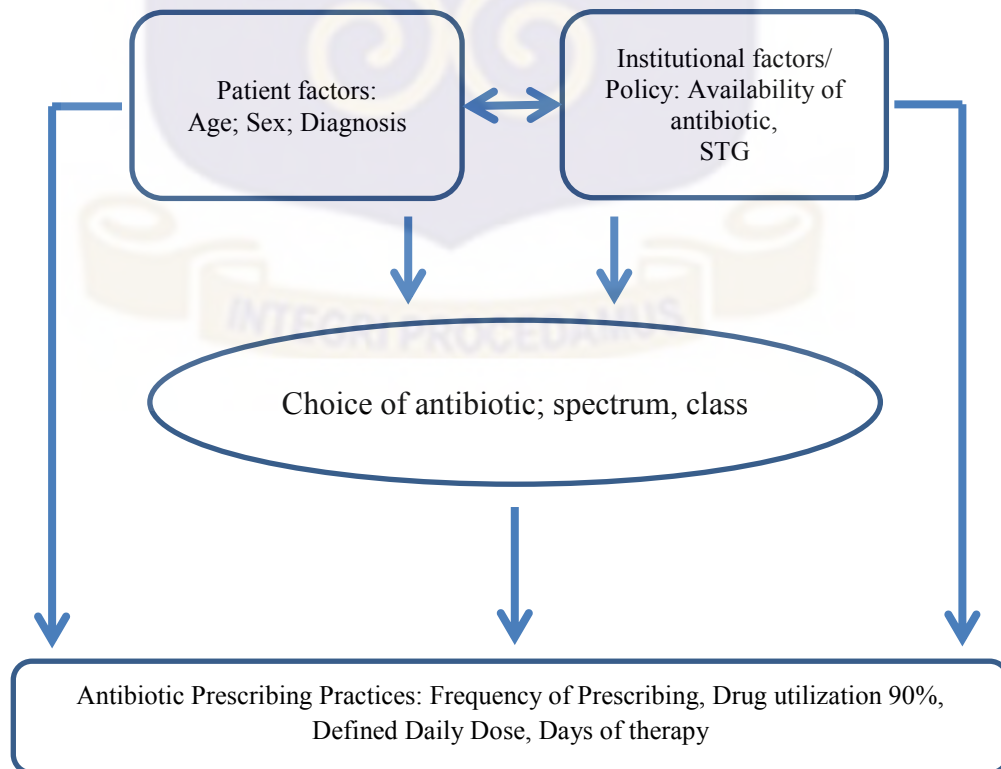


Figure 1: Conceptual framework showing factors that influence antibiotic prescribing

The patient factors that determine the antibiotic that is chosen per case are the age and sex of the patient, and diseases that were diagnosed. Institutional factors that influence the choice of antibiotics are the STG recommendations and the availability of antibiotics at the facility. The STG recommendations influence the diagnoses made. The age and sex of the patient are factors considered in the development of the STG recommendations. Patient factors determine daily doses for patients and the STG recommendations provide guidelines as to the days of antibiotic therapy. Patient and institutional factors are predictors of the choice of antibiotic (that is, the spectrum and class of the antibiotic). Aggregate data on choice of antibiotics determine the drug utilization 90% (DU90%) and the frequency of prescribing.

1.5 Research questions

- What are the antibiotics prescribing practices at the outpatient department of Sunyani Municipal Hospital?
- Which antibiotics are prescribed at the outpatient department?
- What are the defined daily doses (DDD) prescribed at the outpatient department of the Sunyani Municipal Hospital?
- What are the days of therapy (DOT) prescribed at the outpatient department of the Sunyani Municipal Hospital?

1.6 General objective

1. To determine antibiotics prescribing practices at the outpatient department of Sunyani Municipal Hospital.

1.7 Specific objectives

1. To identify the antibiotics prescribed at the outpatient department of the Sunyani Municipal Hospital.
2. To determine the defined daily doses (DDD) prescribed at the outpatient department of the Sunyani Municipal Hospital.
3. To determine the days of therapy (DoT) prescribed at the outpatient department of the Sunyani Municipal Hospital.



CHAPTER TWO

LITERATURE REVIEW

2.1 Antibiotics and inappropriate prescribing

Antibiotics are medicines used to prevent or destroy the growth of microorganisms. They are a category of medicines which was discovered in the mid-twentieth century. The discovery was revolutionary for modern medicine in that it led to a significant reduction in the hospitalization and death due to infectious diseases (Strengthening Pharmaceutical Systems, 2012). This underscores the need to keep the integrity of antibiotics. However, the World Health Organization (2015a) reports that antibiotics have a high potential for inappropriate use particularly in Africa where they are easily accessible without a prescription. More so, prescribing standards where available are largely unenforced. Antibiotics misuse can be traced to inappropriate prescribing by physicians, irrational dispensing and sale by pharmacists and incorrect administration by the general public. The prescribing of antibiotics without evidence of an infection or for managing viral infections or non-infectious diarrhoea constitutes inappropriate prescribing (Strengthening Pharmaceutical Systems, 2012). According to the World Health Organization (2015a) patients in several countries surveyed believe that infections such as common cold, coughs and fever of viral origin could be treated with antibiotics. Prescribing a higher or lower dose or indicating it for use for longer or shorter period or more or less frequently than is recommended all constitute inappropriate prescribing. Using the right medicine via the wrong route of administration also constitutes inappropriate use (Strengthening Pharmaceutical Systems, 2012).

This is a matter of interest because of the several implications of high and inappropriate use of antibiotics on individuals and on populations. It is well established that the high use of antibiotics is associated with the emergence and spread of antibiotic resistance (WHO, 2015a). Meanwhile, antibiotic use for treatment of human illnesses is reported to be increasing significantly. Antibiotics resistance poses a serious threat to the treatment of infectious diseases. In developing economies a number of common illnesses such as dysentery, respiratory tract infections cannot be treated with previously recommended antibiotics because of resistance. In these countries however, access to quality and efficacious antibiotics can save the lives of children with similar diseases.

With the growing emergence of resistance there are fewer alternatives of antibiotics to choose from. Additionally, patients would have to stay in hospitals for longer durations with attendant increase in the cost of treatment for the patient and the entire health system. Also, with high antibiotics use comes high occurrence of adverse drug reactions. Antibiotics prescribing needs to be monitored closely to ensure optimal use in the fight against antibiotic resistance (WHO, 2015b).

In the Ghana Ministry of Health, (2010) produces and reviews the Standard Treatment Guidelines to aid in the optimization of resources to assure cost-effective, accessible and safe treatments for all people in the country. A systematic process is used to review its content periodically and consensus is built into the recommended interventions it proposes. For the National health Insurance scheme, it is meant as a cost containment mechanism aimed at reducing inefficiencies and over prescription of medicines. The recommended interventions are based on scientific evidence that apply generally in the Ghanaian context. It defines inappropriate prescribing as non-compliance to the standards recommended by the guidelines.

2.2 WHO classification of antibiotics

To facilitate the measurement of drug use it is necessary to have a classification system and a unit of measurement. The Nordic Council on Medicines (NCM), established in 1975, collaborated with Norwegian researchers to come up with the Anatomical Therapeutic Chemical (ATC) classification system and the defined daily dose as the international unit of measurement. The ATC system is used by the WHO collaborating centre for drugs statistics methodology as an instrument for presenting drug utilization studies so as to optimize drug use (WHO Collaborating Centre for Drug Statistics Methodology, 2010). In this classification system, the drugs are grouped according to the organ or system they act on and their pharmacological properties. There are five levels of classification. Table 1 shows the criteria by which each level is classified.

Table 1: Level and criteria for classification according to the ATC classification system

Level of classification	Criterion for classification
First	Anatomical site of drug action
Second	Therapeutic subgrouping
Third	Pharmacological subgrouping
Fourth	Chemical subgrouping
Fifth	Chemical substance subgrouping

Every drug is coded based on the numbers or alphabets assigned for it or its subgroup at each level. Antibiotics for systemic use are classified as JO1 according to the ATC classification system.

2.2.1 JO1A Tetracyclines

This class of antibiotics have extended spectrum of action against a broad range of both gram positive and gram negative bacteria. They are clinically used to treat infections of chlamydia, mycoplasmas, rickettsia, cholera and protozoan parasites. They can be used in combination with some anti-malarial agents to treat or prevent malaria. Over the years they have been used extensively and abused. They work by preventing bacterial protein synthesis (Chopra & Roberts, 2001; Hash, Wishnick, & Miller, 1964).

2.2.2 JO1B Amphenicols

This class of antibiotics work by inhibition of the bacterial protein synthesis (WHO Collaborating Centre for Drug Statistics Methodology, 2010).

2.2.3 JO1C Beta-lactam Antibacterials, Penicillins

These antibacterials act by preventing cell walls of bacteria from being synthesized, thereby making them susceptible to external influence. They are sub-categorized into

A. JO1CA Penicillins with extended spectrum

This group of penicillins have a broad spectrum of activity against gram negative bacteria. Examples include Ampicillin and Amoxicillin (Galbraith, Bullock, Manias, Hunt, & Richards, 2007).

B. JO1CE Beta-lactamase sensitive penicillins

This group of penicillins are inactivated by beta-lactamase, an enzyme produced by resistant bacteria. They have a narrow spectrum of activity; effective against most gram positive bacteria, a few gram negative bacteria and spirochaetes. Examples are

benzylpenicillin and phenoxymethylpenicillin (Galbraith, Bullock, Manias, Hunt, & Richards, 2007).

C. JOICF Beta-lactamase resistant penicillins

Antibacterials in this sub-category are not inhibited by beta-lactamase. Examples are Flucloxacillin and Methicillin

D. JOICG Beta-lactamase inhibitors

This group of antibacterials do not have antibacterial activity innately but interrupt the action of beta-lactamase. Examples include clavulanic acid and sulbactam.

E. JOICR Combinations of penicillins, including beta-lactamase inhibitors

This sub-category has penicillins which are combined with other penicillins or beta-lactamase inhibitors. A common combination is Amoxicillin with clavulanic acid.

2.2.4 JO1D other Beta-lactam antibacterials

Other beta-lactam antibacterials other than penicillins are grouped under this class. They are sub-categorized from first generation cephalosporins to fourth generation cephalosporins, monobactams, carbapenems and other cephalosporins. Compared with penicillins they have a wider spectrum of activity against gram negative bacteria, are sensitive to penicillin-degrading enzyme producing bacteria and have longer half-lives. The classification from first to fourth generation is based on range of activity against gram negative bacteria. DDDs are assigned based on use in moderate to severe infection (Galbraith, Bullock, Manias, Hunt, & Richards, 2007).

A. JO1DB First generation cephalosporins

They have a relatively narrow spectrum of action against gram negative bacteria. Their activity is mainly against gram positive cocci. Examples are Cephalexin and Cefaclor.

B. JO1DC Second generation Cephalosporin

This group of Cephalosporins have an increased activity against gram negative bacteria and have varying activity against gram positive cocci. They are more resistant to beta-lactamase producing bacteria than the first generation cephalosporins. An example is Cefuroxime.

C. JO1DD Third generation Cephalosporin

They have significant activity against a broad range of gram negative bacteria. Their activity against gram positive cocci is diminished. They are not susceptible beta-lactamase and have a wide range of activity against Enterobacteriaceae and *Pseudomonas* species. Examples are ceftriaxone, cefotaxime, cefpodoxime and ceftazidime.

D. JO1DE Fourth generation Cephalosporin

These cephalosporins have a broad spectrum of activity against gram negative bacteria. They rapidly penetrate cell walls. They have activity against gram positive bacteria too. Examples are Cefepime and Cefpirome.

2.2.5 JO1E Sulphonamides and Trimethoprim

Sulphonamids and trimethoprim both act by antagonizing the metabolic process of folic acid production at different bacterial sites. Co-trimoxazole is in this class. DDD is assigned based on treatment for acute urinary tract infection.

2.2.6 JO1F Macrolides, Lincosamides and Streptogramins

They are sub-categorized into 3 groups

A. JO1FA Macrolides

They act by selectively interfering with the function of bacterial ribosomes while sparing human ribosomes. Their spectrum of activity is narrow; mainly active against gram-positive and a limited spectrum of gram-negative bacteria. Some types have a slightly enhanced activity against gram-negative bacteria. Erythromycin, Azithromycin and Clarithromycin are classified in this group. DDD was assigned azithromycin based on five day regimen.

B. JO1FF Lincosamides

They are narrow spectrum antibacterials with activity against most gram-positive bacteria and a very limited range of gram-negative bacteria. Clindamycin is a lincosamide antibacterial. DDD for oral and parenteral clindamycin is assigned based on intestinal and systemic infections respectively.

C. JO1FG Streptogramins

They exert their pharmacological activity by interfering with protein synthesis at the ribosome. They have activity against gram-positive and gram-negative bacteria. Dalfopristin is in this class.

2.2.7 JO1G Aminoglycoside Antibacterials

Clinically relevant ones include streptomycin, gentamycin, tobramycin, amikacin and neomycin. They inhibit bacterial protein synthesis. They have a wide spectrum of activity against a broad range of gram-negative bacteria. DDDs are assigned based on use in severe infections.

2.2.8 JO1M Quinolone Antibacterials

They act by inhibiting bacterial DNA replication. They are effective against a narrow range of gram-positive and gram-negative bacteria implicated in gastrointestinal and genitourinary tract infections. They are sub-categorized into two classes.

A. JO1MA Fluoroquinolones

The DDDs assignment is based mainly on respiratory tract infections. They include Ciprofloxacin, norfloxacin, levofloxacin, ofloxacin.

B. JO1MB Other quinolones

The DDDs are assigned based on acute urinary tract infection. Rosoxacin is in this class.

2.2.9 JO1R Combinations of Antibacterials

Two or more antibacterials for systemic use combined in a single formulation are categorized in this class.

2.2.10 JO1X Other Antibacterials

All other antibacterials for systemic use not classified elsewhere are put in this category irrespective of their mode of action. Of particular interest is the nitroimidazole, metronidazole. Only parenteral metronidazole is in this class. Oral metronidazole is categorized under P01AB- Antiprotozoal. Clinically the imidazoles

are used mainly for protozoal infections. They are of interest in bacterial infections because of their specific activity against obligate anaerobic bacteria. Though not very clear it is argued that they act by attacking and inhibiting DNA replication. DDD assignment of parenteral metronidazole is based on anaerobic bacteria infection.

2.3 Measuring Antibiotic use

The defined daily dose (DDD) is defined by the WHO as the assumed average maintenance dose per day for a drug used for its main indication in adults (WHO Collaborating Centre for Drug Statistics Methodology, 2010). In its computation, no regard is given to the duration of therapy. It is re-defined for every drug in the Anatomical Therapeutic Classification (ATC) system at least every three years and it is the unit of measurement in drug use studies recommended by the WHO. The DDD makes it possible for prescribed substances to be presented in a standard way for comparison among hospitals, regions, and countries. The European Centre for Disease Prevention and Control (2012) for example, use the DDD to compare antibiotic consumption among European countries. In the 2012 surveillance report a consumption of antibiotics ranged from 11.3 DDD per 1000 inhabitants per day in the Netherlands to 31.9 DDD per 1000 inhabitants per day in Greece. The average consumption of antibiotics was 21.5 DDD per inhabitants per day. Though highly recommended as a unit of measurement for comparative utilization of drugs, the DDD methodology has limitations. Appropriate doses of a particular drug for different indications may vary. The DDD methodology does not account for such variations in diagnoses and severity and as such may overestimate or underestimate exposure to the drug (Truter & Kotze, 1996; Grimmsmann & Himmel, 2011). Researchers came up with the prescribed daily dose defined as the average dose prescribed per day calculated from a representative number of prescriptions (Truter & Kotze, 1996). The

researchers argue that the PDD provides a more accurate measure of drug exposure than the DDD since it's based on the strength of the drug actually prescribed rather than on a theoretical dose (Truter & Kotze, 1996). Provided the dosing instruction is available, the PDD can be computed from medical records, patient interviews and prescription studies. The PDD is limited as a measure of drug use unless the indication for which the medicine was prescribed is identified (Truter & Kotze, 1996). The PDD is calculated as the total doses given divided by the number of days of treatment (Muller, Monnet, Talon, Hénon, & Bertrand, 2006). Studies have shown that the PDD of antibiotics can vary based on the severity of the infection treated. The DDD of antibiotics are based on moderately severe infections.

The duration of therapy as a means of measuring antibiotic use has also been studied. In a study involving 130 hospitals in the United States of America researchers compared the use of the DDD and the days of therapy (DoT) for measuring antibiotic use (Polk, Fox, Mahoney, Letcavage, & MacDougall, 2007). When calculating DDD the duration of therapy is not factored in. The DoT methodology also disregards the daily doses prescribed. Thus, 1 DoT is defined as the administration of a drug given on a day without regard for the number of doses or strength of dose. Their study found that the DDD per 100- patient-days (792 ± 147) and the DoT per 1000 patient days (776 ± 120) were marginally different. There was high correlation between the two measures for antibiotics for which the dose were administered once or twice daily. They identified the advantages of the DDD methodology for measuring drug use as follows: it allows for benchmarking and comparison of drug use among hospitals at the country-level, regional-level and even global-level, countries without adequate computer systems can evaluate drug use easily, changes in local recommended doses will affect estimate of drug use. On the use of the DOT

methodology, they found that it does not allow for estimate of drug use to change based on changes in recommended DDD as well as prescribed DDD.

2.4 Evaluation of the WHO DDD

Haug & Reikvam, (2013) did a study that compared the WHO DDD and DDD adjusted for doses recommended by local guidelines in Norway (hospital-adjusted DDD). The hospital-adjusted DDD was defined as the mid-value of the doses recommended by treatment guidelines for moderately severe and severe infections. This study was premised on the fact that the WHO DDD does not represent what is recommended by national or local guidelines and for that matter what is really prescribed for patients. The WHO DDDs are set at values that are too low and may underestimate drug use. The study included all health enterprises in Norway and data were collected for 6 years, from 2005 to 2011. They found that generally the hospital-adjusted DDDs in grams were considerably higher than the WHO DDDs. However, when units were converted to bed-days the opposite was true.

The average WHO DDD and hospital-adjusted DDD for all antibiotics used was 67.1/100 bed-days and 49.3/100 bed-days respectively. There was an average difference of 10.4% and 56.8% between WHO DDD and hospital-adjusted DDD for broad-spectrum antibiotics and narrow-spectrum penicillins respectively. Using the WHO DDD to calculate the percentage change in antibiotic use there was a 16.5% increase in use and a 17.15 increase using the hospital-adjusted DDD. It is quite clear that the WHO DDD overestimates the use of antibiotics beyond the recommended doses. Setting the WHO DDD too low would mean an overestimation of antibiotic use. If this is not taken into account, information from DDD calculations could be misinterpreted. This study demonstrates the importance of comparing measures of drug use calculated differently when studying the use of drug. The researchers ranked

the antibiotics based on both metrics. Twenty four antibiotics were within the 90th percentile of overall antibiotics usage. Each hospital had at least 13 antibiotics on their medicines list within this percentile. When the WHO DDD was used to rank, the penicillinase-sensitive penicillins ranked first in all of the health enterprises. When the hospital-adjusted DDD was used this group of penicillins ranked first in 8 health enterprises and other antibiotics such as metronidazole, cefuroxime and cefotaxime ranked first in the other facilities.

For in-patient care higher doses of antibiotics may be required than in out-patient care. For this reason, the PDD is expected to exceed the DDD in the case of the former. Studies show that this may not necessarily be the case (Ansari et al., 2009). In their studies, Ansari et al., (2009) found that the dosage form of the antibiotic was a key determinant of the difference between the WHO DDD and the PDD and that the former was invariably greater than the latter for oral and parenteral medicines. Another interesting finding was that a change in antibiotic policy from parenteral ciprofloxacin to parenteral amoxicillin-clavulanic acid would lead to as much as a 50% reduction in DDD even if the number of patients and duration of therapy remained the same. As such when comparing consumption of antibiotics using DDD, common explanatory factors are the choice of drugs, the number of patients and duration of treatment. This reinforces the position that using the WHO DDD as sole measure of antimicrobial use is problematic.

Muller et al. (2006) found that the average PDD and the DDD varied. They established that though average dosages of fluoroquinolones and cephalosporins were prescribed close to the DDD, penicillins, macrolides and aminoglycosides were not, and that the DDD overstated the number of days of treatment by 40%. The PDD for

the most consumed antibiotic in the hospital, amoxicillin-clavulanic acid was 3 times the DDD and was consistent with the nationally recommended dose.

2.5 Describing and monitoring prescribing of antibiotics

Several studies to describe antibiotics prescribing in health facilities and to compare same among hospitals have been conducted over the years. These studies based on their objectives are guided by the relevant portions of the publications –“How to investigate drug use in health facilities” (World Health Organization, 1993), the –“Guidelines for ATC classification and DDD assignment” (WHO Collaborating Centre for Drug Statistics Methodology, 2010) and –“How to Investigate Antimicrobial Use in Hospitals : Selected Indicators” (Strengthening Pharmaceutical Systems, 2012).

According to Varley, Sule & Absalom (2009) broad-spectrum antibiotics have a wide bacterial coverage and as such is preferred for use in critically ill patients before laboratory tests are performed to identify culpable microorganisms. They further indicate that because of their higher likelihood to select resistant organisms they should be switched to narrow-spectrum antibiotics as soon as the results of the sensitivity test shows which organisms are responsible for the infection. They explain that fluoroquinolones and aminoglycosides are concentration-dependent antibiotics while erythromycin, beta-lactams (penicillins and cephalosporins) and clindamycin are time-dependent antibiotics. Concentration-dependent antibiotics exhibit optimal bacterial action when their concentration is high enough. Thus, their concentration is more correlated with effective treatment than the time duration they are exposed for. Time-dependent antibiotics on the other hand require a certain minimum duration of exposure at a concentration above the minimum inhibitory concentration for them to be optimally efficacious.

Robert et al. (2012) conducted a study designed to evaluate the feasibility of using a point prevalence survey to monitor antibiotic use in eighteen teaching and twenty two non-teaching hospitals in France. In total 3,964 patients were surveyed, out of which 1,619 (40.9%) were given antimicrobials, 32.2% being on treatment and 8.7% on prophylaxis. The proportion of patients admitted on medical wards and surgical wards was 29.5% on 39.5% respectively.

Out of 143 patients on medical prophylaxis, 11 received two antibiotics as did 16 out of 200 patients on surgical prophylaxis. The most frequently prescribed antimicrobials for medical and surgical prophylaxis were trimethoprim/sulfamethoxazole (43.4%), penicillin (16.1%) and first-generation (43%) or second-generation (26%) cephalosporins and penicillins with beta-lactam inhibitors combinations (10%).

Of the 1,279 people on therapy, 75.2% were given beta-lactams. The proportion of patients who were prescribed two or more antibiotics was 40.6%. The proportion of combinations including beta-lactams was 88.4%, while 18.7% included aminoglycosides and 36.5% included fluoroquinolones. The median number of days of treatment was 4 days (interquartile range: 2 to 8 days). The proportion of patients on aminoglycosides put on treatment for 3 days was 21.4%. The duration of surgical prophylaxis and antimicrobial therapy were 21% and 27.2% beyond the recommended duration respectively. The extensive use of combination therapy outside the intensive care unit raises the question of appropriate use. Also, the utilization of third generation cephalosporins and fluoroquinolones were higher than expected. The percentage of patients on surgical prophylaxis given antimicrobials (21%) for 1 day is higher than the standard. The frequency of prescribing of the carbapenems is high (8%). This study showed that it is possible to use such surveys to evaluate and describe antibiotic use in the hospital setting. A weakness of this study,

however, is that the 38 hospitals represent only 1.4% of hospitals in France. Another weakness is that not all patients on admission in the participating hospitals were included. This fact coupled with the fact that inclusion into this study was voluntary and arbitrary makes generalizations from the results problematic.

In a study to assess the strengths and weaknesses of using the drug utilization 90% (DU90%) for assessing the quality of prescribing, Bergman, Popa, Wettermark, & Einarson, (1998) concluded that it is a simple, inexpensive and reliable method for quality assessment. This concept is explained as the proportion of medicines that constitute 90% by volume of DDD of all drugs used in a health system. The researchers explain that the choice of 90% is arbitrarily chosen but it reasonably captures the bulk of drug use. They point out that a small proportion is desirable as it suggests limited and controlled use of medicines. The study was done among 24 primary health care facilities in Stockholm. According to their work, 27% of all medicines used made up the DU90% with variations from one health facility to the other. They found the mean adherence of choice of drugs to guidelines to be 67%. This means that 67% of the DU90% is made of medicines from the local guidelines. While the DU90% represents well limited use of drugs the adherence to guidelines is low and requires improvement.

Dong, Yan, & Wang (2008) conducted a study in forty counties and ten provinces in Western China. Their study included 20,125 prescriptions which were grouped into four categories based on the number of antibiotics prescribed per visit to the health facilities. The prevalence of antibiotics prescribing ranged from 41.12 to 57.47. Out of these 40.64% were prescribed exactly one antibiotic (range: 31.41% - 48.28%). The proportions prescribed exactly two and more than two were 7.08% and 72% respectively. According to the fourth and fifth level of the ATC classification, 20 and

49 classes of antibiotics respectively were in use. The choice of antibiotics among the 10 provinces varied widely. Penicillins, macrolides and cephalosporins were mainly used in each province with significant differences in the proportions of each class used. Except for one province where cephalosporins were prescribed most, the Penicillins were predominantly used in all the other provinces. Macrolides prescribing was more prevalent in eight provinces than cephalosporins. In these two provinces, the reverse was the case. The extent of prescribing of the others such as sulphonamides, quinolones, aminoglycosides and tetracyclines were not clear. The drug utilization 90 (DU90) which is the number of antibiotics which are prescribed 90% of the time consisted of seventeen antibiotics. The remaining 32 antibiotics made up the 10%. Of all prescriptions, 11.66% had amoxicillin and that translated to approximately one-fifth of all antibiotics prescribed. It was the most prescribed antibiotic. Amoxicillin, benzylpenicillin, norfloxacin, cephalexin and cotrimoxazole were most frequently prescribed (Dong et al., 2008).

Though the elderly had a higher likelihood of being prescribed multiple antibiotics than the younger patients, the general proportion of people prescribed more than one antibiotic was low (Dong et al., 2008). Broad-spectrum antibiotics were found to be more prescribed than narrow-spectrum ones. The advantage in this is that even without identifying the exact pathogen there is a high likelihood of being able to treat the infection when broad-spectrum antibiotics are used. On the other hand, however, this practice poses a threat to the normal flora and has potential for accelerating antibiotic resistance. Frequent prescribing of third generation cephalosporins for ambulatory care as was observed in a few of the provinces leads to an increase in acquisition of extended-spectrum beta-lactamase producing pathogens (Gerber et al., 2013). The strength of this study is in the fact that health facilities in a wide

geographical area in rural China were included. Also, data collection was directly from the written prescriptions and as such is very reliable. However, the limitation is that the study does not provide a complete description of antibiotics use in rural China because it was a study based on health facilities which did not include self-prescribed use of antibiotics. It is important also to note that prescribing the medication does not necessarily mean ingestion which actually leads to the ultimate effects on people's health. Another limitation of the study is that data was collected only in one month. Seasonal variations in the need and prescribing of antibiotics have therefore not been accounted for.



CHAPTER THREE

METHODS

3.1 Study area

The study was conducted in the Sunyani municipality in the Brong Ahafo region. It covers a land area of 506.7km and is one of the twenty seven districts in the region. It lies between Latitudes 70 20'N and 70 05'N and Longitudes 20 30'W and 20 10'W sharing borders with the Sunyani West District to the north, Dormaa East District to the west, Asutifi District to the south and Tano North District to the east. Predominantly, inhabitants are of Akan ethnicity with tribal minorities from various Northern tribes, Ewes and Ga-Adangbes. The population is 123,224 representing 5.3% of the region's population. Females form 50.1% of residents. People in the municipality are mainly resident in the urban parts. Until recent increase in commercial activities the local economy was mainly agrarian. Currently, however, 58.3% of the population are employed in the service sector. Sunyani the Municipal capital also doubles as the regional capital. There are six hospitals, three health centres, twelve clinics, three maternity homes and seven Community Health Planning Service (CHPS) compounds providing health services within the municipality (Ghana Statistical Service, 2014).

3.1.1 Sunyani Municipal Hospital

Sunyani municipal Hospital serves as the primary care referral centre within the municipality. It was used as the regional hospital for the Brong Ahafo region until October, 2004 when it attained the current status. It is a sixty-three (63) bed capacity Hospital which offers Out Patient, In Patient, Obstetrics/ Gynaecology, General surgery, Antenatal clinic (ANC)/Postnatal clinic (PNC), prevention of mother to child

transmission (PMTCT), Ultrasound/ X-ray, Pharmaceutical care, Antiretroviral Therapy/Tuberculosis and Mortuary services. The top ten morbidity pattern in 2015 from the highest to the lowest was; malaria, upper respiratory tract infection, acute eye infection, rheumatism and joint pains, urinary tract infection, skin diseases, anaemia, diarrhoea, enteric fever and pneumonia (Sunyani Municipal Hospital, 2015). The average daily out-patient attendance was 188 persons.

3.2 Study design

The medical records of patients 18 years and above who visited the out-patient department of the Sunyani Municipal hospital and were prescribed antibiotics from January to December 2015 were sampled and reviewed.

3.3 Variables

The outcome variable was:

- Prescribing of antibiotics

The independent variables of interest were:

- Demographic characteristics (age and sex)
- Diagnoses
- Antibiotics
- Availability of antibiotics at the hospital

Table 2: Description of dependent variable

Category	Variable	Operational definition	Scale of measurement
Dependent	Prescribing of antibiotics	Defined daily dose = assumed daily maintenance dose expressed per 1000 residents per day	Numeric
		Prescribed DDD = prescribed daily dose divided by the WHO DDD per observation	Numeric
		Days of therapy = number of days antibiotic is used for treatment of an episode of disease	Numeric
		Antibiotic spectrum (Broad-spectrum = Penicillins with enzyme inhibitor, 2 nd , 3 rd and 4 th generation Cephalosporins, fluoroquinolones; Narrow-spectrum = All other antibiotics not categorized as broad-spectrum)	Binary Broad-spectrum or Narrow-spectrum
		STG recommendation = whether prescribed antibiotic is recommended for use in diagnosed disease by the STG	Binary Recommended or Not recommended

Table 3: Description of independent variable

Category	Variable	Operational definition	Scale of measurement
Independent	Age	Age (≥ 18 years) at the time of attending the hospital	Categorical 18-34 35-51 52-68 ≥ 69
	Sex	Gender of patient treated	Binary Male or Female
	Diagnoses	Clinically identified disease of patient to be treated	Categorical (Nominal)
	Appropriateness of antibiotic combination	Antibiotic is combined or not combined with other antibiotics as in STG	Binary Yes or No
	Antibiotic	Antibiotic for systemic use, JO1 and P01AB (according to WHO ATC classification) prescribed for patient by Prescriber	Categorical (nominal)

3.4 Inclusion and exclusion criteria

Folders of patients who were 18 years and above and were prescribed antibiotics for the treatment of a new episode of disease at the out-patient department of the Sunyani Municipal Hospital from January to December, 2015 were included in the study. Patients who were 18 years and above were chosen because the defined daily dose as a measure of drug use is practicable only for such, as the WHO DDD has not been determined for children. For each patient the first visit for which an antibiotic was prescribed was sampled.

Folders of patients prescribed antibiotics on review visits were excluded.

3.5 Sampling

3.5.1 Sample size determination

According to the Sunyani Municipal Hospital (2015) the total number of out-patient and in-patient encounters from January to December 2015 were 61,942. Also, the percentage of patients prescribed antibiotics was 61.13%. Using the Cochran formula for sample size calculation, a confidence level of 95% and confidence interval of 5%:

Population size (N) = 61.13% of 61,942

$$N = 37,865.1446 = 37,866$$

$$n = z^2 pq / d^2$$

$$Z = 1.96; P = 0.61; q = 1 - 0.61 = 0.39; d = 0.05$$

$$n = 365$$

$$\text{Assuming 10\% of folders are duplicates} = 10/100 \times 365 = 36.50 = 37$$

$$\text{Sample size} = 365 + 37 = 402$$

$$\text{Sampling interval} = 37,866/402 = 94.19 = 94$$

3.5.2 Sampling procedure

The OPD register was used to randomly sample 402 folders of patients 18 years or older who visited the out-patient department of the hospital from January to December 2015. All the folders of patients who visited the hospital in the year were sequentially numbered from the first to the last. The first folder was picked by a simple ballot of the first 94 sequential numbers. Every 94th folder number from the first randomly selected folder was chosen until the 402 folders were selected. Folders which met the inclusion criteria were sampled and the process repeated, each time

excluding all the folders previously sampled. This process was repeated until the 402 folders with antibiotics were obtained.

3.6 Training of research assistants

One records officer, one pharmacist and one Pharmacy assistant at the Sunyani Municipal Hospital were engaged to assist in the data collection. They were trained on the significance of the study, ethical considerations, the sampling procedure and data collection and security.

3.7 Data collection

Data were collected from the patient folders, inventory control cards and standard treatment guidelines. A data collection tool (Appendix 1) was used. Relevant data included age, sex, diagnoses, antibiotics prescribed, doses, frequency of administration and days of therapy of prescribed antibiotics, and the dispensed-to-user consumption of antibiotics.

3.8 Data Processing and Statistical analysis

Data were collected on 402 patients at the Sunyani Municipal Hospital. The data collected were coded and put into a table in Microsoft Excel 2010. One patient record was dropped because it had missing values.

For each diagnosis of a bacterial infection made, the Standard Treatment Guidelines (STG) recommended dose, frequency and duration of administration were recorded. These were considered indeterminate for cases where non-specific diagnoses were made. For the purpose of this research non-specific diagnoses were defined as broad category of diseases for which the STG does not provide recommended treatment. These include respiratory tract infections (RTI), chest infections, sexually transmitted infections (STI) and skin infections. It was assumed that antibiotics were prescribed

for the management of bacterial infections or non-bacterial diseases (such as chicken pox and human or animal bite) for which the STG recommends adjunctive treatment using antibiotics.

Diseases were grouped according to anatomical sites of the infections with comparable modes of disease presentation as in Table below:

Table 4: Disease categories and the diagnoses categorized under each

Disease Category	Diagnoses put under disease category
Respiratory tract Infection (RTI)	Pneumonia, Otitis media, Pharyngitis and upper respiratory tract infection (URTI) or Respiratory tract infection
Sexually transmitted Infections (STI)	Sexually Transmitted Infection (STI) , Vulvovaginitis, and Pelvic Inflammatory Disease
Skin Infection	Skin infection, skin rashes, furunculosis or boils, laceration or abrasion, cellulitis, human or animal bite and superinfected chicken pox
Multiple diagnoses	Multiple diagnoses include all cases where more than one bacterial infection was diagnosed
Urinary tract Infection (UTI)	UTI and pyelonephritis
No bacterial infection (NBI)	Cases for which the STG does not recommend treatment with an antibiotic at all
Diarrhoea	Diarrhoea, gastroenteritis or enteritis, cholera
Others	Less frequently diagnosed infections (ie. less than 5% of all diagnosed bacterial infections) that do not fall into any other category

Descriptive statistical analysis was used to obtain summary tables containing age, sex, diagnoses and antibiotics prescribed. The frequency of prescribing of each antibiotic was determined. The Drug utilization 90% (DU90%) was determined by ranking antibiotics in descending order of DDD percentage. The proportion of antibiotics that make up 90% of total DDD percentage was determined. Box plot, scatter plot and bar chart were used to describe antibiotics and prescribing practices. Averages and proportions that describe antibiotic prescribing relative to standard treatment guidelines recommendation were determined.

Chi square test was used to determine the association between broad-spectrum antibiotics prescribing and disease category, age, sex, STG recommendation and appropriateness of antibiotics combination. Simple logistic regression was used to determine the measures of association between prescribing recommended antibiotics and the various disease categories. A *p*-value of < 0.05 was considered statistically significant.

The WHO DDD was taken from the website of the WHO Collaborating Centre for Drug Statistics Methodology (http://www.whooc.no/atc_ddd_index) for each antibiotic on 29th May, 2017 using the searchable version of the complete ATC index. They were used to measure antibiotic prescribing expressed as DDD per1000 inhabitants per day. The population size used was from the 2010 population and housing census (Ghana Statistical Service, 2014).

To assess the difference between the recommended and prescribed days of therapy, the days of therapy for non-specific diagnoses (RTI, SI, diarrhoea) for which the corresponding days of therapy in the STG could not be determined were excluded. For days of therapy for which the STG recommends ranges, the duration prescribed

was recorded as the recommended provided the prescribed duration was within the range. Otherwise, the closest duration to the prescribed was chosen; the lower limit was chosen if the prescribed duration was shorter than the lower limit of the range and the upper limit was chosen if the prescribed duration was longer than the upper limit of the range. Independent-samples *t*-test was used to test the hypothesis that the mean recommended days of therapy was different from the mean prescribed days of therapy. A *p*-value of 0.05 or less was accepted as being statistically significant.

One sample *t*-test was used to assess whether the mean prescribed DDD was greater than 1 to ascertain if doses are higher, lower or equal to the assumed average daily maintenance dose.

Multiple logistic regression was used to determine the magnitude of association (adjusted odds ratio) of the relationship between broad-spectrum antibiotics prescribing, each disease category, sex and to determine the association between recommended antibiotics prescribing, each disease category, sex and age.

3.9 Quality Control

The data collection tool was pretested at Goaso Municipal Hospital. It is a municipal and government Hospital like the Sunyani Municipal hospital, as such it was assumed that the medical records system and prescribing practices will be comparable. The tool was adjusted based on the outcome. The pretesting of the tool served to provide a good guide to the data entry and analysis process. The data collected was cross-checked for completeness and validated.

3.10 Ethical consideration

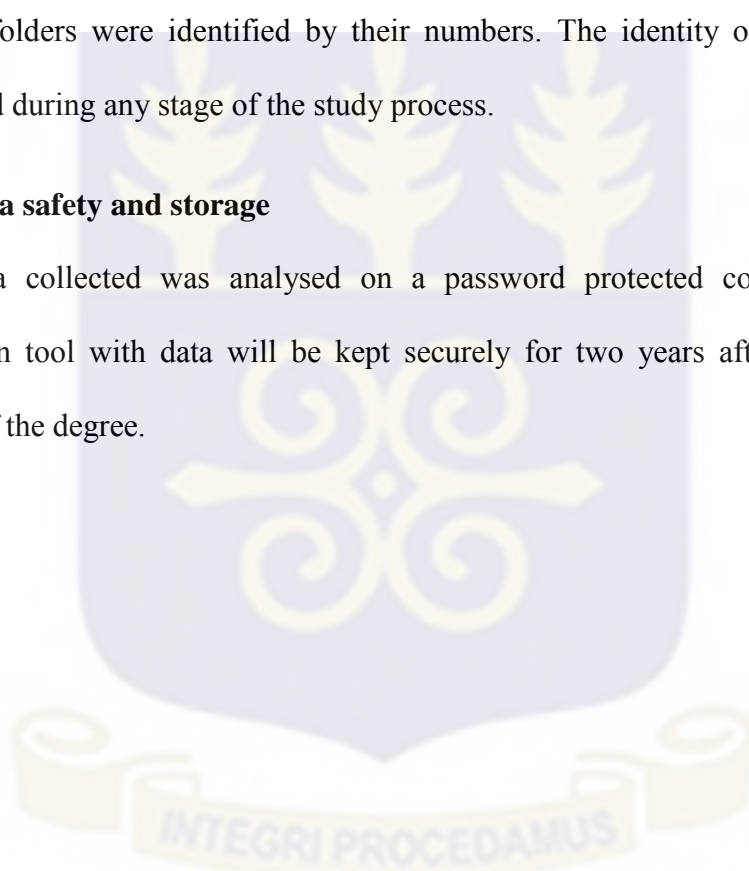
A proposal was submitted to the Ghana Health Service Ethical review committee for review and ethical clearance. The Identification number of the approval for implementation of the study protocol was GHS-ERC: 32/12/2016. A copy is attached as Appendix 2. A copy was sent to the hospital administration before data collection was started.

3.11 Privacy and confidentiality

Patient folders were identified by their numbers. The identity of patients was not disclosed during any stage of the study process.

3.12 Data safety and storage

The data collected was analysed on a password protected computer. The data collection tool with data will be kept securely for two years after the dissertation award of the degree.



CHAPTER FOUR

RESULTS

4.1 Introduction

Diseases were grouped according to anatomical sites of the infections with comparable modes of disease presentation. The following diagnoses were categorized as RTI (25.9%): pneumonia (1.2%), Otitis media (1.9%), pharyngitis (4.4%) and non-specific respiratory tract infection (17%). Diagnoses of non-specific STI (4.4%), vulvovaginitis (1.7%), and Pelvic Inflammatory Disease (5.2%) were categorised as STI (11.2%). Skin infection (20.5%) was categorised to include diagnoses of furunculosis or boils (0.83%), laceration or abrasion (2.7%), cellulitis (1.5%), human or animal bite (2.7%), superinfected chicken pox (0.8%) and skin infection (2.7%). Multiple diagnoses (6.6%) included all cases where more than one bacterial infection was diagnosed. Urinary tract infection (9.7%) includes all diagnoses of UTI and pyelonephritis. The no bacterial infection (7.9%) category refers to cases for which the STG does not recommend treatment with an antibiotic at all. These included malaria and dermatitis. Diagnoses categorized as others (8.3%) were those that did not qualify to fit into any of the above categories and were less frequently diagnosed (ie. less than 5% of all diagnosed bacterial infections). They included sepsis, haemorrhoids, gingivitis and stomatitis.

4.2 Assessment of antibiotic prescribing practices at the outpatient department

From Table 5 below, 42.6% of broad-spectrum antibiotic prescribing was for the treatment of RTIs and 3.6% was for cases in which antibiotic use was not indicated. Narrow-spectrum antibiotics were mostly used for the treatment of skin infections, representing 35.9% of all narrow-spectrum antibiotic use. Proportion of antibiotics

prescribed singly was 83% (95% CI: 79.0 – 86.4%). Those with exactly two and more than two antibiotics prescribed were 13.7% and 3.2% respectively. The proportion of antibiotics inappropriately combined (or not combined) with other antibiotics against the recommendation of the STG was 65.6% with 60.9% of these being broad-spectrum antibiotics. The proportion of antibiotics prescribed to treat diseases for which they were not recommended by the STG was 30.0%; 49% were broad-spectrum antibiotics. The rates of non-adherence to the STG were 16.7% for amoxicillin, 19.1% for flucloxacillin, 13.3% for amoxicillin/clavulanic acid, 54% for cefuroxime, 8.2% for ciprofloxacin, 43.6% for metronidazole and 22.2% for doxycycline.

The average number of antibiotics per prescription was 1.20 (SD=0.49) ranging from 1 to 4. The proportion of broad-spectrum antibiotics prescribed singly was 76.4%. The availability of drugs was 89.4%. The antibiotic classes prescribed were Penicillins (41.4%), Fluoroquinolones (15.9%), Imidazoles (15.1%), Cephalosporins (13.9%), tetracyclines (4.6%), macrolides (3.5%), lincomycin (1.5%) and combinations such as cotrimoxazole (1.2%), Ciprofloxacin-Tinidazole (2.7%) and Ceftriaxone-Sulbactam (0.2%). Antibiotics that made up approximately 90% of total antibiotic prescribing by frequency ranked from Amoxicillin/clavulanic acid (15.5%), Ciprofloxacin (15.1%), flucloxacillin (14.1), cefuroxime (13.0), metronidazole (12.8%), amoxicillin (11.2), doxycycline (4.6%), azithromycin (2.7%) to ciprofloxacin-Tinidazole (2.7%).

Table 5: Bivariate analysis of antibiotic spectrum and factors

Variable	n (%)	Antibiotic Spectrum		Chi Square <i>P-value</i>
		Broad	Narrow	
Diagnoses				<0.001
Respiratory Tract Infection	125(25.9)	83(17.2)	42(8.7)	
Multiple Diagnoses	32(6.6)	21(4.4)	11(2.3)	
STI	54(11.2)	21(4.4)	33(6.8)	
Skin Infection	99(20.5)	9(1.9)	90(18.6)	
Urinary Tract Infection	47(9.7)	42(8.7)	5(1.0)	
Diarrhoea	48(9.9)	27(5.6)	21(4.3)	
Others	40(8.3)	23(4.8)	17(3.5)	
No Bacterial Infection	38(7.9)	7(1.5)	31(6.4)	
Sex				0.022
Male	202(41.8)	85(17.6)	117(24.2)	
Female	281(58.2)	148(30.6)	133(27.6)	
Age				0.376
18 - 34	291(60.2)	142(29.4)	149(30.8)	
35 - 51	110(22.8)	47(9.8)	63(13.0)	
52 - 68	52(10.8)	26(5.4)	26(5.4)	
≥ 69	30(6.2)	18(3.7)	12(2.5)	
Recommendation for use by STG				0.834
Recommended	338(70)	162(33.6)	176(36.4)	
Not Recommended	145(30)	71(14.7)	74(15.3)	
Appropriateness of combination regimen				<0.001
Appropriate	166(34.4)	109(22.6)	57(11.8)	
Not appropriate	317(65.6)	124(25.6)	193(40)	

ABBREVIATION: STI, Sexually transmitted infections; STG, Standard Treatment Guidelines

Table 6 below shows that, the age and sex adjusted odds of prescribing a recommended antibiotic for the treatment of RTI was 7.49 times higher compared to the odds of prescribing a recommended antibiotic for the treatment of diarrhoeal diseases. After adjusting for age and sex the odds of prescribing a recommended antibiotic for the treatment of UTIs was 81% less compared to the odds of prescribing

a recommended antibiotic for the treatment of diarrhoeal diseases. The odds of prescribing recommended antibiotics for the treatment of less frequently diagnosed diseases was 69% less compared to the treatment of diarrhoeal diseases. Prescribing recommended antibiotics for patients with multiple bacterial infections, sexually transmitted infections and skin infections was not significantly associated with prescribing recommended antibiotics at $p < 0.05$ when compared with prescribing antibiotics for treatment of diarrhoeal diseases. The odds of prescribing recommended antibiotics for patients without a bacterial infection was not practicable as no antibiotics are recommended by the STG for treating them. After adjusting for sex and diagnoses the odds of prescribing recommended antibiotics for patients aged 35 to 51 years was 2.26 times greater compared to those aged 18 to 34 years.

Table 6: Logistic regression of factors associated with prescribing of broad-spectrum

	Prescribing recommended antibiotics			
	Unadjusted OR	P-Value	Adjusted OR	P-Value
Diagnoses (Ref: Diarrhoea)				
RTI	6.98 (2.04 - 23.93)	0.002**	7.49 (2.16 - 25.97)	0.002**
MD	0.69 (0.24 - 2.04)	0.504	0.79 (0.26 - 2.38)	0.678
STI	0.39 (0.16 - 0.98)	0.044*	0.47 (0.19 - 1.19)	0.112
SI	0.81 (0.34 - 1.92)	0.629	0.86 (0.35 - 2.10)	0.747
UTI	0.19 (0.07 - 0.47)	< 0.001***	0.19 (0.07 - 0.48)	< 0.001***
Others ^a	0.28 (0.11 - 0.73)	0.009**	0.31 (0.12 - 0.83)	0.019*
NBI	Not applicable		Not applicable	
Sex (Ref: Male)				
Female	0.83 (0.56 - 1.23)	0.35	0.86 (0.52 - 1.43)	0.561
Age (Ref: 18 - 34 years)				
35 - 51	1.93 (1.16 - 3.23)	0.012*	2.26 (1.20 - 4.26)	0.012*
52 - 68	1.62 (0.83 - 3.17)	0.16	1.70 (0.66 - 4.40)	0.271
≥ 69	2.16 (0.85 - 5.45)	0.104	2.22 (0.67 - 7.36)	0.191

ABBREVIATION: RTI, respiratory tract infection; STI, sexually transmitted infection; SI, skin infection; UTI, urinary tract infection; MD, multiple diagnoses; NBI, no bacterial infection diagnosed; OR, odds ratio; CI, confidence interval
a - Diagnosed bacterial infections with frequency of less than 5% that do not fall into any other category (Enteric fever, gingivitis, stomatitis, haemorrhoids, sepsis)

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 7 below shows that after adjusting for age and sex the odds of prescribing broad-spectrum antibiotics for the treatment of skin infections was 92% less compared to the treatment of diarrhoeal diseases. Having adjusted for age and sex, the odds of prescribing broad-spectrum antibiotics for the treatment of UTIs was 6.83 times greater compared to the treatment of diarrhoeal diseases. The odds of prescribing broad-spectrum antibiotics for the treatment of diseases for which antibiotics are not indicated was 83% less compared to prescribing broad-spectrum antibiotics for the treatment of diarrhoeal diseases, after adjusting for age and sex. Prescribing broad-spectrum antibiotics was not significantly associated with treatment of RTIs, multiple bacterial infections, STIs and less frequently diagnosed bacterial infections when compared to treatment of diarrhoeal diseases.

Table 7: Logistic regression of factors associated with prescribing of broad-spectrum

Prescribing broad-spectrum antibiotics				
	Unadjusted OR	P-Value	Adjusted OR	P-Value
Diagnoses (Ref: Diarrhoea)				
RTI	1.54 (0.78 - 3.04)	0.216	1.52 (0.76 - 3.06)	0.23
MD	1.48 (0.59 - 3.75)	0.403	1.55 (0.60 - 3.98)	0.366
STI	0.49 (0.22 - 1.09)	0.081	0.47 (0.21 - 1.06)	0.067
SI	0.08 (0.03 - 0.19)	< 0.001***	0.08 (0.03 - 0.20)	< 0.001***
UTI	6.53 (2.20 - 19.40)	0.001**	6.83 (2.28 - 20.48)	0.001**
Others ^a	1.05 (0.45 - 2.46)	0.906	1.02 (0.43 - 2.40)	0.973
NBI	0.18 (0.06 - 0.48)	0.001**	0.17 (0.06 - 0.47)	0.001**
Sex (Ref: Male)				
Female	1.53 (1.06 - 2.21)	0.022*	1.35 (0.86 - 2.10)	0.189
Age (Ref: 18 - 34 years)				
35 - 51	0.78 (0.50 - 1.22)	0.278	0.68 (0.40 - 1.16)	0.154
52 - 68	1.05 (0.58 - 1.89)	0.873	0.90 (0.45 - 1.82)	0.777
≥ 69	1.57 (0.73 - 3.38)	0.246	1.30 (0.52 - 3.23)	0.576

ABBREVIATION: RTI, respiratory tract infection; STI, sexually transmitted infection; SI, skin infection; UTI, urinary tract infection; MD, multiple diagnoses; NBI, no bacterial infection diagnosed; OR, odds ratio; CI, confidence interval
 a - Diagnosed bacterial infections with frequency of less than 5% that do not fall into any other category (Enteric fever, gingivitis, stomatitis, haemorrhoids, sepsis)

*p<0.05 **p<0.01 ***p<0.001

4.3 Identification of antibiotics prescribed at the outpatient department.

From table 8 below, the disease category most frequently treated with antibiotics was RTIs (25.9%) and the disease category least frequently treated with antibiotics was multiple bacterial infection group (6.6%). Amoxicillin/Clavulanic acid and Cefuroxime were prescribed 12.4% and 4.8% of the time for the treatment of RTIs. Amoxicillin/clavulanic acid was not prescribed on any occasion for the treatment of UTI while the frequency of cefuroxime prescribing for UTI was 3.7%. The frequency of prescribing of ciprofloxacin for the treatment of less frequently diagnosed bacterial infections was 3.1%. 7.9% of antibiotics were prescribed for the treatment of diseases for which antibiotics are not indicated at all, with metronidazole being the most frequently prescribed antibiotic in this category (2.3%). The proportion of people aged 18 to 34 years who were prescribed antibiotics was 60.2%. The proportion from 53 years of age to 67 was 10.8% and that for those aged 68 years or more was 6.2%. The proportion of antibiotics prescribed for females was 58.2%.



Table 8: Distribution of antibiotics prescribing according to patient factors

Variables	Antibiotics n= 483 (%)							Total
	AMC	CIP	FCC	CXM	MTZ	AMX	Others ^b	
Diagnoses								
RTI	60(12.4)	0(0)	1(0.2)	23(4.8)	0(0)	24(5.0)	17(3.5)	125(25.9)
STI	0(0)	7(1.5)	1(0.2)	4(0.8)	12(2.5)	0(0)	30(6.2)	54(11.2)
SI	8(1.7)	0(0)	55(11.4)	0(0)	10(2.1)	21(4.4)	5(1.0)	99(20.5)
Diarrhoea	0(0)	18(3.7)	0(0)	4(0.8)	18(3.7)	0(0)	8(1.7)	48(9.9)
UTI	0(0)	20(4.1)	0(0)	18(3.7)	2(0.4)	0(0)	7(1.5)	47(9.7)
MD	4(0.8)	9(1.9)	0(0)	7(1.5)	3(0.6)	0(0)	9(1.9)	32(6.6)
NBI	1(0.2)	4(0.8)	9(1.9)	2(0.4)	11(2.3)	8(1.7)	3(0.6)	38(7.9)
Others ^a	2(0.4)	15(3.1)	2(0.4)	5(1.0)	6(1.2)	1(0.2)	9(1.9)	40(8.2)
Total	75(15.5)	73(15.1)	68(14.1)	63(13.0)	62(12.8)	54(11.2)	88(18.2)	483(100)
Age								
18 - 34	45(9.3)	40(8.3)	40(8.3)	42(8.7)	35(7.2)	34(7.0)	55(11.4)	291(60.2)
35 - 52	12(2.5)	22(4.6)	20(4.1)	8(1.7)	13(2.7)	12(2.5)	23(4.8)	110(22.8)
53 – 67	9(1.9)	6(1.2)	6(1.2)	10(2.1)	8(1.7)	5(1.0)	8(1.7)	52(10.8)
≥ 68	9(1.9)	5(1.0)	2(0.4)	3(0.6)	6(1.2)	3(0.6)	2(0.4)	30(6.2)
Sex								
Male	25(5.2)	33(6.8)	35(7.7)	19(3.9)	23(4.8)	28(5.8)	39(8.1)	202(41.8)
Female	50(10.4)	40(8.3)	33(6.8)	44(9.1)	39(8.1)	26(5.4)	49(10.1)	281(58.2)

ABBREVIATION: RTI, respiratory tract infection; STI, sexually transmitted infection; SI, skin infection; UTI, urinary tract infection; MD, multiple diagnoses; NBI, no bacterial infection diagnosed; AMC, Amoxicillin/clavulanic acid; CIP, Ciprofloxacin; FCC, Flucloxacillin; CXM, cefuroxime; MTZ, Metronidazole; AMX, Amoxicillin.

a - Diagnosed bacterial infections with frequency of less than 5% that do not fall into any other category (Enteric fever, gingivitis, stomatitis, haemorrhoids, sepsis)

b - Antibiotics with prescribing frequency of less than 5% (Doxycycline, Secnidazole, Benzyl penicillin, Benzathine penicillin, Erythromycin, Azithromycin, Cotrimoxazole, Levofloxacin, Ceftriaxone, Cefixime, Clindamycin, Ciprofloxacin-Tinidazole, Ceftriaxone-Sulbactam)

4.5 Assessment of defined daily doses

Table 9 below shows that averagely, Amoxicillin/clavulanic acid consumption during the year was equivalent to 0.13% of inhabitants consuming 1 DDD per day. Averagely, 0.1% of inhabitants consumed 1 DDD of cefuroxime and amoxicillin each per day during the year. In total, antibiotic consumption was equivalent to an average of 5 per 1000 inhabitants consuming 1 DDD per day during the year.

Table 9: Defined daily doses of antibiotics

Antibiotic	DDD per year	DDD Percentage	Cummulative DDD percentage	DDD per 1000 inhabitants per day
Amoxicillin/Clavulanic acid	59,592.5	26.7	26.7	1.3
Cefuroxime	44,000	19.7	46.4	1.0
Amoxicillin	43,650	19.5	65.9	1.0
Metronidazole	21,100	9.4	75.4	0.5
Ciprofloxacin	19,700	8.8	84.2	0.4
Doxycycline	11,250	5.0	89.2	0.3
Flucloxacillin	10,675	4.8	94.0	0.2
Clindamycin	3,075	1.4	95.4	0.1
Erythromycin	2,750	1.2	96.6	0.1
Ceftriaxone	2,631.5	1.2	97.8	0.1
Clarithromycin	2,600	1.2	99.0	0.1
Azithromycin	2,310	1.0	100.0	0.1
Total	223,334	100		5.0

ABBREVIATION: DDD, defined daily dose

Cumulative DDD%

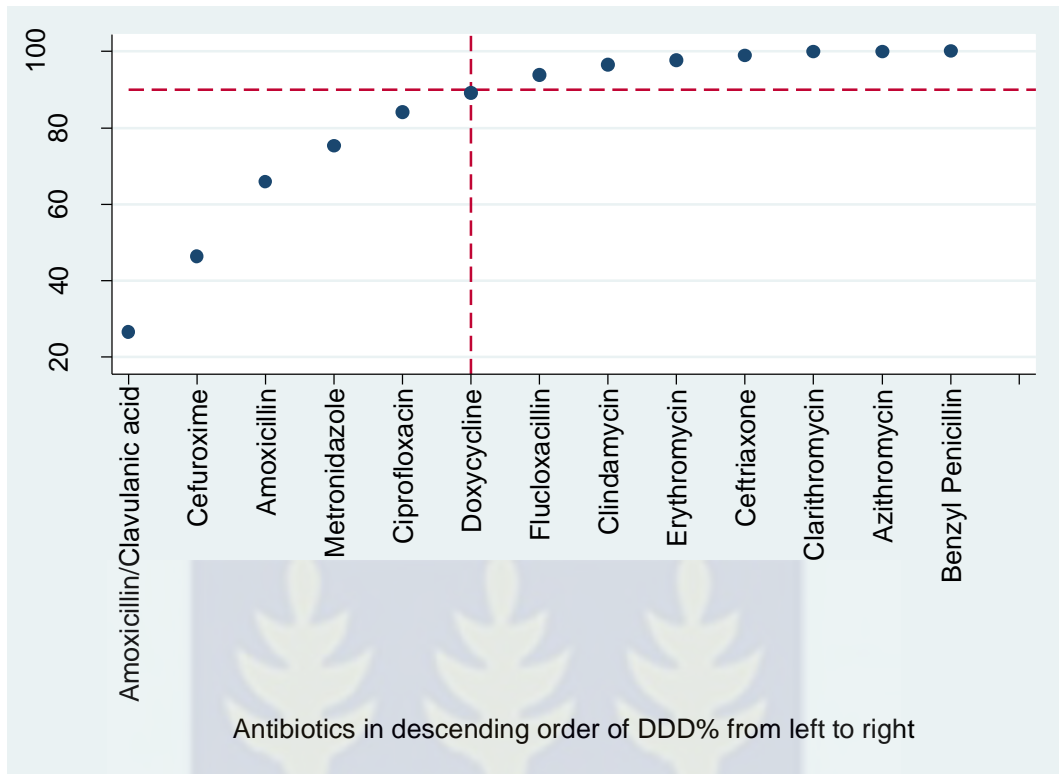


Figure 2: Cumulative defined daily dose percentage of antibiotics at the Sunyani Municipal Hospital.

The proportion of antibiotics that made up the drug utilization 90% (DU90%) was 31.6% (6 out of 19 antibiotics) and they were, Amoxicillin/clavulanic acid (26.7%), cefuroxime (19.7%), amoxicillin (19.5%), metronidazole (9.4%), ciprofloxacin (8.8%) and doxycycline (5.0%). The level of adherence to the essential medicines list was 100%; all of them are listed in the essential medicines list.

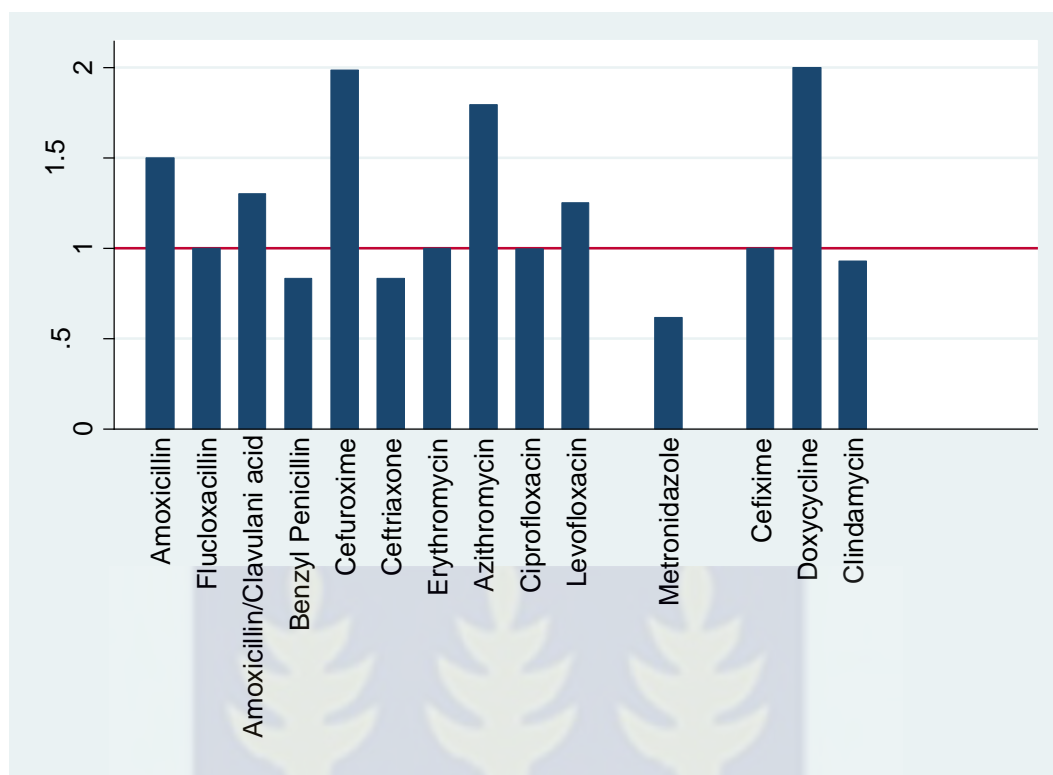


Figure 3: Mean prescribed defined daily dose for each antibiotic

Figure 3 shows that cefuroxime and doxycycline were prescribed in doses averaging twice as high as the assumed average maintenance. The prescribed daily doses of Amoxicillin/clavulanic acid, levofloxacin and doxycycline were higher than their corresponding defined daily doses. Metronidazole, benzyl penicillin, ceftriaxone and clindamycin were averagely prescribed in smaller doses than their respective assumed average maintenance doses. Flucloxacillin, erythromycin, ciprofloxacin and cefixime were prescribed average daily doses equal with their respective defined daily doses.

One sample *t*-test was used to test the hypothesis that the mean prescribed DDD is greater than 1, where 1 is the reference value (ie. the expected prescribed DDD for all antibiotics whose mean prescribed DDD equals the WHO DDD). The mean prescribed DDD was 1.27 (95% CI: 1.22 – 1.31). The mean prescribed DDD is greater than 1; $t(449) = 12.17, p < 0.001$.

4.6 Assessment of days of therapy

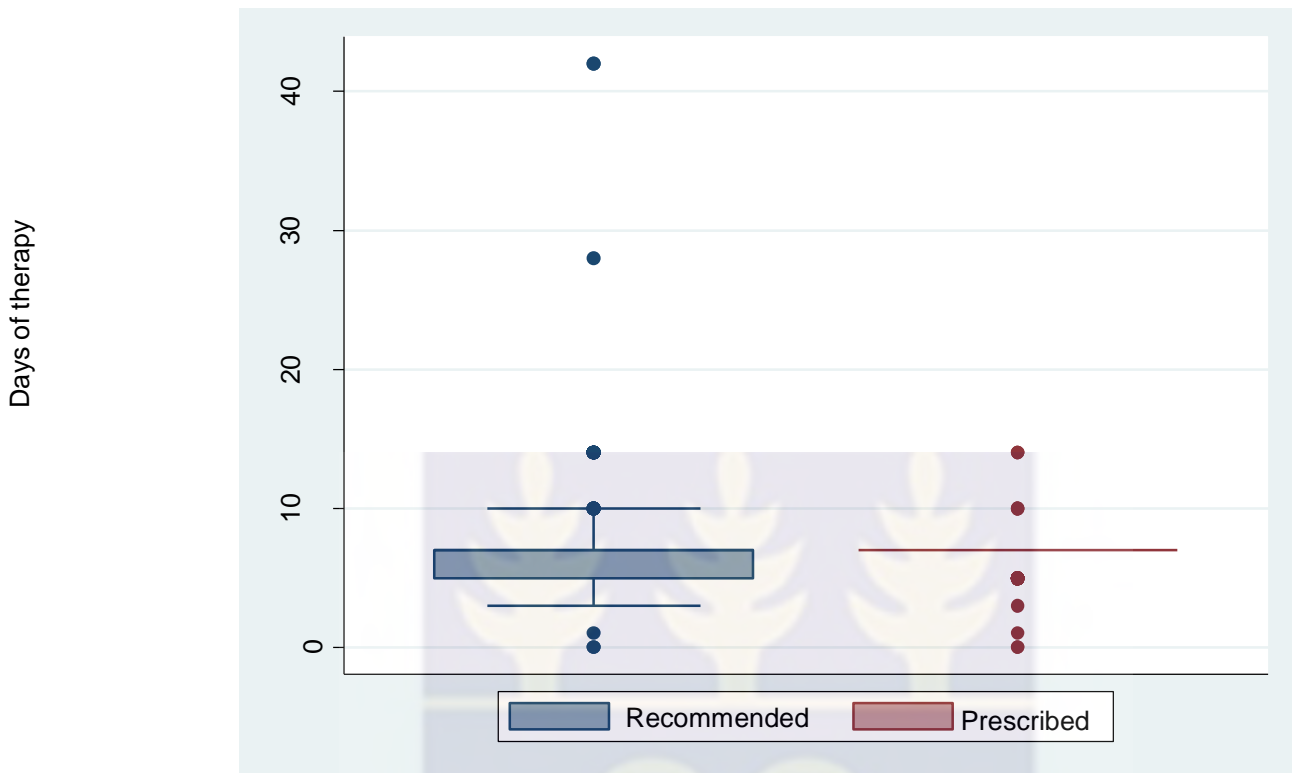
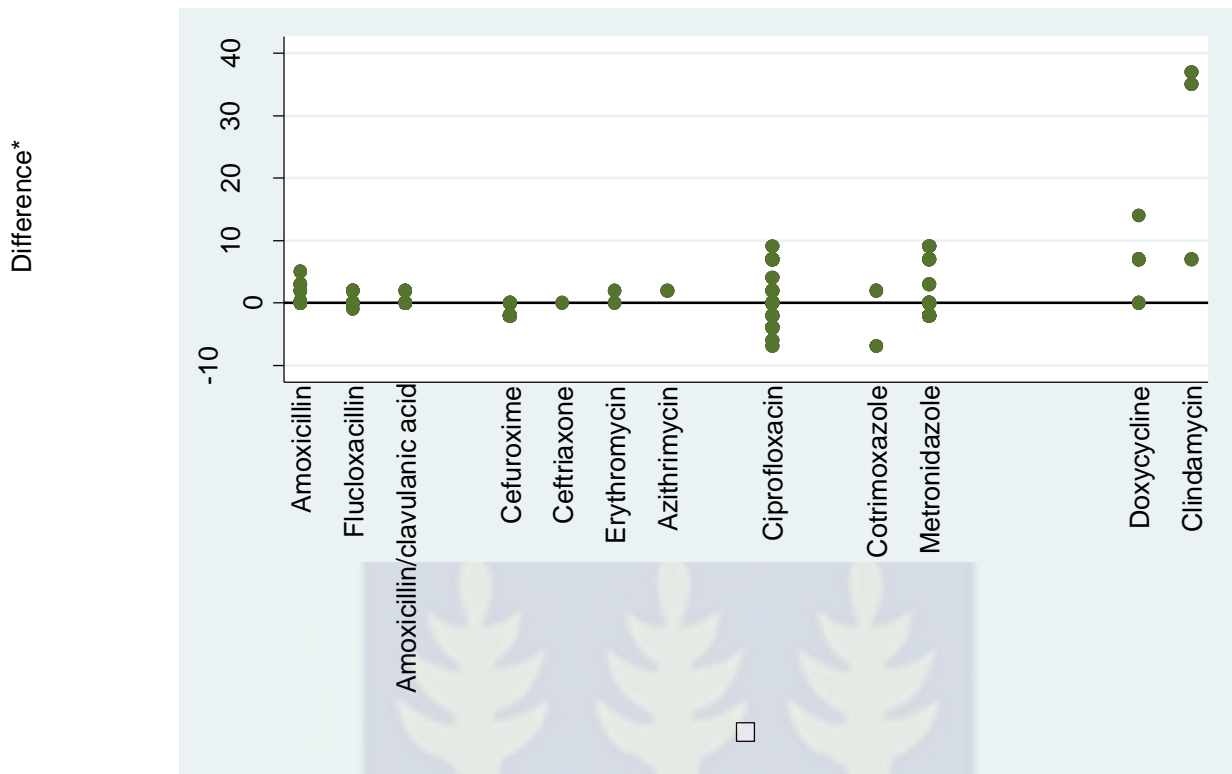


Figure 4: Box plot showing distribution of recommended and prescribed days of therapy of antibiotics at the outpatient department.

The median recommended days of therapy was 7. The upper quartiles and lower quartiles were 10 and 3 days respectively. The distribution of prescribed days of therapy shows that 7 was the upper, middle and lower quartile.



Difference* = Recommended Days of therapy – Prescribed Days of therapy

Figure 5: Scatter plot showing the difference between the recommended and prescribed days of therapy for each antibiotic

Figure 5 above shows that clindamycin has the widest difference between the recommended and prescribed days of therapy. Recommended and prescribed days of therapy for ceftriaxone did not vary on any occasion. Ciprofloxacin has the most varying differences between the recommended and prescribed days of therapy than any other antibiotic.

Independent-samples *t*-test was used to compare the days of therapy as recommended by the STG and as prescribed at the outpatient department. There was a statistically significant difference between the mean recommended days of therapy (7.51 ± 4.44) and the mean prescribed days of therapy (6.78 ± 1.21); $t(500) = 2.542, p < 0.01$.

CHAPTER FIVE

DISCUSSION

In this study, the proportion of females prescribed antibiotics was 58.2% and that of males was 41.8%. These were identical with the outpatient department attendance rates of females and males recorded for the year 2015 (Sunyani Municipal Hospital, 2015).

5.1 Determination of prescribing practices and antibiotics prescribed

The average number of antibiotics prescribed per prescription was 1.20. This value was low and did not fall within the standard range of 1.6 and 1.8 (Isah, Ross-Degnan, Quick & Laing, 2004). In a similar study at the Hawassa University teaching and referral centre in Southern Ethiopia, the average number of antibiotics prescribed per prescription was 1.90 (Desalegn, 2013). Explanations for why facilities have lower than standard average number of antibiotics per prescription include constraints in medicine availability and appropriate therapeutic training. While the latter could be subscribed to in this case, the former is questionable in that the availability of the antibiotics used at the hospital was high (89.4%). Another reason for which the average was low at the outpatient department could be that the frequency of broad-spectrum antibiotics prescribing (48.2%) was almost equal to that of narrow-spectrum antibiotic use (51.8%). The use of broad-spectrum antibiotics makes the combining of antibiotics in most cases redundant and thus reduces the number of antibiotics per prescription. This explanation is corroborated by the fact that 76.4% of broad-spectrum antibiotics were prescribed singly.

Prescriptions with a single antibiotic were 83% of all prescriptions. Those with exactly two and more than two antibiotics prescribed were 13.7% and 3.2% respectively. This trend was different from a point prevalence survey of French hospitals conducted in 2009 where 60% of antibiotics were prescribed singly (Robert et al., 2012). It was higher still compared to a study in Tanzania where the proportion that received a single antibiotic was 71.5% (Gwimile, Shekalaghe, Kapanda, & Kisanga, 2012). The combination of antibiotics in the treatment of diseases is generally justified in severe cases such as in intensive care units. Particularly, beta-lactam antibiotics have shown no benefit when combined with other antibiotics according to meta-analysis by Paul, Lador, & Leibovici (2014). However, the proportion of antibiotics that were prescribed singly or in combination with other antibiotics as recommended by the guidelines was 34.4%. This was rather low and it suggests that prescribers may not be paying due attention to the combination regimen within the framework that informed the recommendations.

The DU90% is suggestive of acceptable quality of prescribing as the proportion of antibiotics accounting for it was quite low (31.6%). This is quite similar to research done by Bergman, Popa, Wettermark, & Einarson, (1998) in Stockholm where the DU90% was made of 27% of antibiotics in use among 24 primary health care facilities. When it is this low it indicates quality prescribing because it suggests that only few antibiotics are used mostly at the outpatient department; restricting exposure to antibiotics has value for controlling antibiotic resistance. However, it must be noted that amoxicillin/clavulanic acid and cefuroxime, both broad-spectrum antibiotics together contribute 46.31%. This observation cannot be overlooked. It is suggestive of overuse of these broad-spectrum antibiotics. The distribution of the prescribed DDD showed that the average daily dose of cefuroxime prescribed was 2 times the WHO

defined daily dose. This practice must be checked. The routinely recommended daily dose of oral cefuroxime, when indicated, is consistent with the WHO DDD. While the mean dose of Amoxicillin/Clavulanic acid prescribed was higher than the DDD, the prescribed doses seem consistent with recommendations by the STG. Another observation of interest was the absolute adherence to the essential medicines list. This means that all antibiotics constituting 90% by volume of antibiotics used at the hospital were listed in the essential medicines list.

The results show that there was high use of broad-spectrum antibiotics (66.4%) in the treatment of respiratory tract infections. This observation, though higher, is comparable to an investigation done in the United States of America where 54% of patients diagnosed with acute respiratory tract infection were prescribed broad-spectrum antibiotics (Steinman, Landefeld, & Gonzales, 2003). In the current study, this was the case, in part, because cefuroxime was prescribed to treat a number of respiratory tract infections. The STG recommends its use only as an alternative in the treatment of otitis media and in combination with other antibiotics for the treatment of retropharyngeal abscess. While Otitis media was infrequently diagnosed and retropharyngeal abscess not diagnosed in any of the sampled folders, it was found that 18.4% of antibiotics prescribed for the treatment of RTIs was cefuroxime. Another reason why broad-spectrum antibiotic use was high in the treatment of RTI was that Amoxicillin/clavulanic acid, recommended to be used for the treatment of specific RTIs as an alternative was routinely prescribed as a first-line agent.

There is empirical evidence that most respiratory tract infections may not require treatment with antibiotics (Snow, Mottur-Pilson, & Gonzales, 2001). This evidence also indicates that those who require treatment with antibiotics respond well to narrow-spectrum ones. Thus, the frequency of narrow-spectrum antibiotics

prescribing was expected to be higher than that of broad-spectrum antibiotics prescribing for RTIs. It is important to note, however, that the high use of broad-spectrum antibiotics prescribing observed may be due to increasing antibiotic resistance to narrow-spectrum alternatives. Work by Obeng-Nkrumah et al. (2013) at the Korle Bu Teaching Hospital in Accra found that about 50% of all isolates of respiratory tract infections had bacteria which had developed resistance to narrow-spectrum antibiotics. Subsequently, broad-spectrum antibiotics intended to be used as second line agents end up being routinely prescribed as first-line agents. Exposing patients to broad-spectrum antibiotics in this manner selects resistant microorganisms.

The rate of non-adherence to the STG recommendations ranging from 53.97% for cefuroxime to 8.22% for ciprofloxacin is of concern. There was a 7.49 greater odds of prescribing recommended antibiotics for the treatment of RTIs compared to treatment of diarrhoeal diseases. The odds of prescribing recommended antibiotics for the treatment of UTIs and less frequently diagnosed diseases was 81% and 69% less, respectively, compared to treatment of diarrhoeal disease. These suggest that recommended antibiotics are more likely to be prescribed for the treatment of RTIs than for the treatment of any other disease category. It is more likely to prescribe broad spectrum antibiotics for the treatment of UTIs than any other disease category. Only the treatment of UTI is significantly associated with the prescribing of both recommended antibiotics and broad spectrum antibiotics. For the treatment of UTIs there are lower odds of prescribing recommended antibiotics than diarrhoeal diseases but higher odds of prescribing broad spectrum antibiotics. The use of cefuroxime in the treatment of Urinary tract infection in adults is not recommended by the treatment guidelines. Ciprofloxacin was prescribed in 42.55% of UTI cases. It is worth mentioning that the recommended antibiotic, ciprofloxacin, was used only 4.44% in

excess of cefuroxime which is not recommended at all for use in adult treatment of urinary tract infection. The recommended alternative, amoxicillin/clavulanic acid, was not used at all for UTI treatment. These explain the observed relationship between UTI treatment and prescribing of recommended antibiotics and broad-spectrum antibiotics. It must be noted that cefuroxime has spectrum coverage of some bacteria that cause UTIs and as such is recommended for use in children in Ghana and in adults elsewhere. This notwithstanding, there is the need to restrict its use. Restricting its use and for that matter its exposure and thereby decreasing selective pressure cannot be overemphasised.

5.2 Assessment of defined daily doses

The mean Prescribed DDD shows that the prescribed daily dose was averagely 27% higher than the assumed average maintenance dose. While this magnitude of variation is peculiar to the hospital, it is consistent with other works that suggest that the DDD as a measure of drug use underestimates drug utilization (Grimmsmann & Himmel, 2011; Berrington, 2009). In a similar study at a university hospital in France the prescribed DDD varied from as low as 0.53 to as high as 3 (Muller et al., 2006). It must be said that the dose of antibiotics are prescribed based on a number of factors including anatomical site of infection, severity of infection, susceptibility of pathogen, toxicity profile of the drug, health status of patient (health of kidney and liver) among others. For this reason the DDD provides but a standard method of measuring antibiotic use and cannot be expected to reflect the standard in practice. The difference between the prescribed daily dose and the defined daily dose is possibly due to the toxicity profile, recommendations by treatment guidelines and what the routine practice has been overtime.

The DDD expressed per 1000 inhabitants per day is known to approximate the prevalence or incidence of disease at a hospital (WHO Collaborating Centre for Drug Statistics Methodology, 2010). In this case it provides an estimate of bacterial disease incidence at the hospital. That means the average incidence of bacterial infections at the hospital was 5/1,000 inhabitants per day. This compares quite differently with the study by Mölsted et al. (2008) which found the national DDD per 1000 inhabitants per day in Sweden to be 14.6. The difference can be explained by the fact that the scope of the current study did not include antibiotics used by all the community pharmacies, and health facilities in the municipality. The current study does not estimate antibiotic use within the municipality, it does for only the hospital.

5.3 Assessment of days of therapy

The distribution of the days of therapy in figure 4.1 suggests that most antibiotics were routinely prescribed for 7 days. This is at variance with the distribution of the recommended days of therapy, suggesting non-compliance to recommended standards. This suggests that prescribers do not give much attention to the appropriateness of the duration of therapy. This may be the reason for which differences were observed between the recommended and prescribed days of therapy. The recommended and prescribed duration of therapy were matched for each observation on the diagnoses made. Therefore, it was expected that if at all any difference were observed due to severity of infections it would not be significant. The test to assess the difference, however, suggests that the two were significantly different. Specifically, the mean prescribed days of therapy (6.78 ± 1.21) was shorter than the mean recommended days of therapy (7.51 ± 4.44). The implication of this is that treatment was not optimal as far as duration of therapy was concerned. Reducing

duration of antibiotic therapy is suggested as an effective means of reducing antibiotic use in general. However, reducing the duration of therapy haphazardly is unsafe as it is ineffective (Rice, 2008). It is reasonable to assume that these were considered in recommending duration of therapy in the treatment guidelines. As such, variations from the recommended duration, if any, were expected to be minimal and insignificant for that matter. A study by Tunger, Karakaya, Cetin, Dinc, & Borand (2009) similarly found short duration of therapy as an important inappropriate prescribing practice. The routine prescribing of 7 days of treatment may favour the selection of resistant strains of antibiotics. Prescribers may be ignoring the need to pay particular attention to the precise duration of treatment for the therapeutic indications. The result is the sub-optimal use of antibiotics, which is especially important for those said to exhibit time-dependent antibacterial action like the beta-lactams, erythromycin and clindamycin. The distribution of the difference between the recommended and prescribed days of therapy showed that the differences varied widely for most antibiotics, particularly clindamycin.

5.4 Strengths and limitations

One of the strengths of this study is that various measures of drug utilization were used to characterize prescribing of antibiotics. This is recommended for institutional drug utilization studies. Another strength is that this study is one of few studies in a Ghanaian health facility aimed at assessing prescribing antibiotics. There were some limitations to this study. Firstly, children were excluded from the study and as such findings cannot be generalized to include prescribing of antibiotics for people less than 18 years of age. Secondly, the study design was retrospective. Prescribing practices may have changed between 2015 and 2017 when this study was conducted.

Thirdly, specific prescribers were not identified and associated with specific prescribing practices. It therefore remains unclear if practices as found apply equally to all prescribers. Fourthly, prescribed medication may not necessarily be ingested by patients. Patients may ingest medicines at dosages and for durations different from those prescribed. The identified effects of misuse apply on condition that antibiotics are consumed as prescribed. Another limitation is the potential for information and misclassification bias because the study was based on one Municipal hospital. Finally, the appropriateness or otherwise of diagnoses were not assessed in this study.



CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The use of combination therapy in the treatment of bacterial infections was low. This implies a high rate of mono-therapy in bacterial infections treatment, underpinned by high utilization of broad-spectrum antibiotics. Broad-spectrum antibiotics were most likely to be prescribed for the treatment of urinary tract infections and least likely for the treatment of skin infections. Recommended antibiotics were most likely to be prescribed for the treatment of respiratory tract infections and least likely for the treatment of urinary tract infections. Prescribing quality as determined by the drug utilization 90% was high but also points to the high use of broad-spectrum antibiotics. Specifically, Amoxicillin/clavulanic acid was frequently used as a first line agent for the treatment of respiratory tract infections. There was high non-recommended use of cefuroxime and the imidazoles. The prescribed duration of therapy was averagely shorter than the recommended duration of therapy. Thus, the prescribed duration of therapy was sub-optimal. The doses of antibiotics prescribed were averagely 27% higher than the assumed average daily maintenance doses. Therefore, using the defined daily dose as a measure of antibiotic utilization underestimates the prescribed doses.

6.2 Recommendations

The following are recommended to help improve antibiotic prescribing

1. Hospital Management

- The Drugs and Therapeutics committee as part of antibiotic stewardship efforts should assess antibiotics utilization at least once a year
- Prescribers and dispensers should be trained on the standard treatment guidelines. Specifically, they should be trained on the framework within which the interventions were chosen and the concepts that underlie them. This would help improve adherence to recommendations. They should also be trained on the use of combination regimen where possible to reduce the use of broad-spectrum antibiotics. The training should also address the appropriate duration of therapy of each antibiotic for the treatment of specific bacterial infections for which they are recommended.

2. Ministry of Health/Ghana Health Service

- A comprehensive surveillance system of antibiotics utilization linked to National health Insurance Scheme reimbursement should be set up
- Further studies characterizing antibiotic resistance with linkages to antibiotic consumption are needed.
- A national survey of antibiotic prescribing to provide country-level data for benchmarking practices in hospitals has become necessary.

References

- Ansari, F., Erntell, M., Goossens, H., & Davey, P. (2009). The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, 49(10), 1496–1504. <http://doi.org/10.1086/644617>
- Aryanti, R., & Hilbrand, H. (2002). Determinants of Antimicrobial Use in the Developing World, 4(1), 1–36.
- Bergman, U, Popa, C, Wettermark, B, Einarson, T. . (1998). Drug Utilization 90 % - A simple method for assessing the quality of drug prescribing the quality of drug prescribing, (May). <http://doi.org/10.1007/s002280050431>
- Berrington, A. (2009). Antimicrobial prescribing in hospitals: Be careful what you measure. *Journal of Antimicrobial Chemotherapy*. <http://doi.org/10.1093/jac/dkp399>
- Chopra, I., & Roberts, M. (2001). Tetracycline Antibiotics : Mode of Action , Applications , Molecular Biology , and Epidemiology of Bacterial Resistance Tetracycline Antibiotics : Mode of Action , Applications , Molecular Biology , and Epidemiology of Bacterial Resistance. *Microbiology and Molecular Biology Reviews*, 65(2), 232–260. <http://doi.org/10.1128/MMBR.65.2.232>
- Desalegn, A. A. (2013). Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. *BMC Health Services Research*, 13(1), 1–6. <http://doi.org/10.1186/1472-6963-13-170>
- Dong, L., Yan, H., & Wang, D. (2008). Antibiotic prescribing patterns in village health clinics across 10 provinces of Western China. *Journal of Antimicrobial Chemotherapy*, 62(2), 410–415. <http://doi.org/10.1093/jac/dkn153>
- Esposito, S., Esposito, I., & Leone, S. (2012). Considerations of antibiotic therapy duration in community- and hospital-acquired bacterial infections, (July), 2570–2575. <http://doi.org/10.1093/jac/dks277>
- European Centre for Disease Prevention and Control (ECDC). (2012). *Surveillance of antimicrobial consumption in Europe 2012*. <http://doi.org/10.2900/32937>
- Gerber, J. S., Prasad, P. A., Fiks, A. G., Localio, A. R., Grundmeier, R. W., Bell, L. M., ... Zaoutis, T. E. (2013). Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *Jama*, 309(22), 2345–52. <http://doi.org/10.1001/jama.2013.6287>
- Ghana Statistical Service. (2014). 2010 Population & Housing Census, District Analytical Report, Sunyani municipality. *Ghana Statistical Service*. Retrieved from 1. Project, A. S. No Title. at <http://sunyanimunicipal.blogspot.com/2010/06/chapter-two-district-profile-2_22.html>\n2. Report, A. EXCELLENCE ?. (2008). at <[58](http://sunyanimunicipal.blogspot.com/2010/06/chapter-two-district-profile-</p>
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2_22.html>\n3. Sunyani

- Grimmsmann, T., & Himmel, W. (2011). Discrepancies between prescribed and defined daily doses: A matter of patients or drug classes? *European Journal of Clinical Pharmacology*, 67(8), 847–854. <http://doi.org/10.1007/s00228-011-1014-7>
- Gwimile, J. J., Shekalaghe, S. A., Kapanda, G. N., & Kisanga, E. R. (2012). Antibiotic prescribing practice in management of cough and/or diarrhoea in Moshi Municipality, Northern Tanzania: cross-sectional descriptive study. *The Pan African Medical Journal*, 12, 103.
- Hash, J. H., Wishnick, M., & Miller, P. A. (1964). On the Mode of Action of the Tetracycline Antibiotics in *Staphylococcus aureus*. *The Journal of Biological Chemistry*, 239(6), 2070–2078.
- Haug, J. B., & Reikvam, A. °smund. (2013). WHO defined daily doses versus hospital-adjusted defined daily doses: impact on results of antibiotic use surveillance °, 68(July), 2940–2947. <http://doi.org/10.1093/jac/dkt268>
- Hutchinson, J. M., Patrick, D. M., Marra, F., Helen, William R Bowie, L. H., Muscat, Mark, D. L. M., ... Marra, F. (2004). Measurement of antibiotic consumption : A practical guide to the use of the Anatomical Therapeutic Chemical classification and Defined Daily Dose system methodology in Canada, 15(1).
- Isah AO, Ross-Degnan D, Quick J, Laing R, M. A. (n.d.). The development of standard values for the WHO drug use prescribing indicators. *ICUM/EDM/WHO*. Retrieved from http://archives.who.int/prduc2004/rducd/ICIUM_Posters/1a2_txt.htm
- Lee, C., Cho, I. H., Jeong, B. C., & Lee, S. H. (2013). Strategies to Minimize Antibiotic Resistance, 4274–4305. <http://doi.org/10.3390/ijerph10094274>
- Mannan, A., Shohel, M., Rajia, S., Mahmud, N. U., Kabir, S., & Hasan, I. (2014). A cross sectional study on antibiotic resistance pattern of *Salmonella typhi* clinical isolates from Bangladesh. *Asian Pacific Journal of Tropical Biomedicine*, 4(4), 306–11. <http://doi.org/10.12980/APJTB.4.2014C770>
- Ministry of Health, G. (2010). *Standard Treatment Guidelines*.
- Ministry Of Health Ghana. (2009). WHO pharmaceutical situation assessment – level II – health facilities survey in Ghana, (June), 41. Retrieved from http://www.moh-ghana.org/UploadFiles/Publications/Ghana_baseline_WHO_level_II_Health_Facility_Survey140204075637.pdf
- Mölstad, S., Erntell, M., Hanberger, H., Melander, E., Norman, C., Skoog, G., ... Cars, O. (2008). Sustained reduction of antibiotic use and low bacterial resistance : 10-year follow-up of the Swedish Strama.
- Muller, A., Monnet, D. L., Talon, D., Hénon, T., & Bertrand, X. (2006). Discrepancies between prescribed daily doses and WHO defined daily doses of antibacterials at a university hospital. *British Journal of Clinical Pharmacology*,

61(5), 585–591. <http://doi.org/10.1111/j.1365-2125.2006.02605.x>

- Naaber, P., Ko, S., & Maimets, M. (2000). Antibiotic usage and resistance — trends in Estonian University Hospitals, *16*, 309–315.
- Ntšekhe, M., & Tjipura, D. (2011). Antibiotic Prescribing Patterns at Six Hospitals in Lesotho. *Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health. Strengthening*, 40.
- Obeng-Nkrumah, N., Twum-Danso, K., Krogfelt, K. A., & Newman, M. J. (2013). High levels of extended-spectrum beta-lactamases in a major teaching hospital in Ghana: The need for regular monitoring and evaluation of antibiotic resistance. *American Journal of Tropical Medicine and Hygiene*, *89*(5), 960–964. <http://doi.org/10.4269/ajtmh.12-0642>
- Olofsson, S. K., & Cars, O. (2007). Optimizing Drug Exposure to Minimize Selection of Antibiotic Resistance, *45*(Suppl 2), 129–136. <http://doi.org/10.1086/519256>
- Paul, M., Lador, A., & Leibovici, L. (2014). Beta lactam antibiotic monotherapy versus beta lactam- aminoglycoside antibiotic combination therapy for sepsis (Review), (1). <http://doi.org/10.1002/14651858.CD003344.pub3>. www.cochranelibrary.com
- Polk, R. E., Fox, C., Mahoney, A., Letcavage, J., & MacDougall, C. (2007). Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, *44*(5), 664–70. <http://doi.org/10.1086/511640>
- Rao, G. G., Cooper, B. S., & Wade, P. (2011). Impact of guidelines and enhanced antibiotic stewardship on reducing broad-spectrum antibiotic usage and its effect on incidence of Clostridium difficile infection ", (June), 2168–2174. <http://doi.org/10.1093/jac/dkr253>
- Rice, L. B. (2008). The Maxwell Finland Lecture : For the Duration — Rational Antibiotic Administration in an Era of Antimicrobial Resistance and Clostridium difficile, *44106*, 491–496. <http://doi.org/10.1086/526535>
- Robert, J., Péan, Y., Varon, E., Bru, J. P., Bedos, J. P., Bertrand, X., ... Greder-Belan, A. (2012). Point prevalence survey of antibiotic use in French hospitals in 2009. *Journal of Antimicrobial Chemotherapy*, *67*(4), 1020–1026. <http://doi.org/10.1093/jac/dkr571>
- Samore, H. (2003). Evaluation of antibiotic use in a hospital with an antibiotic restriction policy. *International Journal of Antimicrobial Agents*, *21*, 308–312. [http://doi.org/10.1016/S0924-8579\(02\)00392-8](http://doi.org/10.1016/S0924-8579(02)00392-8)
- Singh, Z., Chowdhary, Q., Bashir, A., Abbas, Z., Assistant, S. F., & Lecturer, S. (2012). Rationalizing antibiotic use to limit antibiotic resistance and novel, *17*(4), 1–6. http://doi.org/IndianJMedRes_2011_134_3_281_85559 [pii]

- Snow, V., Mottur-Pilson, C., & Gonzales, R. (2001). Principles of Appropriate Antibiotic Use for Treatment of Nonspecific Upper Respiratory Tract Infections in Adults. *Annals of Internal Medicine*. <http://doi.org/10.7326/0003-4819-134-6-200103200-00014>
- Springer. (2010). *Antimicrobial Resistance in Developing Countries*. (& O. I. N. Sosa A. de J., Byarugaba D.K., Amabile-Cuevas C.F., Hsueh P., Kariuki S., Ed.). Springer New York Dordrecht Heidelberg London. <http://doi.org/10.1007/978-0-387-89370-9>
- Steinman, M. A., Landefeld, C. S., & Gonzales, R. (2003). Predictors of Broad-Spectrum Antibiotic Prescribing for Acute Respiratory Tract Infections in Adult Primary Care, *289*(6), 719–725.
- Strengthening Pharmaceutical Systems. (2012). How to Investigate Antimicrobial Use in Hospitals : Selected Indicators. *Published for the U.S Agency for International Development by the Strengthening Pharmaceutical Systems Program. Arlington, VA: Management Sciences for Health*, (February). Retrieved from http://www.msh.org/projects/sps/SPS-Documents/upload/Indicator-based-Study-on-Hospital-Antimicrobial-Use_Manual_Final.pdf
- Sunyani Municipal Hospital. (2015). Annual report 2015, Sunyani Municipal Hospital.
- Thomas P Van Boeckel, Sumanth Gandra, Ashvin Ashok, Quentin Caudron, Bryan T Grenfell, Simon A Levin, R. L. (2014). Global antibiotic consumption 2000 to 2010 : an analysis of national pharmaceutical sales data. *The Lancet Infectious Diseases*, *14*(8), 742–750. [http://doi.org/10.1016/S1473-3099\(14\)70780-7](http://doi.org/10.1016/S1473-3099(14)70780-7)
- Thompson, S. (2009). Rational antibiotic use in surgery. *Surgery*, *27*(10), 435–440. <http://doi.org/10.1016/j.mpsur.2009.08.008>
- Truter, I. (2008). A review of drug utilization studies and methodologies. *Jordan Journal of Pharmaceutical Sciences*, *1*(2), 91–104. Retrieved from <http://journals.ju.edu.jo/JJPS/article/viewFile/1068/1060>
- Truter, I., & Van W Kotze, T. J. (1996). A drug utilisation study investigating prescribed daily doses of 4hypolipidaemic agents. *South African Medical Journal*, *86*(11), 1397–1401.
- Tunger, O., Karakaya, Y., Cetin, C. B., Dinc, G., & Borand, H. (2009). Rational antibiotic use. *J Infect Developing Countries*, *3*(2), 88–93.
- Varley AJ, Sule J., A. A. (2009). Principles of antibiotic therapy. *Continuing Education in Anaesthesia, Critical Care and Pain*, *9*(6), 184–188. <http://doi.org/10.1093/bjaceaccp/mkp035>
- WHO. (2005). Containing antimicrobial resistance. *World Health Organization Geneva*, *10*, 1–6. <http://doi.org/10.2471/BLT.10.084236>
- WHO. (2014). Antimicrobial resistance. *Bulletin of the World Health Organization*, *61*(3), 383–94. <http://doi.org/10.1007/s13312-014-0374-3>

- WHO. (2015). Worldwide country situation analysis: response to antimicrobial resistance. *WHO Press*, (April), 1–50. <http://doi.org/ISBN: 978 92 4 156494 6>
- WHO Collaborating Centre for Drug Statistics Methodology. (2010). *Guidelines for ATC classification and DDD assignment. Vegetatio* (Vol. 70). <http://doi.org/10.1021/la902623c>
- World Health Organization. (1993). How to investigate drug use in health facilities. Retrieved from <http://apps.who.int/medicinedocs/pdf/s2289e/s2289e.pdf>
- World Health Organization. (2015). Global action plan on antimicrobial resistance., Geneva: World Health Organization. Retrieved from http://www.who.int/drugresistance/global_action_plan/en/
- Yawson, AE, Nimo, K., & Biritwum, R. (2013). Challenges of health care delivery at a municipal health facility under Ghana ' s national health insurance scheme. *Postgraduate Medical Journal of Ghana*, 2(2). Retrieved from <https://gcps.edu.gh/wp-content/uploads/2014/09/Challenges-of-health-care-delivery-at-a-municipal-health-facility-under-Ghana's-national-health-insurance-scheme.pdf>



APPENDIX 2

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted.



Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
Tel: +233-302-681109
Fax + 233-302-685424
Email: ghserc@gmail.com

My Ref. GHS/RDD/ERC/Admin/App/17/99-1
Your Ref. No.

Michael Mireku Opoku
School of Public Health
University of Ghana
P. O. Box LG 13
Legon-Accra, Ghana

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	GHS-ERC: 33/12/2016
Project Title	"Assessment of Antibiotic Prescribing at the Sunyani Municipal Hospital in 2015"
Approval Date	14 th March, 2017
Expiry Date	13 th March, 2018
GHS-ERC Decision	Approved

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report **after completion** of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....
DR. CYNTHIA BANNERMAN
(GHS-ERC CHAIRPERSON)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra