LONDON'S GLOBAL UNIVERSITY

Optimising antibiotic prescribing in Nigerian hospitals

Thesis submitted in accordance with the requirements of University College London for the degree of Doctor of Philosophy

By

Eneyi Edith Kpokiri

Department of Practice and Policy
University College London
School of Pharmacy

February 2019

PLAGIARISM STATEMENT

This thesis reports research that was conducted at the University College London (UCL) School of Pharmacy between 2014 and 2018 under the supervision of Professor Felicity Smith and Professor David Taylor. I, Eneyi Kpokiri at this moment confirm that the work submitted in this report is my own and where information has been derived from other sources have been clearly stated. I have not violated the University College London, School of Pharmacy's policy on plagiarism.

Signature: [redacted] **Date:** 21/02/2019

ACKNOWLEDGMENTS

I am most grateful to God Almighty whose grace saw me through this programme.

I am also grateful to my supervisors Professor Felicity, J. Smith and Professor David, G. Taylor for their expert supervision, support, and guidance throughout my study. I use this opportunity to say thank you for your excellent feedback that has encouraged me so much.

Thanks to the Nigerian tertiary education trust fund, for providing the initial funds needed for this programme.

My sincere appreciation goes to my family. My dad (you would have been so proud) and my mum who prays for me endlessly, my brothers Edwin-Spiff and Lawson and my sister Joy I say thank you for your support. Special thanks also go to my dear friends Dr. Arit Udoh, Dr. Frederick Pessu, Dr. Abarasi Hart, Olusegun Folarin, Fabian Pappoe and Peter Owonaro for your encouragement throughout this programme.

I also want to appreciate Professor Bryony Dean-Franklin, Dr. Jani Yogini my senior colleagues’ Dr. Ebiowei Orubu, and Dr. Kehinde Ganiyu for your timely inputs. To my friends and colleagues in room 336, School of Pharmacy (Dalal, Mona, Asmaa, Sherly, Liz and Rebekah) many thanks for all your support you’re amazing.

Finally, a special thank you goes to my husband Dr. Ebiegberi Kpokiri for his unwavering support and believing so much in me. Thank you for your love, patience, and encouragement all the way.

ABSTRACT

Background: Antimicrobial resistance (AMR) is a major concern facing global health today. It is severe in developing countries where the burdens of infectious diseases are much higher. Studies from developed countries suggest that antibiotic stewardship can improve antibiotic prescribing; however, these interventions are not directly applicable to developing countries. The aim of this study is to identify potentially feasible and effective strategies that will lead to improvements in antibiotic prescribing practices in hospitals in low and middle-income countries.

Methods: A mixed methods approach was employed. First, a quantitative retrospective survey of antibiotic prescribing using patient's case notes was conducted and then a qualitative prospective survey of prescribers and stakeholder's perceptions of antibiotic prescribing. The qualitative survey employed semi-structured interviews to explore determinants of current antibiotic prescribing practices, suggestions to improve practice and the likely barriers. This study was carried out in four hospitals including two secondary and two tertiary care hospitals in Nigeria.

Results: The results show that 72% of antibiotics were prescribed empirically. Only 28% of antibiotic prescriptions studied had complete compliance with the guidelines and relevant diagnostic tests were carried out in 15% of antibiotics prescriptions retrieved. Main determinants of current antibiotic prescribing practices include drug costs and availability, limited diagnostic resources and services, the excessive workload for healthcare providers, lack of policies/guidelines, and physicians' attitudes. Recommendations prioritised by stakeholders for improvements to practice include provision of resources to support training and education, documentation and monitoring, improved diagnostic services and availability of antibiotics.

Conclusion: This research extends our knowledge on antibiotic prescribing practices and strategies for implementing antibiotic stewardship programmes in resource poor settings. Establishing effective locally developed approaches can possibly improve antibiotic prescribing patterns. Achieving appropriate use and prescribing of antibiotics in Nigeria is a potentially achievable goal, provided the necessary resources are provided and funds allocated.

IMPACT STATEMENT

Earlier studies conducted in high-income countries have shown how antibiotic stewardship programmes can improve antibiotic prescribing in hospital settings, but these interventions are poorly employed in low and middle-income countries (LMICs) owing to differences in the healthcare settings. Until now, the literature published does not provide sufficient guidance on feasibility and potentially effective interventions to improve antibiotic prescribing in these settings. In addition, not much is known about the specific barriers that needs to be addressed to support the effective implementation of antimicrobial stewardship programmes in LMICs and other developing countries around the world.

This research describes the antibiotic prescribing patterns in Bayelsa state, Nigeria across the different levels of care. This is the first study on antibiotic prescribing carried out in the area. Firstly, the results obtained here contributes to national antibiotic use database, which has not been available before now. Secondly, the findings obtained provides valuable information to guide antibiotic use and procurement and will also inform local policies on antibiotics prescribing.

In this research, a bottom-up approach was employed to identify the main determinants of antibiotic prescribing practices. Also, the barriers that impact on the feasibility and the implementation of antimicrobial stewardship in resource-poor settings were highlighted. These barriers were found to exist at all levels of the healthcare delivery process, from the government level, to the institutional and also at the individual level. Consequently, practical recommendations were developed to address the barriers at the different levels with potential to improve antibiotic use using an established framework for behaviour change (The Behaviour Change Wheel by Michie *et al.,* 2011).

The findings from this project have been able to demonstrate a clear need for more training on the antimicrobial resistance (AMR) subject for prescribers and the need for collaboration among healthcare personnel to deliver better and more optimised health services. It has also highlighted the impact of poor healthcare financing and weak regulatory and surveillance systems on the rational use of medicines in developing settings.

This work provides insights for the next steps to be taken to support the implementation an antibiotic stewardship programme in low and middle-income countries. The findings from this project have informed a set of recommendations for the implementation of antimicrobial stewardship (AMS), in a low-resource setting. The study highlights the opportunities and challenges and presents a series of recommendations derived from observation of practice and consultation with practitioners and other key stakeholders.

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
ABR	Antibiotic Resistance
ABS	Antibiotic Stewardship
A&E	Accident and Emergency
AMR	Antimicrobial Resistance
AMS	Antimicrobial stewardships
ANAPE	Average Number of Antibiotic drugs Per Encounter
APEASE	Acceptability Practicability Effectiveness Affordability Safety Equity
ASP	Antibiotic stewardship programmes
ASU	Antibiotic Smart Use
ATC-DDD	Anatomical Therapeutic Classification-Daily Defined Doses
ATS	American Thoracic Society
BCT	Behaviour Change Technique
BCW	Behaviour Change Wheel
BNF	British National Formulary
CAQDAS	Computer Assisted Qualitative Data Analysis Software
CASP	Critical Appraisal Skills Programme
CDC	Centre for Disease Control Nigeria
CMAC	Chairperson, Medical and Advisory Committee
CMD	Chief Medical Director
CME	Continuing Medical Education
COM-B	Capability Opportunity Motivation Behaviour
CPD	Continuous Professional Development
CRE	Carbapenem-Resistant Enterobacteriaceae
DA	Director of Administration
DAD	Drug Actually Dispensed
DDD	Daily Defined Doses
DH	Department of Health
DKMH	Diete Koki Memorial Hospital

DTC	Drug and Therapeutics Committee
EML	Essential Medicines List
ENT	Ear Nose and Throat
EPOC	Effective Practice and Organisation of Care group
EU	European Union
ESBL	Extended Spectrum Beta Lactamase
FCT	Federal Capital Territory
FDA	Food and Drug Association
FMC	Federal Medical Centre
FMoH	Federal Ministry of Health
HBM	Health Belief Model
HIV/AIDs	Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome
HM	Her Majesty
GARDP	Global Antibiotic Research and Development Partnership
GDP	Gross Domestic Productivity
GHA	Government Hospital Amassoma
GLASS	Global Antibiotic Resistance Surveillance System
GOPD	General Out Patient Department
IACG	Intra Agency Coordination Group on antimicrobial resistance
IB	Innovator Brand
ICG	Infection Control Group
ID	Infectious Disease
IDRT	Infectious Disease Research and Treatment
IDSA	Infectious Diseases Society of America
LMICs	Low and Middle-Income Countries
LPG	Lowest Priced Generic
MCS	Microbial Culture and Sensitivity

MD	Medical Director
MDCN	Medical and Dental Council of Nigeria
MDR	Multi Drug Resistant
MDRO	Multi Drug Resistant Organism
MoH	Ministry of Health
MRSA	Methicillin Resistant Staphylococcus Aureus
NAFDAC	National Agency for Food and Drug Administration and Control
NDLEA	National Drug Law Enforcement Agency
NDUTH	Niger Delta University Teaching Hospital
NHIS	National Health Insurance Scheme
NMA	Nigerian Medical Association
NPC	Nigerian Population Commission
OBY&GYNAE	Obstetrics and Gynaecology
PEA	Percentage Encounter for Antibiotics
PRB	Prescriber
QA	Quality Assurance
RCGP	Royal College of General Practitioners
RDT	Rapid Diagnostics Tests
REC	Research and Ethics Committee
SCBU	Special Care Baby Unit
SPSS	Statistical Package for the Social Sciences
STG	Standard Treatment Guidelines
STI	Sexually Transmitted Infections
STKH	Stakeholder
STRAMA	Swedish Strategic Programme Against Antibiotic Resistance
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
SWOT	Strength Weaknesses Opportunities Threat
TB	Tuberculosis
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Actions
UCL	University College London

UK	United Kingdom
UNFPA	United Nations Population Fund
UNICEF	United Nations International Children's Emergency Fund
USAID	United States Agency for International Development
USD	United States Dollars
VINARES	Vietnam Resistance Programme
VRE	Vancomycin Resistant Enterobacteriaceae
WAAW	World Antibiotic Awareness Week
WHO	World Health Organisation

LIST OF DEFINITIONS

Term	Definition
Antibiotics	Chemical substances usually produced by microorganisms such as bacteria, yeasts, moulds which inhibits growth or kills other microorganisms.
Antibacterial	Agents or compounds that kill or inhibit the growth of bacteria.
Antimicrobials	Agents that kill or inhibit growth of microbial organisms such as bacterial, fungi, virus, yeasts and some parasites. Antibiotics and antibacterial medicines are subsets of antimicrobials.
Antimicrobial resistance	This is opposition reaction of microorganisms to antimicrobial agents/ drugs to which they were originally sensitive.
Irrational drug use	Where there is over or under prescribing, multiple prescribing as well as indiscriminate use of drug.
Inappropriate use	Refers to use of the wrong drug, for the wrong indication, or wrong patient; or wrong patient information as well as inadequate doses, or indiscriminate use.
Self-medication	Use of drugs or pharmaceutical products by a consumer to treat self-recognized disorders or symptoms.
Intervention	Refers to various measures that can be used to optimise the use of medicines such as antibiotics/antibacterial/ antimicrobial agents.

Chapter 1 INTRODUCTION

1.1 Background

Antimicrobial resistance (AMR) is a global problem of increasing importance. AMR associated illnesses currently cause an estimated 50,000 deaths annually in the United States of America and Europe, increasing to several hundred thousand deaths when other countries are included (HM Government, 2014). If the current situation does not change, this continuous rise in AMR is projected to result in 10million deaths annually by the year 2050 (Review on AMR, 2014, see Figure 1.1 below). This will have serious economic consequences as further research suggests that this projected death rate will reduce the world's total GDP by an estimated 3.5% which will may lead to a loss of between 60 and 100 trillion USD globally by 2050 (Review on AMR, 2014).

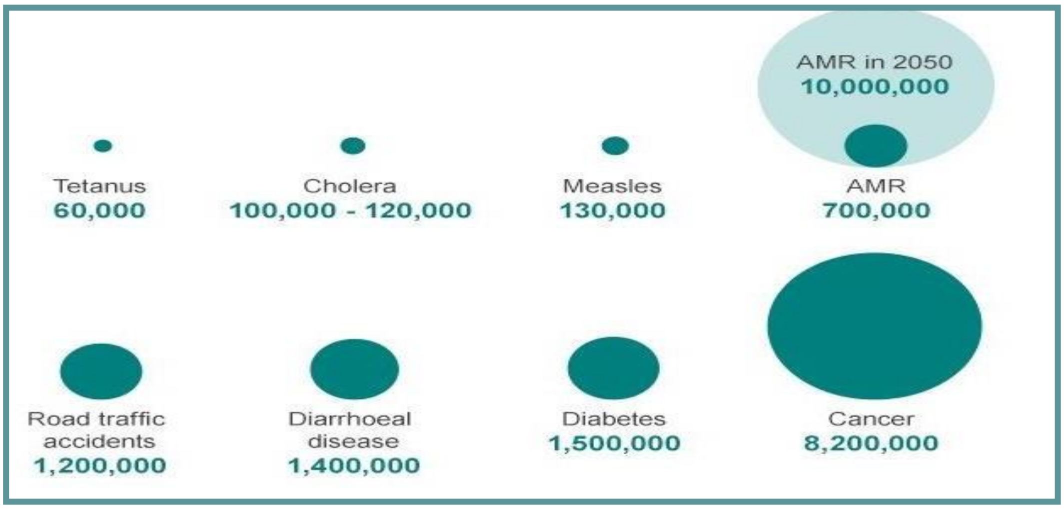

Figure 1.1: Estimated deaths due to AMR by the year 2050 (Review on AMR, 2014)

Factors that have contributed to increased antimicrobial resistance over time include inappropriate use of antibiotics such as prescribing antibiotics for viral and non-bacterial illnesses, poor adherence to guidelines and use of antibiotics in animals and agriculture (WHO, 2015). Other factors especially in low and middle-income countries include high burden of infectious diseases and uncontrolled access to antimicrobial drugs (Nguyen *et al.,* 2013). Recent research shows continuous increase in rates of bacterial resistance to antibiotic drugs ((Review on AMR, 2014).

Unfortunately, there has been a steady decline in the number of new antibiotics that have been successfully developed in the last few decades. Discovering and testing new antibiotics is very costly and takes a lot of time (Hughes & Karlén, 2014). Antibiotics are mostly taken as short course therapies for the duration of an infection and as such represent a poor return on investment when compared to other classes of drugs used in the long term like anti-hypertensives. Furthermore, the more antibiotics are used, the less effective they become as bacterial organisms develop mechanisms of resistance against the drugs. This contributes to the lack the incentive on the part of pharmaceutical companies to invest in antibiotic drug development. As a result, conservation of the antibiotic drugs we have by promoting rational use is now essential.

1.1.1 Antibiotic discovery

Traces of tetracycline were discovered in the fossils of the Sudanese Nubia tribe dating to 350-550 CE. This distribution of tetracycline in bones was believed to be possible due to exposure to tetracycline-containing materials in the diet of these ancient people (Bassett *et al.,* 1980; Nelson *et al.,* 2010). However, modern antibiotic era reports the discovery of antibiotics approximately eight decades ago, which was novel and marked a major turnaround in the management of infectious diseases in clinical medicine practice. Morbidity and mortality rates from bacterial infections reduced drastically owing to lack of primary resistance at the time. The use of antibiotic drugs became a necessary intervention for many medical conditions relating to bacterial infections. Since then, the use of antibiotics has increased; newer antibiotics were developed and used in the therapeutic management of a wide range of infectious diseases. Currently, antibiotic drugs are one of the widely used category of drugs worldwide (Buke *et al.,* 2003; Gaash, 2008).

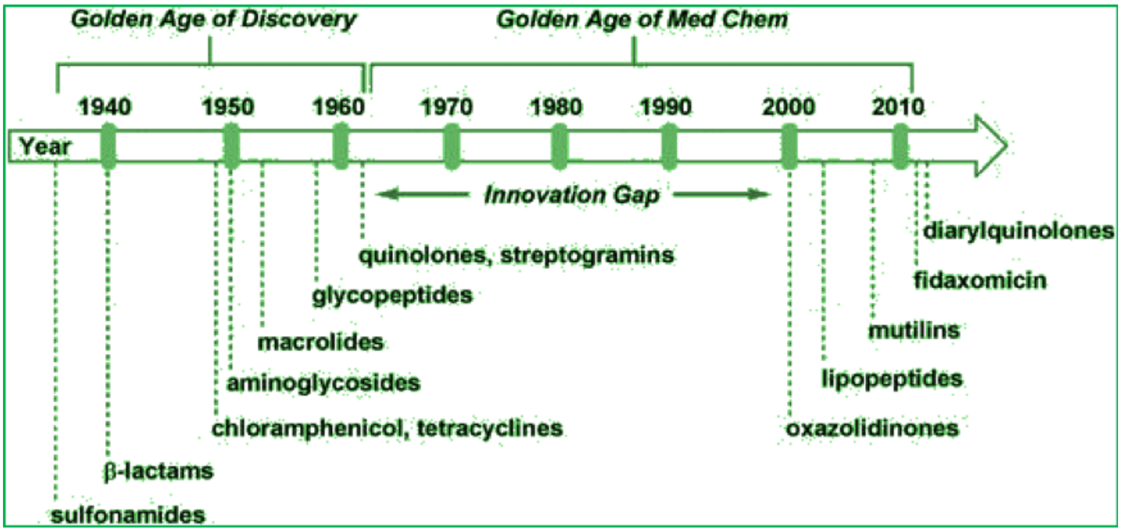

Figure 1.2: Timeline for antibiotic discovery (Adapted from Walsh et al., 2013)

Figure 1.2 above shows the timeline for antibiotic discovery. The pace of antibiotic drug development has markedly slowed in the last 20 years. Without effective interventions, going by current rate of increase in bacterial resistance to antibiotic drugs it is possible we may enter what some have termed the post-antibiotic era, where the world would be faced with previously treatable diseases that have become untreatable (Tenover & Hughes, 1996). As a result, improving the use of antibiotics has become an important patient safety and public health issue as well as a global priority.

1.2 Antibiotic Resistance

The inappropriate use of antibiotics over the years has led to the development of antibacterial resistance which is now a major public health concern globally. Antibiotic resistance has been shown to be directly related to the increased use of antibiotic drugs (Guillemot *et al.,* 1998; Donnan *et al.,* 2004). Other factors that have over time increased the issue of resistance in antibiotic use include over prescribing of antibiotics, use of antibiotics in animals and agriculture, easy access to antibiotics and the use of antibiotics for nonbacterial illnesses (WHO, 2015). This irrational use of antibiotics has been documented in both developed and developing countries (Holloway and Dijk, 2011).

1.3 Impact of Antibiotic resistance

The emergence of resistance to first line antibiotics has led to a shift in using newer and more expensive antibiotic drugs. This is accompanied by extended duration of illness and longer length of stay in hospitals. There is also an increased rate of mortality and morbidity especially in the LMICs where the high cost of second line antibiotic drugs most times restricts their use (Laxminarayan *et al.,* 2013). Given the factors contributing to the problem of antibiotic resistance, strategies and recommendations to address AMR will include efforts from all stakeholders including doctors, pharmacists, nurses, clinical microbiologists, healthcare specialists, educationalists, policy makers, legislative bodies, agricultural and pharmaceutical industry workers, government and the public.

1.4 Antibiotic Resistance: The global burden

With the ease and frequency at which people travel from one country to another, antibiotic resistance is now increasing to alarming levels all over the world. Bacteria develop new mechanisms of resistance to newer and modified antibiotics, which puts the achievements of modern medicine such as basic surgical procedures, organ transplant and chemotherapy at risk. The US Center for Disease Control and Prevention (CDC) estimates that more than two million people are infected with antibiotic-resistant organisms worldwide. Multi-resistant bacteria already cause around 80,000 deaths annually in China**,** 25,000 in Europe and approximately 63,000 annually in the United States (WHO, 2013).

The rate of antibiotic resistance is thought to vary with the different disease conditions. The World Health Assembly in 2005 reported that antibiotic resistance to first line antibiotics was as high as 70-90% in cases of pneumonia, dysentery, gonorrhoea and some other hospital infections. Globally, the resistance to penicillin has been estimated to be between 5-98% for gonorrhoeal and between 12%-55% for pneumonia and bacterial meningitis (Tapsall, 2001; Schrag *et al.,* 2001). A study reports that majority of adults in India, Egypt and Pakistan carry bacteria that are resistant to β-lactam antibiotics such as the carbapenems, considered to be one of the last resort antibiotics (Kumarasamy *et al.,* 2010). This may be due to the high rates of over-the-counter availability of carbapenems in these countries.

1.5 Strategies and interventions to curb antibiotic resistance

With the decline in development of novel antibiotics in the last thirty years, the initial attempts to address antimicrobial resistance were modifications made to existing antimicrobials. Many were successfully developed and overcame resistant bacteria at the time, however new mechanisms of resistance evolved and also resistance to the modified antimicrobials emerged. Another strategy to combat AMR is to reduce antimicrobial drug consumption, and other steps to ensure rational use. Mathematical modelling has demonstrated that reductions in antibiotic use would possibly result in lower resistance rates because genetically less “fit” resistant strains would be outcompeted by susceptible strains (Lipsitch *et al.,* 2000). As a result, this strategy has now been widely pursued globally. Different country governments around the world have released policy interventions, such as regulating where antimicrobials can be sold, restricting the use of last-resort antimicrobials, funding AMR stewardship programmes, and launching public awareness campaigns (Katwyk *et al.,* 2017). Other initiatives include the WHO Global Strategy for Containment of Antimicrobial Resistance, 2001; World Health Day six-point AMR policy, 2011; Department of Health (DH) UK Antimicrobial Resistance Strategy and Action Plan (2000); DH/British Society of Antimicrobial Chemotherapy's ‘Start Smart, Then Focus’ campaign (Ashiru-Oredope *et al.,* 2012; Llewelyn *et al.,* 2014); and the Target Antibiotics toolkit in general practice (RCGP, 2014).

Antimicrobial resistance is of high priority for the WHO, and in their response, they have put in place different strategies to address AMR. Some of the WHO strategies include:

World Antibiotic Awareness Week (WAAW): Held every November since 2015 with the theme “Antibiotics: Handle with care”, the global, multi-year campaign has increasing volume of activities during the week of the campaign.

The Global Antimicrobial Resistance Surveillance System (GLASS): This WHO-initiated system supports a standardized approach to the collection, analysis and sharing of data related to antimicrobial resistance at a global level to inform decision-making, drive local, national and regional action.

Global Antibiotic Research and Development Partnership (GARDP): A joint initiative of WHO and Drugs for Neglected Diseases initiative (DNDi), GARDP encourages research and development through public-private partnerships. By 2023, the partnership aims to develop and deliver up to four new treatments, through improvement of existing antibiotics and acceleration of the entry of new antibiotic drugs.

Interagency Coordination Group on Antimicrobial Resistance (IACG): The United Nations Secretary-General has established IACG to improve coordination between international organizations and to ensure effective global action against this threat to health security. The IACG is co-chaired by the UN Deputy Secretary-General and the Director General of WHO and comprises high level representatives of relevant UN agencies, other international organizations, and individual experts across different sectors.

Also, a global action plan on antimicrobial resistance was endorsed at the World Health Assembly in May 2015. This plan has five strategic objectives and aims to ensure prevention and treatment of infectious diseases with safe and effective medicines. The objectives include:

- To improve awareness and understanding of antimicrobial resistance.
- To strengthen surveillance and research.
- To reduce the incidence of infection.
- To optimise the use of antimicrobial medicines.
- To ensure sustainable investment in countering antimicrobial resistance.

The WHO global action plan aimed at addressing the global antimicrobial resistance issue the strategies are stakeholder-centred, with the interventions directed towards the stakeholders who are directly involved with the use of antibiotics and as a result need to be part of the solution. These include patients, healthcare providers, healthcare facility administrators, policy makers and government, professional societies and the pharmaceutical industry (See Table 1.1 below).

Table 1.1: Stakeholder specific interventions recommended by WHO

Stake holder	Interventions
Patients/ General community	Education-appropriate use of antibiotics, expectations.
Prescribers/Dispensers	Training and education.
Hospital Management	Set up infection control programmes, therapeutics committee, local policies, formulary, monitoring systems, antibiotic stewardships.
Government/ Health ministries	Establish national antibiotic policies, standard treatment guidelines, essential medicines list, and regulations for promotion, supply and sales of antibiotics.

1.5.1 Antibiotic prescribing practices

Improving antibiotic prescribing practices will lead to reduced antibiotic use which will translate to a reduction in antibiotic resistance rates. While antimicrobial stewardships have been able to influence antibiotic prescribing, there is still need for further change. The inappropriate prescribing of antibiotics remains widespread, despite the global response from different organisations and governments to improve antibiotic prescribing. Durkin *et al.,* 2018 conducted a study in the US that showed no changes to antibiotic prescribing practices over a three-year period from 2013 to 2016. There were no significant variations in the individual or overall yearly antibiotic prescribing rates during the study period.

A more focused, strategic and integrated action, informed by high-quality research targeted at prescribing behaviour, is now required (Durkin *et al.,* 2018; Wong *et al.,* 2015). One feasible approach to doing this will be to first understand prescribers' knowledge, attitudes and perceptions of antibiotic prescribing and then to study the factors and determinants of antibiotic prescribing practices in any given setting.

1.5.1.1 Factors and determinants of antibiotic prescribing practices

The factors that impact on antibiotic prescribing vary across different settings. Some general factors already identified as important in promoting resistance include widespread use of antibiotics (91%), inappropriate empiric choices (79%) and use of broad-spectrum agents (70%). Hand-washing was not considered to be important in reducing resistance. (Tennant *et al.,* 2010). In settings without a comprehensive health insurance scheme, some physician's stated that their decision of antimicrobial prescription was influenced by patient's socioeconomic status and patients' demands (Shahid *et al.,* 2017, Faizullah *et al.,* 2017). Thakolkaran, *et al.,* 2017 found in their study that more than half the physicians report that patient or parent expectations or pressure would have no impact on their antibiotic prescribing pattern.

Another study showed that physicians preferred educational interventions, such as specific teaching sessions, availability of guidelines or readily accessible advice from an infectious diseases specialist, to improve antibiotic prescribing, rather than restricting antibiotic prescribing (Pulcini *et al.,* 2011).

1.5.2 Prescribers knowledge, attitudes and perceptions of antibiotic prescribing

Understanding prescribers' knowledge, attitude and perceptions of antibiotic prescribing is crucial for a change in their prescribing behavior. Studies mostly from developed countries demonstrate that prescribers from different levels and across varying specialties are aware that antibiotic resistance is a critical global problem (Alothman *et al.,* 2016; Tennant *et al.,* 2010). However, they are not so much aware of specific resistance rates in their practice facilities. One study showed that only 31% and 26% of *the* doctors knew the correct prevalence of antibiotic misuse and of methicillin-resistant *Staphylococcus aureus* in hospitals in France and Scotland, respectively (Pulcini *et al.,* 2011). In a Pakistani study, only 16% of physicians could correctly estimate the rates of resistance of Klebsiella pneumoniae and pseudomonas aeruginosa to cephalosporin.

Most physicians (80%) reviewed their decisions to prescribe an antibiotic by discussing with a senior colleague (Shahid *et al*., 2017). In India, less than half of the doctors in a study reported awareness of antimicrobial resistance to *S. pneumoniae*; knowledge of this resistance pattern was shown to be lower in physicians who did not receive periodic updates on bacteria resistance patterns, while a high percentage of physicians agreed to use antibiotics for the treatment of common cold or other upper respiratory tract infections (Thakolkaran, *et al* 2017).

Although physicians were aware of the problem of bacterial resistance to antibiotics and the contributory factors, their practice did not reflect measures to reduce it. There is need for continuous educational and training programmes and also institution-specific antibiotic prescribing policies should be put in place (Davey *et al.,* 2017; Salsgiver *et al.,* 2018).

1.5.3 Antibiotic Policies

The use of government policies to promote public health has been rewarding especially when the challenge requires widespread and uniform compliance to a defined set of standards (Magnusson, 2017). This suggests that government level policies released to guide the use of antimicrobial agents may play a key role in reducing AMR in the selected setting. The hospital antibiotic policy would be helpful to guide antibiotic use on prophylaxis, empirical and definitive therapy. The main aim of an antibiotic policy should be to minimise morbidity and mortality due to antibiotic-resistant infections, and to preserve the effectiveness of antibiotic drugs in the treatment and prevention of communicable diseases (WHO, 2011). The antibiotic policy ideally sets the standards for prescribing antibiotics, such that first choice antibiotics can be prescribed by all doctors and the restricted choice antibiotics can only be prescribed only be prescribed by designated experts, or after consultation with a higher authority such as an infectious disease consultant or one of the antimicrobial team representatives. The restricted and reserved antibiotics refers to those antibiotics that could contribute to development of multi-resistant organisms if not used appropriately.

Studies conducted have shown that government policies implemented to prevent over-the-counter sales have led to actual reductions in antibiotics use in Mexico and Brazil (Tellez *et al.,* 2013). In Brazil, over-the counter sales were common until November 2010 when a national restrictive policy requiring medical prescription for the sale was implemented. There was an important drop in antimicrobial sales in Brazil. This impact was higher for the large urban areas and regions with better socio-economic status (Moura *et al.,* 2015). This approach had been applied in other Latin America countries. A less direct intervention has also been used to reduce antibiotic use in Canada when a policy to provide free universal influenza immunization produced appreciable reduction in inappropriate antibiotic prescriptions made out for influenza (Kwong *et al.,* 2009).

In a study conducted in Thailand involving thirty-three Thai hospitals from all five regions of Thailand, it was found that all the hospitals had policies related to infection control and antibiotic use, though different levels of implementation were observed. However, some studies have been able to establish the ability of antibiotic policies to reduce antibiotic use and also show its effects on reducing resistance rates (Gould, 1999).

Table 1.2 gives a summary of interventions in different countries regarding antibiotic policies that were reported to have led to reductions in antibiotic use. This was measured in terms of reduction in resistant strains of bacteria, reduction in antibiotic consumption, reduction in length of hospital stay etc.

Table 1.2: Benefits from antibiotics policies in different countries

Country	Intervention	Effect	Authors/Year
Iceland	Reduction in penicillin and co-trimoxazole use	Reduction in penicillin resistance from 20% to 15%.	Arason, *et al.*, 1996
Finland	Policy on reduction of macrolides usage was issued	Total use of macrolide antibiotics in out-patient therapy decreased from 2.40 defined daily dosesper 1000 inhabitants per day in 1991 to 1.38 in 1992 (P_ 0.007).	Seppälä *et al.*, 1997
America	Introduction of a restrictive antibiotic policy	Sharp decrease in resistant Acinetobacter and Enterobacteriaceae, with no detrimental effect on survival.	White *et al.*, 1997
China	Formulary restrictions in policy, antibiotic use monitoring systems	Reduction in antibiotic sales from 25% to 17%, antibiotic prescriptions reduced from 68% to 58%	Xiao *et al.*, 2013
Greece	Implementation of management protocol	Reduction in length of hospital stay from 3.7 to 2.6days, and 50% decrease in the use of antibiotics in an ICU unit	Price *et al.*, 1997
America	Antibiotic prescribing improvement programme	Reduction in prescribing broad spectrum antibiotics and corresponding decrease in the rates	Frank *et al.*, 1996

		of Nosocomial bacteraemia	
France	Reduction in gentamicin prescribing	Reduced prevalence of gentamicin resistant MRSA	Aubry-Damon *et al.,* 1997

For the effect of the antibiotic policies to be sustained over time, there is need for implementing other interventions alongside, such as stakeholders' involvement to promote changes in prescribing behaviour and also public education campaigns that can enhance the uptake of the policy measures. Developing routine public awareness campaigns to these policies as well as systems to monitor compliance to the policies are important (Wirtz *et al.,* 2013).

1.5.4 Antibiotic Stewardship Programmes (ASP)

Antibiotic stewardship is a coordinated program that promotes the appropriate use of antibiotics, improves patient outcomes, reduces antibiotic resistance, and decreases the spread of infections caused by multidrug-resistant organisms. It is a valuable approach to optimising antibiotic therapy. It is a key component in various multifaceted strategies being put in place to prevent emergence and reduce antibiotic resistance. Good antibiotic stewardship involves optimising drug dose and duration to cure an infection while minimising toxicity and conditions for selection of resistant bacterial strains (See Figure 1.3).

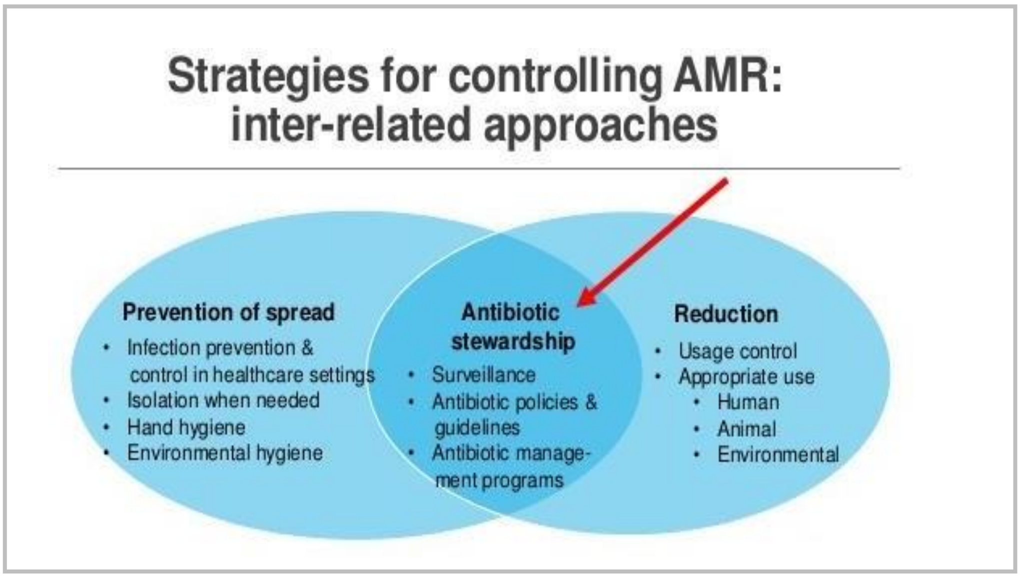

Figure 1.3: Strategies for controlling AMR and their interrelated approaches (Lansang, 2017)

Antibiotic stewardship is built on a framework of existing antibiotic policies and achieves "uniformity of prescribing" with adherence to policies, guidelines and formularies. This makes it practically impossible to implement in settings where policies and guidelines are non-existent. Even in settings with existing policies, this uniformity of prescribing may actually be harmful at times as the best defence against resistance is probably "diversity of prescribing". Common barriers to the implementation of antimicrobial stewardships include lack of funds, human resource and manpower, lack of information and technology, higher priorities and prescriber opposition (Mani, 2014).

A review identified many studies assessing the effectiveness of antibiotic stewardship programmes (Hulscher and Prins, 2017). They concluded that antibiotic stewardship programmes can ensure that professionals use antibiotics appropriately, improve patient and microbial outcomes, costs or some combination of these. In most studies included in the review, the stewardship programmes are multifaceted i.e. having a combination of interventions beneficial effects of antibiotic stewardships are measured as a reduction in antibiotic prescribing and consumption, reduction in patient length of hospital stay and hospitalization costs.

1.5.5 Prevalence and benefits of stewardship programmes

Antibiotic stewardship programmes are widely employed in optimising of antibiotics use in most developed and in some developing countries today**.** Multidisciplinary groups set up in the hospitals usually act as drivers and custodians of the stewardship programmes. Examples of such groups include

Drugs and Therapeutics Committee (DTC) and Infection Control Groups (ICG). A lot of interventions can be employed by the antibiotic stewardship to achieve improved use of antibiotics (Przybylski *et al.,* 1997), a non-binding treatment counselling initiated for patients on broad spectrum antibiotics therapy (Del-Arco *et al.,* 2014). These stewardship programmes are able to reduce the consumption of antibiotics as well as reduce patients' length of stay in hospital (Hulscher and Prins, 2017).

Various degrees of success in curbing antibiotic misuse and over use have been documented with the implementation of antibiotic stewardship programmes in many countries. In Belgium, antibiotic prescriptions reduced by 36% in one year, between 1999 and 2000 through mass media campaigns, this prompted France to initiate their own antibiotic campaign which was titled **"Antibiotics are not Automatic anymore"** this campaign was directed at the public and general practitioners. This French campaign led to a reduction in antibiotics prescription by 26.5% between 2002 and 2007 which was even higher than the national target of 25% (Huttner *et al.,* 2009).

In Thailand, the Antibiotics Smart Use (ASU) programme was initiated between 2007 and 2012 to foster a more responsible use of antibiotic medicines by directly engaging prescribers, dispensers and patients. The phase 1 of the ASU programme, which was the pilot phase aimed to reduce antibiotic prescriptions by at least 10%, to increase by at least 10% the number of patient-provider encounters not resulting in antibiotics prescriptions and satisfactory patient outcomes in up to 70% of targets.

The outcome of phase 2 confirmed the outstanding results of the pilot phase of the program, and then focused on svaling up effective interventions from phase 1 to ensure the benefits of the Antibiotic Smart Use programme are maintained

(Sumpradit *et al.,* 2012). Other hospital based National stewardship programmes implemented include the newly introduced Vietnam Resistance Programme (VINARES), the Swedish Strategic Programme Against Antibiotic Resistance (STRAMA), the European Union's Antibiotic Stewardship International (EU's ABS International) and the South Africa's Best care…Always (Boyles *et al.,* 2013).

With no clear prospects of developing new antibiotics, stewardship programmes should be developed and implemented in the different settings to optimise use and preserve the antibiotics we already have.

Table 1.3 below shows the impact of some forms of antibiotic stewardship programmes implemented in different developing countries.

Table 1.3: Implemented antibiotic stewardship programmes with success in developing countries					
Strategy	**Intervention Description**	**Effect on antibiotic use**	**Study location**	**Year**	**Reference**
Antibiotic policies	Formulary restrictions in policy, antibiotic use monitoring systems	Reduction in antibiotic sales and antibiotic prescriptions also reduced	China	2013	Xiao *et al.,*
Education and an antibiotic control programme	Education for resident doctors and medical students, antibiogram, antibiotic prescription sheets and prescribing controls	After the intervention, there was a 24% reduction in the rate of antibiotic prescribing. Inappropriate antibiotic use was reduced, 42% Vs 20%, reduction in incidence of antibiotic resistance and also reduction in cost of antibiotics prescribed to patients was recorded.	Thailand	2006	Apisarnthanarak *et al.,*
Antibiotic use control programme	Introduction of antibiotic prescription form,	Sustained reduction in antibiotic consumption, reduction in antibiotic cost. Total cost savings was $913,236 during the study. Decreased	Argentina	2003	Bantar *et al.,*

	education and prescribing control	rates of MRSA and increased susceptibility to ceftriaxone by previously resistant *Proteus mirabilis* and *Enterobacter cloacae.*			
Antibiotic restriction policy	Introduction of a restrictive antibiotic prescribing Policy	Expenditures for antimicrobial drugs decreased by 50%, from $699 543 during 1995 and 1996 to $347 261 during1997 and 1998. Susceptibility rates of staphylococci Improved for restricted antibiotics with >35% reduction in utilization	Panama	2000	Saez-llorens *et al.*,
Antibiotic prescription chart and weekly antibiotic ward rounds	An antibiotic prescription chart and weekly antibiotic stewardship ward rounds were introduced in two medical wards of a teaching hospital	Reduction in antibiotic consumption without harm to patients. There was a 19.6% decrease in volume of antibiotic consumption in terms of defined daily doses (DDD) with a corresponding cost reduction of the pharmacy's antibiotic budget.	South Africa	2013	Boyles *et al.*,

Hand hygiene campaign and WHO pocket book guidelines for prescribing	The intervention was two phases; a hand hygiene campaign and introduction of the WHO pocket book guidelines as standards for antibiotic prescribing in a teaching hospital	There was major reduction in hospital acquired infections from 22.6% to 8.6% through the hand washing campaign. Inappropriate antibiotic use declined by more than 50%. From 43% to 20.6% with the use of WHO pocket antibiotic prescribing guidelines. There was also significant reduction in deaths, 6% decline in in-hospital deaths in the post intervention period.	Indonesia	2014	Murni *et al.*,

1.5.6 Overview of antibiotics use in LMICs

In emerging economies, antibiotics are the most widely sold and used class of drugs in a variety of ailments and there have been significant flaws in the use of antibiotics (Calva, 1996; Anyanwu& Arigbe-Osula, 2012). From the literature published so far on antibiotic use in developing countries, major themes have been highlighted from the patterns of use, and these factors are thought to impact greatly on the rising burden of antibiotic resistance in developing countries.

1.6 Inappropriate prescribing

There is generally a high level of antibiotic prescribing in the hospitals across different developing countries. Studies on drug utilisation and antibiotic use have continuously reported values higher than the WHO recommendation of 20% - 26% encounter with antibiotics. Percentage encounters with antibiotics greater than 50% have been recorded from different studies in Ethiopia, Nigeria and in Ghana (Odusanya, 2005; Desalegn, 2013). Some studies have identified factors that may contribute to overprescribing of antibiotics to include poor pharmaco-therapeutic knowledge, perceived patient demands, absence of guidelines/ policies, economic incentives more in the community pharmacies (Akinyedanu and Akinyedanu, 2014), fear of bad clinical outcomes and poor laboratory investigation services (Radyowijati and Haak, 2003).

In a study in Yemen, more than half of antibiotic prescriptions were without diagnosis and none of the antibiotic prescriptions included in the study had a sensitivity test result (Al Akhali *et al*, 2013). Again, in a cross-sectional study carried out in three developing Asian countries, Yemen, Saudi Arabia and Uzbekistan, 40% of antibiotics were prescribed for cough and 34% were for influenza (Belkina *et al*, 2014).

1.6.1 Over-the-counter sale and Self-medication

It has long been estimated that about two-thirds of global antibiotic sales occur in the community settings and without any prescription (WHO, 2004). This practice of over-the-counter sale of antibiotics without medical prescriptions is more pronounced in low and middle-income countries. Almost all the classes of antibiotics are freely available for sale without a prescription in developing countries, and the penicillins are mostly purchased. The lack of regulations or the poor implementation where regulations exists is a motivating factor for the continuous over-the-counter sale of antibiotics. Other factors influencing the use of antibiotics for self-medication in developing countries include easy access to antibiotics, saves time by avoiding the long queues and delays in hospitals, and less costs as other hospital charges are avoided (Olayemi Olayinka & Musa, 2010; Ekwochi *et al*, 2014 and Donkor *et al*, 2012). This practice will limit clinical efficacy, favour self-medication with antibiotics and ultimately increase the emergence of antibiotic resistant bacteria**.** It is evident that this practice of self-medication with antibiotics cuts across culture, gender, race, health and social status, educational level and occupation (Awad *et al*, 2005). Community pharmacists are now seen as retailers and businessmen as they easily hand out antibiotics without prescriptions for economic benefits rather than rationally dispense antibiotics as professional healthcare providers in the primary care (Akinyedanu and Akinyedanu, 2014). There is need for the implementation of strict regulations and policies to address the sale of antibiotics without a prescription in developing countries. However, due to poor access to healthcare in these settings, a complete ban of over-the-counter sale of drugs may have higher risks than the immediate benefits to the citizens.

In LMICs, self-medication with antibiotics has been found to be of high prevalence and is thought to be motivated by easy access to antibiotics, no regulations, cheap costs, and influence from friends and family, shortages in healthcare services /professionals, etc. The main sources of antibiotics used for self-medication are the community pharmacies and patent medicine stores, other identified sources include family and friends, and remains from previous prescription (Osemene and Laminkanra, 2012).

1.6.2 Antibiotics availability

Due to the high prevalence of infectious diseases in developing countries, access to appropriate therapy is vital. There are often cases of drug stock outs in the general public hospitals and clinics. Two secondary analyses studies (Lee *et al*, 2014) and (Cameron *et al*, 2008) looked at availability of medicines and access to antibiotics in LMIc's. Lee *et al*, 2014 found regional availability of 15 medicines on the WHO essential medicine list, (27% of which were antibacterial) was at 29.4% in Africa. Availability of antibiotics is generally higher in the private sector compared to the public sector in developing settings. Public sector availability is consistently low due to a range of factors including poor compliance to national medicines list and inadequate incentives for maintaining stocks. The connection between antibiotics procurement prices and availability most strongly affects low-middle income residents as the public sector is often their only source of antibiotics. In the WHO AFRO region, a common antibiotic like ciprofloxacin had private sector availability of 93.2% which is about double that of public sector availability at 45.2% (FMoH Nigeria, 2006). Availability of medicines also differ between the Innovator Brand (IB) and Lowest Priced Generic (LPG) even in the private sectors that records higher availability of medicines than the public sectors. See Figure 1.4 below.

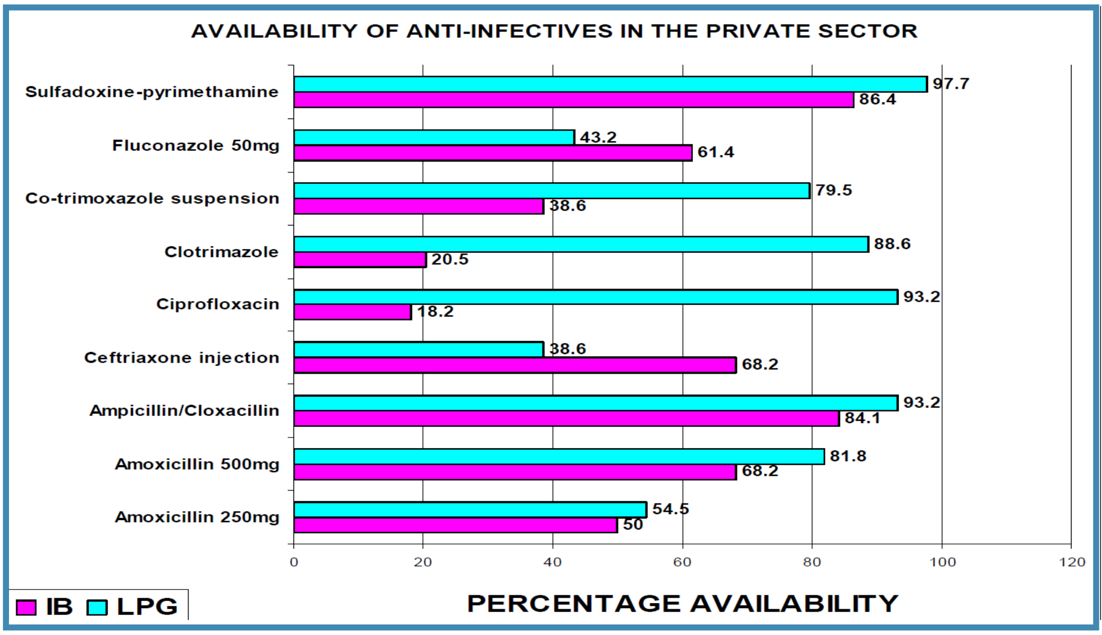

Figure 1.4: Availability of innovator brands versus lowest priced generics of common antimicrobials in Nigeria (FMoH, Nigeria, 2006)

Results from the Lee *et al*, 2014 review showed that first line injectable antibiotics used to treat neonatal infections have low availability in Africa, which is a concern because the region still suffers a significantly high rate of infant mortality due to infectious diseases (Lee *et al.*, 2014).

1.6.3 Antibiotics costs and affordability

In developing countries, antibiotics could be up to fourteen times more expensive than international prices. A study assessed the relative cost of antibiotics for in patients in a tertiary setting and found that almost all the antibiotics assessed were more expensive than the international reference prices (Arute *et al*, 2011). This is especially alarming because a significant amount of the population in developing settings live below the poverty line of $2 a day and antibiotics are still relatively beyond the reach of over half the population. Cost, as a factor of accessibility needs to be addressed by the government and health policy makers to maximise rational use and minimise AMR.

A Nigerian study explored the influence of health insurance scheme on the patterns of drug prescribing in a tertiary care setting. They found out that patients who pay out of pocket were less able to afford antibiotic therapy for their infectious diseases as those patients covered under the National Health Insurance Scheme (NHIS) were found to receive more antibiotics than those who pay for their medicines out-of-pocket (Fadare *et al.,* 2015).

1.6.4 The burden of antibiotic resistance in developing countries

Bacterial resistance significantly increases healthcare costs, mortality and morbidity while decreasing national productivity and economic output, and this impact is exacerbated in developing countries (Founou *et al.,* 2017). The WHO reports that 45% of deaths in Africa and South-East Asia can be attributed to multi-drug resistant (MDR) bacteria (WHO, 2014).

As high as 95% of adults in India, Egypt and Pakistan carry bacteria that are resistant to β-lactam antibiotics such as the carbapenems, considered to be one of the last resort antibiotics (Kumarasamy *et al.,* 2010). A contributory factor to this will be high rates of over-the-counter availability of carbapenems in these countries. In Nigeria, some studies suggest that as much as 88% of *Staphylococcus aureus* infections cannot be treated with methicillin, and the prevalence rates of Methicillin Resistant *Staphylococcus aureus* (MRSA) reported is between 21-40% of population (Fayomi *et al.,* 2011). Drivers of increasing antibiotic resistance in developing countries include inappropriate prescribing of antibiotics, over-the-counter sale and self-medication practices, poor infection, prevention and control measures, poorly enforced regulations and the lack of systematic surveillance data. This paucity of data on the actual situation of national antibacterial resistance rates in most resource poor settings limits implementation effective control measures and stewardship programmes.

1.7 Improving antibiotics use in developing countries

Most of the evidence on the effectiveness of interventions in improving use of medicines comes from studies conducted in developed countries. Only few studies have been carried out in developing countries and directly applying these interventions from these developed settings with highly advanced medical practice is unlikely to yield similar results as other factors may interfere in the developing settings. However, some of the interventions already implemented in some resource poor settings are discussed below:

1.8 Educational and training programmes

Most interventions targeted at improving antibiotic use and prescribing are educational in nature. Continuing education, antibiotic seminars and workshops can serve as a useful opportunity in educating antibiotic prescribers, pharmacists, nurses and other stakeholders in antibiotic use in developing countries. In Zambia, continuing education for prescribers resulted in patients being prescribed antibiotics less frequently at intervention centres (34%) when compared to control centres (42%), there was also marked improvements in drug choices and dosing. In Indonesia, one-on-one educational interventions and seminars for medical prescribers reduced antimicrobial prescriptions by 17 (Santoso, 1996). Educational programmes in Thailand led to a 24% reduction in antibiotic prescribing plus significant reductions in antibiotic resistance and costs (Apisarnthanarak *et al*., 2006).
However, in a review by WHO on the interventions to improve medicines use, it was found that providing education alone for prescribers had little overall impact (<10%) in improving use of medicines. Whereas when used in combination with other interventions (multicomponent interventions), use of medicines improved by more than 20%-30%.

1.8.1 Formulary restrictions and antibiotic policies

The first line antibiotics can be prescribed by all doctors and the restricted choice antibiotics can only be prescribed after consultation with a higher authority like the infectious disease consultants or one of the antimicrobial team representatives. On the other hand, only designated experts can prescribe the reserved antibiotics. There has always been a debate as to whether antibiotic policies are effective in regulating the use of antibiotics and curbing the increase in resistance rates. However, some studies have been able to demonstrate the impact of antibiotic policies in reducing antibiotic use and show the corresponding effects on reducing resistance rates (Saez-llorens *et al*, 2000; Boyles *et al*, 2013 and Xiao *et al*, 2013;). In China, introducing formulary restrictions in their antibiotic policy, led to reduction in antibiotic sales from 25% to 17%, and also the amount of antibiotic drugs in patients' prescriptions reduced from 68% to 58% (Xiao *et al*, 2013).

1.8.2 Stewardship programmes

While antibiotic stewardship programmes has shown effectiveness in improvements to antibiotic prescribing in developed settings, most of the interventions are not directly applicable to developing countries owing to differences in healthcare systems and other local factors. The evidence of implementation and effectiveness of antibiotic stewardship programmes in developing countries is limited. However some of these initiatives both at the international and local levels are potentially feasible in LMIC's with contextualisation (Cox et al., 2017).

1.8.3 Barriers in implementing antibiotic stewardships in developing countries

Major issues stand against the full implementation of antibiotic stewardship programmes in developing economies. The health systems in developing countries are in a transitional stage and may not be sufficiently prepared to take on newly emerging issues in infectious disease management. A few studies have identified barriers in the implementation of antibiotic stewardship programmes in developing countries. In India, stewardships are not available in over 50% of the hospitals; common barriers identified in India include lack of funds, human resource and manpower, lack of information and technology, higher priorities and prescriber opposition (Mani, 2014). Other barriers highlighted in implementing antibiotic stewardships in hospitals include lack of appropriately trained personnel such as infectious disease physicians and pharmacists, no additional compensation or remuneration for the added responsibility, lack of funding and loss of physician autonomy in making clinical decisions as there is a perceived antagonism from colleagues in other specialties (Drew, 2009).

In majority of developing countries, all the barriers mentioned above come into focus in addition to poorly developed healthcare systems, paucity of data on the status of antibacterial resistance, lack of infrastructure, lack of technology such as expert diagnostics and little allocations to healthcare in national budgets. Also, the lack of teamwork efforts among the different professionals in healthcare delivery comes into play.

1.9 Overcoming these barriers

Attempts to overcome these barriers will include education and training for prescribers and other health professionals, awareness and enlightenment campaigns for health administrators and the government in a bid to reorder priorities, increased employment for health staff to strengthen workforce and training of current employee on infectious disease management, provision of modern diagnostic tools and laboratories, conducting research in the area which will provide essential information on current status and also inform future decisions to improve practice. Increasing funds and budg*et al*location for healthcare is also vital in facilitating easy implementation of the interventions.

The issue of rising antibiotic resistance is obviously a huge healthcare burden in developing economies. The healthcare systems are not fully developed to tackle the persistent increase in antibiotic resistance. Major factors causing the increase in antibiotic resistance in developing countries include over prescribing of antibiotics, massive over the counter sales of antibiotics without a legal prescription and self-medication with antibiotics. Other factors that aggravate this burden include the availability and use of fake and substandard antibiotics and the continued use of antibiotics in animal and livestock production. Governments should respond to the issue of antibiotics resistance in the developing world as a healthcare priority and funds available to support the needed stewardships programmes, training of specialist personnel and other resources needed like improved laboratory diagnostics to address the problems of antibiotic resistance.

1.10 Antibiotics use in Nigeria

Healthcare in Nigeria is provided by both public and private sectors. The public sector include the government owned hospitals, while the private sector include specialist hospitals and clinics run by individuals, companies and other co-operate bodies. Health services is available from the three levels of care; primary, secondary and tertiary. Cost of health care in Nigeria is mostly financed through out-of-pocket payments as the National Health Insurance Scheme (NHIS) is yet to be fully implemented across the country. The Nigerian health systems continues to face many challenges including poor financing, shortage in skilled professionals, poor access to good quality medicines and lack of other infrastructure and resources.

Challenges with antibiotics use in Nigeria have been identified that are currently promoting the spread of various strains of resistant bacteria. These challenges are due to a complex mix of factors in the healthcare delivery ranging from the healthcare settings to the different stakeholders involved in service delivery such as the health professionals, drug manufacturers, the government and patients (Chukwuani *et al.,* 2002). Some of these factors are discussed in the sections below.

1.11 Irrational prescribing

Irrational prescribing of antibiotic has been documented in several studies in different parts of Nigeria. There is generally a high level of antibiotic prescribing seen across the three levels of healthcare in Nigeria (Odusanya, 1999, Iliyasu *et al.,* 2015). The WHO recommends a percentage encounter for antibiotics (PEA-percentage of patients receiving antibiotics in their prescriptions) to be 20-26%. The highest percentage of antibiotic prescriptions is seen in the secondary care levels. The tertiary levels of care have lower antibiotic prescriptions with some within the WHO recommendations. Not many studies have been carried out in the primary care settings; however antibiotic prescribing seemed to be quite high even in primary care settings with 50.1% PEA reported in one study retrieved (Babalola *et al.,* 2011). Table 1.4 below illustrates the findings. Several studies have documented PEA's ranging from above 50% to almost 100% in the secondary care settings. The southern part of Nigeria also seemed to have higher antibiotic prescribing than in the Northern region with the highest five readings from the southern regions.

Table 1.4: Percentage Encounter with Antibiotics (PEA) in different locations across Nigeria

Location	Level of Care	PEA (%)	Setting	Authors and Year
South-West	Secondary	96.7%	In-patients	Chukwuani *et al.,* 2002
South-South	Secondary	75.0%	Out-patients	Erah *et al.,* 2003
South-West	Secondary	68.9%	Out-patients	Akinyede *et al.,* 2000
South-West	Secondary	55.0%	Out-patients	Odusanya, 2005
South-South	Secondary	54.2%	Out-patients	Isah *et al.,* 1995
North-Central	Tertiary	51.0%	Out-patients	Enato and Chima, 2011
South-West	Primary	50.1%	Out-patients	Babalola *et al.,* 2011
South-West	Primary	44.2%	Out-patients	Odusanya, 1999
North-West	Secondary	43.8%	Out-patients	Tamuno, 2011
North-West	Tertiary	34.4%	Out-patients	Tamuno & Fadare, 2012
South-West	Tertiary	23.0%	Out-patients	Eze & Olowu, 2011
North-Central	Tertiary	13.0%	Out-patients	Akande & Ologe, 2007

Overall, some factors that influence overprescribing and poor prescribing in antibiotics use in Nigeria may include poor pharmacotherapeutic knowledge, perceived patient demands, absence of policies, economic incentives, fear of bad clinical outcomes and poor laboratory investigation services as have been reported in similar resource poor settings (Radyowijati and Haak, 2003).

1.11.1 Over-the-counter sale of antibiotics

The practice of over-the-counter sale of antibiotics is more pronounced in and low and middle-income countries. It has been reported in India, Pakistan and China (Duong *et al.,* 1997; Xiao *et al.,* 2013; Salunkhe *et al.,* 2013). In Nigeria, almost all classes of antibiotics are freely available for sale over-the-counter even without a prescription**.** This is very common in the community pharmacies and is largely due to the lack of regulations and deficiencies in quality of current professional practice. Anecdotal evidence suggests that community pharmacists tend to easily hand out antibiotics without prescriptions for economic benefits rather than rationally dispense antibiotics as professional healthcare providers in the primary care. Of course, it would be better if complications wrought by antibiotic-resistant bacteria did not happen. Howbeit, this practice has some benefits mostly in developing countries as it provides immediate primary healthcare needs in the community. But by restricting the availability of antibiotics, especially in middle to low income countries like Nigeria, where obtaining a doctor's prescription is not readily available and even where available can be very costly and time-consuming (Enato and Uwaga, 2011), this would also cause more people to die who might have lived.

1.11.2 Self-medication with antibiotics

Findings from studies in developing countries reveal that 60-80% of health-related problems are treated through self-medication (Awad *et al.,* 2007 and Abay *et al.,* 2010). Self-medication with antibiotics has been identified by various studies as one of the main forms of irrational use of antibiotics in developing countries and is a leading cause of antibiotic resistance. Prevalence of self-medication with antibiotics among tertiary level students is as high as 70% in Ghana (Donkor *et al.,* 2012), 79.5% in Sudan (Awad *et al.,* 2007), 70.66% in India (Patel *et al.,* 2012). In Nigeria, antibiotics self-medication has been reported in various regions and is thought to be motivated by easy access, no regulations, cheap costs, shortages of healthcare services /professionals, etc. Antibiotics have been used as self-medication drugs for menstrual symptoms (Sakpota *et al.,* 2010), skin, genitourinary and respiratory tract infections (Olayemi *et al.,* 2010), and the management of diarrheal diseases in children by the parents (Ekwochi *et al.,* 2013).

1.11.3 Lack of antibiotic guidelines/policies in Nigeria

Given the evidence on antibiotics misuse in Nigeria, and the consequent increase in antibiotic resistant bacteria, more practical steps are needed to improve prescribing practices. It is still not clear as to whether antibiotic polices exist in practice in Nigeria or not. If these have been formulated, are physicians and other healthcare workers compliant or not? A study was carried out on the determinants of physician's antibiotic prescriptions in Nigeria and found out that 97% of physicians prescribe antibiotics frequently, of which, 93.9% is based on their clinical judgements, 87.8% based on experience, and over 70% based on senior colleague's decisions. There was no place for guidelines and policies in the decision process when prescribing antibiotics. The authors concluded that there was no evidence for existence of institutional policies regarding antimicrobial therapies (Ogunleye and Ogunleye, 2012).

In Nigeria, interventions are needed to control antibiotics use and the question now is "***how"*** can this be done? A very key step in optimising the use of antibiotics in Nigeria will be to regulate the current antibiotic prescribing practice with policies. Studies that looked into antibiotics use have recommended the implementation of local and national policies on antibiotics use in Nigeria. Several professional societies have also issued statements to reduce the use of antibiotics in Nigeria by means of strict antibiotics policy. These policies can act as a working document for infection control groups and also serve as the frame work on which antibiotic stewardship programmes can be developed. A lot of national policies on antibiotic use have been issued in Europe and in the United States. These could be adapted and adequately modified to suit the Nigerian setting as local issues are to a large extent addressed by local solutions.

The Provost of the College of Medicine, University of Lagos, Professor Folasade Ogunsola has urged the Nigerian Federal Government to introduce a national policy on antibiotics use and prescribing in a bid to curb antibiotic drug misuse. Delivering a paper titled, 'Apocalypse Now: A Call for a Coordinated National Response to Antibiotic Resistance', she said *"At present, no public hospital in Nigeria has a fully functional infection control programme* *or antibiotic stewardship programme*," (Swank Pharm® news, 2014). Until now, not many studies have looked at the availability and use of antibiotics policy in Nigeria or the barriers to implementing these policies in Nigeria.

1.11.4 Wide spread use of antibiotics in animals and livestock

The use of antibiotics in animal rearing has been documented in different settings and locations in Nigeria. Antibiotics are continually used in poultry and other livestock for prevention of infectious disease, treatment and even fattening which has contributed to increased resistance rates (Apata, 2009).

Antibiotics are given in sub-therapeutic levels usually mixed with the animal feed to promote their growth and prevent disease. This leads to selection pressure of the bacterial strains that become resistant to the antibiotic. A high amount (69.74%) of selected sample of edible beef placed for sale in an abattoir in Nigeria was found to contain antibacterial residues (Olatoye and Ogundipe, 2009).

In July 2005, the Food and Drug Administration (FDA) finally withdrew its approval for the use of fluoroquinolone antibiotics in poultry due to concerns on the spread of antibiotic resistant bacteria to humans from animal foods. Despite this ban, fluoroquinolone antibiotics are the most common class of antibiotics still used in poultry in Nigeria (Alo and Ojo, 2007; Ogunleye *et al.,* 2008; Oluwasile *et al.,* 2013;). Reducing the use of antibiotic drugs in Agriculture is very important today because the issue of antibiotic resistance in humans cannot be effectively controlled when resistant genes are still being transferred through food intake.

1.11.5 Antibiotic resistance: The burden in Nigeria

In Nigeria, antibiotics are the most widely used class of drugs in a variety of ailments and there have been significant flaws in the use of antibiotics (Anyanwu and Arigbe-osula, 2006). A number of studies have documented irrational prescribing of antibiotics (Olayemi *et al.,* 2006; Akande *et al.,* 2009). Also, of interest is the high rate of self-medication with antibiotics (Osemene and Lamikanra, 2012; Olayemi *et al.,* 2010; Akinyede *et al.,* 2011), poor adherence to course of antibiotic therapy (Igbeneghu, 2013) and the over-the-counter/ non- prescription sale of antibiotics in Nigeria (Akinyandenu and Akinyandenu, 2014). All of which are contributing factors to increasing antibiotic resistance.

The initial reports on antibiotic resistance in Nigeria came in the 1970's and presently, there are reports from all over the country of antibacterial resistant strains. Some studies suggest that as much as 88% of *Staphylococcus aureus* infections cannot be treated with methicillin, and the prevalence rates of methicillin resistant Staphylococcus *aureus* (MRSA) reported is between 21-40% (Fayomi *et al.,* 2011) (See Table 1.5).

Table 1.5: Prevalence rates of methicillin resistant Staphylococcus aureus (MRSA) in Nigeria

Sn	Region	Isolates/Samples	Prevalence	Authors and year
1	South-south	Pus, wounds and swabs	79%	Samson & Anthony 2013
2	North	Wound isolates	75%	Udobi *et al.,* 2013
3	North central	Urine samples	69%	Onanuga *et al.,* 2005
4	South	Clinical samples	38%	Akande 2008
5	West	In-patient specimen	31%	Fayomi *et al.,* 2011

However, there is paucity of data on the situation of national antibiotic resistance rates in Nigeria. This is likely due to methods not being standardised and individual studies used different parameters for measurement. Also, Nigeria has no data yet on national consumption of antibiotics using the World Health Organisation (WHO) recommended Anatomical Therapeutic Chemical classification of Defined Daily Dose (ATC-DDD) methods of consumption estimation or other internationally recognised methods of measure.

1.12 Antibiotics use in Nigeria: The future

From the literature reviewed on antibiotics use in Nigeria, there has been inappropriate use of antibiotics documented as irrational prescribing in hospitals, over-the-counter sale and self-medication with antibiotics poor implementation of treatment guidelines and high use of antibiotics in animal and livestock rearing. Based on these findings, recommendations like continuous education and training for prescribers, design and implementation of antibiotic prescribing guidelines, establishment of national/local antibiotic policies and setting up of antibiotic stewardships programmes/ infection control groups have been suggested. However, there is paucity of data so far on the implementation of these recommendations (Kamaldeen *et al.,* 2013; Ilayasu *et al.,* 2015; Oduyebo *et al.,* 2017).

1.13 Justification for the proposed research

The healthcare systems in Nigeria still has a lot of challenges in practice that needs follow up to effectively carry out the WHO and other international recommendations to improve the use of antibiotics and to curb resistance.

Until now, the successful implementation of antibiotic stewardship programmes has not been documented anywhere in the country. This may be largely due to the fact that the Nigerian healthcare system at present may not support some stewardship strategies. The absence of antibiotic policies and guidelines will make stewardship programmes almost impossible to enforce, the health sector is also clearly understaffed. The healthcare workers on ground are currently burdened with excess workload and will not be ready to take on extra roles without additional incentives.

There is paucity of standardised data on the antibiotic consumption, usage and occurrence of resistance in Nigeria. This is because only few regions have data on antibiotics use studies and the methods used in these studies are not standardised thus making direct comparisons and compilations difficult. To facilitate national steps in designing stewardship programmes and policies, national data should be available for the entire country which can be obtained by conducting more antibiotic use studies in areas or regions where this data is lacking.

Also, the information on the feasibility, facilitators and the barriers in the implementation of antibiotic stewardship programs in Nigeria is limited. There is need for more research in this area to identify stakeholder's perceptions and the barriers that exists in implementing effective antibiotic stewardship programmes in Nigeria.

Policies support implementation of stewardship strategies therefore, for the effective implementation of antibiotic stewardships programmes in Nigerian hospitals, and other WHO strategies to improve the use of antibiotics, there is a need to put in place functional antibiotic policies in place. Practical steps for the design and implementation of policies should be taken.

The overall aim of this project is to identify potentially effective strategies and priorities for implementing antibiotic stewardship programmes in a typical LMIC hospital setting.

Chapter 2 LITERATURE REVIEW: ANTIBIOTIC PRESCRIBING PATTERNS IN NIGERIAN HOSPITALS

2.1 Introduction

Antibiotics are widely used in Nigerian hospitals across all levels of care, and some flaws exist so far in the prescribing patterns of antibiotics in different locations in the country. According to WHO, resistance to antibiotics is presently one of the biggest threats in global health. Globally, more than 50% of all antibiotics are prescribed, dispensed or sold inappropriately, while 50% of patients fail to take their antibiotics correctly (Nambiar, 2003 and Brahma *et al.,* 2012.) In developing countries, there has been reports that about 75% of antibiotics are prescribed inappropriately in hospitals (Nambiar, 2003). This is similar to findings of a study conducted in a secondary care hospital in Nigeria, where, antibiotic therapy was irrational in 74% of the antibiotic prescriptions studied (Odusanya, 2002). Therefore, a review of the existing literature on antibiotic prescribing patterns in Nigerian hospitals was conducted to assess the situation of antibiotic prescribing and to understand the factors that interplay in antibiotic prescribing.

Optimising antibiotic prescribing is one strategy that can help to address this growing concern of AMR especially in resource poor settings with higher infectious diseases burdens. In other to implement any feasible stewardship programmes, there is the need for a more detailed understanding of the antibiotic prescribing patterns in Nigerian hospital settings.

The research question adopted for this literature review is '***What are the patterns and determinants of antibiotic prescribing in Nigerian hospitals***'? This review explores what antibiotics are routinely used and what factors inform the decisions in antibiotic prescribing across Nigerian hospitals. It highlights the challenges for antibiotic prescribing and identifies the gaps in knowledge that is useful to design future research.

2.2 Method

2.2.1 Search strategy

Some bibliographic databases were searched for articles relevant to the research question. Databases searched were PubMed, Scopus, OvidSP platform for EMBASE and MEDLINE and some articles were also retrieved from google scholar citations. Websites of selected journals were also searched. These included the African Journals online and the International Journal of Pharmacy Practice. The key words used to conduct the search include "antibiotics", "antimicrobial", "prescribing", "prescription", "use", "pattern", "practise", and "Nigeria". Keywords were combined using the Boolean operators "OR" & "AND". Keyword truncation like antibiotic* and prescri* were used in some databases like PubMed to ensure all the related Medical Subject Headings (MeSH) terms were not left out in the search.

Relevant articles were selected from the initial hits. The references of selected articles were also hand searched for inclusion of more relevant articles and then duplicates were eliminated. Table 2.1 below shows the search results and the number of relevant articles retrieved in the different databases.

Table 2.1: Electronic database search results

Database	Number of hits	Relevant papers
EMBASE	368	11
PubMed	272	6
Medline	196	12
Scopus	302	9
Google scholar	294	7
Total	1432	**45** **-32** (duplicates) **+ 2** (from references) **=15** (Included for review)

2.2.2 Eligibility criteria

Studies were included in the review based on the main subject discussed and its relevance to the research question set for the review. Articles that studied antibiotic or antimicrobial prescribing anywhere in a Nigerian hospital were included. Studies reported in English language and carried out in hospital settings that used either retrospective review of patients' case notes and/or prescription sheets or prospective follow up of patients receiving antibiotics were also included. Studies reporting antibiotic use only in community settings or conducted in countries other than Nigeria were excluded. These inclusion/exclusion criteria were set to ensure all relevant articles were retrieved, see Table 2.2. As the findings will be used to develop a theoretical frame work for the current study as well as give guidance on objectives and methods to be employed and also to allow for easy comparison of findings.

Table 2.2: Eligibility criteria for studies included in the review

Factor	Inclusion criteria	Exclusion Criteria
Country	Nigeria	Countries other than Nigeria
Drug class	Antibiotics/Antimicrobials	Other drug classes
Setting	Hospital (Primary, Secondary and Tertiary care)	Community, population use
Subject	Use in human populations	Use in animals/ agriculture
Language	English	Languages other than English
Design	Descriptive, surveys and epidemiological studies	
Publication type	Original research article	Conference abstracts, news articles

2.2.3 Search results and selection process

The total number of papers identified from the database search with key words was 1432. The titles of citations were reviewed accordingly, and 954 studies were excluded as they did not meet the eligibility criteria set for the review, leaving 478 papers. From these 433 papers were removed after in-depth screening of the abstracts because they did not provide any information on the research question for the literature review. Out of the 45 papers left, 32 were further removed as duplicates and 13 retrieved. The reference list and citations of the 13 relevant papers were manually searched and 2 more relevant articles were added. This brings the final number of papers to 15 included for the review. Figure 2.1 below gives a flow chart of the literature search.

After the initial screening of titles for relevance, studies were included for the review based on the inclusion criteria. The abstracts of studies conducted in Nigeria were assessed, and those investigating antibiotic prescribing in a Nigerian hospital were selected. Others set in the communities or household settings were excluded. The abstracts were reviewed for outcomes measured and papers reporting the quantity, types of antibiotics prescribed, the indications and other related outcomes were included. Full copies of 15 papers that reported antibiotic prescribing patterns in hospitals in across different states in Nigeria and met the other inclusion criteria were retrieved.

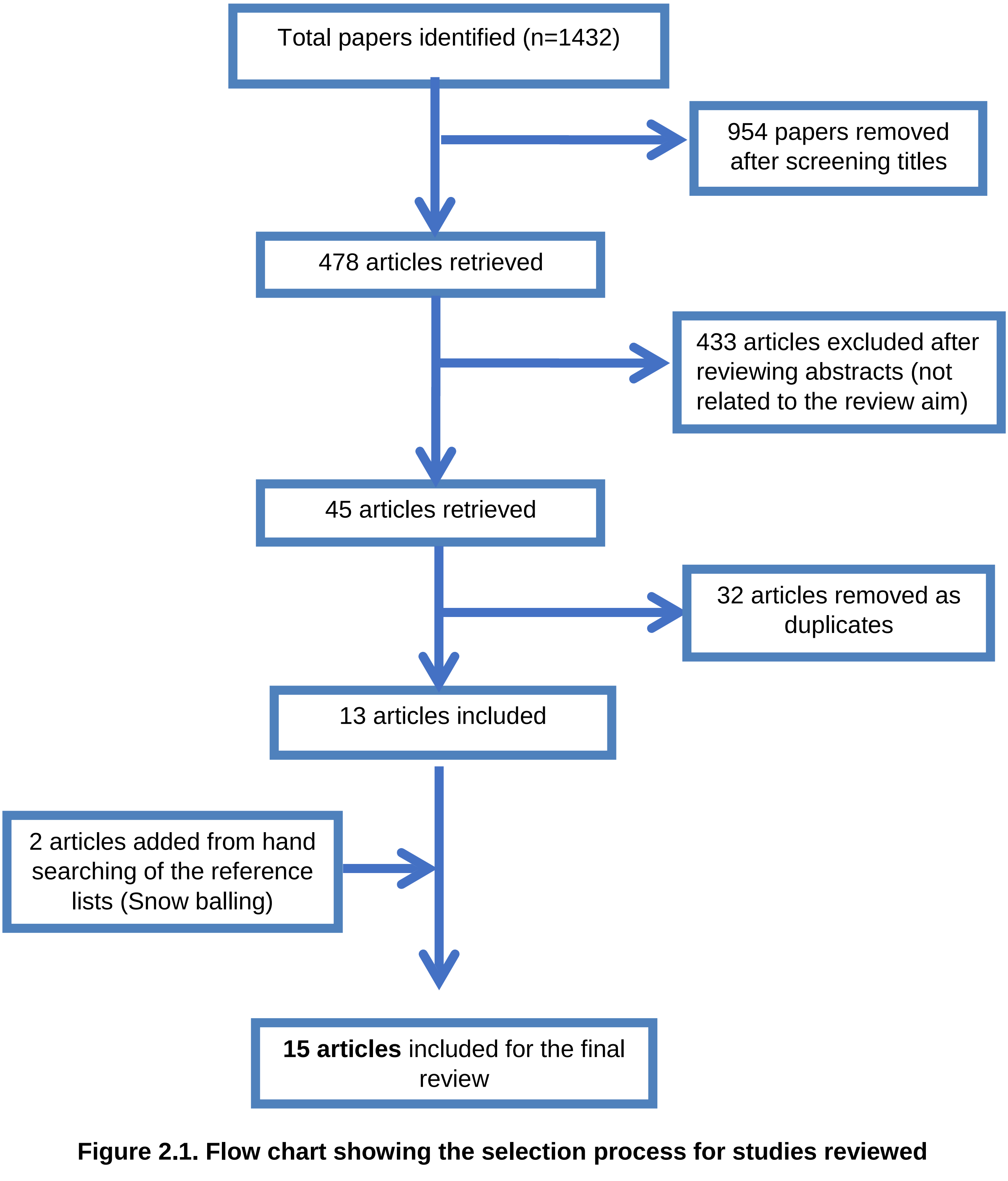

Figure 2.1. Flow chart showing the selection process for studies reviewed

2.2.4 Quality of studies

In order to facilitate critical appraisal and interpretation of results, the Critical Appraisal Skills Programme (CASP) tool and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist was used to assess reporting of outcomes in the studies included in the review (Von-Elm *et al*, 2007). Both tools were used to develop quality criteria for review of included studies.

The CASP tool was used to extract data and appraise each of the study, the methods were assessed for suitability to achieve the study aim and objectives. The processes were checked for any bias and the results were matched with objectives set. The strengths and weaknesses of the studies were also captured. Some of the critical appraisal reports of the studies are presented in appendix VII.

Based on STROBE checklist, items were scored as either 'adequately reported' or 'inadequately reported'. If an item on the checklist was not applicable for that study design, it was scored as 'not applicable'. See appendix VIII for the 22 items in the STROBE checklist. The fifteen studies selected were adequately reported according to the STROBE check list for reporting.

2.2.5 Data extraction

Data extraction was done at two levels. First, the abstracts were assessed and then, the complete research papers were examined. A data extraction form was purposely created from the CASP tool used to assess the quality of the studies. This made it easy to retrieve information from each study for further synthesis and presentation of the literature review results. Identity and explanatory variables retrieved from the selected papers include: the year the study was published and location in Nigeria where the study was carried out, study setting and level of care, study aims and design, outcomes measured, results, strengths and weaknesses.

2.2.6 Data synthesis

An inductive approach was employed to retrieve information, establish links between the research objectives of the studies and to summarise the findings. The outcomes measured in the studies were identified and listed and this was used to develop a framework for the underlying patterns of antibiotic prescribing patterns in Nigerian hospitals. Analysis was conducted based on the objectives of the studies. Similar objectives from the different studies were put together as themes e.g. studies that reported the amount and different classes of antibiotics were grouped together to obtain the theme: commonly prescribed antibiotics. Other themes identified from the results of the studies reviewed include common indications for which antibiotics are being prescribed, use of diagnostic tests, generic/brand name prescribing, appropriateness of antibiotic prescribing and costs/availability of the prescribed antibiotics. The themes identified were also discussed in relation to the level care of the different hospitals and the location to determine if these may be associated the outcomes.

2.2.7 Data analysis

A narrative approach was used to analyse the data generated from the review. Data were retrieved from each study from the outcomes measured using the CASP tool and data extraction forms developed. Studies measuring same outcomes were grouped together under the themes emerging from the studies' results. These outcomes were used to develop the themes for analysis and the results were then discussed together making reference to the settings, level of care and the geopolitical zone which is the location of the study site in the Nigeria.

2.3 Overview of selected studies

Fifteen articles that studied antibiotic prescribing patterns in Nigerian hospitals were included for the review. The studies retrieved are Chukwuani *et al.,* 2002; Odusanya, 2002; Akande *et al.,* 2009; Odili *et al.,* 2010; Mgbahurike *et al.,* 2010; Enato and Uwaga, 2011; Jimoh *et al.,* 2011; Olugbenga *et al.,* 2012;

Abu-Saeed *et al.,* 2013; Iliyasu *et al.,* 2015; Israel *et al.,* 2015; Nsofor *et al.,* 2016; Ogbonna and Eze*,* 2016; Oduyebo *et al.,* 2017 and Umar *et al.,* 2018.

Ten of the retrieved studies were conducted in tertiary care settings (Akande *et al.,* 2009; Mgbahurike *et al*. ,2010; Odili *et al.,* 2010; Jimoh *et al.,* 2011; Olugbenga *et al.,* 2012; Iliyasu *et al.,* 2015; Israel *et al.,* 2015; and Ogbonna and Eze*,* 2016; Oduyebo *et al.,* 2017 and Umar *et al.,* 2018.). Three were carried out in secondary care settings (Chukwuani *et al.,* 2002; Odusanya, 2002 and Abu-Saeed *et al.,* 2013); and two other studies were multicentre involving different hospitals at different care levels (Enato and Uwaga, 2011 and Olugbenga *et al.,* 2012).

The studies retrieved were conducted in different parts of the country. Each geo-political zone had at least one study which will therefore enable this review to provide some insight of the situation with antibiotic prescribing practices from different regions across the country. Twelve of the studies retrieved used retrospective methods to assess antibiotic prescribing practices from patient's medical notes or prescription sheets (Chukwuani *et al.,* 2002; Odusanya, 2002; Akande *et al.,* 2009; Odili *et al.,* 2010; Mgbahurike *et al*.*,* 2010; Enato and Uwaga, 2011; Jimoh *et al.,* 2011; Olugbenga *et al.,* 2012; Abu-Saeed *et al.,* 2013; Iliyasu *et al.,* 2015; Ogbonna and Eze*,* 2016 and Umar *et al.,* 2018). Two other studies used a point prevalence method to assess antibiotic prescribing by taking a snap shot of antibiotics use across different units or sites (Nsofor *et al.,* 2016 and Oduyebo *et al.,* 2017). Only one study used a cross sectional prospective method, studying patients' case notes who are on antibiotics (Israel *et al.,* 2015).

All these details of the studies retrieved, together with their aims, outcomes measured and final conclusions on antibiotic prescribing practices across Nigeria are summarised in Table 2.3 presented below.

Table 2.3: Summary of Studies assessing antibiotics prescribing in hospital settings in Nigeria							
Authors (Year)	**Location**	**Setting**	**Methods**	**Aim of Study**	**Outcomes measured**	**Conclusions**	**Recommendations**
Iliyasu *et al*., (2015)	Kano (North West)	Tertiary	A retrospective survey using patient case note for over 6 months	To examine the pattern of antibiotic prescription in a tertiary hospital	PEA, commonly used antibiotic, route, indication empirical prescribing	Inappropriate antibiotic prescribing.	Need for introduction of antibiotic guidelines
Akande *et al*., (2009)	Ilorin (North Central)	Tertiary	A retrospective study using prescriptions sheets the from pharmacy unit	To examine antibiotic prescription pattern and related costs in a Tertiary hospital.	PEA, commonly used antibiotic, route, availability, cost and generic prescribing.	High prescription of antibiotics.	Formulate antibiotic policies to promote rational prescribing
Odili *et al*., (2010)	Benin (South south)	Tertiary	A retrospective study using 406 patient case notes	To assess the prescribing patterns and antibiotic use	Route, commonly used antibiotic, generic prescribing availability, compliance to STG.	Poor generic prescribing and compliance to STG.	Establish restrictive guide to antibiotic use.
Jimoh *et al*., (2011)	Sokoto (North West)	Tertiary	A retrospective study using patient records	To study the pattern of antibiotic prescribing in a tertiary hospital	Indication, commonly used antibiotic, use of diagnostic test and common combinations	Only one fifth of antibiotic prescriptions used a diagnostic test of only less than half (40%) of which the results was used	Formulate antibiotic policies and implement continuing education for prescribers.

						as a guide to prescribe.	
Israel *et al.*, (2015)	Uyo (South south)	Tertiary	A cross sectional prospective study using patients case note who are on antibiotics	To determine the use of antibiotics with specific focus on use of investigations as a guide to prescribing	Indication, use of diagnostic test, dose and duration, appropriateness of therapy.	Irrational us e of antibiotics, investigations was used in less than one fifth of prescriptions.	
Kamaldeen *et al.*, (2013)	Abuja (FCT)	Secondary	A retrospective review of prescription sheets containing antibiotic prescriptions	To assess the prescription pattern of antibiotics in a secondary care hospital	Commonly used antibiotic, route, generic prescribing and appropriateness based on frequency and duration.	High compliance to National drug policy and STG. Poor generic prescribing**.**	There is need for education of prescribers in that regard.
Odusanya (2002)	Lagos (South west)	Secondary	A retrospective study auditing prescribing data containing antibiotics	To investigate patterns of antibiotic prescribing and the rationality of antibiotic use	Indication, commonly used antibiotic and appropriateness of therapy.	Antibiotic use in this centre is largely irrational.	There is need for patient education, prescriber training, guidelines and improved diagnostic tools.
Chukwuani *et al.*, (2002)	Lagos (South west)	Secondary	A retrospective audit of patient's prescriptions	To describe current drug use practices at the centre and gather baseline data for the design of an	PEA, indication, commonly used antibiotic, use of diagnostic test, and occurrence of errors.	Appreciable gaps exist in the rational use of drugs.	There is need for a concerted continuing educational programme for healthcare

				intervention programme			providers, review of policies and establishment of hospital formulary and STG.
Mgbahurike *et al*., (2010)	Lagos (South west)	Tertiary	A retrospective study of patient's prescriptions	To identify prescribing patterns and antibiotic usage pattern in a Nigerian tertiary hospital	Average number of drugs per encounter (ANDPE), drug actually dispensed (DAD), Average number of antibiotics per encounter (ANAPE), PEA, use of diagnostic test	Antibiotics are often prescribed in the hospital and many prescribers base their diagnosis for antibiotic prescription on personal experience and prevalent disease.	The correct knowledge of antibiotic prescribing is evident but not followed in practice.
Enato and Uwaga (2011)	Port Harcourt (South south)	Multi-centre	A retrospective review of medical records containing antibiotic prescriptions in the different settings	To evaluate patterns of prescribing antimicrobials and self-medication practices	Commonly used antibiotic, indication, appropriateness of therapy, self-medication practice.	Inappropriate use of antimicrobial drugs by the public and health facilities.	Need for more studies on the subject to understand the public health implications.

Ogbonna and Eze, (2016)	Anambra (South East)	Tertiary	A cross sectional retrospective descriptive study of systematically selected prescriptions	To assess the prescribing patterns of cephalosporin antibiotics in two tertiary healthcare centres.	Adherence to generic prescription, classes of antibiotic prescribed, the reasons for prescribing and cephalosporin combination prescriptions.	There was non-adherence to generic prescribing and use of drugs from the essential medicines list.	This is an indication of irrational use of antibiotics which can lead to increase in bacterial resistance and treatment failure.
Olugbenga *et al.*, (2012)	Uyo (South south)	Tertiary	A descriptive retrospective study using patient folders to study the prescription patterns of antibiotics	To study the prescription patterns of antibiotics	Indications for antibiotic prescribing, antibiotic prescribing errors, commonly prescribed antibiotics and the patient population receiving antibiotics.	There were high prescription errors seen in antibiotics dosage formulations, high use of broad-spectrum agents.	The participation of pharmacists in clinical ward rounds is highly recommended to improve drug use safety.
Nsofor *et al.*, (2016)	Owerri (south East)	Multicentre	A point prevalence study conducted across nine hospitals	To describe the prevalence and characteristics of antimicrobial use in 9 major hospitals to provide data for improvements	Commonly prescribed antibiotics, common combinations and the indication for antibiotic prescribing, type of therapy for antibiotic prescribing.	The results dhow high rates of antibiotic use in the hospitals.	There is need to develop an effective antibiotic manage and surveillance programme and strengthen training for medical staff.
Oduyebo *et al.*, (2017)	Abuja, Ife Lagos	Multicentre (Tertiary)	A point prevalence	To describe the rate and characteristics	Commonly prescribed antibiotics,	The prevalence of antibiotic	The country needs to institute a

	and Zaria		survey conducted across all wards in four tertiary hospitals in Nigeria.	of antibiotic prescriptions in Nigeria.	indications for prescribing antibiotics, antibiotic prescribing by wards and quality indicators on antibiotic prescribing.	prescription in Nigeria is high, which is evidence that:	cohesive antimicrobial stewardship intervention programme.
Umar *et al*., (2018)	Zaria (North central)	Tertiary	A descriptive retrospective study assessing antibiotic prescribing from in-patient prescription orders	To investigate antibiotic prescribing and antibiotic use using the WHO core prescribing indicators	Commonly prescribed antibiotics, percentage encounter for antibiotics, availability of prescribed antibiotic, generic name prescribing, availability in the EDL and common combinations of antibiotic drugs.	The antibiotic drug prescribing was generally inappropriate compared with ideal standards.	There is need for continuous training and retraining on rational drug use, periodic monitoring and the use of treatment protocols in tertiary hospitals

2.4 Themes identified from the selected studies

Table 2.4: Emerging themes from the literature review

Themes identified from the selected studies
Commonly prescribed antibiotics
Common indications for antibiotic prescriptions
Use of diagnostic test and laboratory investigations in antibiotic prescribing
Generic/brand name prescribing of antibiotics
Appropriateness of the prescribed
Availability of prescribed antibiotics
Cost and affordability of prescribed antibiotics

2.4.1 Commonly prescribed antibiotics by class

Eleven studies documented the frequency of prescribing different classes of antibiotics. Of these nine studies, six studies reported penicillins to be the most commonly prescribed class of antibiotic (Akande *et al.,* 2009; Ogbonna and Eze*,* 2016; Odili *et al.,* 2010; Enato and Uwaga, 2011; Abu-Saeed *et al.,* 2013; and Umar *et al.,* 2018). Three others reported quinolones as the most commonly prescribed antibiotic class (Odusanya,2002; Jimoh *et al.,* 2011; and Israel *et al.,* 2015.) while Iliyasu *et al.,* 2015 and Oduyebo *et al.,* 2017 reported cephalosporin's as the commonly prescribed antibiotic class. All the studies reporting quinolones as the commonly used antibiotic had penicillins as the second most prescribed class.

This indicates the three major classes of antibiotics being prescribed in Nigerian hospital settings are the penicillins, cephalosporins and the quinolones. The level of care however had no relationship with the commonly prescribed class of antibiotics as the penicillins were mostly prescribed across the primary secondary and tertiary levels of care and the only multicentre study included in the review also reported penicillin as the highly prescribed class. Also, the location had no association with the class of antibiotic prescribed as penicillins were widely prescribed across all the geopolitical zones represented by the studies. The most commonly prescribed penicillin was found to be amoxicillin (Enato and Uwaga, 2011, Odili *et al.,* 2010; Abu-Saeed *et al.,* 2013; and Israel *et al.,* 2015). This may be due to cost reasons as amoxicillin is one of the cheapest penicillin antibiotics available. The commonly prescribed quinolone was found to be ciprofloxacin (Jimoh *et al.,* 2011, Odusanya, 2002). Both commonly prescribed classes of antibiotics are broad spectrum antibiotics of which over prescription of these will promote increase in resistance rates.

2.4.2 Common indications for antibiotic prescriptions

Seven studies in all reported common indications for which antibiotics were frequently prescribed. These are Chukwuani *et al.,* 2002; Odusanya,2002; Enato and Uwaga, 2011; Jimoh *et al.,* 2011; Olugbega *et al.,* 2011; Iliyasu *et al.,* 2015; Israel *et al.,* 2015 and Nsofor *et al.,* 2016. Six of these studies reported respiratory tract infections as the most common indication for which antibiotics were prescribed. Respiratory tract infections are wide ranging, some of which are viral infections that would not necessarily need an antibiotic therapy. Prescribing antibiotics in such cases is also an indication of inappropriate antibiotic use. Only Jimoh *et al.,* 2011, reported gastrointestinal infections as the condition that received the most antibiotic prescriptions. While gastrointestinal and genitourinary infections were the second and third most indications for antibiotic prescriptions respectively. All the studies reported use of antibiotics for non-bacterial illnesses. Malaria was recorded as the leading non-bacterial disease with the highest prescription for antibiotics (Jimoh *et al.,* 2011, Israel *et al.,* 2015, Nsofor *et al.,* 2016, Enato and Uwaga, 2011) this was closely followed by cardiovascular diseases mainly hypertension. One study reported prescription of antibiotic for diabetes even when the patient had no trace of an underlying infection (Israel *et al.,* 2015).

Table 2.5: Top three infectious and non-infectious diseases for which antibiotics were prescribed

COMMON INDICATIONS FOR ANTIBIOTIC PRESCRIPTIONS			
	Infectious diseases		Other non-infectious diseases
	Bacterial diseases	**Non-bacterial diseases**	
	Respiratory tract infections	Malaria	Arthritis
	Gastrointestinal infections	Fungal skin infections	Cardiovascular diseases
	Genitourinary infections	Retroviral diseases	Diabetes

2.4.3 Use of diagnostic tests and laboratory investigations in antibiotic prescribing

There was mostly limited use of diagnostic test results as guide to antibiotic prescribing in studies that assessed the use of laboratory test as an outcome measure. Nine studies investigated the extent to which diagnostic tests and laboratory investigations were a guide to prescribing antibiotics (Odusanya, 2002; Chukwuani *et al.,* 2002; Jimoh *et al.,* 2011; Iliyasu *et al.,* 2015, Israel *et al.,* 2015; Mgbahurike *et al.,* 2010**;** Odili *et al.,* 2010; Oduyebo *et al.,* 2017 and Umar *et al.,* 2018). In some studies, majority of the antibiotic prescriptions were written empirically without the use of laboratory tests results (Odili *et al.,* 2010; Iliyasu *et al.,* 2015 and Oduyebo *et al.,* 2017). Odili *et al.,* 2010 studied 406 case notes of patients in Benin City who received antibiotic prescriptions and in all of these, there was no diagnostic testing. In Kano, microbial culture and sensitivity tests results were available for less than one-fifth of the cases studied and not all cases with lab results were further reviewed with the test results obtained. However, it is of concern that a significant number of initial empirical antibiotic prescriptions even among the few later de-escalated were not according to the standard treatment guidelines (Iliyasu *et al.,* 2015). In a secondary care hospital in Lagos, only 4.2% of the inpatients using antibiotics had microbial culture and sensitivity tests carried out before prescribing the antibiotics as diagnostic services were not readily available (Chukwuani*et al.,* 2002). In another secondary care hospital in Lagos, sensitivity test was requested in only 6.0% of the total study population receiving antibiotic prescriptions (Odusanya, 2002). Israel *et al.,* 2015 reported that in a university teaching hospital in Uyo, Nigeria, laboratory investigations were requested and used as a guide in only 15% of all antibiotics prescribed in their study centre which is less than one fifth of the study population. Also, about one fifth (20%) of the study population in Sokoto, South-west Nigeria had laboratory investigations done, of which only less than half of such results were used as a guide for the antibiotic prescription (Jimoh *et al.,* 2011). This demonstrates that there is limited use of laboratory investigations as a guide to the choice of antibiotics being prescribed and the subsequent review of antibiotic therapy for inpatients across different Nigerian hospitals.

2.4.4 Generic prescribing/brand name prescribing of antibiotics

Drug utilisation studies in Nigeria have reported irrational prescribing and drug use, and very little or no interventions have been instituted to address this issue, an attempt to solve this problem by the government on a large scale was the implementation of the Essential Medicines List (EML). The EML contains a list of all essential medicines in the generic names that covers a wide range of conditions that must be available in hospital formularies for dispensing. The Federal Ministry of Health (FMoH) released the National Drug Policy (NDP) document that states all medicines should be prescribed using the internationally recognised non-proprietary or generic names (FMoH, 2005). However, a study report demonstrates that implementing the EML has not showed much impact in drug prescribing practices (Chukwuani *et al.,* 2011). Seven studies assessed the degree of prescribing antibiotics in generic form. They are Jimoh *et al.,* 2011; Iliyasu *et al.,* 2015, Odili *et al.,* 2010, Abu-Saeed *et al.,* 2013; Akande *et al.,* 2009; Ogbonna and Eze, 2016 and Umar *et al.,* 2018. The use of trade and brand names as opposed to generic names in antibiotic prescribing is common in antibiotics studies in Nigeria. Three studies reported higher brand name prescribing (Jimoh *et al.,* 2011, Odili *et al.,* 2010 and; Ogbonna and Eze, 2016). Two other studies, secondary healthcare facility in Abuja, Abu-Saeed *et al.,* 2013 and a tertiary healthcare in the north central region (Akande *et al.,* 2009) facility found no major difference between brand and generic prescribing of antibiotics. However, contrary to previous reports on generic and brand name prescribing of antibiotics, Iliyasu *et al.,* 2015 and Umar *et al.,* 2018 found a significant number (63.0% and 66.8% respectively) of antibiotic prescriptions to be in generic form. Majority of antibiotics prescribed in the studies were found in the essential medicines list and Kamaldeen *et al.,* 2013 and Umar *et al.,* 2018 recorded 100% and 95.5% of antibiotic prescriptions to be in the essential medicines list which is in line with recommendations of the Nigerian Drug Policy.

2.4.5 Appropriateness of the prescribed antibiotics/ compliance to guidelines

Antibiotic prescribing was found to be inappropriate in seven studies that measured appropriateness of the antibiotic therapy. These are Odusanya, 2002, Akande *et al.,* 2009, Enato and Uwaga, 2011, Jimoh *et al.,* 2011, Abu-Saeed *et al.,* 2013; Israel *et al.,* 2015; and Umar *et al.,* 2018. Appropriateness of antibiotic therapy was measured using different criteria in the different studies. Parameters used to determine appropriateness include compliance to treatment guidelines, use of diagnostic and sensitivity tests and absence of a bacterial infection. The criteria for judging appropriateness to therapy was unclear in one study (Odusanya, 2002).

Only one study measured the Prescribers' compliance to the Nigerian standard treatment guidelines in antibiotic prescribing and concluded that there was a wide variation between defined recommendations and the clinical use of antimicrobial agents (Odili *et al.,* 2010). Israel *et al.,* 2015 reported that antibiotics were prescribed for patients with conditions such as malaria, diabetes mellitus and hypertension without a documented indication of an underlying infection for antibiotic use. Also, drug-drug interaction was considered possible in 3.1% of antibiotic prescriptions in a tertiary care hospital in north central Nigeria (Akande *et al.,* 2009).

In a secondary care hospital in Lagos, antibiotic therapy was reported irrational in 74% of antibiotic prescriptions studied. The cases of irrational antibiotic prescribing were classified as wrong choice of antibiotic (55%), no indication for an antibiotic (40%) and dosage problems (5%). However, the author did not mention what standard or guideline was used to judge the appropriateness of therapy in the study (Odusanya, 2002). Another study conducted in Lagos also reported that in about 75% of antibiotic prescription cases, prescribers base their decision for antibiotic prescription on individual experience, disease prevalent in the community at the time and the signs and symptoms of the patients (Mgbahurike *et al*., 2010).

Enato and Uwaga, 2011, used selected physicians to assess the appropriateness of antimicrobial prescribing. This revealed that about one-fifth of the prescriptions studied (23%) were classified inappropriate. No attempt was made by the authors to verify the accuracy of the assessor's judgements, meaning inappropriate prescribing is more likely to be higher than reported as physicians are likely to be less critical of their colleagues or they may very well share the same prescribing habits (Enato and Uwaga, 2011). However, contrary to other findings, Abu-Saeed *et al.,* 2013 reported that 95% of antibiotics prescribed in a secondary care centre in Abuja, were appropriate in terms of frequency and duration of use, and there were also no drug-drug interactions or adverse drug reactions reported in antibiotic prescriptions in Sokoto (Jimoh *et al.,* 2011). From the studies reviewed antibiotic prescribing is generally inappropriate across different locations in Nigeria, even though the correct prescribing practices may be known this is not followed in practice.

2.4.6 Availability of prescribed antibiotics

The availability of required antibiotics is an important factor that affects antibiotic prescribing practices especially in LMICs where access to medicines is still a concern for healthcare delivery. Very few studies reviewed the availability of antibiotics prescribed in Nigerian hospitals. Two studies found (Abu-Saeed, 2013 and Odili *et al.,* 2010) assessed antibiotics availability. Abu-Saeed *et al.,* 2013 found out that all the antibiotics used in their study facility were in the essential drugs list and almost all of the prescribed antibiotics were available at the pharmacy unit as at the time they were prescribed. Odili *et al.,* 2010 also reported a high number (85.8%) of prescribed antibiotics being available in the hospital pharmacy for antibiotic dispensing.

However, there are differences in the level of availability between the public and private sector hospitals. One study found that the difference in Co-trimoxazole availability was high with private sector availability (88.6%) almost double that of public sector availability (45.2%). Ciprofloxacin, another antibiotic used to treat a wide range of infections, had a mean availability of 18.2% in the public sector but had a 93.2% availability when acquired privately (FMoH Nigeria, 2006). This indicates that the commonly used antibiotics are mostly available in the hospitals.

2.4.7 Cost and affordability of prescribed antibiotics

Two studies assessed the cost and affordability of antibiotics. One study (Arute *et al.,* 2011) assessed at the relative cost of antibiotics for in patients in a tertiary setting. The study found that antibiotic costs could be much more expensive in the hospital settings than the national agreed prices. They studied costs of fifteen different antibiotics and found that 80% of these were more expensive than the national reference prices. Without a comprehensive national health insurance scheme, this suggests antibiotic costs has implications on the antibiotics being prescribed, as patients may not be able to afford the medicines. In a study conducted in north central Nigeria, Akande *et al.,* 2009 it was also reported that the cost of antibiotics per prescription is relatively high. In their study, they reported the mean cost of all drugs on a prescription sheet is USD9.25, the mean cost of antibiotics on the prescription sheet is USD6.72. This means that about 72.7% of total costs of drugs on a prescription can be attributed to antibiotics (Akande *et al.,* 2009). Another study looked at the influence of health insurance on drug prescribing patterns in a tertiary setting in Nigeria. They found that patients covered under the National Health Insurance Scheme (NHIS) and those who paid ‘out of pocket’ encountered antibiotics 49.4% and 33.6% respectively. This implies patients who pay out of pocket are less able to afford antibiotic therapy (Fadare *et al.,* 2015).

2.5 Discussion of the literature review findings

The most prescribed class of antibiotics in Nigeria are the penicillins, of which amoxicillin alone or in combination with clavulanic acid was the most common antibiotic drug prescribed within the class. This is likely due to amoxicillin being cheap, readily available, having high efficacy and good safety profile (Abu-Saeed, 2013; Israel *et al.,* 2015). However, amoxicillin is a broad-spectrum antibiotic which covers a wide range of bacterial organisms and it's over prescription empirically compounds the situation of increasing antibiotic resistance.

The findings show a high rate of empirical broad-spectrum antibiotic prescribing in Nigeria. There was limited use of microbiological testing prior to antibiotic prescribing as documented in most studies. Ideally, selection of antibiotics should be done based on microbiological test results, bacterial sensitivity and on the prevalence of resistance in the local hospital (Jimoh *et al.,* 2011). This may be partly due to poor diagnostic facilities. Antibiotics were also prescribed for non-bacterial illnesses such as malaria, hypertension and diabetes, this suggests limited use of diagnostic testing, lack of established guidelines and high patient demands may have contributed to this. The presence of fever was found to increase the likelihood of prescribing antibiotics as some physicians tend to consider fever as a sign of bacterial infection which is not always the case (Odili *et al.,* 2010). Also, the lack of a national or local antibiotic prescribing guideline designed based on the local resistance patterns compelled some clinicians to use other guidelines such as the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) guideline on infectious disease cases. This may be misleading as resistance patterns differ from one country or continent to another (Iliyasu *et al.,* 2015).

The studies in this review show that in Nigeria, the use of generic names when prescribing antibiotics is low with a rather high of use of branded names instead. This has been linked to the high marketing strategy of pharmaceutical company representatives to hospitals, with frequent incentives and gifts to clinicians prescribing their brands. Also, pressure from patients on prescribers based on previous use of a particular brand has been linked to high prescribing in brand names (Odili *et al.,* 2010 and Jimoh *et al.,* 2011). Although the antibiotics being prescribed to a large extent was in compliance with the national EML.

Also, the prescribed antibiotics were mostly available for dispensing in the hospital's formulary or available for sale in community pharmacies. Cost of antibiotics per prescription is relatively high, antibiotics alone accounted for about 72.7% of total costs of drugs on a prescription (Akande *et al.,* 2009). The high rate of inappropriate antibiotic prescribing seen is greatly influenced by the lack of antibiotic guidelines and policies and also the limited use of microbiological tests and sensitivity results. Jimoh *et al.,* 2011 also mentioned lack of proper documentation of antibiotic use and prescribing to be a compounding factor.

From the studies reviewed, there is inappropriate prescribing of antibiotics and the patterns of antibiotic prescribing in the hospital are similar across the country. The reasons for poor antibiotic prescribing in Nigeria are multifactorial some of which are socioeconomic pressures, inadequate managerial systems, poor infrastructure, knowledge and attitude of healthcare providers. With the studies conducted so far on irrational prescribing of medicines and drug use in Nigeria, very little or no intervention has been implemented to solve the problem. The attempt made so far the by the government on a large scale was the development and implementation of the EML. This intervention had limited success and has still not addressed the issue of irrational drug prescribing (Chukwuani *et al.,* 2002).

The above findings have important public health implications in Nigeria. The main recommendations suggested to improve antibiotic prescribing so far include formulation and implementation of antibiotic policies and guidelines both at the national level and locally in the hospitals, continuous training and education for prescribers, improvement of laboratory and diagnostic services, monitoring and evaluation with routine audits for antibiotic prescribing and use within the hospitals. Cost savings is possible if restrictive antibiotic policies are implemented and prescribers are compliant with these policies (Ibrahim, 2004 and Akande *et al.,* 2009).

2.6 Limitations of the studies reviewed

The studies reviewed have sufficiently highlighted and discussed the main issues with antibiotic prescribing in Nigerian hospitals across different levels of care i.e. both in the secondary and tertiary care facilities in different locations of the country. A number of studies were conducted in only one unit or ward in the hospitals. This will not be providing a fair representation of all prescribers in the study setting. Some studies have very short duration of two or three months only. This will not capture any seasonal variations in antibiotic prescribing leading to a bias in reporting of commonly prescribed antibiotics. Some studies did not report using any form of pre-piloted data collection instruments to ensure uniformity of the data collected. This will impact on the reliability of the final results reported. Furthermore, there was no attempt to check the compliance to existing guides such as the standard treatment guidelines or the nationally accepted British National Formulary (BNF) for appropriateness. The study reporting appropriateness measured these using fellow prescribers who will be less critical of their peers leading to bias in the results provided. Finally, some studies failed to provide any practical recommendations to improve practice even when their study findings suggest significant flaws in the patterns of antibiotic prescribing in the study centres.

2.7 Conceptual frame work from literature review

The findings and evidence base from the literature reviewed has provided a conceptual frame work around which the proposed study will be built. With the emerging themes being the factors to be studied further to understand the issues raised clearly. These themes will be explored in this study. Figure 2.2 highlights these themes.

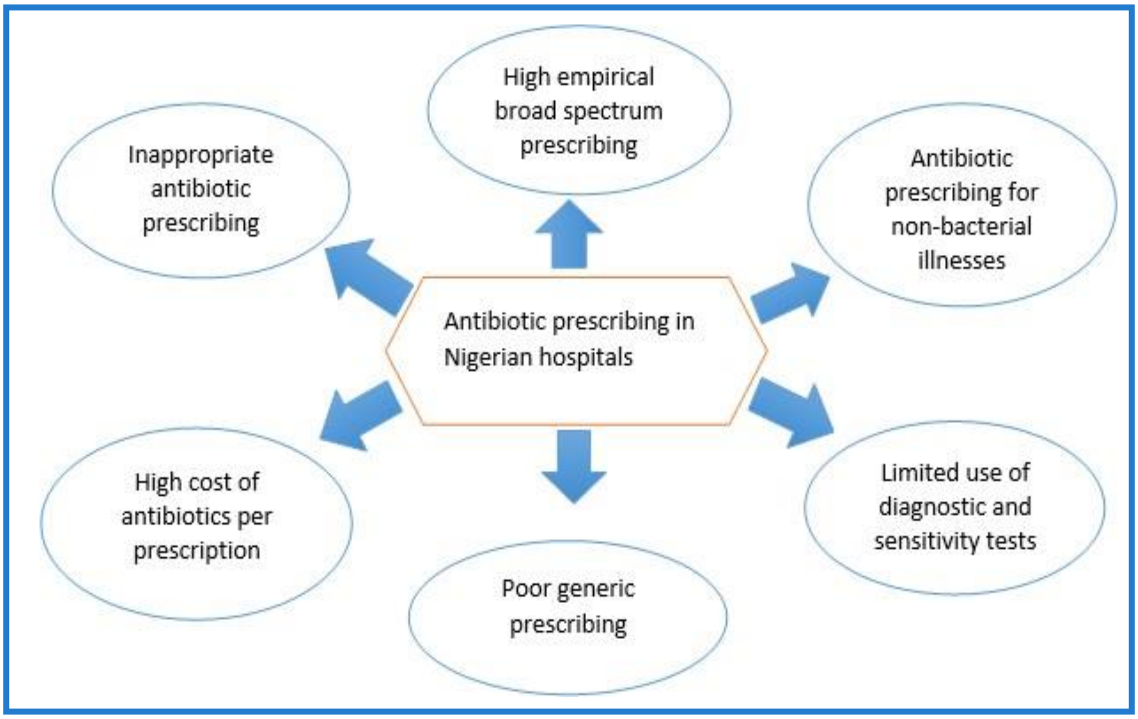

Figure 2.2. Conceptual framework from literature review

2.8 Justification and implication for current study

From the literature reviewed on antibiotics prescribing and use in hospital settings in Nigeria, there has been inappropriate prescribing of antibiotics documented as over prescribing of antibiotics, high empirical broad spectrum prescribing in hospitals, limited use of diagnostic and sensitivity tests, poor use of antibiotic policies and guidelines, poor generic prescribing. Based on these findings, recommendations like continuous education and training for prescribers, design and implementation of antibiotic prescribing guidelines, establishment of national/local antibiotic policies and setting up of antibiotic stewardships programmes/ infection control groups have been suggested. However, there is paucity of data so far on the implementation of these recommendations. There is also a need to assess the reasons for the inappropriate antibiotic prescribing patterns from the prescriber angle so as to determine what interventions will be feasible in addressing the issues discovered.

One of the first steps to improving the use of antibiotics in Nigeria will be to optimise the prescribing patterns in the hospitals. This is because a significant proportion of antibiotic prescribing in the hospital settings are still inappropriate and also, the hospital is a more controlled environment with a management structure in place to implement any improvement strategies as compared to the community settings. More research on this subject is needed to generate data that will help identify the next steps to improving antibiotics use in the local settings. Further research is needed to provide information on the following questions that will be useful for implementing feasible strategies that will improve antibiotic prescribing practices in the area.

- What is the current antibiotic prescribing pattern in the Niger Delta region?
- Are the recommendations from earlier studies being implemented and any improvements so far?
- What are prescribers' knowledge, attitudes and perceptions on antibiotic prescribing, resistance and the use of guidelines?
- What are the opinions of other stakeholders in the improvement of antibiotics prescribing and use?
- What forms of antibiotic stewardship programmes will be feasible and effective in the Nigerian health systems?
- How can these programmes be implemented with the available resources and manpower?
- What are the barriers to successful implementation?
- How can these barriers be addressed?

This study seeks to assess the antibiotic prescribing practice and patterns in the Niger Delta region of Nigeria as a needs assessment for the local setting, evaluate the knowledge, attitude and perceptions of prescribers and other stakeholders on the rational use and prescribing of antibiotics. And also, to make recommendations for interventions based on findings and consultation with stakeholders as a way forward to addressing the AMR situation in Nigeria and other LMIC's.

Chapter 3 PRELIMINARY FIELD WORK, AIMS & OBJECTIVES AND METHODS

3.1 Introduction

The purpose of this research is to assess the prescribing patterns with antibiotics, sample prescribers and other stakeholders' opinions on the current antibiotic prescribing patterns and to determine what interventions will be practical in improving antibiotic prescribing in the local setting. This chapter begins with the details of the preliminary data collection conducted to guide the research aims and specific objectives. It provides a summary of the research design employed, information needed to answer the research questions and how they were obtained. Detailed accounts of the location and settings involved, research sample and participants, organisation and analysis of data collected and the ethical issues around these are presented.

3.2 Preliminary fieldwork

The preliminary field work and initial data gathering was conducted in the early stages of this research. This was done to assess the current situation and to provide relevant contextual information about the local settings. This information obtained will be useful for developing the specific objectives for the proposed study.

3.2.1 Aims of the preliminary data collection

The aims of the preliminary data collection are:

1. To have a background understanding of the study settings and their situation with antibiotics use.
2. To guide and inform the aims and objectives of this current study
3. To inform the appropriate choices of population to be targeted for data collection
4. To provide basic information in addition to literature sources that will be used in the design of data collection forms and interview topic guides.

3.2.2 Methods of preliminary data collection

The methods employed for the preliminary data collection were mostly in the form of informal interviews. This was conducted in two phases. An initial informal face to face discussion interview was conducted in December 2014 with a senior pharmacist in one of the tertiary hospital settings. This was to get a general background understanding of the systems and practice pattern with drug prescribing in the area. The points gathered were then used as a guide to draw up questions for the second phase which was conducted through telephone interviews. Questions on antibiotic prescribing use, and monitoring were asked to get a background for the proposed study.

3.2.2.1 Settings

The data for the preliminary fieldwork was retrieved from hospitals in Bayelsa state located in the Niger Delta region of Nigeria. This is because the proposed study is to be carried out in hospitals in this area. Two tertiary and two secondary care hospitals were selected and included for the preliminary data collection.

3.2.2.2 Sampling strategy

A convenience non-random, purposive sampling was employed. This is because the goal for this preliminary work is to obtain general background information about the medicines use and prescribing practices in the settings. This information is needed to inform the objectives of the main study as the research will be in the same settings. The two main tertiary hospitals in the study location and two other secondary care hospitals were selected. The researcher purposely identified healthcare professionals involved with the prescribing and dispensing of antibiotics in the hospital settings. This was theoretically informed from the studies published earlier, hence one prescriber and one pharmacist each were contacted from the hospitals.

3.2.3 Results of the preliminary data collection

The data gathering that make up the preliminary data collection work was done in different ways at different times.

Firstly, an initial informal discussion interview was conducted with a senior pharmacist (JFE) in one of the tertiary hospital settings. Some background information was gathered. The summary of the discussion is;

- Antibiotics are mainly prescribed by doctors and dentists in the hospitals
- There is no specific antibiotic prescribing policy or guidelines.
- General treatment guidelines exist at the national level but the extent to which they are available for use and followed in the local hospital settings is not known.
- No form of antibiotics use monitoring or surveillance exists
- Antibiotics are procured from pharmaceutical companies directly and new brands are added based on clinical presentations from the companies
- An initial survey of antibiotics use patterns will be helpful and serve as a needs assessment for developing the study outcome measures.

Based on the data collected, a data collection form was designed to get specific information from the proposed study settings (See appendix II). The form was developed to retrieve information needed for designing the proposed research. This form was sent to identified contacts in the study settings via email. Completed forms were returned via email also. Brief phone calls were made by the researcher to centres not responding and to gather more information.

The questions asked about individual settings during these phone calls are given in the Table 3.1***:***

Table 3.1: Preliminary data gathering questions

SN	Questions
1	Is there a drug and therapeutics committee in the hospital?
2	Are there policy documents for prescribing medicines in the hospital?
3	Are treatment guidelines available for prescribers?
4	Are there specific antibiotic prescribing guidelines/policies?
5	Is there an infection control group?
6	Is there is formulary list of antibiotics available for prescribers?
7	Is there restricted use of some antibiotics (i.e. reserved antibiotics)?
8	What informs or guides the choices of antibiotics being prescribed?
9	Is there any monitoring or surveillance of antibiotics use and consumption?
10	Is there a trained infectious disease specialist in your facility?

Information retrieved from the different levels of healthcare delivery are presented below. They include responses from the tertiary care hospitals and the secondary care hospitals.

3.2.3.1 Tertiary care settings:

The following specific information was collected from the tertiary settings contacted:

- There is a drug and therapeutics committee and infection control groups in the tertiary care settings. However, no information was retrieved on their impact as regards antibiotics use in the hospitals.
- Prescribing patterns of antibiotics in these settings are not known and there is no monitoring or surveillance on antibiotics use and consumption. The prescribing physicians are aware of the existence of standard treatment guidelines and copies are available in only few consulting rooms the extent of compliance with these guidelines is not known.
- No hospital specific antibiotic prescribing guidelines or policy documents exist. Prescribing of antibiotics in these settings is mostly empirical as laboratory investigations are not carried out in most cases.

- Only the paediatrics units in one of the tertiary settings mentioned restricted use of imipenem and amikacin as reserve antibiotics, the other site has no practice of reserve antibiotics.

3.2.3.2 Secondary care settings:

In the secondary care settings, the following information was retrieved:

- There are no drugs and therapeutics committee or infection control groups in place.
- The prescribers are aware of the existence of the standard treatment guidelines, but this is not available in the consulting rooms for physicians when prescribing.
- There is no antibiotic policy document or prescribing guidelines. Hence antibiotics are prescribed mostly empirically and sometimes based on laboratory culture results.
- Antibiotics use or consumption is also not being monitored.
- In the secondary settings, the pharmacy unit makes a list of drugs in the hospital's formulary to guide the prescribers' choices.
- There were no reserved antibiotics in the secondary care settings.

3.2.4 Impact of Preliminary field work on the proposed study

The information retrieved from the preliminary data gathering has provided useful information for this proposed study. It served as a situation analysis and has given a clear insight as to the current practice systems in the study settings which now guide the aims and objectives for the proposed research work.

Firstly, the fact that the exact patterns of antibiotic use and prescribing is not known due to lack of monitoring and surveillance suggests that an initial survey of the antibiotic prescribing practice in these settings will be useful both as data for the hospital management and also serve as a needs assessment for developing strategies to improve antibiotic prescribing which is the second part of this study that was conceived based on the data obtained in the literature reviewed from other locations in the country.

Secondly, the information gathered the second phase of this study was used to determine prescribers' perceptions on the determinants antibiotic prescribing. The information retrieved here was then used to guide the target participants and also inform the interview topic guides and questions to include.

3.3 Aims and objectives for the proposed study

The main goal of this research work is to identify feasible and practical interventions to improve antibiotic prescribing patterns in the Nigerian hospital settings.

3.3.1 Broad aims

The broad aims for the proposed study include:

1. To assess the antibiotic prescribing patterns in the Niger Delta region of Nigeria.
2. To evaluate the knowledge and perceptions of prescribers and factors that influence prescribing of antibiotics.
3. To develop and propose a set of practical recommendations based on the study findings that will lead to improvement in antibiotic prescribing.

3.3.2 Specific Objectives

Based on the broad aims, the following specific objectives are to be achieved. Table 3.2 summarises specific objectives of this study and the methods to be employed in achieving the objectives.

Table 3.2: Study aims and objectives

Broad aims	Specific objectives	Population targeted
To assess the antibiotic prescribing patterns in Hospitals in the Niger Delta region of Nigeria.	1. To determine what antibiotic drugs/classes are commonly prescribed	Retrospectively, using data collection forms to extract information from patients' case notes.
	2. To identify the indications for which antibiotics are mostly prescribed	
	3. To explore the use of laboratory tests and treatment guidelines as a guide to the choice of antibiotics being prescribed	
	4. To assess the availability and costs of commonly prescribed antibiotics in the hospitals	Data collection forms with pharmacy prescription sheets and dispensing notebooks.
To evaluate the knowledge, attitude and perceptions of prescribers on the rational use and prescribing of antibiotics.	5. To explore prescribers' perceptions of the current situation with antibiotic prescribing in Nigerian hospitals	Use of semi-structured interviews With relevant stakeholders e.g. prescribers, healthcare providers and clinical and administrative heads etc.
	6. To identify the determinants of antibiotic prescribing practices	
	7. To explore prescribers' views on the availability and use of guidelines/policies in antibiotic prescribing	
	8. To explore prescribers' suggestions on strategies to improve antibiotic prescribing practices	
To determine feasibility of recommendations proposed to improve antibiotic prescribing.	9. To develop a set of recommendations from prescribers' suggestions and existing literature in similar settings	
	10. To identify and recruit the relevant stakeholders in the study area antibiotics use in for interviews.	
	11. To explore their perceptions and acceptability of the proposed recommendations.	

	12. To determine if the recommendations have been put in place or exists already in any form.	
	13. To identify the likely barriers in the implementation process of the proposed recommendations to improve antibiotic prescribing.	

The flow chart below gives an overview of the sequence in the proposed research study design (see below).

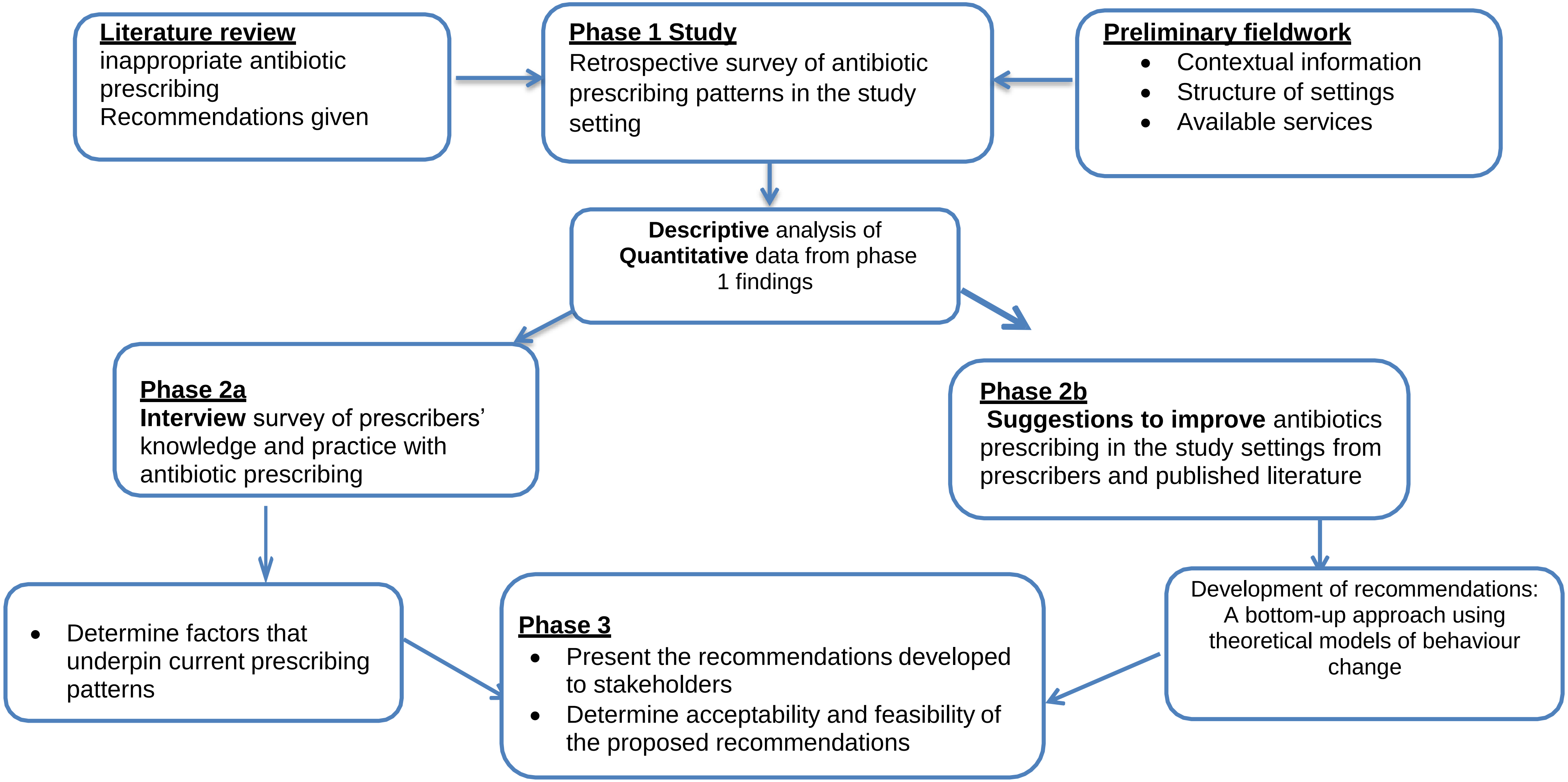

Figure 3.1: Overview of the sequence in the proposed research study design

3.4 Study design

With the problem of increasing resistance to antibiotics partly due to inappropriate use and prescribing in the hospitals, and the lack of established solutions in the local settings, this study adopts a bottom-up approach using theoretical models to assess the problems explore options of potentially feasible solutions. The bottom-up approach is particularly beneficial as it considers the local issues at the grass root level, and solutions are more likely to work as they are generated by parties directly affected.

A mixed methods design is employed for this study. Mixed methods in research is a form of research design for collecting, analysing and interpreting both quantitative and qualitative pieces of data (Tashakkori and Teddlie, 2003). The mixed methods are employed to give a broader view and a more robust understanding of the research problem.

There are four distinct models of the mixed methods approach and these include the convergent parallel design, the explanatory sequential design, the exploratory sequential design and the embedded design (Hadi *et al.,* 2012). Given the study aims and objectives, the explanatory sequential design is most appropriate and was adopted for this current study.

3.4.1 The explanatory sequential design of the mixed methods

This model involves two distinct phases. In the first phase, the quantitative data is collected, analysed and interpreted. This then guides the data collection for the qualitative phase of the research. The qualitative data is then collected to help understand and explain the findings from the initial quantitative data set retrieved in phase I of the study. This proposed explanatory sequential mixed method is ideal for this study as only one data set will not adequately explore the research objectives and the quantitative results will be better understood and explained by the qualitative methods.

This research involves an initial retrospective review of patients' case notes and prescription sheets. The data collected were used to answer questions such as what are the common antibiotics are being prescribed and for what indications, are these in compliance with existing guidelines and based on laboratory tests etc. The next phase was a prospective cross-sectional survey of prescribers' knowledge, attitude and perceptions on antibiotics prescribing and use, systems and practices. This was used to explore determinants of rational prescribing of antibiotics.

Given the specific objectives, the empirical work is split into three phases. The phases are explained below:

Phase 1- This involved an initial retrospective, cross-sectional descriptive survey to assess the patterns of antibiotic prescribing in the study settings. This phase was designed to achieve objectives 1-5. This study was conducted as a need assessment based on theoretical information obtained from the review of published literature and information gathered from the preliminary field work. Antibiotic prescribing was studied over a fixed time period by retrieving quantitative data from patients' case notes.

Phase 2- This involved a prospective survey of prescribers' perceptions and opinions of antibiotic prescribing patterns in the settings. This phase achieves objectives 6-9. The study made use of findings from phase 1 to further explain and understand the prescribing patterns from the results obtained. This is a qualitative survey of prescribers' knowledge, attitudes and practice with antibiotics. The responses from phase 2 of the research were used to determine the factors that interplay in antibiotic prescribing in the settings and the reasons for the observed practice patterns. Theoretical models were explored, and the behaviour change wheel (BCW by Susan *et al.,* 2011) was adopted to develop of a set of recommendations to improve current practice. This was done by compilation of suggestions made by prescribers combined with successful interventions implemented previously in similar settings and already published.

Phase 3- With the findings obtained from phases 1 and 2 above and the developed recommendations, phase 3 then sought to explore the stakeholders' views on feasibility and acceptability of these set of recommendations. The relevant stakeholders in the local settings were identified and recruited for this phase. In this phase, the behaviour change wheel and its corresponding APEASE criteria was used and the theoretical framework to discuss implementation steps.

The cycle in the Figure 3.2 illustrates how the bottom-up approach is employed in the different phases in this research.

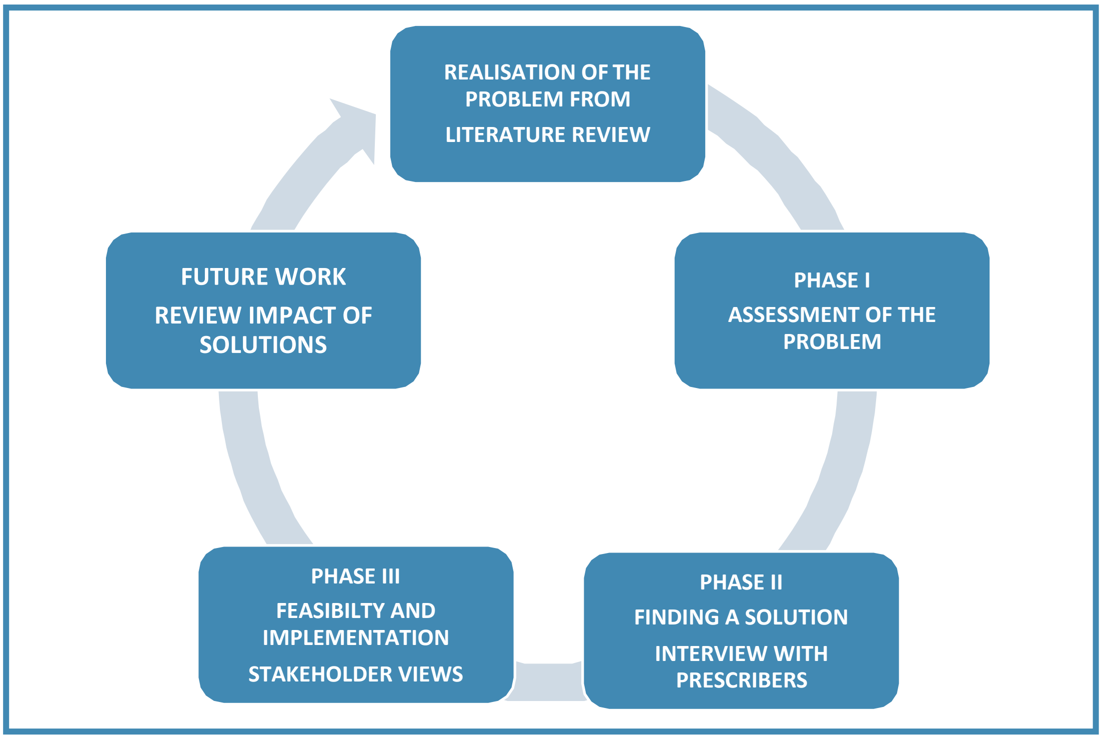

Figure 3.2: The cycle of the bottom-up approach employed

3.5 Study location

This study was carried out in Bayelsa state which is in the Niger Delta region of Nigeria. Nigeria is located on the Gulf of Guinea in the western part of Sub-Saharan Africa and shares land borders with the Republic of Benin in the west, Chad and Cameroon in the east, and Niger in the north. The Federal Bureau of Statistics of Nigeria reports that Nigeria is the seventh most populous country in the world with approximately 193 million inhabitants currently with an estimated 2.6% population growth rate annually (NPC, 2016). It is categorized as a developing nation in the lower-middle income group by the World Bank (World Bank report 2016). It currently operates a democratic system of governance with its capital in Abuja. Nigeria officially has 36 states grouped into six geo-political zones and the Federal Capital Territory (FCT, Abuja) the states are subdivided into 774 local government areas. The geo-political regions are the North Central, North East, North West, South East, South West and South-South regions based on ethnicity and culture, historical origins and background and physical location in the country. Almost half (46%) of Nigeria's populace live in the urban areas (WHO, 2015).

The Niger Delta region of Nigeria, as now defined officially by the Nigerian government, extends over about 70,000 km² and makes up 7.5% of Nigeria's land mass. The Niger Delta is also known as the Nigerian "South-south" geo-political zone which is the major oil-producing region in Nigeria. In the Niger Delta region, the main source of livelihood is fishing and farming, while Christianity is the dominant religion being practised. This study was carried out in Bayelsa state which is one of the youngest states established and it is also the smallest state in Nigeria. Bayelsa state has eight (8) local government areas equally split with four local government areas on the mainland and the other four on the island. It has one state owned university and two colleges of education. Healthcare services are mostly provided by the two tertiary care hospitals, eight general hospitals (secondary care) across each local government area and some private clinics present in the state capital. This is the first study on antibiotics prescribing practices in this state, as other studies have been carried out in other states in Nigeria. It will contribute to generating a more robust data on antibiotic use and prescribing for Nigeria at the national level. Bayelsa state is among the last few states created in Nigeria. It lacks primary data in many areas as not much research has been conducted in the state. There is need for more research in the state to generate the information and data required to inform policies and guide decisions in this area. Based on this and available resources for the project, this research is set in Bayelsa state of Nigeria.

3.5.1 Healthcare Systems in Nigeria

The Nigerian healthcare systems operates from the both the private and the public sector. The private being run by individuals, companies and co-operate bodies while the public is run by the government. However more recently, steps have been taken to initiate highly specialized hospitals jointly owned and managed by the government and foreign corporate bodies. Healthcare costs in Nigeria are financed mostly by out-of-pocket payments, other sources include tax revenue, donor funding, and health insurance (social and community). The Nigerian National Health Insurance Scheme (NHIS) was established in 1999 and later implemented in 2003 (NHIS, 2018). Up until now, access to the scheme remains limited and studies estimate only a 4% coverage (Onoka *et al.,* 2013). Achieving successful healthcare financing system continues to be a challenge in Nigeria (Olakunde BO, 2012).

The country's life expectancy is currently pegged at 53years for males and 56years for females. Maternal and child mortality rates have improved in recent years, but current indices are still high when compared to other Sub Saharan African countries (WHO, 20I5). Infectious disease burden in Nigeria is high as malaria, HIV/AIDs and TB are still leading causes of death. Chronic non-communicable diseases like hypertension and diabetes are also reported to be on the increase (Unachukwu *et al*., 2008).

The provision of healthcare services is at three levels; the primary, secondary and tertiary care levels. In Nigeria, the primary healthcare levels mainly provide preventive services like vaccinations and consists of comprehensive health centres and small clinics usually located in the rural areas. Most times these rural health centres are managed by nurses and a few community health workers. This level of healthcare is basically run and funded by the local government (Alenoghena *et al.,* 2014). The secondary healthcare levels operate from both public and private sectors. The General hospitals are government owned and also most of the private hospitals in Nigeria owned by corporate bodies and private individuals provide healthcare at the secondary level. They receive referrals from the primary healthcare centres and clinics. The tertiary healthcare levels are mainly in the urban areas of the country and they include the Federal Medical Centres, University Teaching hospitals and specialists' referral hospitals. These provide highly specialised services and are usually run by the federal or state government. They receive referrals from both the primary and secondary healthcare levels. The primary healthcare facilities are perceived to provide very low-quality healthcare services making the secondary and tertiary care facilities generally the preferred choice in seeking healthcare (Asuzu, 2004). Community pharmacies and traditional medicine healers also provide primary healthcare services. The Nigerian healthcare system is still developing and has suffered several setbacks, especially at the state and Local Government Levels.

3.5.2 Study settings

The study was conducted in selected hospitals in Bayelsa state. The hospital setting was chosen for this research because it has a management structure in place, and other resources to support the process of achieving the research objectives. Also, the hospital setting has a structure that will support the study findings and recommendations to be channelled for implementation. Although antibiotics are also used in the community and in homes, lack of controls and regulations amongst other factors makes assessment of antibiotics prescribing and use in the community settings difficult. Hence the study of antibiotic prescribing practices is limited to hospital settings only.

The selected hospitals include the two tertiary hospitals in the state and two other secondary care hospitals. The targeted tertiary hospitals included are the state's university teaching hospital and the federal medical centre of the state. Both hospitals have an average of 250 bed spaces, over five specialties/units, of which includes the general outpatient department, surgery, obstetrics and gynaecology, paediatrics, ophthalmology, internal medicine, dentistry, accidents & emergency and others. Staff strength is an average of about 2000 professionals including medical doctors, nurses, pharmacists, medical laboratory scientists and other allied healthcare professionals. The state university teaching hospital is owned and managed by the state government. The staff are mainly indigenes and locals of the state. The federal medical centre is owned and managed by the Nigerian federal government and their staff are drawn from all over the country. The Nigerian healthcare settings at the state and federal levels are similar in structure and services offered across the different states of the country. Hence the results from these setting can be generalised to reflect practice in other locations with same level of care under similar conditions.

A total of four (4) hospitals were selected for this study. The hospitals included are the two tertiary care hospitals in the state and two secondary care hospitals- one from a mainland local government area and the other from an island local government area.

The tertiary care hospitals are:

The Federal Medical Centre (FMC), located in Yenagoa the state capital which is in the mainland urban area. This hospital has around 250 bed spaces and up to 10 specialties/units.

The Niger Delta University Teaching Hospital (NDUTH), located in Okolobiri, which is a semi urban-rural area of the state. Also has up to 250 bed spaces, serves as the teaching hospital for the state-owned university

The secondary care hospitals recruited were:

The Diete-Koki Memorial Hospital (DKMH) which is also located in Yenagoa the state capital. It has four main units: the general outpatient unit, male and female wards and the paediatric ward. Has an average weekly patient turn out of up to 70 patients. And the second is:

The General Hospital Amassoma (GHA). This is hospital is located in Amassoma, a rural community in southern Ijaw island region of the state. Also has four main units: the general outpatient unit, male and female wards and the paediatric ward. Records an average weekly patient turnout of 50 patients.

These four hospitals were purposely selected as they provide a good coverage of both tertiary and secondary care hospitals in the urban and rural areas and also across the mainland and island local governments of the state which provides a fair representation to assess antibiotic prescribing across the state.

An overview of the methods employed in the different phases of the research are presented in Table 3.3 below and explained in detail in the following sub sections.

Table 3.3: Overview of the study design methods

	Phase I	Phase II	Phase III
Location	Bayelsa State, Niger Delta Region of Nigeria		
Settings used	-Two Tertiary care hospitals (1 located in a rural setting and the other in urban area) -Two Secondary care hospitals (1 located in a rural setting and the other in urban area)		
Sampling and recruitment	- Patient case notes retrieved from medical records unit -Prescription sheets retrieved from pharmacy department - Clinic visit within July-December 2015 - Received a prescription for antibiotic(s)	-Purposive sampling of prescribers across hospitals in Bayelsa state. -Invitation leaflets were emailed out - Responding contacts were sent study information leaflets and the interviews were scheduled with them	-Stake holders at different policy levels -Recruitment same as Phase II
Data collection	-Retrospective retrieval of antibiotic prescribing data using pre-designed data collection forms	-Semi structured interviews using a developed interview topic guide	-Semi structured interviews using a developed interview topic guide
Data processing and analysis	-Quantitative data retrieved -Cleaned and entered in SPSS Version 21 - Analysed and reported using basic descriptive frequencies -Presented in tables and charts	-Qualitative data generated from the interviews - Audio recordings were transcribed -Transcripts imputed into NVivo 11 for further organisation of the data -Thematic framework analysis was employed	The same as Phase II

With the overview of the study design presented in Table 3.3 above, the next steps of the study methods are presented in three different parts according to the different phases in the research project. These are phases I, II and III.

3.6 Methods employed for Phase I

This involved a retrospective, cross-sectional descriptive survey to assess the patterns of antibiotic prescribing in the selected hospitals. This phase was designed to achieve objectives 1-5. The study was conducted as a need assessment based on theoretical information obtained from the review of published literature and information gathered from the preliminary field work.

3.6.1 Sampling for Phase I

3.6.1.1 Sampling Strategy

This phase was conducted to retrieve information on antibiotic drug prescribing patterns, assessing the common drugs and classes prescribed, the indications, use of laboratory investigations, generic/brand name prescribing and compliance to treatment guidelines. The antibiotic prescribing patterns was surveyed by studying antibiotic prescriptions from patient's case notes retrospectively in the study hospitals over the last six months based on the time of commencing data collection (December 2015). A simple non-random purposive sampling was used to obtain the patient case notes with antibiotic prescribing. This time frame of six months was chosen as it will provide a more recent account of antibiotic prescribing patterns and not too large a data set, since different study hospitals are included. The eligibility criteria were patients' case notes that received an antibiotic prescription and was seen between July to December of 2015.

This data source and method of sampling within a specified time frame was adopted from the methods employed by similar studies already published. Also, the retrospective method was chosen over the point surveillance method in this study because the point surveillance takes a snap shot and gives the prescribing pattern for only a day across the setting. Many important outcome measures for this research like the antibiotic duration and changes to medication and the use of diagnostic test results will not be captured when using point surveillance method. In addition, this retrospective method prevents bias introduced by prescriber change in behaviour if a prospective data collection method was employed (Mangione-Smith, *et al.,* 2002).

3.6.1.2 Sampling Procedure

The researcher reported to the medical records department of each of the study hospitals. This is where the case notes and other medical records of patients are stored. The researcher presented the ethical approval letter obtained prior and explained the purpose of the research to the head of the medical records department or the most senior staff available at the time of visit. Approval was granted to access patient case notes upon the presentation of the relevant ethical approval for the specific hospital. The patient appointment diaries in the medical records office was used to identify the case notes to be retrieved. The diary held a record of patients reporting to the hospital, the date of visit, department or unit patient was seen, the reason for the visit, diagnosis and drugs prescribed. From the appointment diary the researcher compiled a list of case note numbers belonging to patients seen in the hospital between July and December 2015 who received one or more antibiotic prescriptions. A staff member was assigned to assist the researcher retrieve targeted case notes from the list of case note numbers compiled in each hospital. The researcher visited the medical records department for data collection between 10am and 3pm on weekdays (Mondays to Fridays). A desk and chair were provided in the records units in each hospital for the researcher. A total of 1000 case notes was estimated to be retrieved from the four hospitals visited, 300 cases each from the tertiary hospitals and 200 cases each from the secondary care hospitals. This figure was chosen based on the number of case notes assessed in early studies assessing antibiotic prescribing patterns in similar settings. The number allocated to the tertiary hospitals was slightly higher than for the secondary care hospitals as they are bigger and usually have higher patient encounters. However, missing case notes were encountered from the list supplied in all hospitals which reduced the eventual number of case notes retrived with antibiotic prescriptions to be 809 across the four hospitals.

The same procedure was adopted to retrieve information on the costs and availability for antibiotics prescribed from prescription sheets held in the pharmacy departments.

3.6.2 Data collection

In this phase, data were collected from patient case notes and prescription sheets using data collection tools that were developed.

3.6.2.1 Development of the data collection tools

The data collection tools were developed to achieve the objectives of the first phase. The tool was developed to collect information in line with the study objectives which includes the name of antibiotic prescribed, the class, the dosage regimen (dose, duration route/formulation) and the indication for which it was prescribed. Other prescription information retrieved included use of laboratory tests, compliance to the guidelines and brand/generic name prescribing. Availability and costs of antibiotics prescribed were included in the tools used for the prescription sheets. Some demographic information incorporated in the tool include the age and sex of patient and the unit/department where the patient was seen.

The developed tool for patient case notes was piloted with five case notes after which modifications were made by addition of two more columns. The added columns were to record the use of laboratory tests and compliance to treatment guidelines. The final version of the data collection tools was then adopted for the project (see appendix II and III).

3.6.2.2 Data collection Procedure

The researcher identified patients who received antibiotic prescriptions within the data collection time frame (July to December 2015) from the patient appointment diaries and made list of the case note numbers. This list was handed to the medical records staff who retrieved the case notes and handed them over to the researcher. The researcher was made to sign an undertaken for the number of cased notes received each time. The researcher then proceeded to extract the antibiotic prescribing information from the case notes using the data collection forms. One form was used per case note to retrieve data, and each case was assigned a unique identifier number on the forms. Identifier numbers were anonymous and serial beginning case number 001. On completing the data extraction of each set, the case notes were handed back to the medical records staff who counter signed the undertaken after confirming the correct amount of case notes issued out has been returned. The same procedure was repeated daily until first 300 case notes numbers with antibiotic prescriptions were sent for retrieval in the tertiary hospitals and first 200 case note numbers identified and sent off in the secondary care hospitals. However, there were missing case notes and the total cases retrieved was not up to the initial 1000 targeted for the four hospitals. A total of 809 case notes were retrieved across the four hospitals sampled.

3.6.3 Data Processing

Data from the completed forms were entered manually into the IBM Statistical package for Social Sciences (SPSS) version 22. Each variable was coded by assigning numerical values to each response e.g. yes=1 and no=2 for questions with yes and no responses. A coding frame was developed for questions with more than two answers e.g. the type of antibiotic, the class or the indications. After the data entry, the data set was cleaned by checking randomly for coding errors such as duplicates or skipped entries. Any confirmed missing data was coded 999 to ensure proper output in the analysis.

3.6.4 Data analysis and presentation

Simple descriptive statistics like frequencies, percentages and mean were mostly used for the analysis and results were presented using tables and charts.

The first two objectives of this study: commonly prescribed antibiotics and the common indications for which antibiotics were prescribed were analysed with descriptive frequencies and percentages. The results were presented in tables arranged in descending order.

The use of laboratory test as a guide when prescribing antibiotics was analysed by assigning each case to a category. Categories developed to measure this outcome were: test not required, relevant tests conducted, irrelevant tests conducted, and tests not carried out. After assigning cases to the categories they fit in, analysis was done using frequencies and percentages. The results were presented in tables to display how much of the cases sampled had a laboratory test carried out relevant for antibiotic prescribing. Similar methods of analysis were employed to determine the compliance to treatment guidelines. The Nigerian standard treatment guidelines available in hospitals is a document containing a list of different disease conditions and the drug treatment options listed which includes the drug, formulation, the dose and duration. Each case studied was assigned to a particular category of compliance. The categories developed for this outcome include full compliance which indicates that the antibiotic prescribed was in accordance to the treatment guidelines in terms of the drug, the dose and the duration for the diagnosis documented in that case. Other categories were partial compliance indication when the right antibiotic was prescribed but using a different dose or duration from that stated in the guidelines and then non-compliant for when a completely different antibiotic drug was prescribed for that diagnosis. The cases were assigned to categories and displayed in tables using frequencies and percentages to show how much of all cases surveyed had complete, partial or non-compliance to the treatment guidelines.

In the analysis of availability of antibiotic drugs prescribed, the number of times each antibiotic drug was prescribed was recorded and assigned a category of either “Yes” (available when prescribed) or “No” (not available when prescribed). The availability of each antibiotic drug was then expressed in percentages and presented in tables according to the drug classes.

The costs of antibiotics prescribed were analysed by summing up the costs of all antibiotics present in a prescription and expressed as a percentage of the total costs of all drugs prescribed in the individual cases.

3.7 Methods employed for Phase II

This aim of this phase was to determine prescribers' knowledge and perceptions on antibiotic prescribing practices in the study location and to explore the determinants of antibiotic prescribing practices observed in phase one study. A prospective qualitative design using semi structured interviews was employed. The intent of qualitative research design is to examine a situation by allowing the researcher to enter into the world of others (Locke *et al*, 2000). This approach provides an in-depth understanding of a phenomenon, the reasons for decisions taken by participants as well as enabling an understanding of their attitudes and opinions (Saunders *et al*., 2003).

3.7.1 Sampling strategy

Purposive sampling was used to select the participants for this study. Purposive sampling is a technique widely used in qualitative research. It involves identifying and selecting individuals or groups of individuals that are especially knowledgeable about or experienced with the subject of interest being researched. (Patton, 2002; Cresswell & Plano Clark, 2011). This is to yield the most relevant information on the subject.

The researcher purposely targeted prescribers of antibiotics in the previously selected hospitals. Based on the preliminary data collection carried out in the study setting, doctors and dentists are the official prescribers of medicines within the study settings, hence these set of professionals were targeted for the interviews. A fixed sample is not always required in qualitative studies however, the concept of saturation is the most important factor to consider (Mason, 2010). A sample size of 20 prescribers was aimed for to achieve the objectives of this phase. This sample was chosen based on the results obtained from the initial study that suggests antibiotics were prescribed across nine different units across the elected hospitals in phase one. The researcher anticipated 2 prescribers from each unit would be sufficient. Targeting one senior prescriber (defined in this study as at least 10years post qualification experience) and one junior prescriber (less than 5years post qualification experience) in each unit.

3.7.1.1 Inclusion criteria for participants

- Medical doctor or dentist
- Practicing in any of the hospitals recruited for the phase one study
- Licensed to practice within the last year
- Willing to partake in the study

3.7.2 Sampling procedure and recruitment of participants

The medical directory which contains a list of all medical doctors and dentists practicing in the state alongside their current practice facility, year of qualification and contact information was obtained from Nigerian Medical Association (NMA) office in the state.

Medical doctors from the four hospitals selected for phase I study were then targeted and contacted through emails and invited to participate in the study. An information/ invitation letter was developed containing information on the project. The information contained include the title and aim of the study, the researcher details and contact information, and what the study entails (See appendix IX). Participants who confirmed receipts of the information letters and also indicated willingness to participate were sent further information on the interview process and what it entails. Those who responded interest to partake after follow-up were then booked in as confirmed for an interview session and arrangements for a suitable time and venue to conduct the interviews were made.

3.7.3 Data collection for prescribers' perceptions

3.7.3.1 Development of the interview topic guide used for the participants

A semi-structured interview topic guide was developed for the interview sessions held with prescribers for this study. The questions on the interview guide explored topics on the themes that emerged from the earlier quantitative study which was mostly in line with themes identified in the literature reviewed on antibiotic prescribing patterns in Nigerian hospitals. Questions chosen were informed by the aims and objectives of this phase. This is to get a detailed account of participant’s perceptions on the current situation with antibiotics prescribing and its determinants in the Nigerian hospital settings. The researcher made use of open ended questions, this is to enable the participants to express their views and experiences in their own words (Smith, 2010). For instance, participants were asked to describe their views and experience regarding the value of and use of policies. Some closed ended questions were used just to get factual data: an example is “do you prescribe antibiotics from the essential medicines list?”

After all the questions for the topic guide was set, two mock interview sessions were held with two other post graduate research students to check the researchers’ interviewing technique. The questions were then rearranged to get a more logical flow for the interview discussion. The first two interview sessions carried out with the recruited participants were used as pilots to check the ease of flow of questions and also to estimate timing. After these, the questions were modified to increase clarity to participants and then related questions were organised into categories to avoid sounding repetitive. Four categories which includes knowledge and awareness of antibiotic prescribing patterns, personal prescribing patterns, the decision-making process and individual suggestions to improve current prescribing practice. This final version was then adopted for the rest of the interviews conducted.

Other instruments developed and used during the recruitment and data collection process for the interviews include information and Invitation letters and an informed consent form (Appendix XII).

3.7.3.2 Data collection process

Most of the interviews were conducted in the hospitals using consulting rooms, doctor’s office or staff lounges as was available and a few interviews were conducted in public places outside the hospitals. A total of 17 Interviews were conducted in this phase. Upon meeting with the participants at the agreed place and time, the participants were briefed again on the purpose of the interview, the possible duration and topics to be discussed. Consent to make notes and audio record the session was then sought from participants. The researcher provided the participants an informed consent formed that was developed and the interviews then began after the participants signed and dated the consent forms**.**

Questions were mostly open ended with a few closed ended questions embedded. Use of guided probes during the interviews was also employed to enable participants to expatiate further on relevant topics raised. Leading questions was avoided as much as possible to reduce bias in the data generated. The questions in the interview topic guide aimed to provide an explanation and understanding of the current antibiotic prescribing patterns as observed in the phase 1 study. For example, the reasons for high rates of broad spectrum empirical antibiotic prescribing and poor compliance to the standard treatment guidelines was discussed in the interview sessions with prescribers and other stakeholders. The interview sessions lasted approximately between 45minutes to one hour. All interviews were audio-recorded with consent from the participants. This was done to ensure no piece of information was missed out during transcribing and analysis. However, field notes were also taken during the interview sessions to provide a clearer understanding of the context in which some responses were provided.

3.7.4 Data processing and analysis

The audio recordings from the interviews were transcribed verbatim by the researcher on completion of all scheduled interviews. Reference was made to the field notes taken during the interviews when needed to provide further clarifications. The written transcripts were revised over and over by the researcher, and any missing words were reconfirmed from audio recordings and then the transcripts were updated. All typographical errors were also corrected. Self-transcribing was done by the researcher as this enables the researcher to become more familiar and immersed with the data which makes the analysis and interpretation of finding much easier. Corrected transcripts were sent to research colleagues who helped screen the transcribed interviews against the audio recordings for accuracy. All discrepancies highlighted were resolved. Finalized transcripts were printed out and an initial annotation and manual coding was done on the paper copies of transcripts.

A hybrid approach to analysis was employed here which is a combination of techniques for coding the data and generating the themes (Swain, 2018). Two main coding techniques exist for qualitative data which includes the deductive and inductive approaches. The deductive approach is a top-down theoretical process that produces a set of priori themes obtained from a pre-existing framework such as the research aim and objectives or the interview topic guide. While the inductive approach is more of a bottom-up data driven process with new codes being derived from an examination of the data (Boyatzis, 1998; Burnard *et al*., 2008). Deductive approach was used first. A coding frame was developed using the themes and categories template obtained from the topic guide used for the interviews. The data were coded and then assigned to the themes and categories in the coding frame developed from the interview topic guide. Secondly, new and relevant findings emerging from the data that did not fit into the pre-existing themes and categories were assigned new themes that emerged purely from the data; this formed the inductive approach in the analysis of the results. The coding frame was being updated as the analysis progressed with the inductive approach.

Three of the transcripts were also given to two other colleagues involved in qualitative research for blind coding and the codes were matched with the initial coding of the researcher. The results and main findings from the interview data were then presented.

To further enhance the analysis process, the transcripts were prepared in word document formats and entered in to the NVivo 11® software which is a Computer Assisted Qualitative Data Analysis Software (CAQDAS) and also widely used in qualitative data analysis. This allowed for more flexibility and organisation in the data analysis. This software has a friendly outlook interface making use of colours to differentiate between the nodes and themes identified. It also supports the framework approach of qualitative data making case based thematic analysis much easier. Comparing case classifications in NVivo also helped to reduce the researcher influence on the analysis and interpretation of findings.

The stages in the framework method of analysis was employed for analysing the data obtained from the interviews in this study. The Framework Method for the management and analysis of qualitative data has been used since the 1980s (Ritchie and Lewis, 2003). It was originally developed by researchers, Jane Ritchie and Liz Spencer, from the Qualitative Research Unit at the National Centre for Social Research in the United Kingdom for use in large-scale social policy research. However, this method has become an increasingly popular approach in medical and health related research (Gale *et al.,* 2013).

The framework method is appropriate for thematic analysis of textual data, particularly interview transcripts, where it is important to be able to compare data by themes across many cases and also within a case, while also situating each perspective in context by retaining the connection to other aspects of each individual's account (Srivsatata and Thompson, 2009). The method is easy to follow and also very flexible as it permits researchers to either collect all the data before analysing them or to commence the data analysis while data collection is still on-going (Rabiee, 2004). It provides defined steps in analysing the data in the form of connected stages to achieve the final picture that the data represents. This stage includes familiarization with the interview data, then coding the transcripts, identification of analytical frameworks which is developing main themes and categories. The next stage is charting and indexing, which is matching the related codes to build up the themes they support and finally mapping and interpretation of the data.

3.8 Methodology for Phase III

The third phase of the project was carried out to explore stakeholders' views on acceptability and feasibility of the proposed recommendations. The methods employed for this part are presented below:

3.8.1 Sampling strategy and recruitment

Stakeholders were identified by purposive sampling based on their position in the healthcare settings. Participants in positions of authority to influence the implementation of the different strategies proposed were identified and invited to take part. Although, most of the stakeholders are physicians who still prescribe antibiotics in practice and could share their thoughts from the Prescribers' viewpoint, they were interviewed also for the management positions they hold. Routine prescribers on ground were not recruited this time as they have been interviewed in the previous stage of this project and their views on practical strategies to improve antibiotic prescribing were also sought then. Participants in this phase were selected mostly from the Niger Delta University Teaching Hospital (NDUTH) which is one of the four hospitals used for the earlier stages for data collection. This particular hospital was selected because it is a university teaching hospital, and it already have some committees in place that will take on board the recommendations proposed and facilitate the implementation as this will be in line with certain requirements to either attain or retain accreditation as a teaching hospital. After implementation and evaluation, the interventions can then be rolled out in the other hospitals since the systems and settings are very similar.

Stakeholders at the different policy levels were identified through interactions with staff of the hospital during the data collection period for the previous phase, enquiries from the hospital management staff and some personal contacts of the researcher. Enquiries were made to get more details on their roles and how their position may impact on the information needed for the current study in terms of practicality and implementation of the developed set of recommendations.

A total of ten stakeholders were identified and Invitation/information leaflets (as used in phase II) were sent out to participants via email. Eight responses were received, and they were all then recruited to take part. They include:

1. **Chief Medical Director (CMD):** The CMD of the hospital is responsible for the supervision and overall regulations that affects the hospital as a healthcare institution. He oversees and approves all policies, protocols

and interventions presented for continuous quality improvements in this hospital. He was recruited to take part in the interviews as all the recommendations will need his input and final approval before implementation in the hospital.

2. **Chairperson Drugs and Therapeutics Committee (DTC):** The chairperson of the DTC was also recruited as the DTC ensures responsible and rational use of medicines in the hospital which is the goal of the recommendations being presented to improve antibiotic prescribing. It will be the sole responsibility of the DTC chairperson and it members to actually implement the recommendations agreed upon through inclusion in the committee work plan.

3. **Secretary Research and Ethics Committee (REC):** The secretary of the research and ethics committee was recruited as the chairperson was not available at the time of the interviews. This committee will be directly responsible for certain aspects of the recommendations and intervention plan like conducting local studies and audits. The REC will also be responsible for monitoring improvements in practice following implementation and feedback to relevant persons.

4. **Chairperson Nigerian Medical Association (NMA), Bayelsa:** The Nigerian Medical Association is the professional association for registered doctors in Nigeria. The NMA holds training courses for doctors, has several on-going projects on health issues in collaboration with UNICEF, WHO, USAID, UNFPA and other bodies. It is also involved with health policy formulations by making recommendations to the government. The NMA in the study location will be involved in the implementation of some of the recommendations proposed i.e. training and implementing the guidelines and hence the chairperson was recruited and interviewed.

5. **Head of Drugs Procurement (Pharmacy):** The pharmacist in charge of procuring medicines in the pharmacy unit was also recruited as one

of the recommendations was to stock effective generic drugs. Drug costs and drug availability in the brands/generics forms were among the factors affecting the use of antibiotics in the study centre.

6. **Chairperson State Health Insurance Scheme:** Healthcare costs to the citizens was another factor identified as impacting on the choice and decision of an antibiotic being prescribed. The hospitals mostly run an out-of-pocket payment system and implementing health insurance was a proposed recommendation to improve the patterns of antibiotic prescribing, hence the chairperson of the new state health insurance scheme was also recruited to discuss the practicalities this recommendation.

7. **Head of dispensing unit (Pharmacy):** The pharmacist in charge of the dispensary was also recruited as one of the strategies proposed was to restrict antibiotic dispensing in the pharmacy unit and also monitoring of dispensed antibiotics prescribed in the hospital.

8. **Drug use and documentation pharmacist:** The pharmacist responsible for documenting drug use was also recruited to discuss the strategies of monitoring antibiotics drug use and availability of antibiotics in the formulary. This will help to highlight and also address practical steps in the implementation of these strategies.

3.8.2 Data collection

The procedure for data collection in phase 3 is similar to the steps used in the phase 2 interviews.

3.8.2.1 Development of Interview topic guide

The interview topic guide was developed based on the recommendations being proposed to the stakeholders. It has three main sections. The first section was an introduction that basically informed the participants the study background and more details on the topic to be discussed in the interview. The second section then discussed each recommendation being proposed as a topic to explore the perception and acceptability of the stakeholders. Probes were used for each recommendation to determine their views in terms of feasibility, likely barriers that maybe encountered during implementation, needed resources, man power, funds and the role of government. Also, questions were asked to check if any strategy similar to the recommendations already existed in this hospital. The third and concluding section asked stakeholders to mention any recommendation not already covered in the discussions and finally, they were thanked for their time.

3.8.2.2 Data collection process

A convenient time was then agreed with the participants to meet for the interviews. All interviews were conducted during official hours (9am-5pm) in the hospital and they lasted between 30minutes to 60minutes. At the beginning of each interview, the researcher thanked participants for accepting to take part in the interviews and stressed again that all data will be anonymised and kept confidential being used solely for the purpose of this research. Permission was obtained to audio record and take field notes as the interviews progressed. Open ended questions were asked to allow the participants to discuss their views in detail. The researcher used probes to further explore some areas of interest. And the researcher made some field notes as the interviews went on.

3.8.3 Data analysis

The steps outlined in the framework analysis method of qualitative data analysis was employed in analysing the data obtained. All audio recordings of interviews were transferred onto the work computer anonymously and transcribed verbatim. The researcher transcribed the data personally to familiarise properly with the data. The coding of the data was mostly inductive as there were no pre-existing categories for the subject being explored. The transcripts were studied repeatedly as the coding process progressed. Similar codes were matched into emerging themes directly from the data. Similar themes were put into categories and discussed as the interpretation of the finding in line with the objectives set for the study.

The Behaviour Change Wheel (BCW) was adopted to interpret some of the study findings with relation to implementation of the proposed recommendations and also likely barriers in the implementation process. The BCW is a framework for behaviour change which highlights the elements of behaviour change in a system at the different policy levels.

3.9 Validity and reliability of data

Validity and reliability are important in any research. They are particularly essential in qualitative research and should be considered as most often, the subjectivity and influence of the researcher may interfere in the research process and interpretation of findings. Validity determines whether the research truly measures that which it was intended to measure or how truthful the research results are (Joppe, 2000). Validity means the appropriateness and accuracy of the tools, processes involved, and data generated in the research.

A number of steps were taken to ensure reliability of the data generated in this study. For the phase I retrospective quantitative data collection, the data collection tools were piloted first in the study setting to identify its suitability to record all relevant information needed in this study. All emerging issues were addressed, the forms were duly modified before proceeding to the main data collection for the research.

Secondly, to ensure data generated in the qualitative phase is valid, only relevant stakeholders in antibiotics use and prescribing were recruited as participants for the interviews. Stakeholders for the interviews were targeted for recruitment by virtue of their profession and positions held and are able to discuss in detail their perceptions as regards antibiotic use and prescribing in their hospitals and also express their views on how antibiotic prescribing practice can be optimised in their systems given available resources.

Validation of the topic guide was ensured by trying it out on two students first, after which the questions were slightly rearranged to get a more logical flow of the discussion. Two pilot interview sessions were then carried out again with recruited participants, and the final version was then adopted after making some minor adjustments to the topic guide. In qualitative research, sample selection is dependent on the ability of the participants to provide data relevant to the research aims. As a result, the researcher recruited medical doctors who are directly involved with antibiotic prescribing in the hospital settings to avoid issues with speculation, insufficient and inaccurate data. The doctors have the knowledge and can respond precisely to questions asked. All interviews were audio recorded and carefully transcribed verbatim. Interview audio recordings and matching transcripts were randomly selected and sent to external individuals for independent assessing.

Reliability is concerned with the consistency and repeatability of the informants account. Joppe (2000) defines reliability as: The extent to which results are consistent over time and an accurate representation of the total population under study is referred to as reliability and if the results of a study can be reproduced under a similar methodology, then the research instrument is reliable. In order to ensure reliability in this study, the researcher sent out information about the study on invitation leaflets ahead to participants. Prior to every interview, the research also took time to explain the nature and purpose for the interviews and the proposed dissemination of study findings this was done to reduce the risk of participants withholding any information or giving out false responses to please the researcher.

3.10 Reflexivity

Reflexivity is a process whereby researchers place themselves and their practice under scrutiny, acknowledging the ethical dilemmas that permeate the research process and impinge on the creation of knowledge (McGraw, Zvonkovic and Walker, 2000).

The perspective or position of the researcher shapes all research. A researcher’s background and position will affect what they choose to investigate, the angle of investigation, the methods judged most adequate for this purpose, the findings considered most appropriate and the framing and communication of conclusions (Malterud, 2001). It is therefore imperative to reduce any bias due to the researcher’s influence in qualitative research. In this study, the researcher acknowledges the fact that there may be some researcher influence in the methods analysis and interpretation of findings because the researcher is a pharmacist from Nigeria where the study is being carried out and has worked in the region previously. The implication of this is that prior knowledge of how medicines are being prescribed in the study settings may have influence over the data and findings in this study. However, certain steps were taken to minimize this type of bias. Firstly, the researcher was very open minded and systematic in choosing the study design and project execution, making use of best practices and evidence-based approaches at every stage of the work.

The researcher also engaged in on-going critical reflections and journaling. The project was constantly discussed with research colleagues, project supervisors and other relevant researchers in the field who provided very neutral comments and feedback which was useful in achieving the study objectives. The researcher incorporated these comments into the project execution. During the data analysis, the transcripts were screened against the audio recording for accuracy, also transcripts were sent to different researchers for blind coding. This was then matched to the researcher's initial coding as a check to reduce any bias due to the researcher's influence and knowledge in the study area. Field notes and journals were taken during the data collection phase and these were reviewed with the final results to ensure the context in which data were obtained was well reflected in the interpretation of findings. The use of a Computer Assisted Qualitative Data Analysis Software (CAQDAS), Nvivo□ 11 for data analysis also helped to minimise and the researcher influence and bias that maybe introduced in this work.

In order to ensure reliability of the data sets generated, both quantitative and qualitative data were put together and collectively used to explain the exact situation in a triangulation chapter and presentation of results from phases one and two. The eventual findings were then discussed with other stakeholders at higher levels to determine practicality of recommendations in the settings and any specific barriers in the implementation process.

3.11 Ethical Consideration

Only a formal introductory letter from University College London (UCL) was obtained. The UCL Research and Ethics Committee (REC) was contacted for clarification on ethics requirements and the project was exempted from the REC clearance. This is because it is a Nigerian study involving the examination of records of antibiotics use and also talking to healthcare professionals in the Nigerian hospital settings. The UCL REC contacts advised the researcher that the ethical approvals from the relevant Nigerian hospital authorities would be sufficient.

The researcher contacted the hospital management authorities in Nigeria for details on the procedure for ethical applications. The researcher was informed that ethics approvals were provided by the research and ethics committee present in the tertiary hospitals and for the secondary care hospitals, ethical approval was then obtained from the state hospitals management board through the state ministry of health as these hospitals are being run and managed by the government at the state level. Hence, three different ethics application letters were written, a detailed study proposal was attached and sent off to the REC in both tertiary hospitals and one sent to the state ministry of health. All ethics applications were approved after processing and the researcher received three ethics approval letters covering all the hospitals used (See Appendix XIV: Ethical approval letters)

3.12 Data Protection

All data collected in the study were anonymized. Patient names and hospital registration numbers were not recorded during the data collection to ensure patient anonymity and confidentiality. The researcher ensured data collection and handling processes across the three phases of the study complied with the existing Data Protection Act. No identifying patient or participant information was recorded. Patient case notes were assigned serial numbers and interview participants were allocated participant identity codes which cannot be used to identify any person in particular.

All documents containing study data and related information that was generated during the data processing were stored in secured file cabinets at the UCL School of Pharmacy, Pharmacy Practice department. Other electronic files and data sets were stored in pass worded computers. All primary data collected will be discarded upon completion of the study. And study findings will be disseminated to study participants and the hospital authorities.

Chapter 4 ANTIBIOTIC PRESCRIBING PATTERNS: A SUMMARY FROM SELECTED NIGERIAN HOSPITALS

4.1 Overview of chapter

This chapter presents the results obtained from studying the antibiotic drugs prescribed across four hospitals in the Niger Delta region of Nigeria, Bayelsa state. The aim of this phase of the research is to assess the antibiotic prescribing patterns in the selected Hospitals in the Niger Delta region of Nigeria. The objectives set include:

1. To determine what antibiotic drugs/classes are commonly prescribed
2. To identify the indications for which antibiotics are mostly prescribed
3. To explore the use of laboratory tests and treatment guidelines as a guide to the choice of antibiotics being prescribed
4. To assess the availability and costs of commonly prescribed antibiotics in the hospitals

The prescribing patterns across the different hospitals studied are also compared and presented. Interesting themes emerging from the results such as the use of antibiotic in paediatric patients were further analysed and presented. The chapter concludes with a summary of the main findings from the results obtained and its implications for the next phase of this research.

4.2 Demographics

The characteristics of the patient population who received antibiotic prescriptions were analysed from the data retrieved from patient's case notes. The demographic details analysed and interpreted here includes the antibiotic prescribing data retrieved from the different hospitals, the sex and age of patients receiving the antibiotic drugs and finally the different departments or units where the antibiotic drugs were prescribed.

4.2.1 Antibiotic prescribing retrieved by facility

Data regarding 809 cases having one or more antibiotic drug prescribed were collected from patient case notes across the four hospitals surveyed. Most of the cases were gotten from the FMC- 264 (32.6 %) followed by those from the NDUTH- 246 (30.4 %). The secondary care hospitals had fewer cases with GHA having 151 (18.7 %) while DKMH had 148 (18.3). See Table 4.1 with details of the hospital and how much antibiotic prescription cases were retrieved.

Table 4.1: Number of cases retrieved by facility

Name of Hospital	**Type of Facility**	**Area of location**	**Number of cases retrieved (percentage)**
Federal Medical Centre, Yenagoa (FMC)	Tertiary	Urban	264 (33%)
Niger Delta University Teaching Hospital (NDUTH)	Tertiary	Rural	246(30%)
General Hospital, Amassoma (GHA)	Secondary	Rural	151(19%)
Diete-Koki Memorial Hospital (DKMH)	Secondary	Urban	148(18%)
			809(100%)

Table 4.1 shows that more cases were collected in the tertiary care hospitals than in the secondary care hospitals. This is because the tertiary care hospitals are bigger, with more decentralised units. They have more patient encounters because they receive referrals from the secondary and primary care facilities and also from the private hospitals. The area of location however had no impact in the number of patient case note retrieved as the tertiary hospitals in both urban and rural locations yielded similar number of cases (264 and 246 cases respectively) in same time period which is the same for the secondary care hospitals in the urban and rural areas too (148 and 151 cases respectively).

4.2.2 Sex and of patient population

In this study, a total of 809 patients received antibiotics for different medical conditions from the four hospitals surveyed. Of this number, 351(43%) were males and 458 (57%) were females. Figure 4.1 shows the frequency distribution of patients according to the gender in a pie chart.

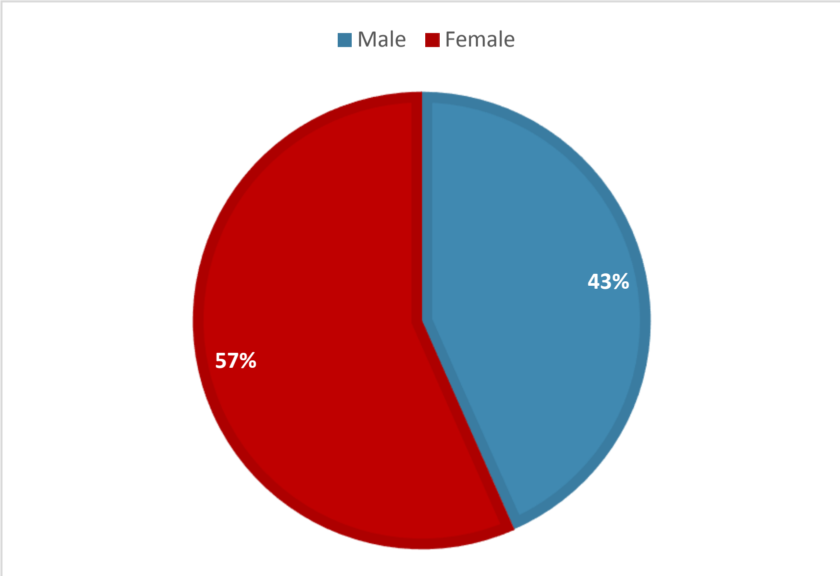

Figure 4.1: Sex of patients that received antibiotics

The chart above shows more females received antibiotic prescriptions. This may be attributed to the fact that more females report to hospitals when ill as reported by earlier studies.

4.2.3 Age distribution of patients

The ages of patients receiving antibiotics were put into different age groups. Infants and children were grouped as 0-16years, from 17-29 years were allocated to young adults, from 30-49years were classified as middle aged. Older patients were from 50-65 years and 66 years and above were elderly patients. This frequency distribution by the age classification is presented in Table 4.2 below:

Table 4.2: Frequency distribution of patient's age

Age range (years)	Number (%)
≤ 16	427 (53)
17-29	173 (21)
30-49	144 (18)
50-65	36 (4)
≥65	18 (2)
Total	798(99)
Missing data (Age not documented)	11(1)
Total	**809**

From Table 4.2, the data shows more than half of the patients receiving antibiotics were aged from 0 to 16years (52.8%). Notably, antibiotic prescribing progressively decreases with increase in patient's age. Hence, elderly patients above 65years of age were the age group receiving the least antibiotic prescriptions (2.2%). This is an indication that most of the antibiotic prescribing in the study settings are for children because the case notes were retrieved centrally from the medical records unit and not from the individual wards.

The sex of the patients was also considered within the age groups. Figure 4.2 below shows the age groups and the sex distribution of patients receiving antibiotics.

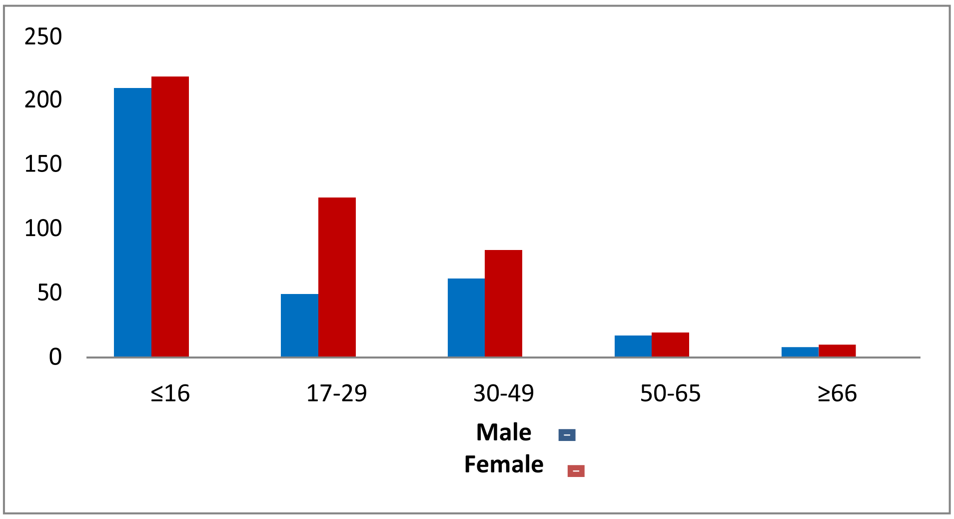

Figure 4.2: Bar chart showing the age and sex distribution of patients receiving antibiotics

In all age groups, it was observed that females received more antibiotics than the males in the same age group across all the age categories. This is consistent with the demographic data results presented earlier which shows that the antibiotic prescriptions being studied has slightly more females than male patients.

4.2.4 Hospital wards/units

The wards where antibiotics were being prescribed for patients was also analysed. More than half of all the antibiotics prescribed being surveyed was seen in the paediatrics unit which is consistent with the frequency distribution for age, having the highest number of antibiotic prescriptions (See Table 4.3 below and Figure 4.2 above). Another unit with significant amount of antibiotic use is the general outpatient department (GOPD) with 28% of antibiotics prescribed, this was followed by accident and emergency unit with 10%, while the ear, nose and throat (ENT) unit and the male wards prescribed the least antibiotics (0.5%). Other units encountered include the female wards, dental, surgery and obstetrics and gynaecology.

Table 4.3: Antibiotic prescribing by the different units

Unit	Frequency(n)	Percent (%)
Paediatric	423	52
General Outpatients Department (GOPD)	224	28
A&E / Casualty	82	10
OBY & GYNAE	33	4
Dental	18	2
Surgery	17	2
Female Ward	6	1
Male ward	3	0.5
Ear Nose & Throat	3	0.5
Total	**809**	**100**

These results indicate that about 90% of all the antibiotics prescribed were in three units (the paediatrics, general outpatients and the accident and emergency unit. The other six departments recorded accounted for the rest of the antibiotics prescribed. Paediatrics unit alone accounted for more than half of all the antibiotics prescribed across the four facilities. There is a need to further investigate the patterns of use of antibiotics in paediatric populations in these settings to understand the reasons for the high rates of antibiotic prescribing observed.

The units where antibiotics were prescribed was also compared across the different sites. The results are presented in Table 4.4 below.

Table 4.4: Antibiotic prescribing by unit across the four hospitals

Unit	Name of Hospital				Total
	FMC N (%)	NDUTH N (%)	DKMH N (%)	GHA N (%)	
Paediatric	127(48)	160(65)	65 (44)	71 (47)	423
A&E	4 (2)	2 (0.8)	0 (0)	76 (50)	82
GOPD	97 (37)	55 (22)	72 (49)	0 (0)	224
OBY & GYNAE	15 (6)	12 (5)	2 (1)	4 (3)	33
Male ward	0 (0)	3 (1)	0 (0)	0 (0)	3
Female Ward	0 (0)	6 (2)	0 (0)	0 (0)	6
Dental	10 (4)	0 (0)	8 (5)	0 (0)	18
Surgery	9 (3)	6 (2)	0 (0)	0 (0)	15
Ear Nose & Throat	1 (0.4)	2 (0.8)	0 (0)	0 (0)	3
Unit not stated	1 (0.4)	0 (0)	1 (0.7)	0 (0)	2
Total	**264**	**246**	**148**	**151**	**809**

The results comparing antibiotic prescribing across the different sites show that although there is still high amount of antibiotic prescribing in the paediatric units across the four hospitals, the absolute highest in paediatrics units were recorded in the two tertiary centres (FMC and NDUTH with 48% and 65% respectively). This may be possible because being tertiary care facilities, they have more advanced specialised services for paediatrics and also receive referrals from the secondary care hospitals. While other units had the greatest encounter for antibiotic prescribing in the secondary care hospitals. The secondary care hospital in the rural area, GHA had the highest antibiotics prescribed in the accident and emergency unit (50%), closely followed by paediatrics (47%). While the secondary care hospital in the urban area, DKMH had the highest amount of antibiotics prescribed in the general out-patient department -GOPD (49%) and followed by the paediatrics (44%).

4.3 Patterns of antibiotic prescribing

The patterns of antibiotic prescribing here describe the number of antibiotic drugs prescribed to patients individually or in combinations, the frequency of antibiotic drugs was analysed to determine the commonly prescribed drugs, antibiotic prescribing by class to also determine commonly prescribed antibiotic classes, indications for which antibiotics were prescribed and also antibiotic prescribing by brand or generic names.

4.3.1 Number of antibiotics prescribed in the study

The number of antibiotic drugs prescribed alone and in combination is shown in Figure 4.3. From the 809 cases entered in the four hospitals, a total of 1059 antibiotic course were prescribed. In 809 cases, at least one antibiotic drug was prescribed, while 219 cases had a combination of two antibiotic drugs and 31 cases had a combination of 3 different antibiotic drugs.

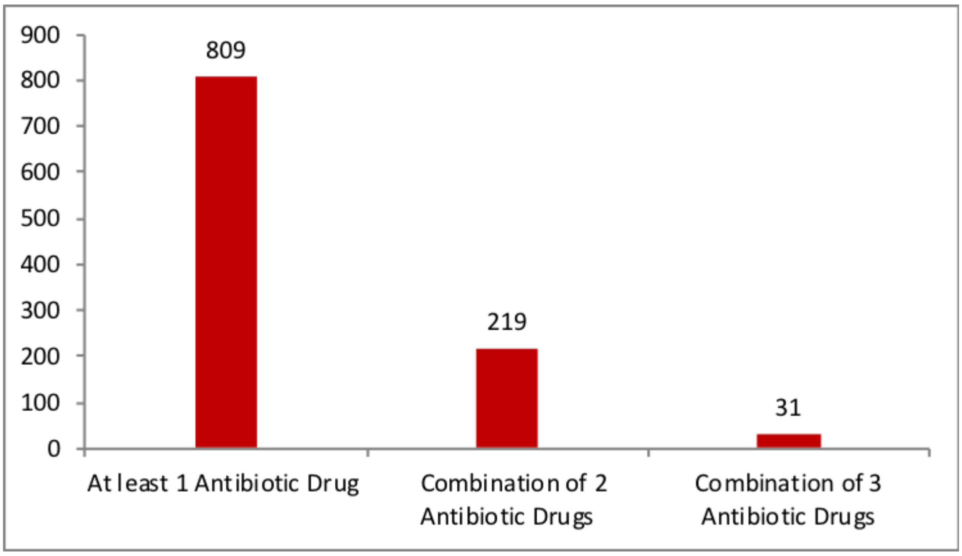

Figure 4.3: Number of antibiotic drugs prescribed alone and in combinations

4.3.2 Antibiotic drugs prescribed

A total of 31 different antibiotic drugs were prescribed. From the frequency of antibiotic drug prescribing presented, the top five commonly prescribed antibiotic drugs were metronidazole (18%), amoxicillin (17%), amoxicillin+ clavulanic acid (16%), cefuroxime (12%) and ciprofloxacin (11%).

While the least prescribed antibiotic drugs are lincomycin, sparfloxacin, secnidazole, flucloxacillin, and tetracycline all being 0.1% each: this is shown in Table 4.5 below

Table 4.5: Frequency of antibiotic drugs prescribed

S/n	Antibiotic drugs	Frequency N (%)
1	Metronidazole	194 (18)
2	Amoxicillin	176 (17)
3	Amoxicillin + Clavulanic acid	166 (16)
4	Cefuroxime	127 (12)
5	Ciprofloxacin	118 (11)
6	Ampicillin + cloxacillin	51 (5)
7	Doxycycline	38 (4)
8	Azithromycin	32 (3)
9	Ceftriaxone	22 (2)
10	Gentamicin	21 (2)
11	Erythromycin	15 (1)
12	Ceftazidime	13 (1)
13	Ofloxacin	13 (1)
14	Co-trimoxazole	12 (1)
15	Clarithromycin	8 (0.8)
16	Ornidazole	6 (0.6)
17	Tinidazole	6 (0.6)
18	Cefixime	6 (0.6)
19	Ampicillin	5 (0.5)
20	Crystalline penicillin	5 (0.5)
21	Cefodoxime	4 (0.3)
22	Nitrofurantoin	4 (0.3)
23	Flucloxacillin	3 (0.3)
24	Levofloxacin	3 (0.3)
25	Cephalexin	2 (0.2)
26	Rifampicin	2 (0.2)
27	Lincomycin	1 (0.1)
28	Sparfloxacin	1 (0.1)
29	Secnidazole	1 (0.1)
30	Flucloxacillin	1 (0.1)
31	Tetracycline	1 (0.1)
	Total	**1059**

The results presented here show that the top five antibiotic drugs commonly prescribed which include metronidazole, amoxicillin, amoxicillin + clavulanic acid, cefuroxime and ciprofloxacin making up about 75% of antibiotics prescribed are broad-spectrum antibiotics which is an indication that most antibiotics are prescribed empirically. Empirical prescribing is prescribing based on experience or an educated clinical guess without being informed by appropriate diagnostic procedures. Fewer narrow-spectrum antibiotics were prescribed, such as the clarithromycin, crystalline penicillin, and rifampicin. Narrow spectrum antibiotics are used for specific infections when the causative organism is known. These types of antibiotics were rarely prescribed.

4.3.3 Class of antibiotic prescribed

Table 4.6 displays the frequency of antibiotic prescribing by class. All the antibiotics prescribed were grouped into thirteen different classes. The five common classes of antibiotics prescribed were penicillins (35%), nitroimidazoles (20%), cephalosporins (17%), quinolones (13%) and macrolides (6%). These were mostly broad-spectrum antibiotics; while rifamycin (0.3%) and lincosamide (0.1%) were the least classes prescribed from.

Table 4.6: Frequency of antibiotic prescribing by class

S/n	Class	Frequency (n)	Percentage (%)
1	Penicillins	371	35
2	Nitroimidazoles	208	20
3	Cephalosporins	176	17
4	Quinolones	133	13
5	Macrolides	64	6
6	Beta Lactam antibiotics	31	3
7	Tetracycline's	31	3
8	Aminoglycosides	13	1
9	Sulphonamides	12	1
10	Nitrofuran	4	0.4
11	Rifamycin	3	0.3
12	Lincosamide	1	0.1
	Total	**1047**	**100**

Table 4.6 shows that penicillin, nitroimidazoles and cephalosporins are the most prescribed classes of antibiotics in this study and collectively make up about 72% of all antibiotic classes. These classes of antibiotics contain mostly broad-spectrum antibiotics which is consistent with results presented earlier on commonly prescribed antibiotics.

An analysis of the class of antibiotic prescribed across the four hospitals was carried out. The results are presented in the bar chart in Figure 4.4 below:

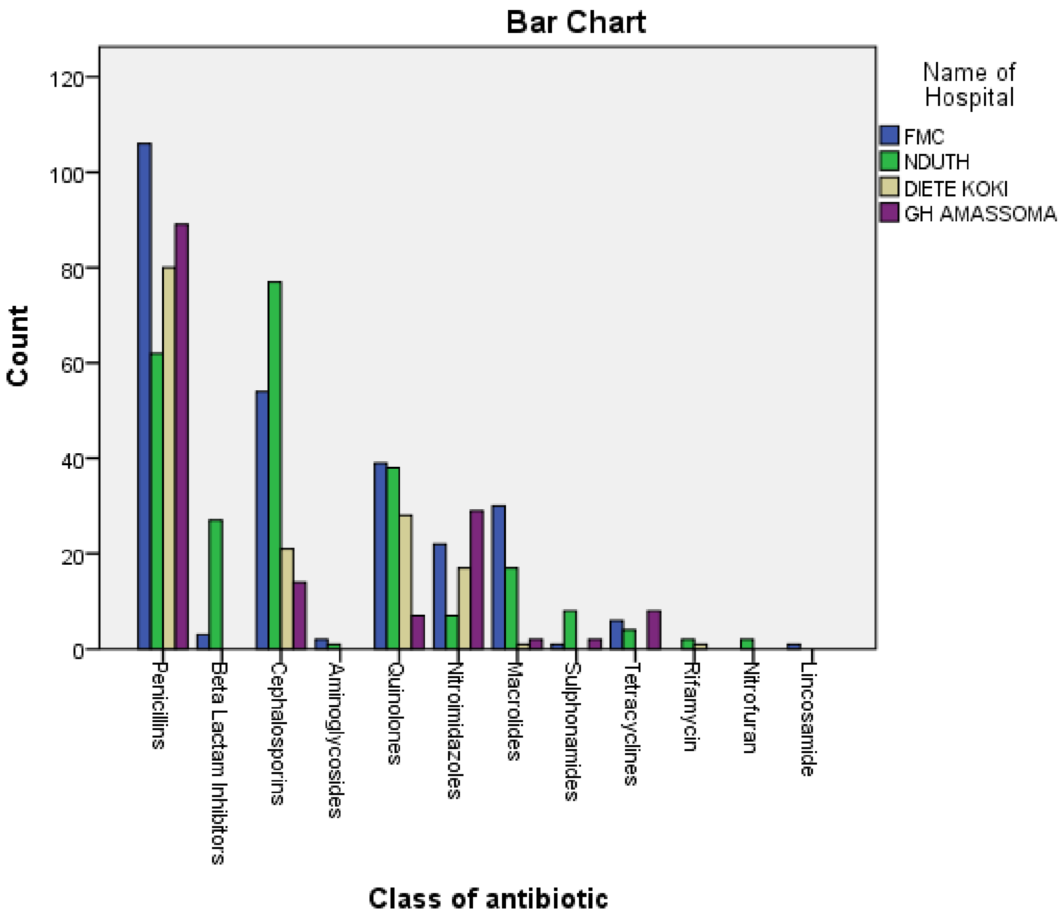

Figure 4.4: Bar chart showing class of antibiotic prescribed by hospitals

The penicillin, the cephalosporins and the quinolones are the top three classes prescribed across the four hospitals. Some other classes like the beta lactam inhibitors and aminoglycosides were prescribed only in the secondary care hospitals.

4.3.4 Generic or brand name prescribing

Figure 4.5 shows antibiotic prescribing by brand or generic names. And it is evident that most of antibiotics were prescribed using brand names 618 (58%), while 441 (42%) of antibiotic prescribing was done using generic names.

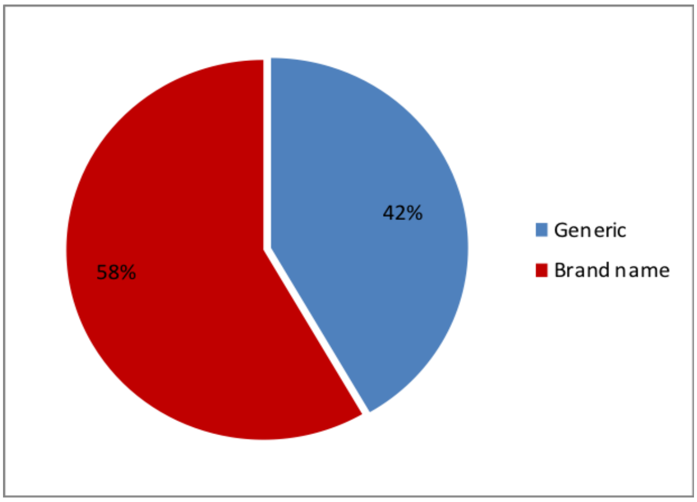

Figure 4.5: Pie chart showing prescribing by brand and generic names

Slightly more antibiotics are prescribed in brand names than in the generic. This may be due to branded medicines being more available for dispensing or the branded antibiotic drugs were preferred more than the generic medicines. The specific reasons for this pattern observed will be explored in the next phase of this study which is the interviews with prescribers. Prescribing by brand or generic names across the four hospitals was also compared. The results are shown in Table 4.7 below.

Table 4.7: Generic and brand name prescribing of antibiotics across the four hospitals

Generic/ Brand prescribing	Name of Hospital				Total
	FMC N (%)	NDUTH N (%)	DKMH N (%)	GHA N (%)	
Generic	109 (41)	137 (56)	49 (33)	37 (25)	332
Brand	155 (59)	109 (44)	99 (67)	114 (75)	477
Total	264	246	148	151	802

Analysis of generic versus brand name prescribing across the four hospitals revealed a similar trend. Brand prescribing was higher than generic prescribing in three out of the four hospitals studied. These include the FMC (59%), DKMH (67%) and GHA (75%). This does not comply with the recommendations for prescribing medicines by WHO and also by the Nigerian National drug formulary that says drug prescriptions shall be made, using the international non-proprietary or generic names. Only NDUTH had slightly more generic prescribing (56%) than the brand prescribing (44%). The NDUTH is a tertiary hospital and serves as the university teaching hospital in Bayelsa State.

4.3.5 Indications for antibiotic prescribing

The indications for antibiotic prescription are presented in Table 4.8. It can be seen that the major indication for which antibiotics were prescribed was respiratory tract infections which accounted for almost a third (31%) of all antibiotics prescribed. Respiratory tract infections here is wide ranging and covers cases like pneumonia, common cold, stubborn coughs, sore throat and other ear nose and throat conditions. Some of which may not be bacterial but viral infections.

Table 4.8: Indications for which antibiotic drugs were prescribed

Medical Indication/Diagnosis	Frequency (n)	Percentage (%)
Respiratory tract Infections	251	31
Gastrointestinal Disorders	174	22
UTIs/STI's	89	11
Surgical prophylaxis	39	5
Other Parasitic infections	60	7
Systemic Infections	47	6
Wounds/ Body injuries	37	5
CNS Disorders	12	1
Skin and soft tissue infections	34	4
Organ disorders	39	5
Non- infectious diseases	22	3
No indication stated	8	1
Total	**809**	**100**

Other common indications for antibiotics prescriptions include gastrointestinal disorders (22%) which includes diarrhoea, cholera, dysentery etc. Urinary tract infections/ STI's accounted for 11% of antibiotics prescribed. Antibiotics were prescribed for other parasitic infections mostly malaria. Other non-infectious chronic disease cases where antibiotics were prescribed include diabetes and hypertension However, in 1% of prescriptions for antibiotics, no diagnosis was documented on the patients' case notes.

4.4 Decision making process in antibiotic prescribing

Data on a combination of factors were entered and analysed for explaining the decision-making process and choice of drug in prescribing antibiotics in the study area. Some of the factors considered include the use of clinical diagnostics and other laboratory investigations as a guide for antibiotic prescribing, compliance with standard treatment guidelines and finally the type of therapy for prescribing, that is empirical prescribing or definitive/therapeutic prescribing. It was found that most of the antibiotics prescribed, were for empirical therapy (72%). There was limited use of relevant laboratory investigations as a guide to antibiotic prescribing and these were carried out in less than one-fifth of the cases studied (15%). Also, complete compliance to standard treatment guidelines was seen in less than a third of all the cases.

4.4.1 Laboratory tests/ investigations for antibiotic prescribing

Table 4.9 below shows the use of laboratory tests and or investigations as a guide for antibiotic prescribing. From the results, it shows that prescribers rarely used laboratory tests or investigations as a guide when prescribing antibiotics as in 78% of cases no tests were carried out. Laboratory investigations relevant for bacterial infections and susceptibility were conducted in only 15% of cases which is less than a fifth of all cases. In 6% of cases, investigations were done but were completely irrelevant to the diagnosis of an infection and antibiotic being prescribed. In about 1% of case entries, use of laboratory investigations for antibiotic prescribing was not required.

Table 4.9: Laboratory tests/ Investigations for prescribing antibiotics

Laboratory investigations	Number of Cases (%)
Yes/ Relevant	118 (15)
Yes/ Irrelevant	49 (6)
Required but not carried out	634 (78)
Not required	8 (1)
Total	**809 (100)**

Laboratory investigations and other clinical diagnostic tests were conducted in just about a fifth of cases studied (21%), and of this number, only 15% of these tests were relevant for antibiotic prescribing while 6% were not related to antibiotic prescribing. These results further explain earlier results analysed that shows most of the antibiotics were prescribed empirically. There is a need to further explore the reasons for this limited use of diagnostic tests in antibiotic prescribing.

4.4.2 Compliance of antibiotic prescribing to Standard Treatment Guidelines (Nigerian STG)

The compliance to the Nigerian Standard Treatment Guideline (STG), last revised in 2008 and still in use is presented in

Table 4.10. The cases were assigned to categories of compliance. Full compliance is when the antibiotic prescribed for the diagnosis was the right drug and the right dosage regimen as stated in the STG. Partial compliance was used when the right drug for the diagnosis was prescribed but in a different dose or duration. The category of non-compliant was assigned to cases where an entirely different drug was prescribed for the diagnosis.

Table 4.10: Compliance to standard treatment guidelines

Compliance to STG	Number of cases (%)
Full compliance	232 (33)
Partial Compliance	304 (43)
Non-compliant	179 (24)
Total	715 (100)
Not applicable	94
Overall total	**809**

In some of the cases studied (12%), compliance to the STG was not applicable such as the cases where the diagnosis could not be found in the STG. After screening all the cases retrieved, 715 cases were eligible for compliance to the guidelines and complete compliance to the STG was seen in about one third of all the cases where compliance was applicable 33% of antibiotics prescribed. Partial compliance was recorded in 43%, while non-compliance was seen in 24% of cases.

4.4.3 The perceived need for antibiotic prescribing

Table 4.11 shows the perceived need for prescribing antibiotics in the four hospitals. In this study, empirical therapy is used to mean all antibiotics prescribed without the use of laboratory tests results and/or not in total compliance with the standard treatment guidelines. It was found out that about 59% of the antibiotics prescribed in this study were given as empirical therapy. The definitive therapy were the cases based on the culture and sensitivity results, other diagnostic procedures relevant for diagnosis of bacterial infection or in compliance with the treatment guidelines. Definitive prescribing of antibiotics was seen in only about one-quarter of antibiotics prescribed (24%). A few of the cases studied (4%) has no clear need as to why an antibiotic was prescribed.

Table 4.11: Perceived need for antibiotic prescribing

<table>
<tr><th colspan="2">The perceived need for antibiotic prescribing</th><th>Cases (n)</th><th>Percentage (%)</th></tr>
<tr><td colspan="2">Definitive therapy (Based on test results and /or guidelines)</td><td>193</td><td>24</td></tr>
<tr><td colspan="2">Prophylactic therapy (according to the guidelines)</td><td>104</td><td>13</td></tr>
<tr><td rowspan="2">Empirical Therapy (based on an educated clinical guess)</td><td>Empirical prescribing</td><td>339</td><td rowspan="2">59</td></tr>
<tr><td>Combination of empirical and prophylactic reasons</td><td>139</td></tr>
<tr><td colspan="2">Unknown (no clear need for the antibiotic therapy)</td><td>32</td><td>4</td></tr>
<tr><td colspan="2">Total</td><td>807</td><td>100</td></tr>
</table>

4.5 Comparing factors that affect the selection of antibiotic drugs across the four facilities

The two main variables directly influencing the choice of antibiotic being prescribed in this study are the use of laboratory investigations and compliance with the standard treatment guidelines. The decision-making process in antibiotic prescribing is now compared among the different hospitals by comparing the percentage use of laboratory tests and degree of compliance to treatment guidelines in the different hospitals.

The two tertiary care hospitals were Federal Medical Centre (FMC) and Niger Delta University Teaching Hospital (NDUTH) and both had higher numbers of antibiotic cases; 33% and 30% of antibiotic prescriptions studied; while the secondary care hospitals General Hospital Amassoma (GHA) and Diete-Koki Memorial Hospital (DKMH) had 19% and 18% of cases respectively. More paediatric patients received antibiotics in all the centres except in DKMH where the most antibiotics were prescribed for patients in the general out patients' department (GOPD). Penicillin was the most prescribed class of antibiotic across the four hospitals, however the most prescribed antibiotic in the tertiary hospitals was co-amoxiclav and the most prescribed antibiotic in the secondary hospitals was amoxicillin. Respiratory tract infections were the highest indication for which antibiotics were prescribed in all sites except in GHA where the indication with highest antibiotic prescriprion gastrointestinal disorders was.

4.5.1 Compliance with STG across the four hospitals

The extent of compliance with STG across the four hospitals is shown in Table 4.12 below. Compliance with standard treatment guidelines was below fifty percent in all the four hospitals studied. Notably, the tertiary care hospitals had higher compliance rates than the secondary care facilities. The highest compliance rate to STG was seen in NDUTH (42.6%), this was followed by FMC (35.2%) both are the tertiary care facilities in this study. Whilst the secondary are hospitals had very low compliance rates with the STG; GH Amassoma had (11.9%) and the lowest was from DKMH with 11.4% compliance rate to STG (See Figure 4.6). Table 4.12 below shows the distribution of compliance to guidelines across the different hospitals, covering complete compliance (that is compliance in drug, form dosage strength and duration), non-compliance, partial compliance (example is right drug, but wrong dose or duration) and those not applicable.

Table 4.12: Compliance with STG across the four hospitals

Name of Hospital	Compliance with STG				Total
	Full compliance N (%)	Non-compliant N (%)	Partial Compliance N (%)	Not applicable N (%)	
FMC	93 (35)	43 (16)	89 (34)	39 (15)	264
NDUTH	104(43)	74 (30)	51 (21)	15 (6)	244
DIETE KOKI	17 (11)	11 (7)	100 (68)	20 (14)	148
GH AMASSOMA	18 (11.9)	49 (33)	64 (42)	20 (13)	151

Figure 4.6: A bar graph showing complete compliance with STG by the different hospitals below shows a graphical representation of complete compliance only by the different hospitals.

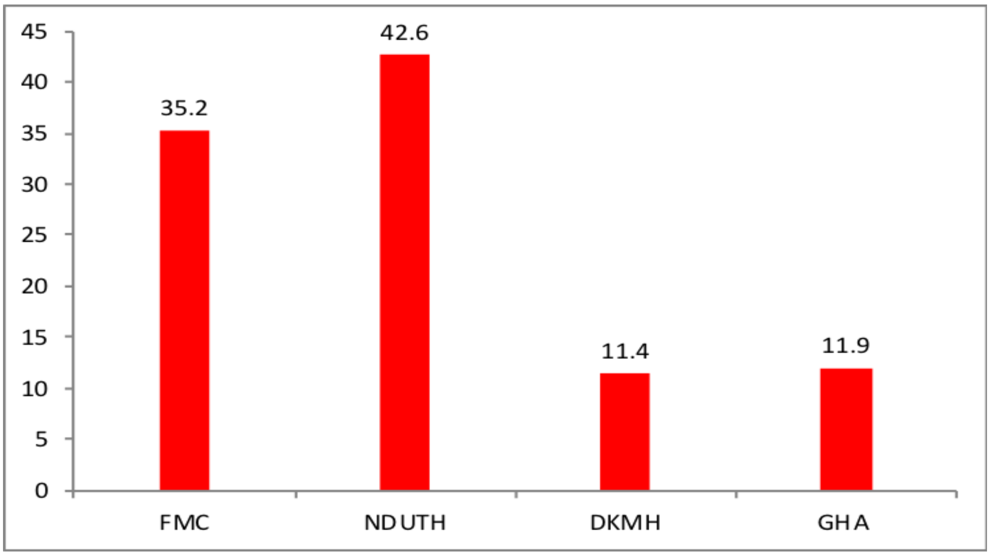

Figure 4.6: A bar graph showing complete compliance with STG by the different hospitals

The bar graph representing full compliance with the treatment guidelines showed that the tertiary care hospitals were more compliant with guidelines than the secondary hospitals studied. However, it was observed from the preliminary data gathered earlier that the treatment guidelines are not readily available in the secondary care hospitals which is likely the main reason for such low compliance rates.

4.5.2 Use of laboratory Investigation

Table 4.13 shows the use of laboratory investigations as a guide to antibiotic prescribing. It can be noticed that the use of laboratory investigations and culture/sensitivity tests was generally poor across all four hospitals studied, which is also consistent with the results obtained for compliance with STG. Use of laboratory tests was higher in the tertiary hospitals. The highest was recorded in FMC (29.2%). Next was NDUTH (10.2%). The secondary hospitals DKMH and GHA were 6.1% and 4.6% respectively.

Table 4.13: Use of laboratory Investigation

Name of Hospital	Investigation done				Total N (100%)
	Done and relevant N (%)	Not done N (%)	Done but not relevant N (%)	Not Required N (%)	
FMC	77 (29)	165 (62.6)	21 (8)	1 (0.4)	264
NDUTH	25 (10)	202 (83)	11 (4.5)	6 (2.5)	244
DIETE KOKI	9 (6)	124 (83)	14 (10)	1 (1)	148
GHA	7 (5)	141 (93)	3 (2)	0 (0)	151

Diagnostic tests were not carried out most of the time before prescribing antibiotics across the four hospitals. Only few relevant tests were carried out and these were slightly more in the tertiary hospitals than the secondary care hospitals. In some cases, tests were carried out that did not indicted presence of a bacterial infection e.g. abdominal scan and fasting blood sugar test. Some other cases were antibiotic prophylactic therapy and as such did not require and prior laboratory tests.

4.6 Availability and cost of antibiotics prescribed

4.6.1 Availability of antibiotics

A total of 595 antibiotic prescriptions were retrieved from 449 prescription sheets studied. Of these, 24 different antibiotics drugs from 10 different classes were prescribed. Eight (33%) out of these 24 antibiotics achieved 100% availability (see Table 4.14 below).

The availability of antibiotics was analysed from prescription sheets as the antibiotics that were actually dispensed when prescribed. Commonly prescribed antibiotics like ampicillin, co-trimoxazole, crystalline penicillin, doxycycline and chloramphenicol achieved 100%, which means they were available, and dispensed every time they were prescribed during the study period. Other less frequently prescribed antibiotics that achieved 100% availability include ofloxacin, cefpodoxime and levofloxacin. Some of the commonly prescribed antibiotics were not available for dispensing sometimes when prescribed. These include amoxicillin (95%), Amoxicillin + clavulanic acid (89%) metronidazole (99%) and ceftriaxone (89%). The data revealed that the average availability of all the different antibiotic drugs prescribed was 93%.

Table 4.14: Availability of antibiotic medicines dispensed

Class	Drug	Items Rx	Was the drug available ?		Availabil i ty	**Mean Availabili ty of class
			Yes	No		
Chloramphenic ol	Chloramphenic ol	7	7	0	100%	100%
Penicillins	Amoxicillin + clavulanic acid	61	54	7	89%	94%
	*Amoxicillin	96	91	5	95%	
	*Crystalline penicillin	2	2	0	100%	
	*Ampicillin	1	1	0	100%	
	Ampicillin +cloxacillin	29	28	1	97%	
	Flucloxacillin	1	0	1	0%	
Cephalosporins	*Cefuroxime	34	31	3	91%	89%
	*Ceftriaxone	35	31	4	89%	
	Ceftazidime	2	1	1	50%	
	Cefotaxime	1	0	1	0%	
	Cephalexin	6	5	1	83%	
	Cefpodoxime	1	1	0	100%	
	Ofloxacin	2	2	0	100%	
Aminoglycoside s	*Gentamicin	10	8	2	80%	80%
Nitroimidazoles	*Metronidazole	125	124	1	99%	99%
Macrolides	Azithromycin	9	6	3	67%	69%
	*Erythromycin	30	25	5	83%	
	Clarithromycin	2	1	1	50%	
Sulphonamides	Co-trimoxazole	19	19	0	100%	100%
Tetracyclines	*Doxycycline	13	13	0	100%	100%
Nitrofurans	*Nitrofurantoin	6	5	1	83%	83%
Quinolones	Ciprofloxacin	94	91	3	97%	97%
	Levofloxacin	9	9	0	100%	
Total		595	555	40		93%
* Medicines in the Essential Medicines List ** Weighted mean calculation						

4.6.1.1 Availability of specific antibiotics prescribed on the Essential Medicines List (EML)

Out of the 24 antibiotics prescribed in the prescription sheets retrieved, 11 are on the Nigerian Essential Medicines List, see Table 4.15 below. Of these eleven medicines, only three were available for dispensing every time they were prescribed. They are ampicillin, crystalline penicillin and doxycycline. Other commonly prescribed antibiotics available in the EML but did not achieve 100% availability include amoxicillin, metronidazole and ceftriaxone.

Table 4.15: Drugs on Nigerian Essential Medicines List

Class	Drug	Availability (%)
Penicillins	Amoxicillin + clavulanic acid	89
	Amoxicillin	95
	Crystalline penicillin	100
	Ampicillin	100
Cephalosporins	Cefuroxime	91
	Ceftriaxone	89
Aminoglycosides	Gentamicin	80
Nitroimidazoles	Metronidazole	99
Macrolides	Erythromycin	83
Tetracycline	Doxycycline	100
Nitrofuran	Nitrofurantoin	83
		Mean= 92%

4.6.1.2 Availability of generics compared to availability of brand name antibiotics

Most of the antibiotic drugs were prescribed as both generics and brand name medicines. Table 4.16: Availability of antibiotics in generics and brand name below shows the distribution of generic and brand name prescribing of the antibiotics studied.

Table 4.16: Availability of antibiotics in generics and brand name

Drug	Number of prescriptions	Generic (n)	Brand (n)
Chloramphenicol	7	5	2
*Amoxicillin + clavulanic acid	61	3	58
*Amoxicillin	96	17	79
*Crystalline penicillin	2	0	2
*Ampicillin	1	0	1
Ampicillin + cloxacillin	29	2	27
Flucloxacillin	1	1	0
*Cefuroxime	34	18	16
*Ceftriaxone	35	27	8
Ceftazidime	2	1	1
Cefotaxime	1	1	0
Cephalexin	6	2	4
Cefpodoxime	1	1	0
Ofloxacin	2	2	0
*Gentamicin	10	5	5
*Metronidazole	125	44	81
Azithromycin	9	4	5
*Erythromycin	30	30	0
Clarithromycin	2	2	0
Co-trimoxazole	19	1	18
*Doxycycline	13	13	0
*Nitrofurantoin	6	6	0
Ciprofloxacin	94	86	8
Levofloxacin	9	9	0
Total (%)	**595**	**275 (47%)**	**316 (53%)**
***Drugs available in the Nigerian EML**			

The frequency of brand name antibiotic prescribing was slightly higher than that of generic drug prescribing with brand name prescribing at 53% and generic prescribing at 47% respectively. This may be due to prescribers' preference for trusted brands when using antibiotics. Some of the commonly used antibiotics were not prescribed in the generic names in the prescriptions studied. These are ampicillin and crystalline penicillin. While the antibiotics mostly prescribed in branded names are amoxicillin + clavulanic acid (Augmentin®), amoxicillin (Amoxyl®), Cephalexin, Metronidazole (Flagyl®) and Azithromycin.

4.6.1.3 Availability of antibiotic drugs in different dosage forms

Eleven out of a total of 24 antibiotic drugs prescribed were available in more than one dosage form. Metronidazole, the most commonly prescribed antibiotic was available in four different dosage forms. Tablets and capsules were the most popular dosage forms as seen in Table 4.17 with a 95% and 97% availability respectively. Topically administered and ophthalmic antibiotics were the least prescribed dosage forms and achieved 100% and 90% availability respectively.

Table 4.17: Availability of antibiotics in the different formulations

Antibiotic dosage form	Number of Prescriptions (n)	Was drug available?		Availability (%)
		Yes	No	
Tablet	318	302	16	95
Capsule	112	109	3	97
Suspension	32	24	8	75
Syrup	21	20	1	95
Injection	99	88	11	89
Topical	3	3	0	100
Ophthalmic preparations	10	9	1	90
Total	**595**	**555**	**40**	

In summary, the availability of antibiotic in the different formulations were found to be broadly similar.

4.6.2 Antibiotic cost

Data for antibiotic prices were collected from hospital dispensaries of the four participating hospitals. The average cost of the antibiotics across all sites, the difference in generic and brand name prices and also the proportion of drug cost due to antibiotics were examined. The study findings allowed deductions to be made regarding availability and cost.

4.6.2.1 Cost of all prescription drugs

This study assumed total drug cost to be same as the cost of prescription items. This means all other costs patient may have incurred such as administration cost, cost of medical investigations etc. have not been included. The average cost of a prescription was found to be ₦1,506 ($4.5) (See Table 4.18).

Table 4.18: Cost of prescription items

Number of prescriptions	Currency	Cost of all drugs	Mean prescription cost
449	Nigerian Naira (₦)	₦661,292	₦1,506
	United States Dollar ($)	$1,983	$4.518
$1= ₦358 (As at 22nd March 2016 from oanda.com)			

4.6.2.2 Cost of antibiotic drug therapy

There was a wide range in the cost of different antibiotic drug therapies. The most expensive antibiotic course prescribed in the prescription sheets studied was ₦6000 ($16.72) while the least expensive being ₦10 ($0.03). The mean cost for an antibiotic therapy calculated was ₦708 ($1.98) see Table 4.19 below. These analyses did not take into account the other supplementary costs associated with some formulations e.g. purchase of the other consumables associated with injectable medicines such as needles and syringes, infusion giving sets etc.

Table 4.19: Cost of antibiotics prescribed

Currency	Minimum cost of antibiotic therapy	Maximum cost of antibiotic therapy	Mean
Nigerian Naira	₦10	₦6000	₦708
United States Dollar	$0.03	$16.72	$1.98

4.6.2.3 Average cost of a course of antibiotic by class

The average cost of a course of antibiotic according to the different classes was also analysed and presented in

Table 4.20 below. The most expensive class is the cephalosporins followed by the penicillins, next is the macrolides and then nitroimidazoles. The least expensive class being the sulphonamides.

Table 4.20: Average cost of an antibiotic course by class

Class of antibiotic	Average cost of antibiotics by class (=NGN=)	Average cost of antibiotics by class (=USD=)
Penicillins	1083.35	3.02
Cephalosporins	1803.83	5.03
Aminoglycosides	571.43	1.59
Quinolones	977.18	2.72
Nitroimidazoles	896.40	2.50
Macrolides	957.73	2.67
Sulphonamides	108.57	0.30
Tetracyclines	554.00	1.54
Nitrofuran	648.00	1.91
Chloramphenicol	383.33	1.07

4.6.2.4 Average cost of an antibiotic therapy

The average cost of the commonly prescribed formulations of antibiotic drugs prescribed were analysed and presented in Table 4.21 below. Innovator brands ranged between 2 to 6 times more of the cost of commonly prescribed generics. The most expensive antibiotic drug prescribed was found to be intravenous ceftriaxone, a third-generation cephalosporin antibiotic. This was closely followed by ceftazidime another third-generation cephalosporin and amoxicillin + clavulanic acid. The cheapest antibiotic prescribed in this study is co-trimoxazole and it had the highest brand cost to generic cost ratio at 600%. Other less expensive antibiotic prescribed include ampicillin, chloramphenicol and doxycycline.

Table 4.21: Cost of an antibiotic therapy per drug

Antibiotic drug	Mean cost of generics N ($)	Mean cost of brands N ($)	Ratio Generic: Brand (Approx. to nearest 100%)
Tabs. Metronidazole	516.80 (1.44)	1566 (4.37)	300
Caps. Amoxicillin	416.41 (1.16)	1780 (4.97)	400
Caps. Ampicillin + cloxacillin	415.53 (1.15)	1920 (5.36)	500
Tabs. Amoxicillin+ clavulanic acid	1356.04 (3.77)	3225 (9.01)	200
Tabs. Erythromycin	583.57 (1.62)		
Tabs. Ciprofloxacin	665.94 (1.85)	1967(5.49)	300
Caps. Doxycycline	289.00 (0.80)		
Tabs. Co-trimoxazole	108.57 (0.30)	655 (1.83)	600
Inj. Gentamicin	528.13 (1.47)	1350 (3.77)	300
IV. Cefuroxime	1048.45 (2.91)	2825 (7.89)	300
IV. Cephalexin	999.50 (2.78)	2710 (7.75)	300
IV. Ceftazidime	1400.00 (3.89)	3650 (10.20)	300
Tabs. Ofloxacin	850.00 (2.36)		
IV. Ceftriaxone	1506.79 (4.19)	4150 (11.59)	300
Tabs. Azithromycin	729.57 (2.03)	2650 (7.40)	400
Tabs Levofloxacin	665.00 (1.85)		
Inj. Crystalline penicillin		950 (2.64)	
Syr. Cefpodoxime	933.00 (2.59)		
Tabs. Nitrofurantoin	404.00 (1.12)		
Tabs. Clarithromycin	577.50 (1.60)		
Caps. Ampicillin		655 (1.82)	
Caps. Flucloxacillin	999.00 (2.78)		
IV. Cefotaxime	1000.00 (2.78)		
Caps. Chloramphenicol	258.33 (0.72)	470 (1.31)	200
1$= ₦358 (As at 22nd March 2016 from oanda.com)			

Commonly prescribed antibiotics were not available to be dispensed every time they were prescribed due to some periods of stock out in the hospital dispensary. This will encourage prescribing and dispensing to patient's other alternatives available different from the specific antibiotic indicated. Findings revealed that branded antibiotics were more available in the hospitals than the generics.

The costs of antibiotic therapy were also found to vary between the different classes and also between the generic and innovator brands of the specific antibiotics. Earlier analysis on availability showed that more brands were prescribed and dispensed than generics.

4.7 Antibiotic prescribing patterns in paediatric patients

The use of antibiotics in children (paediatric patients) in this study was found to be very high as more than half (54%) of antibiotics prescribed in the study was for children seen in the paediatric units. A further analysis was then carried out on the paediatric population of the cases retrieved to determine if the high volume of antibiotics prescribed for paediatric patients reflects just the disease patterns or it is suggestive of irrational use of antibiotics. This sub analysis was done with the following objectives set:

1. What are the commonly prescribed antibiotics for paediatric patients?
2. What are the common indications for which antibiotics were prescribed for paediatric patients?
3. Use of laboratory tests as a guide when prescribing antibiotics for paediatric patients
4. Compliance to the standard treatment guidelines when prescribing antibiotics for paediatric patients.

The following sections will present results on the antibiotic drugs commonly prescribed for children, the indications for which antibiotic drugs were prescribed for children and the decision-making process in choice of antibiotics being prescribed for children that is the use of laboratory investigations and compliance to the treatment guidelines.

4.7.1 Antibiotic Drug prescribed for paediatric patients

Antibiotics from varying antibiotic classes were prescribed for paediatric patients (patients aged 16 years and below). Table 4.22 below shows the distribution frequency of antibiotic drugs prescribed for children. Amoxicillin plus clavulanic acid (24.8%) was the most common antibiotic used in children in the study hospitals. Other commonly prescribed antibiotics include cefuroxime (18.9%), amoxicillin (14.6%), metronidazole (11.8%) and azithromycin (5.9%). It was also discovered that the five most commonly prescribed antibiotics for children in this study are all broad-spectrum antibiotics.

Table 4.22: Antibiotic Drug prescribed for paediatric patients

Drug	Number of prescriptions n (%)
Amoxicillin+ Clavulanic acid	122 (24.8)
Cefuroxime	93 (18.9)
Amoxicillin	72 (14.6)
metronidazole	58 (11.8)
Azithromycin	29 (5.9)
Ampicillin +cloxacillin	21 (4.3)
Gentamicin	15 (3.0)
Ciprofloxacin	15 (3.0)
Ceftazidime	12 (2.4)
Ceftriaxone	12 (2.4)
Co-trimoxazole	9 (1.8)
Cefixime	5 (1.0)
Crystalline penicillin	5 (1.0)
Doxycycline	4 (0.8)
Flucloxacillin	4 (0.8)
Cefpodoxime	3 (0.6)
Cephalexin	2 (0.4)
Rifampicin	2 (0.4)
Nitrofurantoin	1 (0.2)
Tetracycline	1 (0.2)
Total	**492 (100)**

4.7.2 Indication for antibiotic prescribing in paediatric patients

The distribution of indications for antibiotic prescribing in children is shown in Table 4.23 below. The most common indication for antibiotic prescribing was respiratory tract infections (55.8%). Other common indications seen in paediatric patients include gastro-intestinal infections (21.3%), systemic infections and skin infection accounting for 10.5% and 6.1% respectively.

Table 4.23: Indication for which antibiotic was prescribed in paediatric patients

Indication	Number of cases (%)
RTI	202(55.8)
GIT	77(21.3)
Systemic infections	38(10.5)
Skin infections	22(6.1)
UTI/STI	10(2.8)
Wounds/Assault	7(1.9)
Other conditions not requiring an antibiotic	4(1.1)
No diagnosis documented	2(0.6)

4.7.3 Decision making process and choice of antibiotic in paediatric patients

The use of laboratory investigations and the compliance to treatment guidelines when prescribing antibiotics for paediatric patients was also analysed. This was used to study the decision-making process in the choice of antibiotics for paediatric patients.

4.7.3.1 Use of laboratory Investigation in paediatric units

The frequency of use of laboratory investigations in paediatric units is displayed in Table 4.24 below. It is evident that there is very limited use of lab investigations as a guide because in 82.4% of paediatric cases, laboratory investigations were not carried out and in 3.5%, tests were carried out but not relevant for the diagnosis and antibiotic prescription. Only 13.3% had relevant investigations carried out.

Table 4.24: Use of laboratory Investigation in paediatric units

Number of cases	Investigation done				Total
	Yes/ Relevant	No	Yes/ Irrelevant	Not required	
N (%)	57(13.3)	352(82.4)	15(3.5)	3(0.7)	**427(100)**

4.7.4 Compliance to STG in Paediatric patients

Table 4.25 presents the frequency results for compliance to treatment guidelines when prescribing antibiotics for paediatric cases. It is clear that complete compliance was also poor as this was obtained in 28.6% of cases. Partial compliance was 37.7%, non-compliance was 23.2% and the use of a guideline for prescribing was not applicable in 10.5 % of cases seen.

Table 4.25: Compliance to STG in Paediatric patients

Compliance to STG	Number of cases (%)
Yes	122(28.6)
No	99(23.2)
Partial compliance	161(37.7)
Not applicable	45(10.5)
Total	**427(100)**

The sub-analysis for the patterns of antibiotic drugs prescribed in paediatric patients reveals a similar trend with the patterns of antibiotic prescribing patterns observed in the rest of the cases analysed. This is an indication that the patterns of antibiotic prescribing are similar across the different wards in the four hospitals studied. Different factors may have contributed to the extremely high volume of antibiotic prescribing observed in the paediatric units. Some of these factors include high paediatric patient turn out in the government owned hospitals due to subsidized healthcare costs for children under five years of age in Nigeria (Uzochukwu *et al.*, 2015) and high volumes of admissions in the special care baby units (SCBU) where most patients are prescribed prophylactic antibiotics.

4.7.5 Summary of key findings

This is the first antibiotic prescribing study in the area and has been able to provide useful data on antibiotic prescribing patterns in the hospitals. Many problems have been highlighted to be associated with antibiotic prescribing practice in the study area which reveals a trend towards inappropriate prescribing, ultimately contributing to antibiotic resistance. The commonly prescribed antibiotics were broad spectrum antibiotics, these include penicillins (amoxicillin), imidazoles (metronidazole), quinolones (ciprofloxacin) and the cephalosporins (ceftriaxone). A high amount of these antibiotics was prescribed empirically (72%) in the hospitals. Antibiotics were often prescribed in combination of two or three antibiotics together and there were more antibiotics prescribed in brand names than generic names. The high empirical prescribing was supported by the limited use of clinical diagnostics and poor compliance to the treatment guidelines. Similar findings were reported in earlier studies that assessed antibiotic prescribing patterns in other geo-political zones in Nigeria (Abdu-Aguye *et al.,* 2016; Abu-Saeed *et al.,* 2015; Iliyasu *et al.,* 2015) and similar practices have been reported in other developing countries as well. The commonly prescribed antibiotics did not achieve 100% availability in all the study hospitals. The mean cost of an antibiotic therapy was $1.98 and the prices on innovator brands were up to 6 times more the costs of the commonly used generics.

The results presented in this chapter describes antibiotic prescribing patterns in selected hospitals in the Niger Delta region of Nigeria. These results suggest that are some form of inappropriate use and prescribing of antibiotics in the hospitals as evidenced by:

- High empirical prescribing of antibiotics
- Limited use of laboratory results and clinical diagnostics
- Poor compliance with the treatment guidelines

Further discussion of these results is presented in chapter six. The next stage of this research is therefore to explore the reasons and determinants for the observed prescribing practices. These will help to highlight and prioritise areas for improving antibiotic prescribing practices in the local settings which is in response to the study objectives that seeks to develop recommendations on effective strategies to improve practice. The next chapter presents prescribers' knowledge, views and perceptions of antibiotic prescribing practices and their suggestions for improvements to practice.

Chapter 5 PRESCRIBERS' KNOWLEDGE, VIEWS AND PERCEPTIONS OF ANTIBIOTIC PRESCRIBING PRACTICES

5.1 Introduction and background

A summary of the results from the previous phase demonstrates irrational prescribing of antibiotics, which now informs this current phase II. The aim of this second phase study is to explore in-depth the reasons and determinants of the observed antibiotic prescribing patterns in the study settings. Semi-structured interviews were conducted with prescribers in the hospitals to discuss prescribing of antibiotics. The objectives of this second phase study were to:

1) To explore prescribers' perceptions of the current situation with antibiotic prescribing in Nigerian hospitals
2) To identify the determinants of antibiotic prescribing practices
3) To explore prescribers' views on the availability and use of guidelines/policies in antibiotic prescribing
4) To explore prescribers' suggestions on strategies to improve antibiotic prescribing practices

5.1.1 Characteristics of participants and details of interviews conducted

Out of 20 participants initially contacted, a total of 17 interviews were conducted achieving a response rate of 85%. All the participants were physicians who prescribe antibiotics in their practice across the four hospitals selected in the previous stage to access antibiotic prescribing. There were more males (n=12) and the range of participants' professional experience was from less than 5years to more than 16years in practice. Three of the participants are consultants and unit heads who are also prescribers, and one is an infection control lead and a medical director. The participants were purposively selected with the aim of providing maximum variation across different units, care settings and the level of professional experience. Specific characteristics of respondents are presented in Table 5.1 below:

Table 5.1: Characteristics of participants

Characteristics		Number of Participants n (%)
Gender	Males	12 (70)
	Female	5 (30)
Years of practice	≤ 5	7 (40)
	6-10	4 (24)
	11-15	4 (24)
	≥ 16	2 (12)
Rank	Medical officer	7 (40)
	Snr medical officer	3 (18)
	Principal medical officer	4 (24)
	Consultant	3 (18)
Specialty	Internal Medicine	6 (35)
	Paediatrics	5 (30)
	Surgery	3 (18)
	Obst. and gynae	2 (12)
Level of care	Tertiary	11 (65)
	Secondary	6 (35)

Almost half of the participants (40%) were the junior doctors in the medical officer rank as they were easier to reach and more readily available for the interviews compared to the other senior ranks and consultants. Prescribers were from four different specialties with the highest numbers from internal medicine (35%) and paediatrics (30%). The other two specialties were surgery (18%) and obstetrics and gynaecology (12%). Majority of the study participants are from the tertiary care hospitals (65%) because they are bigger and have more doctors. There are generally fewer doctors in the secondary care hospitals and made up 35% of the participants in this study.

5.1.2 Summary of interview process

Seventeen interviews were conducted. All interviews took place just before or after clinic sessions in prescribers' consulting rooms or offices in the hospitals during normal official hours (between 8am-4pm). The timing and choice of place to conduct interviews reduced interruptions to the interview process. The duration of a single interview ranged from 35minutes to 65minutes (an average duration was 45minutes).

At the start, the researcher explained the purpose of the interviews to the participants and sought their consent to audio-record and take notes. There were no objections and all interviews were audio-recorded after signing consent forms (See Appendix XII).

All interviews were conducted smoothly to the end and all the questions in the topic guide were fully explored. The audio-recording of interviews were transcribed verbatim, transcripts were read over the corresponding recordings again and again to ensure no information was missed.

A coding frame was developed using deductive methods informed by the interview topic guide (see Appendix XIII). This was used to organise statements and information arising from the interview data, the coding frame consists the main categories from the topic guides and the corresponding codes obtained. The coding frame was flexible and additional themes arising from the data were added inductively. A research log was kept to document changes made to the coding frame during the analysis process.

5.2 Results

The results and data obtained from the interviews after being analysed are mostly in line with the earlier findings from published literature and similar studies carried out on antibiotic prescribing in Nigerian hospitals. However, exploring prescribers' views further explained the results obtained in phase I providing a deeper understanding of the observed antibiotic prescribing situation. Their knowledge and perceptions on policies and guidelines for antibiotic prescribing was explored. They provided suggestions and recommended strategies to help improve the antibiotic prescribing practices while also highlighting barriers most likely to be encountered. These formed the main domains and themes under which the interview results will be discussed subsequently.

Table 5.2 below shows the main domains and themes and codes arising from analysis of the interview transcripts

Table 5.2: The domains and corresponding themes emerging from the data analysed

Domains	Themes
Perceptions of antibiotic prescribing practices	Poor prescribing practices Inappropriate prescribing Empirical prescribing Relatively good outcomes
Reasons for the current prescribing practices	Poor laboratory services Drug cost/ Patient economic status Lack of knowledge Lack of drug availability Long term prescribing habits No system support in the local settings, Lack of training Pressure from patient Workload in the clinic
Prescribers' views on the availability and use of guidelines/policies in antibiotic prescribing.	Hard to comply with as drugs are not readily available Guidelines would be helpful if available in the local department Not readily available.

Recommendations suggested to improve Antibiotic prescribing	Upgrade laboratory services Training Review policy and guidelines Make antibiotics available Local studies to inform local guidelines Routine audits Restrictive prescribing Pharmacist interventions Regulate drug prices
Barriers to implementing the recommendations	Funding Attitude of prescribers Drug availability

These main themes and categories are further discussed in detail in the following five sections below:

5.2.1 Prescribers' perceptions of current antibiotic prescribing practices

This analysis was carried out to answer the first objective of phase II which is to explore prescribers' knowledge and perceptions of the current antibiotic prescribing practices.

Most prescribers described antibiotic prescribing in the Niger Delta region of Nigeria as inappropriate because antibiotics are prescribed on clinical suspicions of an infection without any empirical evidence. They expressed concerns on poor prescribing practices, making mention of the high rate of empirical prescribing. However, one participant described the antibiotic prescribing in their setting as relatively good because of the treatment outcomes and resolved infections. Achieving the desired outcome of a resolved infection does not directly mean development of resistance a resistance to antibiotics may still be increasing even if infections are resolved. Most of these findings are a confirmation of the results obtained in the quantitative study and review of the published literature also yielded same themes. Below are some quotes from prescribers on their perceptions of antibiotic prescribing in the study area.

“Most doctors don’t have any empirical evidence before prescribing antibiotics” -PRB 001

“I think there is a lot of abuse of antibiotics” -PRB 014

“Some of the laboratory investigations are not readily available”- PRB 002

“They prescribe the wrong antibiotics without any prior MCS {Microbial Culture and Sensitivity} tests” – PRB 012

“I think the major factor is lack of knowledge and core understanding” -PRB 001

Some other responses from the prescribers suggest that while most of the prescribers may know what is ideal and accurate when prescribing antibiotics, this is not followed in practice see quotes from one of the prescribers below:

“Ideally antibiotics are supposed to be prescribed based on clinical suspicions of what disease entity they are trying to treat okay? But the accurate thing to do is to prescribe antibiotics based on not only what you suspect clinically but also based on the patterns of sensitivity when you do the microbiological testing” -PRB 004

5.2.2 Determinants of antibiotic prescribing patterns by prescribers

This second analysis was to determine the factors that influence prescribers’ decisions.

From the data obtained during the interviews, a wide range of factors were highlighted as being important determinants of the current prescribing practices in the hospitals. These include drug costs and availability, pressure from patients, clinicians’ attitudes and prescribing habits over the years, lack of knowledge, excessive workload, and influence from pharmaceutical companies, poor diagnostic resources and laboratory services were reported by participants as common reasons behind the current antibiotic prescribing practices. Of all the factors highlighted, the costs of antibiotics and poor laboratory services were most recurring among the participants' responses.

Table 5.3 below outlines all the factors raised by the respondents and the corresponding numbers of respondents that mentioned the different factors identified.

Table 5.3: Determinants identified for the prescribing patterns

Determinant identified	Number of respondents (n=17)
Drug cost/ Patient economic status	5
Poor diagnostic and laboratory services	5
Excessive workload on prescribers	1
Lack of a variety of antibiotics being available	3
Resources available in the local hospital settings	2
Lack of core prescribing knowledge	4
Influence from pharmaceutical company reps	2
Personal experiences and habits already formed	2
Pressure from patients	2

These main factors are discussed in the subsections below:

Poor laboratory services: The availability and accessibility of diagnostic procedures was identified as a key determinant of the antibiotic prescribing patterns. Prescribers who participated in the interviews stressed the fact that the laboratories are either non-functional or unmanned at some specific work hours. Sometimes, during the call duty hours the laboratories are closed and even when samples are sent off, it takes between 48hours to 72hours to receive the culture results back by which time they would have already started some form of antibiotic cover. This finding provides support to the high rate of broad spectrum and empirical prescribing observed in the phase I study. See quote below:

> ***"**Some of the lab investigations are not readily available"- PRB 012*

> *"We need to strengthen our microbiology laboratories so that the services are more efficient because if you cannot get the culture results as soon as possible, it will be difficult to implement good antibiotic prescribing practices. If we are well equipped to do some of this isolating test and have results within the hour it would be great and help with practice too. We are working towards that in collaboration with other bodies"*
> *PRB 005*

Costs of antibiotics*:* Secondly, the issue of costs and affordability of antibiotics was discussed. In the Nigerian healthcare system, where most patients pay out of pocket for health services and medicines, it becomes a challenge prescribing the ideal antibiotic when patients cannot afford to pay for the requisite tests and drugs. Most prescribers say they are left with no choice but to prescribe cheaper alternatives instead of leaving the patient without any form of antibiotic cover. These cheaper alternatives are sometimes from a different antibiotic class, which may not be highly sensitive to the infecting bacterial organism. All these practices have been highlighted as contributing to the increasing antibiotic resistance. See quote below:

> *"Cost and availability of the required drugs, antibiotics are prescribed just because they are not expensive and are readily available"- PRB 003*

Lack of core antibiotic prescribing knowledge: Misinformation and lack of core understanding in the process of antibiotic prescribing were also highlighted as factors contributing to poor antibiotic prescribing practices. Participants mentioned in their responses that lack of core knowledge in antibiotics use on the part of the prescribers cannot be disputed as a factor. One respondent explained that prescribers who took certain courses like pharmacology seriously while in school will understand the issues with antibiotics use and development of resistance and will therefore be more responsible in prescribing it, as opposed to other prescribers who lack the basic foundational knowledge on antibiotics use.

> *"I think the major factor is lack of knowledge and core understanding"- PRB 001*

Personal experiences and long-term prescribing habits: Some of the interviewed prescribers explained that the antibiotic prescribing patterns also depend on the local settings and unit where the antibiotic drug is being prescribed. Some of the senior prescribers base their antibiotic prescribing on personal experiences with practice over the years. These practices are then handed down from the most senior clinicians to the junior doctors. They explained that some junior doctors just follow the prescribing practices of senior colleagues without having a check themselves, and as such, prescribing practices can be handed down the generation of prescribers in particular conditions seen frequently of a unit. This highlights another possible reason why compliance to the standard treatment guidelines accessed in the previous chapter was low and also prescribers whose prescribing are influenced by such practices may not readily request diagnostic tests and procedures to guide their antibiotic prescribing.

Availability of required antibiotics: A few of the respondents actually stated that the hospital procurement team do not stock a wide range of antibiotics for the doctors to prescribe from and as such are left to prescribe from available options when the required antibiotic is not available. Having highlighted this as one of the factors responsible for poor prescribing practices it's also a fact that the wider the class and range of antibiotics available, the wider the range of antibiotics that would also be prescribed inappropriately as there are no functional prescribing guidelines. This would ultimately lead to antibiotic resistance across a wider range of antibiotics. See quotes from a prescriber below.

> *"In Bayelsa we noticed that we didn't really have some certain kind of drugs. They are not just stocked. We have patients who go around pharmacies and they don't get them. We do tell them that these drugs may be scarce to find and do prescribe them alternatives to start on if they can't find them".......... PRB 015*

Pharmaceutical companies: Pharmaceutical company representatives promoting their drug brands in the hospitals were also mentioned as being another factor responsible for the current prescribing practices. This is because the representatives of the pharmaceutical companies give out enticing incentives to prescribers to prescribe more of their brands. The implication of this is that prescribers are then tempted to prescribe the antibiotics more often if when not ideal or needed, just to earn the incentives offered /by pharmaceutical companies.

Excessive workload: The fact that physicians are faced with excessive workload in the hospital was also reported by one respondent as one of the reasons for the inappropriate antibiotic prescribing. It was highlighted that the number of patients waiting for consultation during clinic hours in the hospitals is so much that it is not practical to spend ample time checking the guidelines or references for prescribing details. So mostly, the choice of antibiotic is based on past experience and the clinical suspicions of an infection by the attending physician.

Pressure from patients: While respondents agreed that some patients actually demand antibiotics, which may lead to prescribing an antibiotic that is not clinically needed by the patient, the majority claimed that such patient demands had no effect in their decision to prescribe an antibiotic drug and would only do so if it clearly benefits the patient in their current clinical condition. See the quote from a prescriber below:

> *"Some patient perceptions are that if they don't get antibiotics when they have a fever, they won't get better, so some practitioners tend to give antibiotics when there is no indication"- PRB 002*

5.2.3 Prescribers' perceptions on the use of policies and guidelines for prescribing

Prescribers' perceptions on the use of policies and guidelines for antibiotic prescribing were explored. This analysis addresses the third objective for the phase II study that seeks to determine prescribers use and perceptions of the standard treatment guidelines for prescribing antibiotics.

Responses gathered revealed although guidelines are not readily available at the moment, prescribers generally have a positive attitude to the use of policies and guidelines and are mostly willing to make use of them for prescribing. One participant pointed out that guidelines make antibiotic prescribing more directed and goal oriented. This will be helpful because many interventions to improve antibiotic prescribing are based on policies and guidelines.

> *"Well it is not readily available. I must be frank with you. It's not readily available in this centre" PRB 004*

> *"Yes, there is a national guideline, but it is not available in my department. I do not think there is any specific antibiotic prescribing guideline" PRB 007*

> *"But guidelines are good to have, it makes it more directed and goal oriented" PRB 004*

These findings indicate that while prescribers maybe willing to use guidelines for antibiotic prescribing choices, these guidelines are not readily available in the clinical settings when prescribing. This also explains some possible reasons for the low and incomplete compliance with the guidelines seen in the results from phase I.

5.2.4 Recommendations and strategies to improve antibiotic prescribing in the hospital settings

This analysis was carried out to answer the last objective of the phase II study that was to explore prescribers' suggestions on strategies to improve the antibiotic prescribing practices in their local settings.

Participants who were all stakeholders in the antibiotic use and prescribing process were asked to comment on and make recommendations that are most likely to help improve current antibiotic prescribing. The recommendations put forward include improvement to laboratory services, training for prescribers, implementing policies and guidelines. Some prescribers recommended carrying out local empirical research and studies on the local sensitivity patterns as this will guide local prescribing guidelines and policies. One respondent stressed the need for proper treatment guidelines suggesting that even though policy documents already exist, this may be lacking in some respects. See quote below:

> *"I think a proper treatment guideline that would cover the different medical conditions"......................PRB 007*

Other recommendations were routine audits and monitoring of antibiotic prescribing and use, and restrictive antibiotic prescribing inform of pharmacist's interventions.

Table 5.4: Recommendations from prescribers to improve prescribing practices

Prescribers suggestions to improve current practice
Improve diagnostic testing and services
Education and training for prescribers
Provide and update local policy and guidelines
Make antibiotic drugs available
Conduct local studies to inform local guidelines routine audits
Restrictive prescribing for some antibiotics
Pharmacist interventions

5.2.5 Likely barriers to implementing recommended strategies

Barriers that might impede the implementation of the recommend strategies were identified by the participants. Most mentioned was finance in the healthcare system as most of the recommendations would need funds and resources for full implementation such as upgrading laboratories both in equipment and staff strength, procurement of antibiotic drugs in the hospital formulary, provision of updated guidelines and organised training sessions for prescribers. Another barrier mentioned was attitudes of the doctors, as they may not be willing to change their current prescribing pattern to imbibe new cultures of using policies and guidelines as recommended. Another barrier mentioned was the lack of awareness on the part of the prescribers regarding antibiotic prescribing and its implications for resistance.

5.3 Discussion of chapter findings

This aim of this phase was to examine prescribers' knowledge and perceptions on antibiotic prescribing in the location, understand the reasons for the antibiotic prescribing practices observed in phase one and the factors that interplay, and what strategies prescribers think might improve their practice. The survey reveals that significant gaps in antibiotic resistance knowledge still exist among prescribers.

Most of the prescribers described antibiotic prescribing in Nigeria as irrational, expressing concerns on poor prescribing practices and also the high rate of empirical prescribing. While they claim to understand the correct process in prescribing antibiotics, it is not being followed in practice as shown by the findings in the phase one study.

The factors discovered to be affecting current antibiotic prescribing practices in this study were observed to be as a consequence of the settings, local resources, prescribers' individual practices and decision making. Some of the contextual factors include poor laboratory services, lack of updated guidelines, poor financing in the healthcare sector, lack of adequate skilled manpower etc. In Nigeria, less than 5% of the annual national budget is allocated for health which directly translates to poor service delivery across the different units in the public healthcare sector (Uzochukwu *et al.,* 2015). Health service provision is better in the private sector, but this service is far beyond the reach of common citizens because healthcare is mostly financed through out-of-pocket payments due to lack of a comprehensive health insurance package. The individual prescriber related factors mostly centred on prescribers' attitudes as seen in and determined by the inner core of the BCW (capability, opportunity and motivation). This include the lack of motivation and willingness to change their antibiotic prescribing practices, and this was dominant across different units. One of the reasons for this might be because their practice is strongly influenced by the prescribing behaviour of the unit head or senior consultants in charge which has been handed down in the particular unit over the years. Apart from the updated guidelines not being readily available, this is another factor contributing to poor compliance. Other factors include patient's beliefs, where patients believe that an antibiotic is able to produce clinical outcomes for every ailment, also physician's beliefs in prescribing antibiotics just to "cover" for fear or negative and adverse outcomes if antibiotics were not prescribed. Also, the pressure to prescribe antibiotics from pharmaceutical companies by offering incentives to prescribers is another factor.

5.4 Implications of findings for the next phase of the research.

The suggestions given by the prescribers to improve antibiotics, with support from existing literature will be used to develop a set of recommendations. These recommendations will aim to target the sources of current prescribing practices at different levels as illustrated by the behaviour wheel change. In additions to these, mores strategies will be sourced from literature published on improving antibiotics use and prescribing in low-income settings, which have been able to show some level of effectiveness.

Chapter 6 DETERMINANTS OF ANTIBIOTIC PRESCRIBING PATTERNS AND DEVELOPMENT OF RECOMMENDATIONS

6.1 Introduction to chapter

Following a survey of antibiotic prescribing patterns in selected hospitals and an examination of prescribers' perceptions of antibiotic prescribing using semi structured interviews, this current chapter seeks to provide further insight and explain the implications of the results obtained from the two preceding studies, addressing questions raised while exploring related literature around these findings to map out possible recommendations. The overall aim of this chapter is to develop a set of recommendations from prescribers' suggestions and existing literature in similar settings.

Emerging themes are discussed in relation to the relevant literature, these include the antibiotic prescribing patterns and the reasons for the observed prescribing patterns.

The recommendations proposed by the prescribers from the interviews were studied in relation to existing literature on effective strategies to improve antibiotic prescribing in similar settings and finally proposing to the targeted stakeholders, a list of interventions based on relevant identified framework. The main findings of this study are discussed below in light with relevant literature already published.

6.2 Antibiotic prescribing practices in the study settings

The antibiotic prescribing patterns were studied as a baseline situation and needs analysis for this study. The main findings indicate that there is still irrational use and prescribing of antibiotics in the selected study hospitals in this region. This is evidenced by a very high rate of empirical prescribing of broad spectrum antibiotic drugs at about 72% this is due to limited use of laboratory sensitivity tests as a guide to the choose antibiotics for prescribing. Diagnostic investigations relevant for bacterial infections and antibiotic prescribing were carried out in less than a fifth of all cases of antibiotics prescriptions studied (15%). Specific aspects of the antibiotic prescribing practices studied are discussed in the subsections below.

6.2.1 Commonly prescribed antibiotic drugs/classes

From the study results, the commonly prescribed antibiotic drugs were metronidazole, amoxicillin, amoxicillin + clavulanic acid, cefuroxime and Ciprofloxacin. As a result, the commonly used classes of antibiotics were the penicillins, nitroimidazoles, cephalosporins and quinolones. These results are in line with findings from earlier studies. Enato and Uwaga, 2011, Odili *et al.,* 2010 and Abu-Saeed *et al.,* 2013 found that the most commonly prescribed penicillin was amoxicillin in their studies. Also, the commonly prescribed quinolone was found to be ciprofloxacin according to Jimoh *et al.,* 2011, Odusanya, 2002). Broad spectrum antibiotics were the most prescribed antibiotics even in other developing countries, similar results have been recorded.

These are all broad-spectrum antibiotics and were mostly prescribed empirically; i.e. without the relevant microbial culture tests being carried out or adherence to the guidelines. This result suggests that right antibiotics were not always prescribed for the right indications. Interviews with prescribers revealed some underlying pointers to these practices. One main issue is the financial status of the patient, the Nigerian healthcare operates mostly on the out-of-pocket payment systems and this affects the treatment process when patients are not able to pay for the medical bills they are faced with when ill.

Prescribers explained sometimes the patients cannot pay for the required culture tests and also do not have enough funds to pay fortheir medicines, so they prefer to prescribe a broad-spectrum antibiotic that will cover most microbes on clinical suspicions of an infection being present. Sometimes the patients are not even able to pay for the indicated antibiotic and can only afford a cheaper alternative which sometimes may be a completely different antibiotic drug to what is being indicated by sensitivity results and prescribers are also forced to prescribe as opposed to leaving the patient with no drug at all. Some other times when the patients are able to pay for the correct medicines, the antibiotics may not be immediately available in the hospital pharmacy.

6.2.2 Indications for antibiotic prescribing

The results from the patient's records of antibiotic prescribing revealed that almost a third (31.1%) of all antibiotics prescribed during the study period were for respiratory tract infections, most of which will be viral infections and wouldn't necessarily need an antibiotic as they are usually self-limiting. Other common indications for antibiotic prescriptions in this study include gastrointestinal disorders (21.6%) and urinary tract infections/ STIs (11.0%). Less than 1% of the prescribed antibiotics had no indication stated. This agrees with six other studies in Nigeria showing large amounts of antibiotic drug being prescribed for upper respiratory tract infections (Abdu-Aguye *et al.,* 2016; Joda and Aderemi-Williams., 2013, Anyawu and Arigbe-Osula, 2012; Enato and Uwaga, 2011, Chukwuani *et al.,* 2002 and Odusanya, 2002). This prescribing practice is further worsened by the limited use of laboratory investigations and guidelines for prescribing antibiotics. Other indications for which antibiotics were prescribed are gastrointestinal infections (21.6%) and urinary tract infections/ sexually transmitted infections (11.0%). Similar indications for antibiotic prescriptions were reported in a study conducted in a Nigerian tertiary hospital where gastrointestinal infections (39.88%), genitourinary tract infections (15.47%) and respiratory tract infections (5.9%) were the top three indications for antibiotic prescriptions (Jimoh, *et al.,* 2011). Iliyasu *et al.,* 2015 also reported that community acquired pneumonia, urinary tract infections and aspiration pneumonia were the main indications for which antibiotics was prescribed in their study.

6.2.3 Generic or brand name prescribing

Brand name prescribing was slightly more than the generic prescribing for antibiotic drugs in the cases studied. The results of earlier surveyon antibiotic prescribing practices showed 59% of antibiotic drugs were prescribed as the branded products while 41% were written out using the generic names. Similar results have been obtained in previous research. A study in a teaching hospital in the south-West region of Nigeria reported generic prescribing of antibiotics to be 45.6% (Akande and Ologe, 2009). A few more studies across Nigeria also reported poor generic prescribing of antibiotics of less than 50% (Akande and Ologe, 2007; Erah *et al.,* 2003; ogbonna and Eze, 2016). However, contrary to this, Iliyasu *et al.,* 2015 and Abdu-aguye *et al.,* 2016 found a higher percentage of antibiotic drugs to be prescribed using generic names in their studies.

Interviews with prescribers showed that while they understand the benefits and importance of prescribing antibiotics as generics in these settings, and the majority of them would prefer to prescribe generics; this is not the actual practice for some reasons. The main reason for having more brand names prescribing of antibiotics according to the prescribers was the issue of clinical efficacy and drug potency. They stressed that in practice they have come to trust certain brands over the years and would not prescribe generics even though they are cheaper as they still perceive some problems with fake and sub-standard medicines being in circulation in Nigeria. It will not be wise to risk prescribing a cheaper generic for a high-risk infection diagnosis, one consultant doctor commented.

> *"We need to prescribe by brand knowing that this particular brand has a higher rate in terms of potency" …. PRB 009*

> *"It is the brand name that will give you the effect you want" … PRB 010*

> *With the knowledge that we have substandard antibiotics in the region, there is need to prescribe certain reputable brands, so you know you are tackling the situation head on……PRB 013.*

“There are so many generics out there that when you prescribe in generic name, people will just use the substandard ones” …PRB 010

Two prescribers highlighted the fact that receiving incentives from pharmaceutical companies is another factor that increases the rate of brand name prescribing over the generics.

“I prescribe by brand names because some companies come with their brands to do presentations” …..PRB 006

“There are doctors who prescribe certain brands due to incentives” …. PRB 008

Another important factor affecting brand name and generic name prescribing is the financial status of the patients. Doctors emphasized they prescribe in brands as long as the patient can afford the costs. They only prescribe generics when the patient is unable to afford the branded medicine indicated for their condition.

“If the patient is well to do and can afford it, we go with brand names as we don’t want to take chances” …PRB 011

One prescriber explained that the generic names of some medicines are not always easy to remember as prescribers are used to the brand names only.

“Some drugs you don’t even remember the generic name like Co-trimoxazole, sometimes forget the generic names and I know this confuses a lot of doctors” …..PRB 011

Consequently, the main factors found to influence the higher brand name prescribing of antibiotic was centered on drug quality and costs. While other factors include influence from pharmaceutical companies and prescriber preferences.

6.2.4 Use of clinical diagnostics in antibiotic prescribing

Initial findings in this research showed that use of laboratory tests as a guide to the choice of antibiotic being prescribed was poor in the study area. The majority of antibiotic prescriptions in the study period were empirical without any laboratory investigations (77.9%). Relevant culture and sensitivity tests were done in only 14.6% and 6.1% of cases tests were carried out but not relevant for bacterial sensitivity or antibiotic prescribing. This is taking into consideration that in some of the cases such as surgical prophylaxis where an antibiotic drug was prescribed, there was no need for any laboratory investigation. Interviews with the prescribers showed the reasons that were contributing to these results. The major factor highlighted was poor laboratory services and delays in results being available. More than half of the prescribers interviewed stressed that laboratory results take up to 2 or 3 days after samples have been sent off, and they need to commence treatment while they wait. Another reason was the cost of running the investigations without any health insurance; indigenous patients are mostly unable to afford the cost of laboratory tests and still pay for drugs. While in some smaller hospitals and rural centres, there are either no laboratory services or shortage of skilled personnel to staff the laboratories adequately. Table 6.1 below summarises the key factors prescribers mentioned as influencing the use of clinical diagnostic testing as a guide to the choice of antibiotics prescribed.

Table 6.1: Factors influencing the use of clinical diagnostics

Factors influencing the use of laboratory tests		
Costs: Additional financial burden on patients due to out-of-pocket payment systems	**Time:** Excessive delays in receiving sensitivity results	**Availability:** Poor availability of services due to lack of resources and skilled personnel

6.2.5 Compliance to treatment guidelines

Complete compliance to the national standard treatment guideline was poor. Sometimes the right drug was given for the indication according to the guidelines but not the right dose or duration. Only 28.7% of the prescriptions studied had complete compliance to the guidelines in terms of right drug for the right indication at the right doses and duration. Partial compliance was seen in 37.4% of the cases studied. There was no compliance at all in 21.9% of cases studied. The main reason prescribers had for this was that the guidelines were not readily available for them in the consulting rooms to use when prescribing. Another reason was that some units confirmed to practices which are established by the consultant physician heading the unit. These practices are viewed as having produced the desired clinical results over the years and they just prescribe accordingly irrespective of what is in the guidelines.

6.2.6 Costs and availability of commonly prescribed antibiotics

This study demonstrates that most of the commonly prescribed antibiotics were not always available in the hospitals for dispensing when prescribed. Metronidazole (99%), Amoxicillin (95%), Amoxicillin + clavulanic acid (89%), cefuroxime (91%) and Ciprofloxacin (97%), the least available antibiotics were ceftazidime (50%) and clarithromycin (50%). The reasons for the observed availability of the prescribed antibiotics were unravelled by responses from interviews with the prescribers. They explained that most times they had to prescribe drugs that were available and affordable by the patients and not necessarily the exact drug that was indicated for the diagnosed condition. This is similar to other study findings looking at the availability of antibiotic drugs prescribed in Nigerian hospitals. Abu-Saeed *et al.,* 2013 found out that all the antibiotics used in their study facility were in the essential drugs list and almost all of the prescribed antibiotics were available at the pharmacy unit as at the time they were prescribed. The essential drug list in Nigeria is a list of medicines put together by the Nigerian ministry of health and the WHO to be made available at all times the hospital formularies. Odili *et al.,* 2010 also reported a high number (85.8%) of prescribed antibiotics being available in the hospital pharmacy for antibiotic.

From the 449 data entries studied, an average cost was calculated for a single antibiotic. This total drug cost was assumed to be the same as cost of prescription. This means all other costs patient may have incurred such as administration cost, substitution cost etc. have not been included. Average cost of a prescription was found to be ₦1,506 ($4.12) and the mean cost of antibiotics prescribed was ₦708 ($1.97). These values are quite lower than findings from the Abdu-aguye *et al.,* 2016 study that reported average cost of prescription to be ₦3,461 ($9.64) with the mean cost of antibiotics to be ₦2,238 ($6.24). This slight variation in price may be due to differences in product pricing in the different geographic locations as the studies were conducted in different geopolitical zones (conversion rate of $1=₦358.88).

The cost of medicines was found to be a major factor in deciding which particular antibiotic was prescribed for patients. This is due to the fact that in Nigeria most settings operate the out-of-pocket payment system, where patients pay 100% for their medical expenses. Most times they are not able to afford the recommended or ideal medication hence they are prescribed cheaper alternatives which may not be the most sensitive antibiotic for the infection diagnosed. This practice encourages the emergence of resistance and subsequently patients develops gradual resistance to the commonly abused cheaper antibiotic medications.

> *"Cost and availability of the required drugs, antibiotics are prescribed just because they are not expensive and are readily available"..PRB 001*

> *"Yeah, cost, the issue of cost and affordability of medications those are very pertinent issues one has to consider when prescribing antibiotic"...PRB 002*

> *"One other limitation is usually finance, because of the setting, we are in a 3rd world country, a developing country and most people that come to us say they don't have money to treat themselves. There is no health insurance, so when you prescribe the test, in my hospital most of their cultures are as cheap as 1000 or 1500 naira but most of the people cannot do it, so you will have to look*

at what's important. We just go straight and give the antibiotics because you have to choose what's best for the patient and prioritise. So, we consider all these things" ……………………………………………………… PRB 004

Inappropriate antibiotic prescribing still exists in the hospitals studied. Prescribing practices are similar in the hospital settings across Nigeria, as findings from this current study are consistent with the prescribing practices reported in earlier studies. The determinants of these antibiotic prescribing patterns are largely due to limited resources in the local settings at the government and institutional levels and prescriber related factors at the individual level. Recommendations to improve antibiotic prescribing in these settings should address the determinants at all levels.

6.3 Improving antibiotic prescribing in hospital settings

The increase in antibiotic resistance due to inappropriate antibiotic prescribing can be effectively minimised through a concerted effort of all stakeholders involved to avoid the occurrence of a post-antibiotic era. Many strategies aimed at improving antibiotic prescribing in hospitals and their effectiveness have been studied. Changing prescribing behaviour is a complex task and this challenge is significant considering up to half of antibiotic usage in hospital settings is inappropriate. Physicians in hospitals maybe unclear about the risks of inappropriate antibiotic prescribing (Wong *et al.,* 2015, Davey *et al.,* 2017). Most of the evidence on the effectiveness of interventions in improving use of medicines comes from studies conducted in developed countries (Davey *et al.,* 2017, Hulscher *et al.,* 2010). Only few studies have been carried out in developing countries and directly applying the interventions from developed and industrialised countries is unlikely to yield similar results as other factors may interfere in the developing countries. Wong *et al,* argued that any evidence synthesis that seeks to make sense of how interventions to change antimicrobial prescribing behaviour in doctors and their effects must consider the context in which the prescribing behaviour takes place.

6.4 Behaviour change models and classification of interventions to improve antibiotic prescribing

At this stage, interventions should be developed based on a suitable behaviour change model for the feasibility of implementation and eventual effectiveness. Different behaviour change models have been applied in healthcare interventions. Some of these models include the Health Belief Model (HBM), the Behaviour Change Wheel (BCW), the Theory of Reasoned Action (TRA), the Theory of Planned Behaviour (TPB) and the Trans-Theoretical Model (TTM). Each model has its own specific features that makes it unique. The HBM is mostly focused on health behaviour, while the TRA and the TPB can be applied in more generic settings, outside of healthcare (Taylor *et al*., 2006). None of these models sufficiently demonstrate the impact of social, cultural and economic/environmental factors except the BCW. The BCW provides a more structured approach for designing behaviour change interventions with considerations of social, cultural and economic/environmental factors. The BCW will be adapted in the design of recommendations to improve antibiotic prescribing in these settings given most of the determinants identified were structural and economic/environmental. The interventions will be classified based on the categories developed by the Effective Practice and Organisation of Care Group (EPOC) in a Cochrane review on interventions to improve antibiotic prescribing practices for hospital inpatients (Davet *et al*, 2017). Different forms of interventions have been documented as effective in improving the prescribing of antibiotics universally (both in developed and developing countries).

6.4.1 Use of EPOC framework for the classification of interventions

The different interventions to improve antibiotic prescribing have been grouped into three main categories by EPOC. These are persuasive, restrictive and structural. See Table 6.2 below. The main comparisons have always been between the persuasive and restrictive interventions. The restrictive interventions have on most occasions reported higher rates of improvement and is thought to be more effective than the persuasive interventions.

Table 6.2: Classification of interventions

Classification of interventions		
Persuasive Encouraging and empowering prescribers to improve on their prescribing behaviours voluntarily	**Restrictive** Limiting prescribing power by selective elimination of options or increased barriers	**Structural** Changes to practice settings, provision of relevant resources and overall improvements to work patterns
(Adapted from the Effective Practice and Organization of Care Group (EPOC by Davey *et al.*, 2017)		

These three categories are further explained with evidence of their effectiveness and impact in practice on improving antibiotic prescribing.

6.4.1.1 Persuasive Interventions

These methods include advice to physicians on how to prescribe or give them feedback on how they have prescribed. It encourages a voluntary change without any force or sanction. They include the distribution of educational materials, leaflets, organizing trainings, outreaches and campaigns, conferences, local opinion leaders, reminders (verbal, on paper or computer) audits and feedback reports or presentations.

6.4.1.2 Restrictive interventions

These methods impose regulations on how physicians prescribe antibiotics. This may include strategies such as selective stocking of antibiotics i.e. formulary restrictions, reserve antibiotic policies and prior authorisation of prescriptions by a higher authority, therapeutic substitutions, automatic stop orders, etc.

6.4.1.3 Structural interventions

These include physical changes in practice settings such as from paper to computerized records, rapid and effective lab testing and reports, quality monitoring mechanisms and computerized decision support systems.

6.4.2 Applying the Behaviour Change Wheel for development of the interventions

The Behaviour Change Wheel (BCW) is a framework that provides developers with a comprehensive, systematic and structural approach for implementing and supporting behaviour change. It was originally developed in 2011 by Michie and colleagues. The BCW has nine intervention functions and seven policy categories developed from a review of 19 previously established frameworks for classifying behaviour change interventions. The BCW is presented as a three-layer wheel that incorporates the sources of behaviour in the inner core of the wheel known as the COM-B (Capability, Opportunity, Motivation and Behaviour) system, the main intervention functions which serves as the agents for behaviour change and the associated policy categories. See Figure 6.1 below. The policy categories are based on the broader population-level strategies that enable the intervention functions to occur (Mangurian et al., 2017). The BCW has a strong focus on behaviour change and is now increasingly being used to develop interventions targeting behaviour change for healthcare providers.

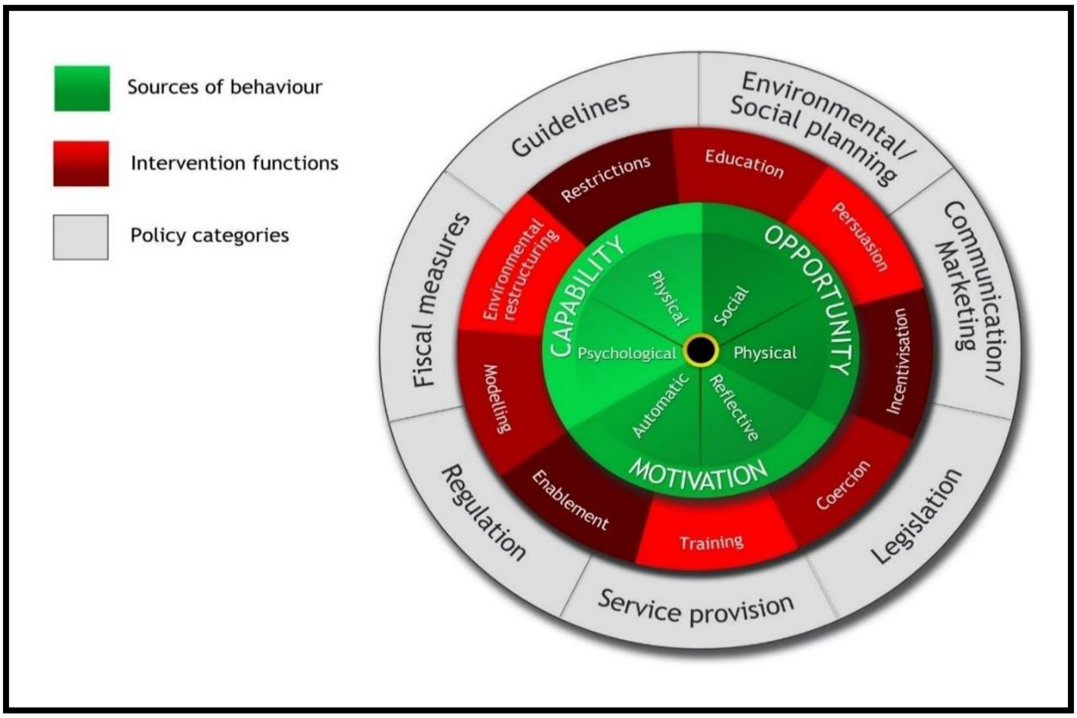

Figure 6.1: The Behaviour Change Wheel (Michie et al., 2011)

The process of intervention development and implementation using the BCW has been applied extensively. It involves three key stages linked to the three layers of the wheel. These are, Stage 1(The inner core): Understanding the intervention to achieve the desired change in the target behaviour(s) and identifying what needs to change; Stage 2 (the middle layer): Identifying Intervention Functions; and Stage 3 (The outermost layer): Identifying content and the relevant 'Mode of Delivery' for the intervention. These stages are discussed in more detail below, along with their application in this research. (See Figure 6.2).

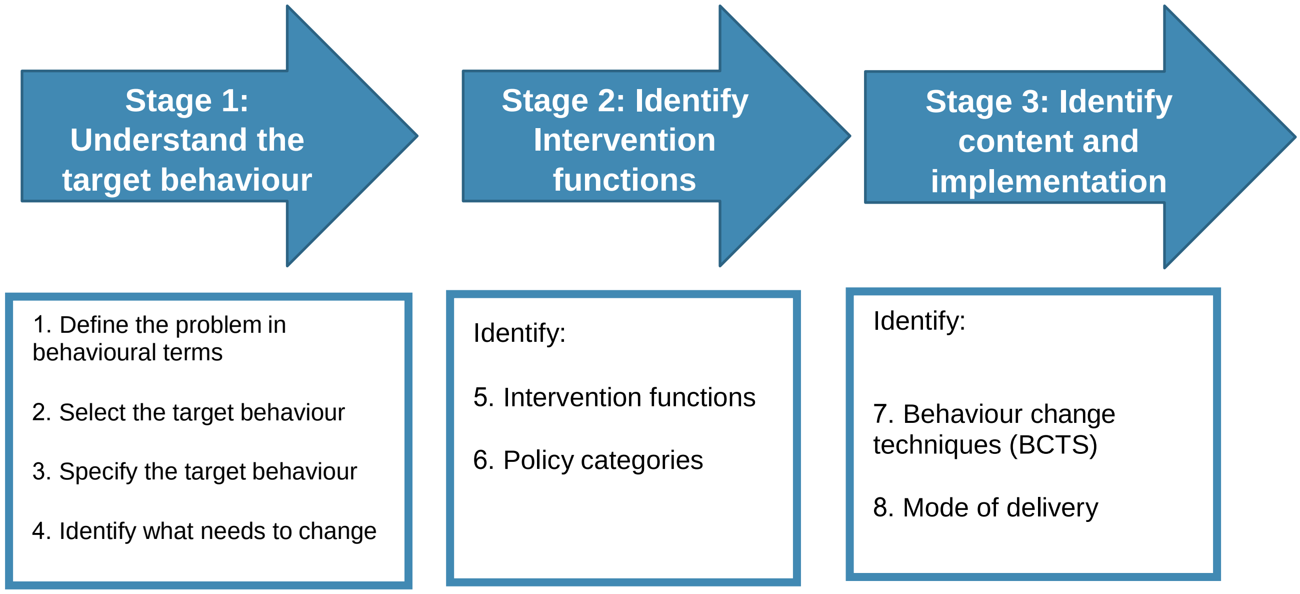

Figure 6.2: Key stages in the development and implementation of interventions using the BCW

6.5 Feasibility and implementation of recommendations using the BCW

Further interviews with stakeholders and the Behaviour Change Wheel (BCW) by Michie *et al.*, 2011 will be used to explore the feasibility and implementation of these strategies. The BCW has three distinct stages, and these are explained below in the context of strategies to improve antibiotic prescribing.

BCW Stage 1: Using the inner wheel (COM-B) to understand and target the behaviour

This initial stage focusses on defining the problems and understanding the target behaviour using four steps in the process. This first step is to define the problem in behavioural terms, then secondly to select the target behaviour after which you specify the target behaviour and finally identify what needs to change. The goal here is overall aim of this research is to identify the effective strategies to that will improve antibiotic prescribing in the study area. The initial results of this research showed that there was inappropriate prescribing of antibiotics and the reasons for this practice was explored further using interviews with prescribers. The target behaviour is antibiotic prescribing and the precise goal here will be intervention to change antibiotic prescribing leading to better outcomes. This will be achieved by analysing the elements of the inner core with regards to prescribers and prescribing antibiotics.

The inner core of the wheel holds the behaviour sources referred to as the **COM-B** system. The COM-B system proposes that for a change in behaviour to occur, the person or persons preforming the behaviour needs to have the physical and psychological **Capability**, the social and physical **Opportunity** and the reflective and automatic **Motivation** to perform this desired behaviour change.

Table 6.3 below summarises how the inner core of the BCW was used to identify the aspect of prescribers that need to change to achieve improved antibiotic prescribing practice.

Table 6.3: Use of inner core identify the aspect of prescribers that need to change to achieve improved antibiotic prescribing practice

CAPABILITY		OPPORTUNITY		MOTIVATION	
Physical	**Psychological**	**Social**	**Physical**	**Automatic**	**Reflective**
Skills Ability Perform	Required knowledge Mental capacity	Patient facing	Hospital Patients	Habits Emotional responses	Conscious decision making Beliefs

Capability: This is both physical and psychological. The physical capability refers to having the required skills and physical abilities to perform the behaviour. Here, antibiotic prescribing being the behaviour desired to change, prescribers mainly doctors will be targeted. Being a medical doctor guarantees the opportunity to prescribe medications by training. However, being a medical doctor, the required knowledge for appropriate prescribing which covers the psychological arm of capability can be enhanced by provision of guidelines and other reference materials.

CAPABILITY	
Physical	Psychological
Poor laboratory services Lack of training Lack of drug availability	Lack of knowledge Long term prescribing habits Pressure from patient Attitude of prescribers

Opportunity: Herein the social and physical opportunity lies which covers all the factors that go beyond the person qualities. It refers to the external factors that prompts or makes the behaviour possible to be carried out. In this context, the fact that prescribers encounter patients with infectious diseases and other cases warranting an antibiotic prescription satisfies the social opportunity. While the physical opportunity will include the hospital / clinic, the presence of patients which provides the opportunity for prescribing medicines.

OPPORTUNITY	
Social	Physical
Drug cost Patient economic status	Poor laboratory services No system support in the local settings Lack of guidelines and policies

Motivation: This refers to the cognitive process that energize and direct a behaviour. It includes the reflective motivation which covers the conscious decision-making based on beliefs about consequences and the automatic motivation driven mainly by habits and emotional responses. The motivation as a source of behaviour in the Behaviour Change Wheel is the target for influencing prescribing behaviour among doctors in this study. The interventions and proposed recommendations aim to change current attitudes, increase knowledge on resistance and also influence the way prescribers make their decisions when prescribing antibiotics in a bid to reinforce the appropriate habits and best practices. All this target the motivation aspect of the BCW inner core.

MOTIVATION	
Automatic	Reflective
Incentives form pharmaceutical companies	Improve health outcomes for patients

Having explained the three components of the COM-B, determinants of behaviour, it is now clear that in the case of antibiotic prescribing behaviours, the interventions developed to improve practice should be targeting the sources of behaviour identified in phase 2 of this study.

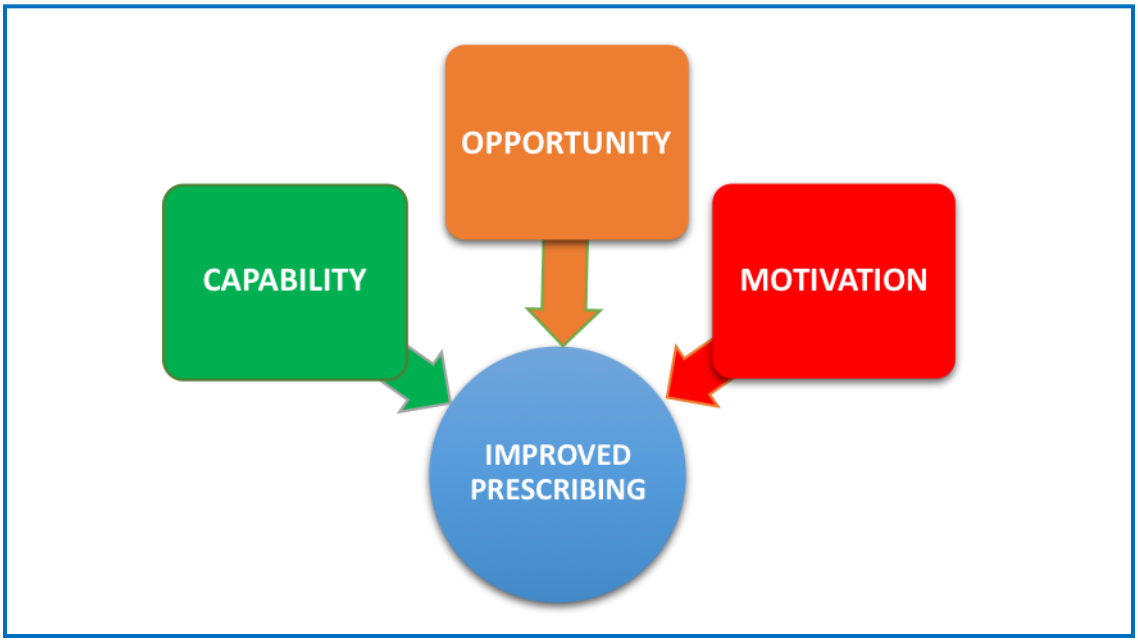

Figure 6.3: Sources of behaviours influencing antibiotic prescribing practices (COM-B)

Stage 2: Identify Intervention functions and policy categories

This stage involves using the behavioural diagnosis achieved with the COM-B system in stage one to identify what intervention functions and policy categories are needed to achieve the desired change. Having established that the motivation component of the inner core is the target for prescribers, question at this stage is what policy functions, demonstrated in the two outer rings will be able to influence the motivation component prescribers.

The BCW has nine intervention functions, and all of these are matched to the recommendations (BCT's) proposed as shown in Table 6.4 below:

Table 6.4: Matching the BCW intervention functions to proposed recommendations

BCW Intervention function	Proposed recommendations
Education	**Yes-** Increasing awareness through trainings and seminars, results from local studies and audits can also be used to educate prescribers on their current practices versus best practices and highlight areas that needs improvements. The use of local data is likely to be more impactful because of originality and ownership.
Persuasion	**Yes-** Guidelines, policies, protocols, fliers, leaflets**,** audits, local studies, are able to provide relevant information on appropriate use of antibiotics and also guide prescribers to make a clinical decision. They can be use also as tools where available to persuade patients not to demand antibiotics if they are nor needed.
Incentivisation	**Yes-** Provision of feedback on prescribing behaviour, Provision of incentives prescribers to encourage compliance with guidelines when prescribing antibiotics e.g. sponsorship to a conference
Coercion	**Yes –** Implementing subtle fines for e.g. inappropriate prescribing such as attending relevant courses on ethics and compliance, making certain workshops or training compulsory for annual licensing.
Training	**Yes-** Education and training on best practices can be organised by specialist in AMR and infectious diseases, this can be done as in-person events or online.
Restriction	**Yes**- Initiating reserve antibiotics policies, and restricted pharmacy dispensing.

Environmental restructuring	**Yes**- Improving lab buildings, setting up quality assay (QA) units and provision of other resources to support antibiotic prescribing.
Modelling	**Yes-** Provide and implement guidelines, reference materials and protocols to model best practices,
Enablement	**Yes-** Lab improvements, guidelines, health insurance, provision of low cost generic antibiotics to enable prescribing the appropriate antibiotic medicines

Education, persuasion, training and modelling are intervention functions that support the goal of increasing AMR awareness among prescribers that will help to impact their decisions and judgements when prescribing antibiotics. Restrictions, environmental restructuring and enablement are other intervention functions that will provide the right conditions and settings to enable the desired changes in antibiotic prescribing in the hospital setting.

Stage 3: Identify content and implementation options

Stage three comes in after applying the layers of the wheel to identify the target behaviour and choose the intervention functions, so this stage is actually outside of the BCW. The first step in this stage is to develop a detailed implementation plan by identifying and choosing from the Behaviour Change Techniques (BCTs). West and Michie, 2015 defined the BCTs as elementary components of interventions such as goal-setting, providing rewards etc. the techniques are the active ingredients within the intervention that leads to observable and replicable behaviour change. The BCT's are matched unto the intervention functions of the middle layer of the BCW according the specified target behaviour that needs to change.

The recommendations chosen and discussed above were selected as a combination of prescribers' suggestions and evidence of impact in similar settings from already published literature which is in accordance with the APEASE criteria. These recommendations were identified as BCT's linked to the BCW component. The BCW suggests that the selected intervention functions likely to be effective for changing prescribing behaviours can also be linked to the range of policy categories on the outermost layer of the wheel. See Table 6.5 below.

Table 6.5: Links between policy categories, intervention functions and the recommendations

Policy categories	Intervention functions	Recommendations proposed (BCT's)
Communication/ marketing	Education Persuasion Training	Increase awareness: Increasing awareness on antibiotic resistance, rational use of antibiotic etc. can be brought about by education and training via short courses, workshops, seminars. The use of fliers and posters on AMR, antibiotics etc. can be placed in relevant areas to support and persuade health care providers on best practices with antibiotic use.
Guidelines	Persuasion Restriction Modelling Enablement	Provision of updated STG's, prescribing references/guides and treatment protocols for prescribers to follow would also persuade and enable physicians to prescribe antibiotics appropriately as these guides' models best practices. While strict protocols can support restricted access to certain antibiotics that may be marked as reserve antibiotics
Fiscal	Environmental restructuring Enablement	Stocking low-cost generic antibiotics enables patients to afford their antibiotic prescribed, setting up quality assurance (QA) units providing health insurance, improvements to labs are all forms or restructuring and also providing the enabling environment for improved antibiotic use and prescribing.
Regulation	Training Restriction Enablement	Provision and implementation of updated guidelines, routine trainings as explained above, and conducting routine audits to regulate practice and identify areas for improvements.

Legislation	Restriction Enablement	Guidelines are able to restrict unnecassry use of antibiotics if adhered to, restricted dispensing of some of the reserved antibiotics and conducting audits as explained above.
Environmental/ social planning	Environmental restructuring Enablement	Increased awareness using planned AMR awareness campaigns, setting up QA units, improvements to labs, restricted pharmacy dispensing, audits
Service provision	Education Training Restriction Environmental restructuring Enablement	Service provision cuts across most of the BCT's already mentioned above. Such as setting up QA units, providing health insurance, improvements to labs, restricted pharmacy dispensing, audits. This sets the scene for effective service provision.

The final step in stage three will involve the sequencing of the activities in the intervention plan. This will depend on the context and goals of the key stakeholders in the different hospitals at the time. For example, while one hospital may start with some aspects of the intervention plan from scratch, in another hospital, they may only need to update an existing strategy. Generally, it will be necessary to cycle back and forth among the activities, while refining and improving the proposed strategies to suit the particular hospital given their own local context.

6.6 Recommendations suggested by prescribers

All attempts to improve antibiotic use in any setting should ideally be directed at the factors that contribute to the inappropriate use of antibiotics in that setting, using a bottom-up approach. The suggestions recommended by the prescribers in this study fits into the three intervention categories discussed above and these have been backed up with evidence of their effectiveness from studies in developing countries.

Given the different reasons identified for the observed inappropriate antibiotic prescribing practices in the study area, there is a need for a more focused, strategic and integrated action plan informed by the stakeholder's views and evidence-based research targeted at prescribing behaviour and how prescribing practices can be improved (See Table 6.6).

Table 6.6: Main factors affecting antibiotic prescribing and the corresponding suggestions by the prescribers to improve antibiotic prescribing

Reasons for the observed antibiotic prescribing practices	Suggestions from prescribers	Classification
Poor diagnostic and laboratory services	Improvements to health care delivery in the local settings: e.g. 1) Upgrading laboratory services 2) Make essential antibiotics available	Structural interventions
Local Settings and healthcare resources		
Cost of drugs and medical care / Patient economic status		
Availability of antibiotics		
Lack of core knowledge on antibiotic resistance	Training and education	Persuasive
Established practices on prescribing antibiotics	Antibiotic policies and guidelines, local studies and audits, restrictive prescribing	Persuasive and restrictive
Influence of incentives from pharmaceutical companies		
Pressure from patient		
Excessive workload on prescribers and healthcare providers	Pharmacists' interventions	Restrictive

Upgrading laboratories and other diagnostic services: Poor laboratory services were given as one of the main reasons for high empirical prescribing of antibiotics in the study area. As a result, more than half of the participants recommended upgrading the lab services available in the hospitals if meaningful improvements in antibiotic prescribing were desired. This is a structural intervention according to the EPOC classification of interventions. Three main factors were discussed under the issue of poor laboratory services of which majorly was the time it took to have results ready after sending off samples, secondly was the costs or running the tests, given that healthcare is pay-out-of-pocket and knowing the financial and social state of indigenes in the study area. Finally, was the complete absence of labs in some settings especially in rural areas, or the lack of equipment or reagent or even man power for effective services. This particular recommendation is one that is particular to this region and supporting literature is still very scarce.

Educational Training for healthcare providers: Many interventions from published literature targeted at improving antibiotic use and prescribing are educational in nature. Continuing medical education, antibiotic seminars and workshops can serve as a useful opportunity in educating antibiotic prescribers, pharmacists, nurses and other stake holders in antibiotic use in developing countries. Conducting educational trainings was also recommended by stakeholders. Several studies have reported insufficient prescriber knowledge about differential diagnosis, the kinds of conditions treatable with antibiotics and the appropriate therapies needed for bacterial infections (WHO, 2001). Davey *et al.,* 2017 also reported that half of the time physicians in hospitals are not prescribing antibiotics properly mostly because they are unclear about the benefits and risks of prescribing antibiotics, which antibiotics to prescribed, at what dose and for how long. Educating prescribers and organizing trainings in different forms is classified as a persuasive intervention. These interventions have been shown to produce some effects in some developing countries. In Zambia, continuing education for prescribers resulted in patients being prescribed antibiotics less frequently at intervention centres (34%) when compared to control centres (42%), there was also marked improvements in drug choices and dosing. In Indonesia, one-on-one educational interventions and seminars for medical prescribers reduced antimicrobial prescriptions by 17% (Santoso,1996). Educational programmes in Thailand led to a 24% reduction in antibiotic prescribing plus significant reductions in antibiotic resistance and costs (Apisarnthanarak *et al.,* 2006).

Antibiotic policy and guidelines: This is another form of persuasive intervention that was recommended by the stakeholders. They acknowledged the fact that guidelines were helpful but not readily available to them in the prescribing spaces, wards and consulting rooms. There has always been a debate as to whether antibiotic policies are effective in regulating the use of antibiotics and curbing the increase in resistance rates. However, some studies have been able to establish the ability of antibiotic policies to reduce antibiotic use and show its effects on reducing resistance rates. In Uganda, dissemination of national standard treatment guidelines alone was able to show marked improvements in antibiotic prescribing practices. (Kafuko *et al.,* 1996).

Improve availability of antibiotics: Although study findings showed that the commonly prescribed antibiotics were mostly available, interviews with stakeholders revealed that this was because they had to prescribe what is available and not necessarily what is indicated or most ideal. For this reason, they recommended that the different drugs and different classes of antibiotic drugs be made available in the hospital formulary to avoid prescribing alternative antibiotics for a bacterial infection that are not the most highly sensitive and this practice also increases the rate of resistance too. This can be classified as a structural intervention as it involves resources and managers at the procurement units. This is another peculiar issue in this study area with not a lot of literature published supporting this particular recommendation even in developing countries.

Conduct local studies and audits: Another recommendation by the stakeholders was that local studies and also routine audits be carried out in the practice settings to guide prescribing. This is also a persuasive intervention as it gives feedback on the prescribing habits of the physicians and points out the areas of defaulting for improvements. In South Africa, an antibiotic prescription chart and weekly antibiotic stewardship ward rounds were introduced in two medical wards of a teaching hospital and this resulted in Reduction in antibiotic consumption without harm to patients. There was a 19.6% decrease in volume of antibiotic consumption in terms of defined daily doses (DDD) with a cost reduction of 35% of the pharmacy’s antibiotic budget (Boyles *et al.,* 2013).

Restrictive prescribing: Some prescribers recommended some level of restrictions to antibiotic prescribing should be implemented. In the form of marking off some antibiotics as reserved antibiotics which can only be prescribed with authorisation from a second level, such as an infectious disease physician or specialist. In China, introducing formulary restrictions in their antibiotic policy, led to reduction in antibiotic sales from 25% to 17%, and also antibiotic prescriptions reduced from 68% to 58% (Xiao *et al.,* 2013).

Pharmacist's interventions: Stakeholders also mentioned some roles of the pharmacists in helping to improve antibiotic prescribing in the area. This includes the provision of updated formulary lists to keep prescribers informed as to what antibiotics are available. And also, that the pharmacist can also query an antibiotic prescription from a prescriber based on their own clinical judgement of the appropriateness of the prescribed antibiotics.

6.7 Recommendations chosen to improve antibiotic prescribing

Prescribing the right antibiotic at the right time for the right patient is not only about having the required knowledge about local formularies, resistance patterns and dosages but also understanding the patients' needs, concerns and comorbidities, while taking into consideration skills, knowledge, behaviours and the local settings (Wong *et al.,* 2015). Uncertainty still lies in deciding which intervention types should be implemented in local settings to get doctors to prescribe antibiotics appropriately. Improving antibiotic prescribing will require strategies to change behaviour. As illustrated by the three layers of the BCW, a multifaceted and multilevel interventions and strategies targeting different stakeholders in antibiotics use will most likely be effective in promoting rational use of antibiotics thereby helping to reduce the development of resistance (Rezal *et al.,* 2015).

Studying the antibiotic prescribing patterns and the factors that underpin the current prescribing behaviours in hospitals in Bayelsa state of Nigeria, provided valuable data which makes it possible to design stewardship programmes likely to be effective. This is because the stewardship programme comprises specific measures directly targeting the highlighted factors to improve prescribing of antibiotic in the local settings of this study. From the reasons affecting prescribing practices given by the stakeholders in the study, the proposed strategies will be grouped into immediate implementation and long-term implementation strategies across both persuasive and restrictive type interventions. Evidence from a review seems to suggest that restrictive interventions tend to have greater immediate impact than persuasive strategies, although the lack of standardization in measuring the effects is a major factor in this comparison (Davey *et al.,* 2017).

The proposed strategies for this study are discussed below in two categories, the interventions can be implemented immediately given that available resources can support the initial start-up, and the recommendations for implementation later due to management deliberations on the resources needed for the implementation.

6.7.1 Strategies for immediate implementation

These strategies were grouped as immediate implementation as they can be set up immediately using resources already available in the hospitals. They can be planned and executed by the already existing committees for example the Drugs and Therapeutics Committee (DTC) as they may not need any approval from a higher authority. These strategies are presented in the table below and explained individually thereafter (See Table 6.7).

Table 6.7: Recommendations presented to stakeholders for immediate implementation in the hospital

Recommendations	Specific issue to address	Target group	How to measure	Impact
Increase antibiotic resistance awareness in the hospital environment	To highlight the need for appropriate use of antibiotic to preserve their potency	All healthcare providers in the hospital	Compliance with the guidelines Reduced empirical prescribing	Reduction in unnecessary prescribing of antibiotics
Monitor antibiotic use and consumption /Audits	Provide the data for action plans (procurement, education and training)	Drug procurement team Prescribers Policy stakeholders	Reports generated	Reduced antibiotic stock out incidents/ Provide useful for procurement
Informed education/training for prescribers	Improve knowledge and create awareness on the need for appropriate prescribing of antibiotics	Prescribers	Compliance with guidelines, Use of lab results	Rational prescribing of antibiotics
Provide/Implement the guidelines	Improve compliance to the Guidelines as they are not readily available for the prescribers in the hospital	Infection control unit, Drug ethics committee	Audits	Appropriate use of antibiotics

Source for rapid diagnostic kits	Reduce the waiting time for less complicated sensitivity tests	Procurement / Laboratory unit	Time to wait for lab results	Reduction in time to arrive at a clinical diagnosis
Conduct local studies	Provide missing data on local resistance and susceptibility patterns that will inform local guidelines	Research and ethics, pharmacy, laboratory unit	Data presented	Informed decision to guide local policy
Stock effective and cheaper generics	To improve affordability of the required antibiotics	Pharmacy and procurement	Reduction in antibiotic stock out	Increased antibiotic drug availability

Increase antibiotic resistance awareness in the hospital environment: In Africa, much of the general public and a significant proportion of health professionals still have very limited awareness on the issues of and the part they play in antimicrobial resistance (Okeke, 2016). This is also supported by findings obtained from initial interviews with prescribers.

The first step will be to improve upon the current level of antimicrobial resistance awareness in the hospital environment. This is important in effecting the behavioural change necessary to reduce resistance and will reinforce the message among health professionals that antimicrobials need to be preserved. This may be achieved by educational trainings and outreaches, distributing printed materials like fliers and posters around the hospital, in strategic points with short messages on antibiotic resistance. A review by Davey and colleagues demonstrated that a combination of persuasive strategies can be effective (Davey *et al.,* 2005). The desired impact of increasing awareness here is not just bringing prescribers to know about antibiotic resistance but awakening a sense of consciousness and responsibility that will influence attitudes towards appropriate and rational prescribing of antibiotic drugs. The outcome of this can be evidenced by increased compliance to guidelines and increased use of lab tests which can be measured by routine audits leading to reduction empirical and unnecessary prescribing of antibiotics.

Routine monitoring: Monitoring antibiotic usage and the consumption patterns will provide reliable and up-to-date data on how antibiotics are prescribed and used. Monitoring in this instance will include what classes of antibiotics are commonly prescribed, the doses, formulations and routes, for what indications, compliance to guidelines and other measures. This will help highlight the priorities that needs to be improved upon while informing current best practices approaches. Delegated members of the infection control team will be assigned this responsibility quarterly or at a more feasible interval. The data generated will be useful feedback for training prescribers and will also enable informed actions for example the drug stocking by the procurement team to avoid issues of antibiotic drug stock out and unavailability.

Audits and local research Unit heads can liaise with research and ethics committee also to carry out local research that will generate data on local sensitivity and resistance patterns to guide local policies. In tertiary hospitals, physicians rely mostly on the local resistance or susceptibility patterns of the pathogen isolated from a patient to decide on the choice of antimicrobial in the absence of an antimicrobial sensitivity test. This will also benefit the health personnel in rural settings without advanced diagnostics and lack the capacity to do antimicrobial testing and sensitivities. The impact will be reduction in empirical prescribing and broad-spectrum use of antibiotics to treat infections as this practice has been shown to contribute to increase in antibiotic resistance (Ayukekbong *et al.,* 2017).

Informed Education and training for prescribers: Previous studies have highlighted the need to continually educate prescribers on appropriate prescribing of antibiotics. A published report has shown that about half of the time physicians in hospitals are not prescribing antibiotics properly as they may be uncertain about whether to prescribe an antibiotic or not, the particular antibiotic to prescribe, the dose, duration and also what the risks and benefits there may be (Davey *et al.,* 2013). Similar findings were observed during the interviews in this present work when prescribers mentioned that lack of core understanding in the process of antibiotic prescribing is among the factors contributing to poor antibiotic prescribing practices. The results from routine audits and monitoring of antibiotic use carried out in the local units and hospitals will be used as part of the informed education and training for prescribers on antibiotic prescribing highlighting areas of deficiencies in the current practice and also stressing the dangers or over prescribing and inappropriate antibiotic use. This will increase awareness of the issue of antibiotic resistance among prescribers as it shows that not many of them are fully aware of the prescribing implications for increase in resistance and the extent of the problem in practice. Such trainings are to stress and emphasize the need for appropriate antibiotic prescribing that is in accordance to the agreed guidelines. This will also serve as a refresher course for prescribers on best practices when prescribing antibiotics.

Update and implement the guidelines: The prescribers interviewed in the phase II study mentioned that the guidelines were out-of-date and are not readily available when needed. The current standard treatment guideline available in Nigeria was last written/revised in 2008 which is almost a decade ago. Clearly there is a need to review this document to reflect current advances in infectious disease management, antibiotics use and the resistance patterns. The section on infectious diseases in the national treatment guidelines can be reproduced in copies of a small booklet and/or other formats and placed in consultation rooms and also on the wards so prescribers can assess it for guidance when prescribing antibiotics. Also, this guideline can be made available electronically for prescribers as a mobile app so they have the guidelines with them on the go via their mobile phones. If prescribers can readily access the guidelines when prescribing antibiotics, this can be effective to improve antibiotic use by reducing the high rate of empirical prescribing and also reduce the volume of unnecessary prescribing of antibiotic drugs. Studies has shown marked beneficial effects on antibiotics use through the use of guidelines in developed settings and also in developing countries.

Stock effective and low-priced generics: According to the World Health Organization (WHO) one third of the worlds' population of today cannot afford the required medicine that they need (Foster, 2010). Studies have shown that affordability is also dependent on whether the drug is an innovator brand or a cheaper generic brand. This factor has been supported by several reports carried out from Health Action International (Cameron *et al.,* 2009; Babar *et al.,* 2007). One major issue that also affects the way antibiotics are prescribed in the study area is the cost of antibiotics drugs. In the study area, cost of healthcare is financed though out of pocket payments. There is still no form of health insurance for some citizens. From the interviews, it was gathered that some patients are not able to pay for the costs of the appropriate antibiotic medication they may need and as such get prescribed a different antibiotic which is cheaper and one that they can afford. The analysis conducted for antibiotics cost and availability in phase I shows that the generic medicines are generally cheaper, but more branded medicines are available in the hospitals. Leisinger *et al.,* 2012 also reported the average availability of generic medicines to be 38% in the public sector in most LMIC's. The procurement of low-priced generics will be increase availability of antibiotics such that patients will have access to the required antibiotics even when they cannot afford the branded medicines which are more expensive. It will also reduce incidence of drug stock outs and help the clinicians comply with guidelines. Prescribers previously mentioned that compliance to the guidelines was difficult when the drugs are not available. However, this recommendation is challenged by the availability of fake and sub-standard medicines particularly available in LMICs.

Provision of Rapid Diagnostic Test (RDTs) kits: Interviews conducted with prescribers showed that there were delays in receiving laboratory sensitivity results, and in some cases, these are not even available due to the lack of diagnostic testing resources or personnel**.** Rapid diagnostic testing kits for bacterial infections that can show sensitivity immediately in not too complex cases will be helpful. These tests kits are designed to be used directly at the site of patient care such as a physician office, outpatient clinic, and patients' homes. They can help to streamline antibiotic prescribing to comply with guidelines, reduce the prescribing of unnecessary antibiotics and also reduce the amount of empirical antibiotic prescribing.

Researcher's report that RDTs may provide some benefit in decreasing the amount of inappropriate prescribing. The impact of RDTs on patient mortality has not yet been established. Three studies used rapid reporting of microbiology test with increase in appropriate antibiotic therapy to measure mortality and in all three studies, there was no significant difference between the intervention and control patients (Bouza, 2004; Bruins, 2005 and Doern, 1994).

While other benefits of RDTs will include shortening the time of a test result and screening for various infectious diseases in an outpatient setting. The decrease in the amount of time to analyse a result compared to standard microbiological procedures benefits the management of infectious diseases considerably (Ogrin and Klepser, 2013). While the provision of these RDTs will support stewardship strategies the cost of procurement makes it difficult to implement in the local settings where healthcare financing is still of national concern.

6.7.2 Recommendations for implementation in the long term

These recommendations were grouped as long-term strategies because they will need more planning, resources and finances in the process of their implementation. This will need proposals to be written and defended and obtaining government approvals and release of funds for project execution which takes time. They are summarised in the Table 6.8 below and then discussed individually in separate sub-headings.

Table 6.8: Recommendations to be presented to stakeholders for implementation on the long term

Long term implementation				
Recommendations	**Specific issue to address**	**Target group**	**How to measure**	**Impact**
Improving laboratory and diagnostic services	To ensure efficient and timely provision of sensitivity results	Management, Government	Measure time it takes to get back lab results,	Reduction in empirical prescribing
Restricted pharmacy dispensing	Providing a check to ensure the right antibiotic is prescribed correctly for the patient/indication.	Pharmacists and Management	Pharmacists queries/ interventions in antibiotic prescriptions	Reduction in amount of antibiotic prescribing
Implement health insurance schemes for vulnerable patients sub groups	Cost of treatment for patients that require an antibiotic course that they cannot afford	Management, Ministry of health	Improve health seeking behaviour, increased patient turn-out in the hospitals	Patients will receive the right antibiotic they need

Improving laboratory and diagnostic services: Access to quality laboratory services is often seen as pivotal to the appropriate use of antimicrobials. Delayed results, poor services and the complete lack of laboratory facilities mostly in low income countries has contributed to over prescribing and high rate of empirical use of antibiotics (Radyowijati and Haak, 2003). Strategies to improve antibiotic prescribing from the lab services will include acquiring the right spaces, machines, reagents to run the required tests such as culture and sensitivity tests, employ more staff in the laboratories and consider operating 24hour services to cover on-call hours. This will ensure tests are run as soon as samples are collected irrespective of the time they get into the laboratory thereby reducing the time for results to be ready from when the tests are requested. This result should be documented also in the laboratory data base as this will provide useful data to determine the sensitivity and resistance patterns in the local hospital and in the different units. This information will then be useful to design the local antibiotic guidelines and also for continuous education and training purposes for prescribers. This has been included in the recommendations as the actual implementation will include management planning, finance budgets and other approvals that will require some amount of time.

Restricted pharmacy dispensing: Another recommendation to help improve prescribing of antibiotics will be to initiate restrictions on some antibiotic prescriptions by pharmacists. In China, introducing formulary restrictions in their antibiotic policy, led to reduction in antibiotic sales to patients from 25% to 17%, and also antibiotic prescriptions reduced from 68% to 58% (Xiao *et al.,* 2013). Pharmacists have an ever-increasing important role in influencing the antibiotics prescribed and dispensed to patients. In some developed settings, clinical pharmacists carryout checks to assess the appropriateness of antibiotics prescribed and actually intervene if and when necessary. This is not so in most developing countries where the practice of clinical pharmacy is still developing and faced with inherent barriers like limited access to patients' case notes, political and professional rivalry with other healthcare professionals and shortage of skilled man power (not enough trained pharmacists). An Australian study was conducted to understand hospital pharmacists' accounts of antibiotic use, and the potential role of the pharmacist in antibiotic optimisation within a tertiary hospital setting. The results show that:

(1) Pharmacists' attitudes are still ambivalent towards the significance of antibiotic resistance with optimising antibiotic use perceived as low priority;

(2) Pharmacists' current capacity to influence antibiotic decision-making is limited by the prescribing power of doctors and the perception of antibiotic use as a medical responsibility;

(3) Inter-professional and organisational barriers exist that prevent change in the hospital setting including medical hierarchies, limited contact with senior doctors and resource constraints resulting in insufficient pharmacy staffing to foster collaborative relationships and facilitate the uptake of their advice.

They concluded that unless these issues are addressed, they will continue to significantly limit the ability of pharmacists to influence antibiotic prescribing (Broom *et al.,* 2015).

Educational training should be organised for pharmacists to build their capacity and inputs in antimicrobial therapy management while increasing their roles and responsibility in ensuring appropriate use of antibiotic medicines. Secondly, hospital institutional policies should support pharmacists' interventions in antibiotic therapy management as part of the multi-professional healthcare delivery team.

Provision of health insurance schemes patients: As the economic condition plays an important role to the irrational use of antibiotics, authorities have to set up a health insurance system to assure the healthcare services to their citizens. The healthcare system in Nigeria still operates an out-of-pocket payment system mostly and it's still a struggle for regular citizens to pay for the required lab tests and prescribed antibiotics when ill. Interviews with prescribers showed that some antibiotics were prescribed for patients not because it was the most appropriate option but just because it is the option the patients could afford, which constitutes irrational use of antibiotics leading to resistance.

Providing insurance for citizens will encourage them to seek medical care in hospitals and this will reassure the healthcare professionals to implement the appropriate antibiotic-use policies such as requesting the ideal diagnostic investigations and prescribing the correct antibiotic medicines according to the guidelines for the patients without worrying if patients will be able to pay for the services or the medicines. Without a health insurance scheme that covers most of the populations, any guidelines and policies regarding the appropriate use of antibiotic will be hard to implement (Abdulah, 2012).

6.8 Justification for the recommendations developed

This chapter brings together finding from phase one and phase two of this work to explain the current antibiotic prescribing practices and the impacting factors. These findings informed the recommendations proposed and discussed above. As a form of response to current issues highlighted in antibiotic prescribing in the study area. Most of these recommendations takes forward some global strategies to address AMR already outlined by the WHO.

In 2001, the WHO released a document for global strategy on containment of antibiotic resistance, to enable countries implement policies on AMR. The strategy includes: Improving use and access to appropriate antimicrobials, strengthening health systems and their surveillance capabilities and enforcing regulations and legislation.

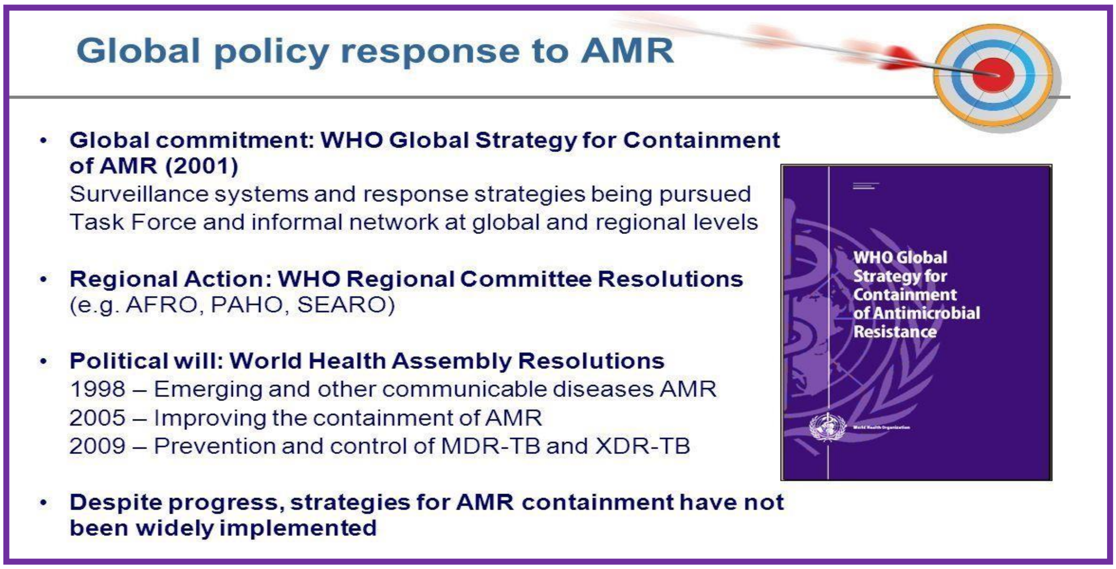

Figure 6.4: The WHO global strategy on the containment of antibiotic resistance

This WHO Global Strategy for Containment of Antimicrobial Resistance (See **Figure 6.4**) provides a framework of interventions to slow the emergence and reduce the spread of antimicrobial-resistant microorganisms through the following strategies:

- ❖ Reducing the disease burden and the spread of infection
- ❖ **Improving access to appropriate antimicrobials**
- ❖ **Improving the use of antimicrobials**
- ❖ **Strengthening health systems and their surveillance capabilities**
- ❖ **Enforcing regulations and legislation**
- ❖ Encouraging the development of appropriate new drugs and vaccines.

This global strategy is people-centred with interventions directed towards the groups of people who are involved in the problem and need to be part of the solution, i.e. prescribers and dispensers, veterinarians, consumers, policy-makers in hospitals, public health and agriculture and professional societies. It highlights the need for further research directed towards filling these existing gaps in knowledge. This research work has been able to provide further insights on some of these strategies (highlighted in bold above), by exploring first hand views and perceptions of relevant stakeholders as mentioned above in resource poor settings where this data is especially lacking. Thereby filling some these existing gaps in knowledge.

Almost two decades later, the national and global responses to these strategies is still inadequate. The findings in this work demonstrate that for global policies to produce the desired response on AMR containment, there is a need to consider the differences across healthcare settings. While developed settings have a robustly financed healthcare system with advanced technology, monitoring and surveillance systems, developing and resource poor settings still struggle with basic things like availability of antibiotics, quality of the drug, cost and affordability, documenting antibiotics use and lack of skilled personnel such as infectious disease specialists etc. As a result, global strategies need to consider the factors that interplay in different settings, if any desired response is to be achieved. For example, international policies encouraging generic prescribing for cost savings in healthcare delivery are not directly applicable in all settings, as the findings presented in this report shows that prescribers would rather prescribe antibiotics as the branded drug, due to the high amounts of fake and substandard medicines in circulation as generics.

Another policy that the study findings impact is the WHO policy package to combat antimicrobial resistance published in the bulletin of the WHO (Leung *et al.,* 2011). The results presented in this project provides ways to take forward as some of the recommended changes and areas of concerns to the policy. These include lack of commitment and data and issues of irrational use and unassured drug quality.

Lack of commitment and data- The need for sustained containment efforts and the paucity of surveillance data on AMR hinders adequate response to control AMR. This research has stressed the need for antibiotic use surveillance and how this can be used to improve practice see Figure 6.5 below. The study findings indicate that there are no working antibiotic stewardship teams in the hospitals studied, hence the recommendation to set up a working antibiotic-use committee in hospitals to oversee antimicrobial stewardship strategies and ensure their execution. This includes monitoring and documentation of antibiotic use in quantity and patterns to generate much needed surveillance data and evidence base on antimicrobial use and resistance. This will inform policies going forward and will help in updating existing local treatment guidelines.

Figure 6.5: How surveillance improves health outcomes (adapted from FutureLearn, UEA)

Unassured drug quality and irrational use- The lack of access to quality-assured medicines at affordable prices, poor provider knowledge and lack of treatment guidelines are key contributors to inappropriate antibiotic prescribing practices (Leung *et al.,* 2011). This is supported by this current study findings, as affordability and costs were key factors affecting prescribing patterns. A recommendation proposed in this project to address this is for the government to increase the allocation of funds for healthcare and provide health insurance for citizens. Then, national policies guiding antibiotic use in the hospitals can be implemented successfully.

6.9 Chapter summary and implications for the next phase

This chapter discusses a triangulation of the results obtained from phases I and II. The reasons and determinants of antibiotic prescribing patterns in the hospital has been identified. Recommendations suggested by prescribers together with other strategies that have proved effective from the literature have been used to develop specific recommendations for the local settings targeting all sources and policy categories as outlined in the BCW.

The next chapter will discuss the stakeholders' views on the recommendations selected to be implemented in the hospital, the feasibility and priorities for implementation as well as the likely barriers. This will be achieved by interviews with selected stakeholders in the study area.

Chapter 7 STAKEHOLDERS VIEWS ON FEASIBILITY AND IMPLEMENTATION OF RECOMMENDATIONS

7.1 Introduction to chapter

The earlier stages of this research work have described the antibiotic prescribing practices in hospitals from the Niger Delta region of Nigeria. Findings from the phase one study showed that there is still inappropriate prescribing of antibiotics across secondary and tertiary care hospitals in the area. This is evidenced by the results that show

- High rates of empirical prescribing of antibiotics (seen in 72% of the cases studied)
- Poor compliance to treatment guidelines (only 28% of antibiotics prescribed had complete compliance with the guidelines)
- Limited use of clinical diagnostics as guide when prescribing antibiotics (84% of the cases studies did not have any relevant sensitivity tests carried out)

These findings informed the phase two study. The reasons for the observed prescribing practices were explored with qualitative methods using interviews with prescribers in the study area. Prescribers were also asked to discuss recommendations they think will be most effective in their settings to improve antibiotic prescribing. This is because they have direct experience of prescribing antibiotics in the settings which puts them in the best position to point out recommendations most likely to be effective. Many stewardship programmes have been implemented in developed settings over the years with notable improvements to antibiotic use and prescribing. However, directly applying the evidence of these interventions in developing healthcare settings is likely to be unsuccessful as other factors such as healthcare financing, manpower and resources, drug availability etc. are likely to interfere in the effectiveness.

After careful analysis of the reasons projected from the interviews, a list of recommendations backed up with evidence from the literature was then developed into a set of proposals and presented to the key management staff and other relevant stakeholders in a selected hospital in the study area. Employing the bottom-up approach, prescribers' suggestions from the previous phase were also used to inform the set of recommendations being presented now to the stakeholders identified at different policy levels in the system.

This was done to obtain acceptability and feasibility of the recommendations by the stakeholders. Acceptability being to what extent were the recommendations accepted by stakeholders to improve current practice with antibiotics and feasibility being to what extent are these recommendations likely to be successfully implemented in the local settings. Most recommendations maybe accepted however, some may not be immediately feasible due to lack of resources and limited financing as highlighted earlier in the healthcare systems. This will include recommendations needing additional funds for implementation like upgrading the laboratory services and other diagnostic facilities such as provision of RDTs. Barriers in the implementation of recommendations was discussed and some of the proposed recommendations already being been implemented in some form are highlighted. Finally, identifying from the stakeholders the top priorities for implementation i.e. the most important recommendations that can be taken forward immediately given the resources currently available in the local settings that will bring about effective and sustainable changes to practice.

7.2 Aim and objectives of this phase

The aim of this part of the work was to obtain the stakeholders views on the feasibility of the proposed recommendations. The specific objectives were:

1. To identify and recruit the relevant stakeholders in the study area antibiotics use in for interviews.
2. To explore their perceptions and acceptability of the proposed recommendations.
3. To determine if the recommendations have been put in place or exists already in any form.

4. To identify the likely barriers in the implementation process of the proposed recommendations to improve antibiotic prescribing.
5. To inform implementation of subsequent antimicrobial stewardship plan in the hospitals.

This will help to identify the given set of recommendations that can then be finally put forward as strategies to improve antibiotic prescribing in the Nigerian hospital setting and would also work in other similar settings.

Previous research on changes to professional behaviour shows that most interventions require further efforts or “implementation plans.” Earlier studies also agreed that there is no superior strategy that works for all innovations and concluded that the way forward will be to build an intervention after careful consideration of the obstacles and on a coherent theoretical base (Marlies *et al.,* 2010; Grol and Grimshaw, 2003 and Grimshaw *et al.,* 2006).

7.3 Procedure

The proposed recommendations were presented to stakeholders in the study area as mentioned above. Key members of the hospital clinical and administrative staff and other relevant stakeholders in the regulatory and policy settings were identified and recruited.The stakeholders recruited include the medical director of a hospital, head of unit, prescribers, pharmacist, representative of drugs and therapeutics committee, chairperson of the medical association in the study state, representative of the state ministry of health etc. A total of eight participants were recruited for the interviews including four pharmacists,two medical practitioners, one medical microbiologist and one administrative staff. Of these, there were six males and two females. All participants had over six years of practice experience and were drawn from different areas of practice including clinical, administrative, and regulatory/policy.

Table 7.1 below shows the demographic characteristics of the participants. Upon acceptance to partake in the study, interviews were scheduled and conducted for the stakeholders to share their views on the proposed recommendations, any forms of implementation so far and the barriers likely to be encountered in the implementation process. This is in line with the stage 3 APEASE criteria of the behaviour change wheel.

Table 7.1: Demographic characteristics of the stakeholders recruited

Characteristics		Number of Participants n=8 (%)
Gender	Males	6
	Female	2
Years of practice	≤ 5	0
	6-10	4
	11-15	2
	≥ 16	2
Profession	Medical practitioner	2
	Pharmacist	4
	Medical microbiology	1
	Other (Administrative)	1
Area of practice	Clinical	4
	Administrative	2
	Regulatory/Policy	2

7.4 Results on stakeholder's views on the feasibility of proposed recommendations

The findings are further discussed below under the individual recommendations in line with the related intervention functions and policy options from the BCW. The acceptability, practicalities and potential impact of these strategies were also explored.

Increase awareness on antibiotic resistance: Most of the stakeholders interviewed agreed that prescribers in the hospital still do not fully understand the reasons for antimicrobial resistance, and there is the need to increase the awareness on antibiotic resistance. The majority of the informants also said that increasing awareness should not only target the prescribers but also other healthcare providers and the patients receiving the drugs too as inappropriate use on their part also leads to resistance. However, some participants mentioned that prescribers are aware of antimicrobial resistance and that the real issue lies in the change of attitudes. It was also gathered that some lectures and sensitization campaigns had been organised on antimicrobial resistance for prescribers by the drug and therapeutics committee.

> *"There is awareness, but the problem is the way to implement the strategies that are being put forward…. we have done quite a number of sensitisation in this area so it's not that they are not aware, they are, but they lack the will and courage to do it" --- STKH 001*

A respondent talked particularly about a recent presentation that held in the hospital on the rational use of antibiotics put together by the drugs and therapeutics committee. This was done to inform and educate the hospital staff on the outcomes of irrational use of antibiotics as some stakeholders agreed that the education and awareness has to be provided for all healthcare providers (multidisciplinary) and the patients also. If the patients are well informed, their expectations to receive an antibiotic for every ailment will greatly reduce and this will further impact on the number of antibiotics prescribed unnecessarily due to pressure from patients.

> *"I think first of all what brings about antibiotic resistance is on the side of the patient because most times patients abuse antibiotics and take antibiotics anyhow without any indication…. The awareness shouldn't necessarily be to the doctors alone but also to the patients to make them know that self-medication with antibiotics leads to resistance" ……. STKH 006*

The main barriers highlighted that impedes awareness include the lack of skilled personnel with the passion for antimicrobial resistance, for example, infectious disease consultants, lack of continuity and poor attendance during the presentations. If prescribers have the right knowledge and attitude on antimicrobial resistance, they would be able to make the right decisions when prescribing antibiotics having considered the implications in the long term. With the barriers highlighted, what would likely work in this setting will be to and employ more Infectious Disease (ID) specialists to champion the cause for AMR sensitisations, campaigns and other related activities. This corresponds to communication/marketing policy category of the BCW, for initiating behaviour change. Also, incentives like Continuing Medical Education (CME) points can be awarded for participation to encourage attendance. The impact of this will be antibiotics being prescribed rationally as measured by increased compliance to the guidelines, used of investigations and reduction in empirical prescribing. This particular recommendation supports the education, persuasion and training intervention functions from the BCW.

Monitor antibiotic use: The stakeholders also accepted the recommendation on monitoring the use of antibiotics in the hospital. They generally agreed that monitoring antibiotic use and keeping tracks on antibiotic consumption is another recommendation that can help to determine if any change in practice is needed towards the improved use of antibiotics. The findings on monitoring will enable informed decisions and identify areas for improvement in practice also. They initially started this practice in the hospital from the pharmacy department as gathered from some of the participants, however, sustaining this practice over time is challenging due to staff shortage especially in the pharmacy departments where monitoring antibiotics use is most feasible.

> *"In the hospital, currently the pharmacy department is now monitoring antibiotic use in the wards mostly, the consumption patterns, and we tried to compare with previous reports from studies. There are similarities, but we need increased workforce to help sustain the monitoring of antibiotic use, if this is continued, we are going to really get so much from monitoring the use of antibiotics" --STKH 003*

Another participant stated that even though antibiotics use was being monitored and documented, there was still no system put in place to adequately present the data obtained and feedback to the clinicians to enable them to reflect on their own practice. However, the overall goal of monitoring antibiotics use goes beyond the documentation. It aims to reinforce collaboration between the prescribers, pharmacists, nurses and microbiologists and other care providers involved in antibiotics use process. It will entail details of what antibiotics are being prescribed, what classes, for what indications, what doses, what formulations, and when exactly are antibiotics prescribed all this coordinated from the pharmacy. The microbiology labs will have to monitor the bacterial sensitivity patterns and then link these results with the antibiotics use data from the pharmacy unit to see the association between what is needed and what is being used. So, this can inform local guidelines and policies, procurement of antibiotics and other improvement plans to practice.

Conduct hospital-specific research: Conducting local studies on infections and resistance trends in the individual hospitals can help to inform education/training for prescribers. This was another recommendation put forward that was agreed upon and accepted widely by the stakeholders interviewed. This has not been implemented in any of the hospitals yet as part of improvement plans on antibiotic use. This recommendation can be linked to audits also discussed above. The research and ethics unit will coordinate the studies in collaboration with the pharmacy and lab units on local resistance and susceptibility patterns, antibiotics drug use charts. Relevant data will then be generated that will inform local guidelines. Findings of the studies will also serve as a check to current practice identifying priority areas that will need changes of some sort. The secretary of the REC stated that it is in the new work plan of the committee and that the microbiology lab has been contacted on it already.

> *"No, it's not being done yet. We spoke to the microbiology lab already and we also need this to create the antibiotic stewardships. So, we are working on that now. Hopefully we would do all of that this year" --STKH 002*

Although one participant mentioned that a few studies have been carried out earlier in the hospital on microbial sensitivity patterns, there was no continuity as this was not done routinely in the hospitals.

> *"The research component is also very weak, we have poor data gathering and poor research foundation. We have also done a baseline study where we took swabs across the different units and it was interesting what we found. We isolated organisms from stored water and suction machines in the SCBU {Special Care Baby Unit} and the resistant pattern was bad. So, the infection control needs to step up and be effective. It's not supposed to be a one-off study, this should be carried out more often and compared*

with previous results. Also finding should be used to influence the prescribing patterns" ----STKH 005.

The issue to address is to source for workforce to strengthen and sustain the research component and ensure the studies are carried out routinely and findings will be communicated through right channels to guide subsequent practice.

Update and implement guidelines: The next proposed recommendation discussed was to update the guidelines and make them available, which all participants agreed to. One participant stated that a major problem in antibiotics use is the fact that guidelines are either out of date or not available in the hospitals, there are current plans to come up with a standard guideline for the hospital. This will be built from the national guideline and reviewed to suit the local hospital.

> *"We are actually working on the development and implementation of Standard Treatment Guidelines {STG} for the hospital. We would build from the national STG as it will be a reference material for us and then we have to look at what is working in our environment and then adopt it and also implement it, that is what we intend to do" ---STKH 001*

The idea of formulating the guidelines into a mobile app for easy access was presented to the stakeholders and it was a very welcome idea, and they definitely agreed this will make prescribing of antibiotics much easier and help to reduce mistakes.

> *"If we can have this it will be good that will be very good, and it will really help compliance because we live in an age now where everything is going paperless everything is on your devices. Technology has made a lot of things easier. But we will work on it together. "-- STKH 001*

> *"Wow. That will be very good and helpful too. The software will definitely be better for the doctors for example if you want to treat bronchitis, you can go to the app and just type bronchitis, and everything comes out like that. I think this will help reduce the mistakes in prescriptions greatly."—STKH 002*

Guidelines is one of the policy categories in the BCW, its intervention functions include persuasion, restriction, modelling and enablement. Providing updated guidelines will model antibiotic prescribing enabling prescribers to prescribe more appropriately.

Rapid diagnostic kits: This was one proposed recommendation that had some uncertainties from the stakeholders' responses. They were not sure such kits were actually available and even if they were, the stakeholders expressed some concerns on the limitations based on the experience they have had using similar rapid tests kits for other parasitic infections like malaria.

> *"How helpful are rapid diagnostic kits? When it comes to infectious diseases? MCS takes minimum of 48hours but with the RDT's I don't think we have those kits for infections except for PCR {Polymerase chain reaction } and Malaria but even that one has its own setbacks" ---STKH 005*

> *"The challenge is how readily will this be available?" ----STKH 003*

> *"When it comes to the labs doing the MCS tests they take up to 48hours I don't think they have any pattern that can reduce that" ---STKH 002*

Cheaper generics: Most of the stakeholders agreed that sourcing for cheaper generics will help improve antibiotics use in the area of costs to the patients. This has been discussed and agreed upon by the drug revolving fund and procurement team. All participants talked about the main issue with generics is that most times the efficacy are questionable, and they have no forms of quality control labs or assay unit. So, in as much as they want to save costs to the patient, they cannot go below certain standards so as not to compromise treatment outcomes.

> *"If we go too low that level to stock generic products whose price is so low that you can save more than 80% of what you are to spend on the brand at the expense of the patients, we can't achieve good outcomes as most non-brands have not been tested for efficacy" ---STKH 003*

Two stakeholders pointed out that due to the unconfirmed efficacy of generics, some clinicians especially from the paediatrics unit will only prescribe branded antibiotics for assured treatment outcomes.

> *"In as much as we want an affordable brand, we need to ensure that it is an effective and efficacious drug too. We still get the brands too because some clinicians especially from the paediatrics unit they stick to certain brands" ---STKH 002*

Improving labs: Stakeholders agreed that the labs currently needs to be strengthened both in terms of improving of the quality of services provided and increasing the staff strength. Top management stays they are actually working on this. An additional point raised was the poor quality of lab scientists being graduated from the universities due to excessively large undergraduate classes and called for in-depth re training of these scientists upon graduation.

> *"The labs need to be strengthened in terms of man power and also technical efficiency and proficiency. Sometimes I go to look at their record books in the lab and some of the things I see are not supposed to be there" ---- STKH 005*

Another important point raised by one participant was the fact that clinicians especially the pathologists do interfere with the labs wanting to claim ownership for the work done which then causes problems with the work flow.

> *"There is this challenge between doctors who are pathologists and scientists so that thing has been there, and the doctors want to claim ownership and they want to be seen as people that control everything but it's not true because it's the scientist that actually do the work" ---STKH 001*

Also, pharmaceutical companies have been asked to supply sensitivity discs for any antibiotic drug they market to enable the labs to run the sensitivity tests without having to source for the discs themselves.

Restricted pharmacy dispensing: From the interviews, it was gathered that this recommendation was already agreed on in the last meeting of the Drugs and Therapeutics Committee (DTC), where there will be a list of restricted drugs that doctors cannot normally just prescribed from casually. These drugs once prescribed will be flagged up by the attending pharmacist and will require second line checks and additional documentations before they can be dispensed.

> *“We earlier had a plan in the DTC and we agreed that we are going to come up with a list of restricted drugs that even the doctors cannot even prescribe if there are no reasons or the proper tests done for such drugs to be prescribed, the pharmacist will have a right to restrict it from being prescribed” ----STKH 002*

Providing health insurance: This recommendation was accepted by all stakeholders interviewed and they agreed it was one way of improving antibiotics use as patients will not bare the direct cost of the lab tests and drugs. The interviews revealed that a health insurance scheme by the state government has just been rolled out for civil servants with plans of extending coverage to other citizens. Some participants pointed out that the health seeking behaviour have changed since the insurance scheme as more people now go to the hospitals for treatment.

> *“our intention is to improve health seeking behaviour instead of people going to chemists to just buy drugs, they should be able to go to the clinics/hospitals, see a doctor and get the necessary investigations done, arrive at a diagnosis before obtaining medications on self-prescriptions as it used to be. Things are changing and people are attending clinic more and seeking for medical services, and they now their rights and benefits that is made available to them in hand bills”--- STKH 007.*

Although the participants commended the government for kick starting the scheme, they pointed out some challenges with funding the scheme which leads to drugs and some services not being available sometimes to civil servants registered under the scheme for now.

> *“This is a very good strategy that the government has put in place to ensure that the people are able to access healthcare readily, but there are some challenges with the funding. Are the resources there to ensure the scheme is effectives? take for example sometimes the drugs are not available for patients under the insurance scheme, even in the labs some reagents are not available for patients to carry out some tests under the insurance” -----STKH 003.*

7.4.1 Barriers in the implementation of these strategies

During interviews with the stakeholders, the challenges and barriers likely to occur in the course of implementing the proposed strategies were also explored. The barriers highlighted in the implementation of the strategies can be grouped into two main categories the behavioural and contextual.

The behavioural level: This borders on individual attitudes, cultural perceptions and the relationships between multi-professional care-delivery systems. Usually different disciplines are involved with antibiotic prescribing in the hospital settings (e.g., clinicians, nurses, pharmacists, microbiologists). Issues arise in care coordination and team work collaboration, (Hulscher *et al.,* 2010). Barriers in the behavioural level include lack of desire to change practice patterns, attitudes towards other care givers, lack of confidence from pharmacists to intervene in a prescription error and lack of interest generally to promote appropriate antibiotic use cultures.

> *"Most of the barriers and challenges are based on human factors, care giver factor, we have a challenge here in the sense that people want to do what they think is right without following the procedures" ---STKH 008*

Some clinicians over the years have developed certain practices which are sometimes handed down by senior colleagues which may not be entirely appropriate with the ever-changing elements in healthcare delivery. This becomes an issue for current practice when they refuse to accept corrections or change this practice. Continuous training and some form of restrictive interventions might be employed in this circumstance to bring about change in behaviour. Attitudes amongst healthcare providers is another major form of behavioural barrier. This is because often times the doctors are reluctant to take any support from other allied medical professionals for lack of trust in their judgements. And until other healthcare providers are seen as equally important to contribute to care, it will be difficult for all healthcare providers to work as a team. Behaviour change models may be used to implement interventions successfully in this light.

The contextual level: This borders on the local settings and organizational policies, the way in which the hospitals organize patient care among caregivers, socioeconomic factors for example the way in which healthcare is funded or re-imbursed.

> *"Some of these things we talk about require some level of funding and when the funding is not there, it's hard to meet some of the standards" --- STKH 001*

> *"What needs to be done is just to improve the system, we have been advocating for a system where we (Pharmacists) should have access to patient's medication profile in the pharmacy" ---- STKH 007*

Other barriers in the implementation of the proposed strategies include lack of funds, poor resource allocations to healthcare sector, shortages in skilled manpower and general workforce, inadequate facilities in the hospital settings. These barriers are higher than the hospital management can be addressed mainly from the government level. A good starting point will be advocacy from health managers and the ministry to the government on the need to increase the annual budget for healthcare in the local settings.

7.4.2 Perceived pharmacist's roles in improving antibiotic prescribing in the hospital settings

The pharmacists among the stakeholders that were interviewed were further asked to share their views on the roles of pharmacists in improving antibiotic prescribing in the hospital and also the barriers the encounter in the delivery of this roles. Majority of the pharmacists agreed that pharmacists have a role to play in ensuring antibiotics as like other medicines are prescribed and used appropriately in hospitals. They said it is the responsibility of the pharmacist to provide basic information about the medicines to prescribers. Information such as availability of the different antibiotic drugs and classes, the strengths and formulation, options for combinations, drug interactions and even side effects. This would help prescribers to prescribe the most suitable option for the patients. They also pointed that pharmacists should vet the prescriptions for accuracy and intervene when any errors are being identified in the prescribed antibiotics. All pharmacists interviewed mentioned only roles relating to the actual prescriptions by doctors. They made no mention of ensuring that antibiotics should always be available, in the different formulations and preparing updated formulary documents. They also seem not to be aware that pharmacists can also improve antibiotic prescribing by monitoring and documenting antibiotic prescribing and consumption patterns, measuring quantities of different drugs prescribed, doses prescribed, the formulations etc. and feeding back to the clinicians.

This is an indication that even pharmacists are not fully aware of their potential roles to improve antibiotic prescribing and therefore need further training and enlightenment on how much contribution they can make in the antibiotic prescribing process.

7.4.3 Barriers in the delivery of pharmacists' roles to improve antibiotic prescribing

The pharmacists also shared on some of the barriers that limit them in fully delivery roles to help improve antibiotic prescribing. Firstly, was lack of manpower as up till date there are still not enough pharmacists in the hospitals and the few already in service are perceived to be overworked already hence additional roles will be very difficult and yield no meaningful results. Secondly pharmacists mentioned the resistance and lack of cooperation from doctors when they try to intervene and feedback in a case of prescribing error. They explained that some doctors are not open to support from other healthcare providers and will refuse any corrections offered. They said there was no form of management support to back them up and there is little or nothing they can do when doctors refuse corrections for obvious prescribing errors. Another factor that limits their input in antibiotic prescribing was the lack of access to patient medical records as they will not be able to fully understand the reasons why the antibiotic was prescribed in that particular manner. Having access to the medical notes will give them a better platform to intervene. And also, the lack of guidelines, prescribing protocols and policy documents is a barrier as this would have given the pharmacists a reference point and base to back up their claims. Finally, pharmacists described the lack of confidence and competence on their part to approach clinicians as another barrier. This is due to the fact that there is no ongoing training programme for pharmacists and pharmacists on their own do not routinely study to keep up with current evidence-based practices. This could be one of the reasons why clinicians may not readily accept corrections from pharmacists on prescriptions

The key findings from this work are summarized in Table 7.2 below:

Table 7.2: Themes and subthemes relating to Stakeholders Perceptions on recommendations to improve antibiotic prescribing practices

Recommendations/Themes	Extracts/ key findings	Inherent barriers
Immediate/short term implementation strategies	Quotes	
Increase awareness on antibiotic resistance and its problems amongst prescribers in the hospital	One presentation on rational use of antibiotics already held They are aware the problem is the will and courage to change The education and awareness have to be provided for all providers (multidisciplinary) and the patients also.	Lack of desire to change practice Lack of reference materials to prescribe antibiotics Poor attendance at the presentation Lack of drivers for the change process to ensure continuity and sustainability
Monitoring antibiotic use and consumption /Audits	Currently run by the pharmacy department in one hospital	Insufficient workforce

	Not done in most hospitals We do not have such practice to monitor antibiotics use here We have created an antibiotic consumption pattern checklist	No system in place for presenting the data and feedback to the clinicians
Conduct local studies and Informed education/training for prescribers	This is not fully operational but will be a very helpful strategy in improving antibiotics use. Will help to guide practice We are going to integrate this aspect as a major point in our next year's work plan	Funds Lack of skilled expertise.
Provide/Implement the guidelines	Providing STG will really go a long way to help We will work towards Developing one for the hospital.	Lack of experts No data and local studies on susceptibility patterns have been

		conducted to inform the guidelines yet
Source for rapid diagnostic kits	This will definitely be of help if available as it will save time and reduce cost to the patient and hospital too Not readily available for MCS tests unless malaria and PCR tests	Not sure it exists yet though and if it does the resources to procure them is also a challenge
Stock effective and cheaper generics	It's okay to stock generics as they are cheaper, but we may be compromising the effectiveness We can save by stocking generics but if we go too low, we can't achieve good outcomes	Fakes and compromised efficacy Lack of trust in generics No quality control labs to check generic drugs Lack of intersectoral collaboration between manufacturing and regulatory bodies
Long term strategies		
Improving lab services	Yes, the labs need to be strengthened	Mainly funds

	We are currently working towards this	In-depth training for lab personnel Lack of skilled manpower
Restricted pharmacy dispensing	We have discussed this in the last meeting and will be included in the guidelines	
Implement health insurance schemes for vulnerable patients sub groups	This is a very good strategy It has been launched in this state now for civil servants	Not enough resources still so some drugs are still not available under the scheme Doesn't entirely cover everyone yet
The role of the pharmacist in improving antibiotic prescribing in the hospital setting		
Perceived roles by pharmacists	Pharmacists have a huge role to play in this regard manly providing basic information to prescribers Pharmacists are to vet prescriptions and drug combinations to ensure they are appropriate We identify any errors in antibiotics being prescribed and intervene	

Barriers in delivery of the roles	Lack of man power (Not enough pharmacists) Resistance from doctors as not all doctors are open to support from other healthcare givers No access to patient's medical records Lack of management support for pharmacists Lack of prescribing protocols to support pharmacists claims during interventions and feed back to the doctors Pharmacists lack the confidence and courage to approach clinicians

7.5 Discussion of chapter findings

All the strategies proposed to improve antibiotic prescribing were generally accepted by all stakeholders with some of the strategies already being implemented to an extent in one of the tertiary care centres. This was discovered from interactions with members of the drugs and therapeutics committee and was confirmed from the latest action plan document presented by the head of the committee. However, some strategies were not immediately feasible for implementation mainly due to lack of resources. These include provision of rapid diagnostic kits, upgrading the laboratories and provision of health insurance. Strategies identified as priorities for implementation include monitoring antibiotic use and consumption, increasing awareness on antibiotic resistance and provision of guidelines and essential antibiotic medicines.

They were mostly happy to take on board the other strategies not put in place already as they agreed to factor these in the subsequent work plans of the drugs and therapeutics committee. Common barriers highlighted by the participants were lack of skilled workforce, poor allocation of funds resources and friction that exists in the relationships amongst different healthcare professionals. Perceived pharmacists' roles in improving antibiotic prescribing were also explored. It was discovered that pharmacists are aware they have a key role in improving antibiotic prescribing and use, however structural limitations, poor working relationships with prescribers and other limitations impedes their delivery of the services. An interesting finding observed was the need for professional collaboration among the healthcare providers to bridge the attitudinal gaps that exist between them. This will facilitate working as a team to achieve the common goal of improved antibiotic prescribing practices.

7.6 Chapter summary

The findings from the interviews show that the stakeholders in the study area are aware of the growing concern of antibiotic resistance as a healthcare problem and all the dangers it proposes if steps are not being put in place to check its continuous increase. While recommendations and strategies outlined for improvements to practice are accepted, the lack of resources and poor healthcare financing impedes immediate feasibility in the local settings. Consequently, for effective and sustained improvements to practice, there is need for provision of needed resources and optimum healthcare allocations in national annual budgets.

Chapter 8 RECOMMENDATIONS AND CONCLUSIONS

8.1 Introduction to chapter

This chapter provides an overview of this research and a summary of the key findings obtained. It presents the final recommendations arising from the results of the stakeholder analysis (presented in chapter seven) and plans for its implementation. The chapter concludes with the implications of study findings for practice, policies and future research.

8.2 Overview of the research

Antimicrobial resistance is a major problem facing global health today. This problem is especially of concern in developing and low-income countries where the stewardship programmes from developed settings with evidence of effectiveness are not directly applicable. This is due to differences in the healthcare structures and service delivery patterns. Internationally designed stewardship programmes have not been successfully implemented because most often, resources are scarce, and the infrastructure needed to execute these stewardship programmes are lacking. Published literature has not sufficiently explored the area of specific barriers that need to be identified and addressed to support effective implementation of antimicrobial stewardship programmes in low income and developing countries.

In this research work, the patterns of antibiotic prescribing in selected hospitals in the Niger Delta region of Nigeria was studied. The enabled a bottom-up approach to explore the determinants of the antibiotic prescribing practices and to develop recommendations for a feasible antimicrobial stewardship programme (ASP) model that will improve prescribing patterns in the region, which can be adopted nationally and even applied to other LMIC's with similar healthcare settings.

In addition to the determinants of antibiotic prescribing patterns, the perceptions of prescribers and their suggestions to improve antibiotic prescribing was also investigated. From the results obtained and other published work, a set of recommendations were developed and presented to the stakeholders in the hospital settings to determine their views on feasibility and priorities for implementation.

8.3 Key findings

8.3.1 Inappropriate antibiotic prescribing patterns

There were no prior studies published on the antibiotic prescribing patterns in the study region. Hence, the antibiotic prescribing practices were studied first as a needs assessment for suggesting and developing strategies to improve antibiotic prescribing in the region. The initial findings demonstrate inappropriate antibiotic prescribing practices. This was evidenced by high rates of empirical antibiotic prescribing (72% of all cases studied), poor compliance with treatment guidelines (28%) and limited/irrelevant use of diagnostic tests as a guide to the choice of antibiotic therapy (84% of antibiotics prescriptions assessed). Commonly prescribed antibiotics were mostly broad spectrum and were not available for dispensing every time they were prescribed. The indications for which antibiotics were prescribed were mostly respiratory tract infections and gastro-intestinal disorders. Antibiotics were prescribed in some instances where there was no clear need or indication for antibiotic therapy. More of the brand name antibiotics were prescribed than the generics, and paediatric patients received more than half of all the antibiotic prescriptions studied. Given these findings, the determinants of these prescribing practices were explored directly from the prescribers.

8.3.2 Determinants of antibiotic prescribing practices

Prescribers were interviewed to explore the reasons for and determinants of the observed antibiotic prescribing practices. The main reasons for the high empirical antibiotic prescribing observed were excessive delays in receiving laboratory test results or the complete unavailability of diagnostic services in some cases, limited availability of treatment guidelines in consultation rooms and other clinical spaces. In some units, the guidelines were not followed as antibiotic prescribing trends are handed down from senior consultants to junior doctors. The cost of antibiotics was also found to be one key factor that impacts on the choice of the antibiotic prescribed. Some patients are unable to afford the ideal antibiotic drug they need and get cheaper alternatives that are not in compliance with guidelines and in line with the sensitivity results (if carried out). Other factors that impact on antibiotic prescribing include the availability of the required antibiotic and lack of core knowledge of antimicrobial therapy. A few prescribers admitted incentives provided by pharmaceutical company representatives influenced the choice of antibiotic prescribed in certain conditions and also the expectations from patients was found to increase pressure on prescribers to prescribe antibiotics.

8.3.3 Recommendations to improve antibiotic prescribing based on findings

Having studied the determinants of antibiotic prescribing using BCW, a set of specific recommendations tailored for the local settings were developed from suggestions of the prescribers and existing literature of effective strategies in similar settings. These recommendations include to increase training and education on AMR for healthcare providers, documentation and monitoring of antibiotics use, regular audits and local research, providing updated guidelines, improving laboratory and diagnostic services, restrictions to antibiotic prescribing, enabling pharmacists' interventions in antibiotic prescriptions, improving availability and affordability of antibiotics (by stocking effective generics) and provision of health insurance. This is to address the problems identified in the context of policy categories, issues with out-of-date guidelines, poor diagnostic service provisions, antibiotic availability/costs and insufficient regulations on medicines use in the hospital settings.

8.3.4 Feasibility and priorities for implementation

These recommendations were presented to the stakeholders in the hospital settings to examine potential feasibility and priorities for implementation. Many were viewed as feasible. Some had already been initiated in some units as part of the requirements to maintain accreditation, especially in the teaching hospital. Top priorities for implementation was training for prescribers, monitoring and surveillance of antibiotics use, provision of guidelines and improved diagnostic testing services.

8.3.5 Barriers in the implementation of the recommendations

The analysis of stakeholders views also highlighted some of the barriers that may interfere in the implementation process. Topmost mentioned was inadequate healthcare financing, lack of sufficient healthcare personnel, the attitudes of the doctors, as they may not be willing to change their practice patterns to imbibe new cultures of using policies and guidelines as recommended. Another barrier mentioned was prescribers not being fully aware of the inappropriate forms of antibiotic prescribing and its implications for resistance. Consequently, an antimicrobial stewardship (AMS) plan considering these highlighted barriers is developed and now recommended for implementation in the hospital. This AMS plan is described in the sections following below.

8.4 The antimicrobial stewardship (AMS) plan

An antimicrobial stewardship plan is now presented with specific recommendations aimed at addressing the determinants of antibiotic prescribing practices. The AMS plan contains strategies operating from both the policy categories, intervention functions and sources of behaviour as outlined in the three layers of the BCW. This plan targets the government at the national level, at the institutional level (hospitals) and at the individual level (i.e., practices and behaviours of prescribers and healthcare providers). These are presented in Table 8.1 below:

Table 8.1: Recommendations to support a stewardship plan

<u>Recommendations at the national level (Government, through the ministry)</u>

- *Increase the allocation for healthcare in the annual budgets*
- *Provide healthcare insurance to cover all citizens*
- *Update and disseminate national treatment guidelines*
- *Organise national antibiotic resistance sensitization programmes to be implemented by healthcare institutions.*

These will then enable the recommendations targeting the institutions below

<u>Recommendations at the institutional level (Hospital)</u>

Increase awareness on antibiotic resistance

- *Posters*
- *Fliers*
- *Billboards*
- *Campaigns, seminars, presentations*

Surveillance

- *Monitor antibiotic use and consumption*
- *Carry out local research on antibiotics use/ bacterial sensitivity patterns*
- *Conduct routine audits on antibiotic prescribing and then feedback*

Policies

- *Develop and review hospital antibiotic policies*
- *Provide the written antibiotic guidelines /antibiotic booklets*
- *Support pharmacists to review antibiotic prescriptions*
- *Set up infection control committee / antimicrobial stewardship groups*
- *Introduce reserve antibiotic policies and restrictions*

Procurement and services

- *Ensure continuous availability of antibiotics, procure affordable generics*
- *Strengthen the laboratory and diagnostic units for improved testing services*
- *Recruit more personnel (ID consultants, pharmacy staff, laboratory staff)*

<u>Recommendations at the individual level (healthcare providers)</u>

Prescribers

- *Attend relevant training on antimicrobial use/resistance (award CME points)*
- *Comply with the guidelines and antibiotic policies, clinical best practices*

Pharmacists

- *Review antibiotic prescriptions (and intervene if needed) before dispensing*
- *Document antibiotics use*

Laboratory and diagnostics personnel

- *Provide all relevant test results as soon as realistically possible*

8.4.1 Next steps in practice and implementation of the AMS plan

The summary of recommendations to support the AMS plan will be presented to the relevant authorities which includes the ministry of health, medical advisory committee chairperson of the individual hospitals and copies made available for health care providers. The following action points will commence in the hospitals immediately:

<u>Procedure</u>:

1. Set up an ASP Team

a). **Leadership-** Appointment of an Infectious Disease (ID) Physician who will be committed to champion and support the safe and appropriate use of antibiotics in the hospital.

b). **Membership-** Appoint other members of the ASP team. This will consist of a pharmacy consultant, medical microbiology/laboratory staff, nursing director, medical records representative.

2. Responsibility

a). This team will be responsible for stewardship activities in the hospital and as a team, they will:

- Develop an ASP mission statement they will work with.
- Develop and agree on local antibiotic treatment guideline from the national guidelines available
- Provision of the printed hard copies of the treatment guidelines by the hospital administration offices to consultation rooms and other clinical spaces like wards
- Review infectious disease cases and monitor the antibiotic use patterns on a regular basis.
- Monitor the patterns of antibiotic resistant organisms in the local hospital (MRSA, VRE. ESBL, CRE, etc.) And other common infectious disease cases such as *Clostridium difficile* infections.
- A laboratory departmental staff should be assigned to document the bacterial sensitivity patterns by reviewing the antibiograms in the

microbiology labs and produce the monthly bacterial sensitivity reports for the hospital.

- Generate monthly antibiotic formulary lists and reports on antibiotics use patterns by documentation of antibiotic use in the pharmacy, (prescribing and dispensing- the number of antibiotics, the drug, dose, duration, dosage forms, etc.) A staff from the pharmacy unit would be assigned to commence daily documentation of these details.
- Document the outcome of antibiotic therapy where possible
- Collect and review the relevant data for clinical and cost efficacy and for feedback

3. Drug Expertise

a). The pharmacist director will be directly involved with the routine procurement of antibiotics drugs in line with the patterns of use, ensuring no stock-out for commonly prescribed antibiotics and all in the EML

b). Ensure the availability of good quality lower priced generics

c). Review all prescriptions and orders for antibiotic drugs for appropriateness before approval for dispensing

4. Surveillance/monitoring

a). Request for clinical diagnostic tests as required in cases of suspected infections to guide appropriate choice of antibiotic therapy.

b). Initiate an antibiotic review process for all antibiotics prescribed in the hospital. This will prompt clinicians to review the need for ongoing antibiotic therapy when diagnostics test results become available, and the clinical picture is much clearer.

c). Laboratory representative will devise a method for flagging off cases of multidrug-resistant organisms (MDRO's). This will be documented alongside antibiograms and used to generate hospital specific antibiotic resistance patterns to guide future empirical treatments.

5. Audits and reporting

a). The ASP team will delegate members to carry out routine audits of the current practice with antibiotics and report findings to enable improvements to practice.

i. A minimum of two antibiotic prescribing audits will be conducted every year (6 monthly)

ii. Suggested audit targets are outlined below:

- 90-100% of antibiotics prescribed are clinically warranted
- 90-100% of antibiotics use is documented in the patient's notes
- 90-100% of antibiotics a prescribing is in accordance with local guidelines
- 90-100% of antibiotics prescribed are prescribed at the correct dose
- 90-100% of antibiotics prescribed are prescribed via the most appropriate route with intravenous to oral switch following local guidance
- 90-100% of antibiotics prescribed which require blood levels are monitored appropriately
- 0-10% of antibiotics are prescribed for longer than is necessary
- 90-100% of patients and their prescription charts are reviewed daily by the clinical team
- 90-100% of health care workers have an annual infection control update including antibiotics prescribing

b). The ASP will conduct local research on antibiotics use and patterns of antibiotic resistance/sensitivity. The findings when reported will be used to inform the development of local and hospital specific guidelines.

6. Feedback/ Education

a). Feedback results from audits and local research conducted in the form of presentations in clinical meetings and ground rounds highlighting areas of good practice and areas where improvements are still needed.

b). ASP team to organise routine seminars and training on the rational use of antibiotics, inviting experts in the area and learning from best practices.

7. Evaluation

The research and ethics committee will conduct service evaluations to assess the impact of the AMS plan following its implementation. This will be measured with outcomes like the compliance with guidelines, reduction in empirical prescribing and increased use of diagnostics tests, reduction in antibiotic stock-out.

8.5 SWOT analysis

Having presented the proposed set of recommendations and the plans for the implementation, a SWOT (**S**trength, **W**eaknesses, **O**pportunities and **T**hreat) analysis is carried out and presented in the sub sections below:

8.5.1 Strengths of the recommendations

- These set of recommendations were developed specifically to address the issues identified in the local settings as opposed to imposing generic recommendations or a set of strategies developed in a different setting.
- The recommendations were equally suggested by the same stakeholders directly involved in the practice settings which gives them an opportunity to contribute to improvements which is a form of ownership. This will most likely encourage them to be actively involved in the implementation process.
- The implementation of these recommendations is likely to provide a more rational improved use of antibiotics, which has the potential financial benefit of cost avoidance to patients and government arising from antibiotic resistance.
- Most of the recommendations at the institutional level can be delivered within the powers and services of the hospital team and existing committee. There will be no need for additional approval from any

external body as services provided are within the duties of the hospital staff.

- Some of these recommendations have been implemented in some low-income settings with evidence impact. These evidence support the feasibility of the recommendations.

8.5.2 Weaknesses

Some of the weakness of the recommendations include:

- Lack of sufficient skilled workforce like an Infectious Disease (ID) physician to champion the cause, a skilled clinical pharmacist that can contribute to clinical management involving antibiotics, and specialised clinical laboratory scientists, etc. There is only one ID physician in the teaching hospital, and none at the secondary care hospitals studied. Also, clinical pharmacist roles in these settings are not fully developed. There is no in-service training designed for pharmacists in clinical practice yet, and they make lack the necessary competencies to support the recommendations.
- Resources in the local settings will not support some aspects of the stewardship programme such as the laboratory services. As is typical with most resource-poor settings, limitations in certain aspects of technology and clinical diagnostics will affect the delivery. For instance, antibiotics may still be prescribed empirically in emergency situations since sample culture requires up to 48hours to run and we still do not have access to rapid diagnostic kits for bacterial infections in the settings yet.
- The readily available prescribing guideline is out of date, this discourages the prescribers to comply with them especially as clinical practice in infectious diseases is always evolving due to the constant development of newer resistant strains. Updating these guidelines will require recent research in bacterial susceptibility and gathering all information needed which may not be immediate.

- No prescribing authority for pharmacists and lack of access to patient's case notes in the Nigerian hospital settings. In addition to lack of clinical competencies for the pharmacists, their roles in the clinical evaluation of patient drug therapy are not sufficiently supported by the systems and processes of care delivery. The clinical pharmacists are not ward based and have limited access to patient treatment records which limits their ability to make meaningful inputs to patient management.

8.5.3 Opportunities

- Implementing these recommendations will require contributions from the different healthcare provides to ensure a more ideal and justified management is delivered. This will improve the collaboration among the doctors, pharmacist, nurses, lab scientist and others as each brings relevant contributions from their field of expertise.
- Reduce the development of resistance and preserve antibiotic drugs. The overall aim of these recommendations is to improve antibiotic prescribing which lead to a reduction in the development of resistance to the antibiotic drugs, thus preserving the effectiveness of the antibiotics available now.
- Implementation of the recommendations will encourage a multi-disciplinary approach to patient management as explained in the point above and this will ultimately lead to improved healthcare delivery and better treatment outcomes for the patients.
- The proposed set of recommendations includes monitoring and documentation of antibiotic use and sensitivity patterns. This will help to generate local data on antibiotics use that can inform guidelines and policy decisions, while also contributing to a wider pool of database needed at the national level and beyond.
- Implementing the recommendations will by default contribute to increasing the knowledge and awareness about antimicrobial resistance and infection control amongst all stakeholders involved.

- The recommendations have the potential to create new job opportunities in the settings are the delivery may require a whole new role in some settings where staff is already being overworked.

8.5.4 Threats

- Not enough funds (for improving lab services, providing healthcare insurance and the logistics of some other interventions).
- Attitudes of healthcare providers. There may be some form of resistance from the healthcare providers refusing to change their current practice patterns and take on additional responsibilities.
- One of the recommendations supports stocking of cheaper generic antibiotics in the hospitals for the bulk of the patients that cannot afford the branded medicines. However, this recommendation is faced with the risk of procurement of substandard medicines as these are in circulation in the drug market still owing to weak surveillance and regulatory services on drug production and importation.

All of these weaknesses and threats identified above are characteristic of the local settings in LMICs and will be adequately addressed upon implementation of the proposed recommendations.

8.6 Implications for practice

The results obtained in this research have implications for practice, targeting stakeholders at different levels (micro and macro) in the systems and processes of healthcare delivery. The micro level in this context includes the stakeholders in the process of service delivery within the hospital having direct involvement with the prescribing practices. While the macro level includes other higher stakeholders in the process of service delivery, not directly within the hospitals, but whose actions also influence the prescribing practices. The discussion presented here shows the next steps for practice based on study findings.

8.6.1 Implications for practice at the micro level

The stakeholders at the micro level includes the healthcare professionals such as the doctors, nurses, pharmacists, laboratory scientists and others, the hospital management staff, such as the unit heads, Medical Director (MD), Director of Administration (DA), Chairman of the Medical Advisory Committee (CMAC) members of hospital sub-committees like Drug and Therapeutics Committee (DTC), Research and Ethics Committee (REC), and others.

The results reported in this study shows that there is a need for comprehensive documentation on antibiotics in the hospitals from the procurement to consumption stages. Specific details to be documented will include details of the antibiotics being procured, such as the drugs, class, the strengths and formulations, and the source of procurement. This in turn will be used to update antibiotic formulary lists to guide prescribers. Also, the documentation of antibiotics being prescribed and dispensed, the drugs and classes, brands, strengths and formulations. This will in turn feedback and inform decisions on procurement of antibiotics in the hospitals as it will provide answers to what antibiotics are a fast line in the local setting to prevent stock outs. This documentation will enable monitoring of antibiotic consumption which is one way to measure improvements to antibiotic use. When antibiotic use documents are available, audits against policy documents and research can be carried out routinely to identify areas for improvement to the current practice. Another place where documentation will be needed is in the labs. There is a need to document the sensitivity and susceptibility patterns of bacteria and other pathogens. This data will guide the development of local guidelines and also help to make a more informed decision when antibiotic prescriptions are needed before clinical diagnostic tests.

All prescribers, pharmacists, laboratory personnel and nurses should endeavour to work as a team, support each other and adhere to local policies when prescribing, dispensing and administering antibiotic medicines. Prescribers most importantly should shift from the traditional prescribing of antibiotic based on clinical suspicion of infection and justify the need for antibiotic prescriptions with clinical diagnostics, recent guidelines and relevant references. This will help reduce the high empirical and unnecessary prescribing of antibiotics. Pharmacists should read up on current guidelines and research on antibiotic drugs, so they can feedback confidently to prescribers if any error or anomaly is identified in a prescription.

Hospital directors and management staff will set up a working antibiotic use committee comprising well motivated individuals from staff members (physicians, pharmacists, nurses, lab scientists and others) to coordinate the activities of the antibiotics use (documentation, monitoring and audits) which essentially makes the stewardship programme. Hospital management would develop local antibiotic policies to guide practice for their settings and ensure the most recent copies of national treatment guidelines are readily available to prescribers both as hard and electronic copies. The medical directors should organise education and training and refresher courses on antibiotics use and AMR for medical staff, results of antibiotics use, and audits should be presented in such training to access practice and identify areas for improvement going forward. The training sessions should be organised quarterly; it can be facilitated by internal staff members or external professionals and attendance should count towards annual Continuing Professional Development (CPD) points for staff, to encourage attendance.

8.6.2 Implications for practice at the macro level

The stakeholders at the macro level in this context includes external policy makers such as the Ministry of Health (MoH), the pharmaceutical companies, the drug use surveillance and regulatory agencies, the government at all levels and other external bodies.

The federal ministry of health should ensure regular reviews and updates to the national treatment guidelines, while hospital management would ensure the updated guidelines are readily available for prescribers as hard copies, electronic copies and even user friendly mobile applications to encourage use on-the-go.

The activities of pharmaceutical companies would be regulated by subjecting them to route supplies of antibiotics through the procurement team in the pharmacy. This way, pressure on doctors to prescribe curtain brands of antibiotics based on incentives offered will be prevented. The procurement teams would procure antibiotics from selected and trusted reps of pharmaceutical companies, this will reduce chances of receiving fake and substandard medicines as there are currently no assay and quality control units in the hospitals. If prescribers are assured to some extent of the quality of medicines, this will encourage antibiotic prescriptions being made out in generic forms which will be more affordable to patients than the branded drugs.

The regulatory agencies on drug circulation and use like the National Agency for Food and Drug Administration Control (NAFDAC) and National Drug Law Enforcement Agency (NDLEA) should intensify pharmacovigilance activities, increase monitoring and surveillance of fake and substandard medicines to decrease the circulation of fake antibiotics, which is a factor contributing to increased antibiotic resistance especially in low and middle-income healthcare settings liked Nigeria.

The government both at the state and national levels should increase allocations to healthcare on annual budgets to facilitate improved service provision in the hospitals. Most of the requirements to improve service with antibiotics use like reinforcing laboratory services, setting up quality control units, ensuring an uninterrupted supply of medicines and staff recruitment is limited by lack of funds. Also, the government should extend already existing health insurance to cover all citizens. This will allow prescribers to request necessary diagnostic tests and also prescribe the appropriate antibiotics needed by the patients if payment is not directly borne by patients through out-of-pocket payments.

8.7 Implications for policies

The study findings also impact on policies at national and international levels.

8.7.1 Implications for policies at the national level

At the national level, the findings in this study suggest that policy makers should develop antibiotic policies that would govern prescribing and dispensing in the hospitals. The policies should support prescribing of antibiotics according to the guidelines when indicted, if possible, supported by clinical diagnostics or local susceptibility patterns. Pharmacists should be adequately supported in their roles to optimise antibiotic prescriptions and reconcile any anomalies in the prescriptions by allowing them access to patient's case notes and not just prescription sheets. The policies should support prescribing of antibiotics from the official formulary lists in the hospital and reserved/ restricted antibiotic will not be dispensed it has been double checked and approved by a higher authority such as the antimicrobial stewardship team, or a designated infectious disease physician. Policies should also support routine audits to practice, results of the audits will be used to feedback to prescribers while identifying areas for improvement to current practice.

8.7.2 Implications for policies at the international level

Policies are finally implemented in local sites and as such, policies should be developed with an understanding of the settings in which they are to be implemented. The issue of antimicrobial resistance containment is not a recent development.

8.8 Generalization of results achieved

The current research focused on antibiotic prescribing practices and was conducted in selected government hospitals in Bayelsa state, located in the Niger Delta region of Nigeria. Due to similarities in the healthcare structure and settings across Nigerian government-owned hospitals, results obtained are likely to be relevant at the national level. Thus, the findings obtained would be broadly applicable to other hospitals in low-income settings, because by exploring the healthcare structure using the behaviour change wheel context, the determinants of antibiotic prescribing practices as outlined in the policy categories intervention functions of the BCW are similar. The results obtained from this work will be expected to inform the next steps for antibiotic prescribing across the country and may also apply to hospital settings in other low/ middle-income settings equally faced with similar resource problems.

8.9 Study limitations

The current research has some limitations in the methods, analysis and findings. These are discussed in the paragraphs below:

Methods: The data collection in phase relied on antibiotic prescription data that was retrieved from hard copies of patient case notes in the medical records unit. A lot of missing information was encountered in this stage such as missing drug chart pages and laboratory report forms which led to incomplete data retrieval in some of the cases. Which eventually affected the overall figures presented in the results for example more laboratories tests may have been conducted, but due to missing forms and pages in case notes not all diagnostic tests were captured and reported in this study. Also, the documentation of antibiotics prescribed did not have any provisions for individualized doses or modified therapy which may have contributed to a lower number of complete compliance with the guidelines as some antibiotic prescriptions are modified to accommodate the patient specific factors such as comorbidities, other medications, side effects and allergies etc. However, the analysis was modified to show cases with complete compliance with guidelines and cases with partial compliance where the right drug was prescribed but the dose and duration was different from the guideline recommendation.

Design: Some stakeholders were not included in recruiting participants for phase two and three, the interviews targeted certain stakeholders at the micro levels within the hospitals only owing to the limited time available to complete the research. The views of patients who consume antibiotics were not captured and other healthcare providers such as the nurses who administer antibiotics and laboratory scientists who perform the diagnostic tests were also not interviewed. External stakeholders at the macro levels like the pharmaceutical company representatives were also not recruited for interviews. Hence, the findings do not represent a comprehensive view of all stakeholders at the different levels.

Validity/ reliability and trustworthiness of findings: Although responses from prescribers reached saturation point, the sample was a fairly small number of respondents when compared to the numbers of prescribers and relevant stakeholders in this region due to time limitations and also their availability for interviews. However, the participants were selected from different specialties in the hospital to provide a more representative judgement of the stakeholders' views. Interviews were mostly conducted in the hospital during work hours and as such encountered some interruptions to the conversations. Some form of bias is also expected as prescribers may not have been entirely honest when they were asked to give an account of their antibiotic prescribing practices. However the key findings are in line with early results from similar studies conducted in LMICs with similar issues.

Being an independent researcher, the data collection, analysis and interpretation was conducted by one person however, views from research supervisors were included and other researchers external to this study were provided with audio recordings and transcripts to go over and notes were compared to reduce bias in the interpretation of study findings.

8.10 Future work

While this study has been able to identify a potentially feasible set of recommendations to improve antibiotic prescribing, more work is needed to see that these recommendations are implemented, and the impact on practice evaluated in the hospitals.

Further research is needed to determine the impact of the recommendations when implemented as an intervention to improve antibiotic prescribing in the hospitals. Priorities for research will include ultimate effectiveness of proposals, measured in changes to key parameters such as compliance to guidelines, reduction in unnecessary antibiotic prescribing, increased use of clinical diagnostic tests etc. These recommendations were made based on current practice in the study hospitals. Other hospitals are at different stages of practice, and these recommendations may have to be modified to some extent to meet hospital-specific needs for implementation.

Also, more research is needed to explore the views of other stakeholders in antibiotic use. These include the patients, extended healthcare providers and others outside of the hospitals that involved in the process of antibiotic prescribing such as ministry of health, pharmaceutical company reps and drug use regulation agencies to generate a more robust data with stronger relevance for internal and external policies. There is also need for recommendations to support patients in achieving appropriate use of antibiotics.

8.11 Innovation in this research

What is already known

The inappropriate prescribing and use of antibiotics is a contributory factor to increasing antibiotic resistance.

Antimicrobial stewardship programmes have proven beneficial in improving antibiotic prescribing use and have been widely employed as a means to address antibiotic resistance.

Global strategies to contain antimicrobial resistance have not been successfully implemented in developing countries.

What this research adds

This work provides insights for the next steps to be taken to support the implementation of antibiotic stewardship in low and middle-income countries

This study has identified important barriers in the successful implementation of antimicrobial stewardships in low and middle-income settings, and also explored the opportunities available for planned improvements to practice in the local settings.

Conclusion

In conclusion, the findings presented in this work demonstrate the impact of poor healthcare financing and weak regulatory and surveillance systems on the rational use of medicines in developing settings, while highlighting the opportunities and challenges. There is still a lot of inappropriate use and prescribing of antibiotics in the hospital settings. Barriers that impact on the current practices were found to exist at all levels of the healthcare delivery process, from the government level, to the institutional and also at the individual level. At the institutional level, there is a need for continuous training and education for prescribers and healthcare providers, reinforcing antibiotic use surveillance and monitoring procedures. The institutional management should ensure availability of antibiotics and provision of updated guidelines and policies on antibiotics use. While at the government levels, healthcare financing needs to be reviewed with increase to allocations for health in annual budgets by governments to support the provision of resources needed such as skill personnel, effective diagnostic services, of good quality medicines and others. These are all essential for creating the enabling environment for successful implementation of antimicrobial stewardship in low and middle-income countries.

This findings presented in this work informed a set of recommendations provides which provides insights for the next steps to be taken to support the implementation of an antibiotic stewardship programme in resource-poor settings.

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APPENDIX IA: Time line for study phases

Below is a table showing the time line of events for study, aims objectives and findings of the work are also presented in the table below.

List of Activity	**Year 1 (Sept 2014- Sept 2015)**					**Year 2 (Oct 2015-Sept 2016)**							**Year 3 (Oct 2016-Sept 2017)**						**Completing research Status (CRS year Oct 2017-Sept 2018)**
	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	
Initial reading																			
Literature Review																			
Initial aims and Objectives																			
Writing up the proposal																			

Preliminary field work																			
Writing first year report																			
Ethics application																			
Initial data collection																			
Data analysis/ interpretation																			
Intervention study																			
Collating final results																			
Writing up thesis report																			
Feedback on drafts, editing and printing																			

APPENDIX IB: Aims, objectives and findings of the research project

Study Design and Methods	Research objectives	Findings
Retrospective quantitative study, using pre-designed data collection forms to obtain data from patient's case notes held at the medical records unit and also the prescriptions sheets held in the pharmacy department of the selected study hospitals.	To determine the commonly prescribed antibiotics and classes	Commonly prescribed antibiotics were the broad-spectrum antibiotics. Penicillin's (Amoxicillin), imidazole's (metronidazole), Quinolones (Ciprofloxacin) and the cephalosporin's (ceftriaxone)
	To identify the indications for which antibiotics are mostly prescribed.	The main indications for which antibiotics were prescribed were Respiratory tract infections, gastro intestinal infections and genito-urinary infections.
	To determine how the prescribed antibiotics are selected, based on laboratory MCS results, empirically or from treatment guidelines and also the purpose for prescribing i.e. prophylaxis reasons or therapeutic.	Majority of the antibiotic drugs were prescribed empirically (72%). Use of clinical diagnostics and MCS results were limited and compliance to the standard treatment guidelines was poor in the study area.
	To assess the costs and availability of commonly prescribed antibiotics in the	Antibiotics are available but not readily affordable. Prices of antibiotics in Nigeria vary from 1 to 39 times

	hospital pharmacy and also in community pharmacies	the international prices. The mean cost of a 5-day antibiotic therapy was above the minimum wage of the average Nigerian worker.
Qualitative study making use of semi structured interviews with prescribers and other relevant stakeholders with a structured interview guide.	To examine stakeholder's perceptions of the current situation with antibiotic prescribing in Nigerian hospitals	The majority of Prescribers' and stakeholders described antibiotic prescribing in Nigeria as irrational, expressing concerns on poor prescribing practice and also the high rate of empirical prescribing.
	To identify and understand the reasons for the current antibiotic prescribing practices observed in the phase one study.	Factors responsible for the current prescribing practices include poor labs, lack of guidelines, high drug costs and availability, patient's pressure, clinician's attitude, lack of knowledge, excessive workload, and the practice settings.
	To explore Prescribers' views on the availability and use of guidelines/policies in antibiotic prescribing	Prescribers generally have a positive attitude to the use of policies and guidelines They acknowledged the fact that guidelines were helpful but not readily available to them in the prescribing spaces, wards and consulting rooms.

	To determine recommendations to improve antibiotic prescribing suggested by the stakeholders	The interventions recommended by stakeholders to improve antibiotics use are education and training, guidelines and policies, adequate procurement of antibiotics. Other recommendations were routine audits to check practice; restrictive antibiotics prescribing inform of pharmacist's interventions.
	To identify the likely barriers to implementing the recommendations	Top most mentioned was finance, attitudes of the doctors, as they may not be willing to change that practice patterns to imbibe new cultures of using policies and guidelines as recommended. Another barrier mentioned was the lack of awareness on the part of the stakeholders. Not being fully aware of the issue of irrational antibiotic prescribing and its implications for resistance.
	To determine the best course of action to be taken to improve antibiotic prescribing based the study findings and consultations with stakeholders. This may be in form of recommendations, enforcing already existing protocols or the design and implementation of a tool.	

APPENDIX II: Preliminary data collection form

Study Title: A survey of antibiotics use in the Niger delta region, the issue of resistance and the options we have today.

Facility Name:

Location:

Level of Care:

Number of Doctors**:**………………………………………………………………

Number of Pharmacists**:**…………………………………………………………….

Number of nurses**:**……………………………………………………………..

Number of laboratory scientists**:**…………………………………………………

Others relevant**:**……………………………………………………………………..

Number of functional units:……………………..………………………………..

Please outline units counted………………………………………………………..

Number of beds: ………………………………………………………………..

Average daily patient turn out:…………………………………………………..

Personnel(s) authorised to prescribe:………………………………………….

Presence of Drug and therapeutics committee?...

Presence of Infection control group?...

Presence of infectious disease i) Clinician…….. **ii) Pharmacist**…………

APPENDIX III: Data collection form for patients case notes

DATA COLLECTION FORM- PATIENTS CASE NOTES				
Title: A survey of antibiotic use and prescribing practices in the Niger Delta region of Nigeria				
Form No:			**Date:**	
Hospital:	Level of Care:		Ward/Unit:	
Patient sex: M ☐ F ☐	Age:	Admitted: Y ☐ N ☐	No. of days: if yes	
Name of Antibiotic:	Class:		Route:	
Dose:	Duration:		Indication:	
S/no	**Outcomes**	**Yes**	**No**	**Any additional comments**
1	Generic prescribing?			
2	Antibiotic prescription based on lab culture results?			
3	Compliance with STG? Based on Drug, dose, route, duration?			
4	Prescribed antibiotic available in the hospital?			
5	Were there any laboratory test results to guide prescribed antibiotic			
7	Reason for prescribing: Empirical ☐ Prophylaxis ☐ Therapeutic ☐			
8	Total number of drugs prescribed:			
10	Prescriber: Doctor ☐ Pharmacist ☐ Nurse ☐ Others ☐			
<u>**Form completed by:**</u> **KPOKIRI, Eneyi Edith……………………………….** [redacted]				

APPENDIX IV: Data collection form for prescription sheets

DATA COLLECTION FORM- PRESCRIPTION SHEETS

Title: A survey of antibiotic use and prescribing practices in the Niger Delta region of Nigeria

Form No: **Date:**

Hospital: Level of Care:

Patient sex: M ☐ F ☐ Age:

Name of Antibiotic: Class: Route:

Dose: Duration: Total no of drugs on prescription:

S/no	Outcomes	Yes	No	Any additional comments
1	Generic prescribing?			
2	Is the prescribed antibiotic present in the essential drug list?			
3	Appropriate prescription based on STG? Drug, dose, route, duration?			
4	Any DTP/Potential interaction with other prescribed medicines?			
5	If yes to 3 and /or 4 above, any intervention from the pharmacist?			
6	Prescribed antibiotic available in the hospital?			
7	Was the prescribed antibiotic dispensed?			
8	Nature of antibiotic prescription error if any:			
9	List the other classes of drugs in the prescription			
10	Estimated cost of antibiotic therapy in NGN:			

Form completed by:
KPOKIRI, Eneyi Edith

……………………………………

[redacted]

APPENDIX V: Ethic's application letter

Department of Practice & Policy,
University College London,
School of Pharmacy,
29-39 Brunswick Square,
London, WC1N 1AX,
United Kingdom.
2nd July 2015.

Dear Sir,

APPLICATION FOR ETHICAL APPROVAL TO CONDUCT A STUDY ON ANTIBIOTIC USE AND PRESCRIBING PATTERNS IN YOUR HOSPITAL

I am a PhD student in the above-named university on study leave from the Niger Delta University seeking to conduct a survey in your hospital. This survey is based on antibiotics use and prescribing patterns.

Antibiotic are widely prescribed across the globe. There has been reported increase in bacterial resistance to antibiotics. Also, the rate of discovery and production of new antibiotic drugs have massively declined over the last decade. Hence there is an urgent need to preserve the existing antibiotics we have through effective strategies to reduce antibiotic resistance.
This study seeks to determine the patterns of antibiotic use and prescribing and the reasons for current practice, whist identifying key areas that will need improved practice.

The findings of this study will show case important areas for intervention in antibiotic prescribing that will lead to improved prescribing and monitoring of antibiotic drug use in the area.

Please find attached a proposal providing further details on the study. I will be grateful if my application is granted.

Yours faithfully,

Eneyi Kpokiri
[redacted]

APPENDIX VI A: Data collection coding for patient case notes

S/n	Variable	Coding
1	Unit/Dept./Ward	Pead =1 A&E=2 GOPD=3 O&G =4 Male =5 Female =6 Dental= 7 Surgery= 8 ENT = 9
2	Sex	Male= 1 Female =2
3	Age	Rounded up to the next year. Ages 1yr and below=1
4	Formulation	Tab= 1 Caps= 2 Syrup= 3 Susp=4 Parenteral=5 Topical =6 Pessaries =7 Gutt=8
5	Drug	Flagyl=1 Amoxil=2 Ampiclox=3 Augmentin=4 Erythro=5 Cipro=6 Doxy=7 Co-trimoxazole=8 tetra=9 Genta=10 Cefuroxime=11 Cephalexin=12 Ceftazidime=13 Ofloxacin=14 Sparfloxacin =15 Nevirapine=16 Cefixime=17 Ceftriaxone=18 Azithromycin=19 Levofloxacin=20 Crystalline Penicillin=21 Rifampicin=22 Cefodoxime=23 Nitrofurantoin=24 Clarithromycin=25.
6	Class	Penicillins=1 Beta lactam=2 Cephalosporins=3 Aminoglycosides=4 Quinolones =5 Nitroimidazoles=6 Macrolide=7 Sulphonamides=8 Tetracycline’s=9 Antiviral=10 Rifamycin=11 Nitrofuran=12
7	Strength	None. Just state the figure (for mg or mls)
8	Frequency	OD=1 BD=2 TDS=3 QDS=4 5=STAT
9	Duration	None. Just enter the number of days
10	Indication	RTI=1 GIT=2 UTI/STI=3 SURGICAL PRO=4 PARASITIC INFECTIONS=5 SYSTEMATIC =6 WOUNDS=7 CNS=8 SKIN=9 Organ problems=10 OTHERS NOT COVERED=11

11	Test /investigations	Yes & relevant=1 NO=2 Yes & irrelevant=3 Not required=4
12	Prescribing	Generic prescribing=1 Brand Prescribing =2
13	Basis / reason	Therapeutic=1 Empirical=2 Prophylaxis=3 Unknown=4 Combination of either of the above=5
14	Compliance to STG	YES=1 NO=2 Partially comply=3 Not Applica=4
15	Facility	FMC=1 NDUTH=2 DIETEKOKI=3 GHA=4

APPENDIX VI B: Data collection coding for prescription sheets

S/n	Variable	Coding
1	Formulation	Tab= 1 Caps= 2 Syrup= 3 Susp=4 Parenteral=5 Topical =6 Pessaries =7 Gutt=8
2	Drug	Flagyl=1 Amoxil=2 Ampiclox=3 Augmentin=4 Erythro=5 Cipro=6 Doxy=7 Co-trimoxazole=8 tetra=9 Genta=10 Cefuroxime=11 Cephalexin=12 Ceftazidime=13 Ofloxacin=14 Sparfloxacin =15 Nevirapine=16 Cefixime=17 Ceftriaxone=18 Azithromycin=19 Levofloxacin=20 Crystalline Penicillin=21 Rifampicin=22 Cefodoxime=23 Nitrofurantoin=24 Clarithromycin=25, Ampicillin=26 Lincomycin=27 Tinidazole=28 Secnidazole =29 Flucloxacillin=30 Ornidazole=31 Cefotaxime=32
3	Class	Penicillins=1 Beta lactam=2Cephalosporins=3 Aminoglycosides=4 Quinolones =5 Nitroimidazoles=6 Macrolide=7 Sulphonamides=8 Tetracycline's=9 Antiviral=10 Rifamycin=11 Nitrofuran=12
4	Prescribing	Generic prescribing=1 Brand Prescribing =2
5	Availability	Yes =1 No=2
6	Facility	FMC=1 NDUTH=2 DIETEKOKI=3 GHA=4

APPENDIX VII: Data extraction sheets for the studies reviewed using the casp tool

DATA EXTRACTION SHEETS FOR THE STUDIES REVIEWED USING THE CASP TOOL

Number		1
Title		Pattern of antibiotic prescription and resistance profile of common isolates in the internal medicine wards of a tertiary referral centre in Nigeria.
Authors		Iliyasu G, Farouq M D, Tiamiyu, A B, Zaiyad, G H, Isa M T, Abdulrazaq G H.
Sponsor		None
Source/ Year		Journal of global antimicrobial, resistance, 2015. Volume 138
Location		Kano. (North West Nigeria)
Aim and objectives		To examine the pattern of antibiotic prescription in a tertiary hospital
Design / Method		A retrospective survey using patient case note for over 6 months. Systematic random sampling was used to select case notes and a pre-formed questionnaire was used to seek socio-demographic data, drug information and other relevant data.
Setting	Tertiary referral healthcare centre	
Outcomes measured		Percentage Encounter for Antibiotics, Commonly used antibiotics, Route, Indication, Empirical prescribing
Result	PEA	49.0% of study population received an antibiotic
	Commonly prescribed antibiotic	Ceftriaxone =39.5%, imidazole's (20.4%) Penicillins (12.6%).

	Routes and Indication	Parenteral =80.8% which accounted for the most of antibiotics prescribed. Community acquired pneumonia (33.2%) and UTI (18.3%) were the commonest indications for which antibiotics were prescribed.
	Empirical prescribing Use of tests	96.7% of all antibiotics were prescribed empirically. 21% of which were wrong. Culture was requested in only 19.8% of the study population. There was an 80% prevalence rate of resistant staphylococcus to cloxacillin
Suggestions to improve practice		Need for introduction of antibiotic prescribing guidelines and stewardship programmes. Further studies needed to highlight the economic burdens of inappropriate antibiotic use.
Comment	Strengths	Good choice of study design, being retrospective. Data were sourced from patient records over a 6-month period a large and appropriate sample size was set which was realistic to achieve the study objectives.
	Weaknesses	The clinical appropriateness of the prescriptions was not assessed. The study was limited to a small number of isolates, hence resistance to a wide range of commonly used antibiotics were not reported.

Number		2
Title		Antibiotic prescription pattern and cost at university of Ilorin teaching hospital, Ilorin Nigeria.
Authors		Akande , T M, Ologe, M, Medubi, G F. 2009
Sponsor		Non
Source/ Year		The international Journal of Tropical medicine, 2009. Volume 4(2)50-54
Location		Ilorin (North Central, Nigeria)
Aim and objectives		To examine the pattern of antibiotic prescription in a tertiary hospital
Design / Method		Retrospective study using prescriptions sheets the from pharmacy unit. 630 prescriptions selected by systematic random sampling.
Sample	Participants	Prescriptions sheets the from pharmacy
	Setting	Tertiary- A university teaching hospital
Outcomes measured		PEA, commonly used antibiotic, route, availability, cost and generic prescribing.
Results	PEA	83.5%
	Commonly prescribed antibiotic,	Penicillins, made up 35.9% of all the antibiotics prescribed, followed by quinolones which was 27.1% and then cephalosporin's were 13.9%
	Route, Availability	Oral route was mostly prescribed with 85.8%, 10.4% parenteral and all other routes were 3.9%. 92.3% of all antibiotics prescribed were available
	Cost and Generic prescribing	Antibiotics accounted for 72% of the cost of drugs on a prescription sheet Only 45.6% of antibiotics were prescribed in generic names
Suggestions to improve practice		Formulate antibiotic policies to promote rational prescribing in developing countries like Nigeria.

Comment	Strengths	The study was descriptive and cross sectional, data collected were manually checked before being analysed. Systematic random sampling was used to select prescriptions included for analysis.
	Weaknesses	Data was only collected for a time period of only 2 months this is a very short duration for data collection which will not allow variations in seasonal prescribing to be observed.

Number		3
Title		Pattern of antibiotic prescription at the general practice clinic of the University of Benin teaching hospital.
Authors		Odili V.E.; Awhonukeh I.A.; Arigbe-Osula M.E.; Igbinaduwa P.O.
Sponsor		Non
Source/ Year		Research Journal of Pharmaceutical, Biological and Chemical Sciences Volume 1 (4) 2010
Location		Benin (South south, Nigeria)
Aim and objectives		To examine the pattern of antibiotic prescription in a tertiary hospital
Design / Method		A retrospective survey using 406 patient case notes who had antibiotic prescriptions.
Setting		The University of Benin teaching hospital, a tertiary care hospital
Outcomes measured		Commonly prescribed antibiotic, route, diagnostic testing empirical prescribing and availability
Results	Commonly prescribed antibiotic	The penicillins were the most prescribed class (45.5%) of which amoxicillin was the highest drug in the class
	Route, Indication	There were no parenteral antibiotics prescribed in this study, URTI were the most reasons for which antibiotics were prescribed (36.7%)
	Empirical prescribing	More than half (64.9%) were prescribed using brand names
Suggestions to improve practice		Establish appropriate restrictive guidelines for antibiotic prescribing and use should be a high priority in the study setting and other settings with similar practices.
Comments	Strengths	The study was retrospective which allowed for the practice to be observed properly and also the General Practice Clinic was used which will give a fair representation of antibiotic use as different cases present to the GPC
	Weaknesses	The study had a very short duration of data collection which will not allow variations in seasonal prescribing to be observed

Number		4
Title		The Pattern of Antibiotic Use in a Family Medicine Department of a Tertiary Hospital in Sokoto, North Western Nigeria
Authors		Jimoh A.O.; Etuk E.U.; Sani Z.; Shuaibu, A.
Sponsor		Non
Source/ Year		Journal of Clinical and diagnostic research. Vol-5(3) 2011
Location		Sokoto (North West, Nigeria)
Aim and objectives		To study the pattern of antibiotic prescription in a tertiary hospital's general outpatient department
Design / Method		A cross sectional retrospective study using patients records with antimicrobial agents within the study period using a pre-piloted data collection form.
Setting		Tertiary hospital
Outcomes measured		Commonly used antibiotic, route, indication and use of diagnostic tests
Results	Commonly prescribed antibiotic,	Quinolones was the highest antibiotic class prescribed (35.83%) followed by penicillins (26.29%)
	Indication Generic prescribing	Gastrointestinal infections (PUD) had the highest prescription for antibiotics (39.88%), URTI. Incessant use of trade names in place of generics
	Use of diagnostics	Only 20.53% had requested for laboratory investigations before prescribing which only about one –fifth of the study population

Suggestions to improve practice		This study reported the prescribing patterns in the study settings and did not provide any suggestions to improve practice even though there were poor practices in antibiotics
Comments	Strengths	Good choice of study design, a large and appropriate sample size collected in the time frame. Data collection forms were pre- piloted and used.
	Weaknesses	Reported and objective of the study subjectively without any exact figures and did not provide any suggestions or recommendations to improve antibiotic prescribing even when flaws were clearly identified.

Number		5
Title		The Use of Antibiotics in a Nigerian Tertiary Healthcare Facility
Authors		Israel U. I.; Effiong G. S.; Akwaowoh, A.E.
Sponsor		Non- recorded
Source/ Year		American journal of Biomedical Science and Engineering Volume 1(3) 2015
Location		Uyo (South South, Nigeria)
Aim and objectives		To determine the pattern of use of antibiotics in a tertiary hospital with particular focus on use of laboratory diagnostics as a guide for prescribing
Design / Method		A retrospective survey using patient case note for over 6 months
Setting		Tertiary
Outcomes measured		Commonly prescribed antibiotic, indication, appropriateness and use of diagnostic test as a guide for antibiotic prescribing.
Results	Commonly prescribed antibiotic	Floroquinolones were the most prescribed with 26.40% and the 24.58%. Amoxicillin and metronidazole was the most prescribed combination.
	Indication Appropriateness	Respiratory diseases were the most (29.94%) followed by the GIT infections (22.7%). Non -bacterial infections also had antibiotic prescriptions such as diabetes, malaria and cardiovascular diseases.
	Use of diagnostics	Only 18.8% carried out lab investigations. Only 15.66% used relevant investigations as a guide for antibiotic prescribing

Suggestions to improve practice		Policies promoting rational use of antibiotics should be formulated. Also strengthen the curriculum of continuing professional development for practitioners to ensure that they have the necessary knowledge and skills to prescribe rationally.
Comments	Strengths	Appropriate study design, and chosen methods. Went into details to report the lab investigations conducted, the percentage documented in the case notes and what proportion was used as guide and even stated the relevance. Suggests practical recommendations to improve practice
	Weaknesses	The validity of clinical appropriateness of the prescriptions reported was not validated with any standards. Only 3 month period was allocated for data collection which is rather small in achieving a comprehensive and reliable result to achieve the objectives of the study.

Number		6
Title		Prescription pattern of Antibiotics among Physicians in a secondary Health Facility in Abuja, Nigeria.
Author		Abu-Saeed, K., Joseph, G. S., & Joseph, F.
Sponsor		Non
Source/ Year		British Journal of pharmaceutical Research. Volume 3(4) 2013
Location		Kano (North West)
Aim and objectives		To assess the prescription pattern of antibiotics by physicians in a secondary healthcare hospital
Design / Method		A retrospective survey using patient prescription sheets over 6 months (August 2012- February 2013)
Setting		Secondary healthcare hospital
Outcomes measured		Commonly used antibiotic, Route, Indication, Generic prescribing, Appropriateness of antibiotic prescription.
Results	Commonly prescribed antibiotic, Availability	Amoxicillin was the most prescribed antibiotic (31.79%) followed by metronidazole (27.37%). All antibiotics prescribed were in the EDL and 97.59% of prescribed antibiotics were available for dispensing to patients.
	Route, Appropriateness	Almost all the antibiotics prescribed were in the oral route (98.3%) 95% of antibiotics were prescribed correctly in terms of frequency and duration of use.
	Empirical prescribing	Majority of the antibiotics prescribed were in branded non-generic forms. 78.8% were prescribed in branded forms.
Suggestions to improve practice		Educating physicians on the need for generic prescribing and further monitoring on this.

Comments	Strengths	Good choice of study design, a large and appropriate sample size, suitable to achieve the study aims and objectives, the data collection forms designed were pretested and validated.

	Weaknesses	Different individuals collected data. This may not have achieved uniformity even though the authors claimed to have trained the pharmacist used.
Number		7
Title		Antibiotic prescribing at Primary Healthcare Facilities in Lagos
Author		Odusanya O.O.
Sponsor		National Primary Health are Development Agency
Source/ Year		Journal of the Nigerian Infection control Association, Vol.2(1) 1999
Location		Lagos (South West)
Aim and objectives		To examine the pattern of antibiotic prescribing in primary healthcare facilities in Lagos, Nigeria.
Design / Method		A retrospective survey using patient case note for over 6 months
Setting		Primary Healthcare Facilities in Lagos
Outcomes measured		PEA, commonly prescribed antibiotic, route, indication
Results	Commonly prescribed antibiotic,	The most prescribed antibiotics was Procaine penicillin (36.3%) followed by cotrimoxazole (22.9%) and then Streptomycin (17.6%)
	PEA	40% of all patients received at least an antibiotic prescription
	Route	More than 5o% of all antibiotics prescribed were in the parenteral route
	Indication	Acute respiratory infections were the most cases for which an antibiotic was prescribed (59.3%) followed by diarrhoea.
Suggestions to improve practice		Training of healthcare workers on disease processes, therapeutics and rational drug use are recommended as steps to improve the use of antibiotics
Comments	Strengths	Appropriate methods and study design, a large and appropriate sample size, made use of more than one primary care centre which will provide a more

		representative data, of the antibiotic use patterns in primary care facilities in the setting.
	Weaknesses	The clinical appropriateness of the prescriptions was not assessed.

Number		8
Title		A survey of drug use practices and antibiotic prescribing patterns at a general hospital in Nigeria.
Author		Chukwuani C.M, Onifade M., Sumonu K.
Sponsor		Non
Source/ Year		Pharmacy World and Science Volume 24, Number 5. 2002.
Location		Lagos (South West, Nigeria)
Aim and objectives		To describe the current drug use practices at the institution, gather baseline data which can serve as a basis for designing an appropriate intervention to improve the drug use profile.
Design / Method		A retrospective audit of in and out patient prescriptions for a period of 3 months (January to March)
Setting		Secondary care general hospital
Outcomes measured		PEA, Indication, use of diagnostic tests, prescriber KAP, and drug supply systems.
Results	PEA,	The percentage encounter for out-patients was 50.3% and 96.7% for in-patients
	Indication	Common indications include Bronchopneumonia 18.4%, Septicaemia 15.4% and gastroenteritis 14.0%
	Use of diagnostic tests	Only 4.2% of in-patient's antibiotic prescriptions were based on sensitivity tests
	Appropriateness	In 18.5% of the in-patient encounters, there was evidence of drug incompatibilities.
	KAP, drug supply.	Prescribers and dispensers rely on different sources such as MIMS, Martindale pharmacopeia for their drug information needs. The drug supply management was found to be inadequate.
Suggestions to improve practice		Review of current policies and systems, concerted continuing education and the establishment of a hospital formulary system and standard treatment guidelines.

Comments	Strengths	Good choice of study design, appropriate for the study objectives, the survey revealed that appreciable gaps still exists among the different cadre of healthcare professionals. It also compares drug use profile between out-patients and in-patients
	Weaknesses	Very short time frame allocated for data collection…may not be completely representative of actual practice and drug use patterns.

Number		9
Title		Profile of Antimicrobial Drug use Patterns in a Nigerian metropolitan city
Authors		Enato F.O.E; Uwaga C.F.
Sponsor		Non
Source/ Year		International Journal of Health Research. Volume 4(1)
Location		Port Harcourt (South South Nigeria)
Aim and objectives		To evaluate self-medication practices and prescribing patterns of antimicrobial agents.
Design / Method		A retrospective survey using patient medical records was used to assess antimicrobial prescribing patterns while a cross sectional survey was undertaken for assessment of anti-microbial self-medication practices.
Settings		Multi-centre study involving six hospitals/clinics (2 government owned and 4 privately owned), four community pharmacies and also the campus of the university of Port Harcourt
Outcomes measured		Commonly prescribed antibiotic, indication, appropriateness of therapy and self-medication with anti-microbial drugs
Results	Commonly prescribed antibiotic	Metronidazole (19.3%) amipicillin+cloxacillin (18.8%) and amoxicillin (16.4%) were the most prescribed antibiotics
	Indication	The common conditions for which antibiotics were prescribed are malaria (21.3%), and URTI (19.4%)
	Appropriateness	Over one-half of the prescriptions (56%) were considered appropriate by physician assessors, 23% were inappropriate, 17% disagreed and 4% were queried.
	Self-medication	65% of respondents said they had recently self-medicated with antibiotics. The most common conditions for antibiotic self-medication were cough

		(20%), stomach upset (20%) and boils (20%). Ampicillin (23%) was the most commonly used antibiotic for self-medication followed by co-trimoxazole (17%) and tetracycline (16%).
Suggestions to improve practice		Inappropriate use of antimicrobial drugs by the public and health facilities. Need for more studies on the subject to understand the public health implications.
Comments	Strengths	Had appropriate methods to achieve the study objectives. It was a multicentre study that used different setting to assess antibiotic use patterns and compared the practice across the government owned and privately-owned settings. The study was also able to show the importance of peer review system in enhancing quality use of medications.
	Weaknesses	The use of physicians to assess the appropriateness of antimicrobial prescribing may have resulted in under reporting of inappropriate antimicrobial prescribing patterns, as physicians are likely to be less critical of their colleagues or they may also share similar prescribing habits as well. Also, being a multi-centre study, finding may not be exactly the same as different settings will have different practice patterns making comparison of results challenging.

Number		10
Title		A study of Antibiotic prescribing at a general Hospital in Lagos Nigeria.
Author		Odusanya O.O.
Sponsor		Study grant from GlaxoSmithKline Pharmaceuticals
Source/ Year		Nigerian Medical Practitioner Volume 42 Number 1 / 2 2002.
Location		Lagos (South west Nigeria)
Aim and objectives		To investigate the pattern of antibiotic prescribing and rationality of antibiotic use at a general hospital in Lagos.
Design / Method		A retrospective prescribing data audit using patient records with antibiotic prescriptions over a 4 month period
Setting		Secondary
Outcomes measured		Commonly used antibiotic, Route, Indication and appropriateness of therapy, use of diagnostic test as a guide for antibiotic prescription
Results	Use of diagnostic test	Antibiotics were prescribed for most patients (94%) without any sensitivity tests being conducted.
	Commonly used antibiotic,	The most frequently prescribed antibiotics were ciprofloxacin, co-trimoxazole and ampicillin/cloxacillin combinations
	Route and Indication	Most antibiotics were prescribed orally (87%), 9% were prescribed parenterally and both routes were used in 4% of cases. Top indications are RTI (15.4%), PUD (12.8%) and malaria (10.5%)
	Appropriateness of therapy	Only 26% of patients receiving antibiotic prescriptions were rationally treated. Irrational antibiotic prescribing was seen in wrong choice of antibiotics (55%), non-

		indication (40%) and incorrect dosages (5%).
Suggestions to improve practice		Regular and effective use of sensitivity tests, patient education to reduce the pressure from patients for antibiotics, prescriber education and also the use of treatment guidelines.
Comments	Strengths	Good choice of study design, a large and appropriate sample size, both sample hospitals had similar sizes and both operated a typical British pharmacy ward service, use disguised observation to reduce Hawthorn effect, a validated scale was used to assess the severity of the errors.
	Weaknesses	The standard for which clinical appropriateness of the prescriptions was measured was not stated in this study. Also, the duration for data collection was rather small to be well representative of the prescribing patterns

APPENDIX VIII: Quality assessment checklist for studies

STROBE Statement—Checklist of items that should be adequately reported in studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org

APPENDIX IX A: Participant information sheets

Information Sheet

Title of Project: A survey of antibiotic use and prescribing patterns in Niger Delta Region of Nigeria and developing strategies to reduce antibiotic resistance.

Name Eneyi Kpokiri

Contact University College London, School of Pharmacy,
29- 39 Brunswick Square
London, WC1N 1AX.
United Kingdom.
[redacted].

I would like to invite you to take part in an interview about antibiotics use and prescribing in your hospital. Before you decide if you want to be interviewed, I would like to provide you with some information. Please read the information below and ask me any question that comes to mind.

Aim of the research

This study aims to assess the antibiotic prescribing patterns in Bayelsa state of Nigeria. To evaluate the knowledge, attitude and perceptions of prescribers on the rational use and prescribing of antibiotics. To identify, design and implement an intervention(s) that will be potentially feasible and effectively lead to improvement in antibiotic prescribing in the chosen settings.

Recruitment

Doctors and dentists are the main prescribers of medicines within the study settings. These set of professionals will be mainly targeted for the questionnaire and interview survey. A bulk SMS text message will be sent out initially. This will be followed by distribution of brief information leaflets about the study. The questionnaires will be distributed by hand in hard copies to participants in the study settings and interviews will be conducted face to face during official hours.

Study type and procedures

If you agree to take part in this study, you will be participating in an interview with me. The interview can be conducted at a time that is convenient to you. The interview can take place during office hours or any other time you are comfortable with. It will be a one-off interview that will last for no more than one hour. I will be the only person present with you during the interview, unless you prefer to have someone else with you. I will take some notes during the interviews, and if you agree, I would like to tape-record the interview so that I do not miss anything you say.

Risks and benefits

There will be no risk to you taking part, but it may help us improve antibiotics use. If you do not wish to answer any questions, it is totally fine to skip the question. You can also discontinue the study at any point if you wish without giving any reason.

Anonymity and Confidentiality

I will keep everything you say confidential by not writing your name on my notes, storing the notes and tape recording securely. If the study team reports your opinions or ideas, your name will not appear, and we will make sure that you cannot be identified. During the interview, I may call your name but when your interview is written up I will give you a code number as opposed to your name so that you cannot be traced.

Voluntary nature of the study

Taking part in the study is voluntary. You do not have to give a reason to refuse to take part or to stop the interview. Refusing to participate will not cause anything bad to happen. We do not pay people for being interviewed.

Any Further Questions

Please feel free to contact me by email, phone or post if you have any further questions. (Contact details have been provided at the beginning of this document). Please discuss the information above with others if you wish or ask me if there is anything unclear or if you would like more information. If you do decide to take part, you are still free to withdraw at any time and without giving a reason.

All data will be collected and stored in accordance with the Data Protection Act, 1998. Thank you for reading this information sheet and for considering taking part in this research.

APPENDIX XB: Prescribers' interview topic guide

ANTIBIOTIC PRESCRIBERS' INTERVIEW TOPIC GUIDE

Date:

Facility:

Respondent ID:

Sex:

Age range:

Specialty:

Length of time in Practice:

Introduction:

Thank you for accepting to take part in this interview. I'd just like to reiterate that everything you say in the interview is confidential to me and my supervisors. All data collected will be anonymised. The interview itself will be open ended and the questions themselves are usually fairly broad. There aren't any right or wrong answers

- I'm simply interested in your experience and your views with antibiotic prescribing. Is there anything you'd like to ask me?

Knowledge/Awareness on antibiotics use in Nigeria

1) What do you think about antibiotic prescribing in Nigerian hospitals?
2) Can you explain to me on factors that might have led to the current prescribing practices?
3) To your knowledge are there any interventions put in place or any steps taken to help with antibiotic prescribing and use in this hospital?
   Probe: Any form of stewardship programmes? Antibiotic prescribing policies/ guidelines? Infection control groups

Prescribing patterns

1) Tell me about the antibiotics that are commonly prescribed in this unit/hospital?
2) How do you choose the classes of antibiotics you normally prescribe from?

3) What are the common indications requiring antibiotic prescriptions in this unit of the hospital?
4) In practice do you normally prescribe antibiotic by brand names or by generic names…tell me about any reasons or factors that will affect generic or brand name prescribing?
5) Do you prescribe antibiotics in the essential medicines list and hospital formulary?

Decision making process

1) What are the factors that influence the choice of antibiotics you prescribe? (Probes: Tests results, PC symptoms diagnosis, availability, cost, co- morbidities).
   a) How do the factors you mentioned affect the choices of antibiotics you prescribe?
   b) When? Are there specific circumstances that certain factors come into play?
   c) Why do you consider these particular factors relevant in choosing antibiotics to prescribe?
2) Tell me about treatment guidelines or antibiotic policies. Are these readily available to guide antibiotic prescribing?
   a) Are they helpful?
   b) Do they influence your prescribing? How?
   c) What are your views and experience regarding the value of and use of policies?
   d) When in particular are the policies useful in prescribing antibiotics?
   e) What are the barriers with the use of antibiotic policies?
3) In your opinion, what proportion of antibiotics do you estimate is prescribed empirically and why?
   a) Under what circumstances would you prescribe antibiotics empirically or as a definitive therapy?
4) How often do you consult guidelines/policies/official books in antibiotic prescribing?
   a) Under what circumstances would you consult guidelines/policies/official books in antibiotic prescribing?

5) How often do you use laboratory investigations/ sensitivity tests as a guide to choice of antibiotics being prescribed?

   a) Tell me about specific situations where you would prescribe without investigations and other situations when you would require a test result before prescribing an antibiotic? Probe: When already prescribed drugs yield no effect?

6) In your opinion, do patients have any role to play in deciding if/ which antibiotic should be prescribed for them?

Recommended strategies

1) In conclusion, how would you describe the antibiotic prescribing pattern in this hospital?
2) In your opinion what interventions should be implemented in this setting to improve prescribing of antibiotics?
3) What would be the likely barriers in implementing this intervention(s)?

investigations and other situations when you would require a test result before prescribing an antibiotic? Probe: When already prescribed drugs yield no effect?

7) In your opinion, do patients have any role to play in deciding if/ which antibiotic should be prescribed for them?

Recommended strategies

4) In conclusion, how would you describe the antibiotic prescribing pattern in this hospital?
5) In your opinion what interventions should be implemented in this setting to improve prescribing of antibiotics?
6) What would be the likely barriers in implementing this intervention(s)?

APPENDIX XI A: Stakeholder's information sheet

STAKEHOLDER'S INFORMATION SHEET

Title of Project: Effective strategies to improve antibiotic prescribing patterns in Niger Delta Region of Nigeria.

Thank you for accepting to take part in this interview. There aren't any right or wrong answers I am simply interested in your views on the proposed strategies to improve antibiotic prescribing here in the hospital. I'd appreciate you sharing your thoughts on the feasibility and also what challenges will be likely encountered when implementing these strategies. Everything you say will be confidential to me and my supervisors. All data collected will be anonymised. The interview questions are open ended.

I'd like to request your permission also to audio-record this interview to help me capture everything during the analysis. Is there anything you'd like to ask me at this time?

The following interventions are being proposed for implementation here what are your thoughts?

- Increase antibiotic resistance awareness in the hospital environment
- Monitoring antibiotic use and consumption /Audits
- Informed education/training for prescribers
- Provide/Implement the guidelines
- Source for rapid diagnostic kits
- Conduct local studies
- Stock effective and cheaper generics

Please add any intervention you think will be beneficial in this system that has not been discussed above.

Okay let's talk about the recommendations that can be put in place over time to improve use and prescribing of antibiotics.

- Improving lab services
- Restricted pharmacy dispensing
- Implement health insurance schemes for vulnerable patients sub groups

Appendix XI B: Stakeholder's interview topic guide

STAKEHOLDER'S INTERVIEW TOPIC GUIDE

Date:

Facility

Position held/Unit:

Respondent ID:

Introduction:

Thank you for accepting to take part in this interview. Everything you say will be confidential to me and my supervisors. All data collected will be anonymised. The interview questions are open ended.

There aren't any right or wrong answers - I'm simply interested in your views on the proposed strategies to improve antibiotic prescribing here in the hospital. I'd appreciate you sharing your thoughts on the feasibility and also what challenges will be likely encountered when implementing these strategies. I'd like to request your permission also to audio-record this interview to help me capture everything during the analysis. Is there anything you'd like to ask me at this time?

The following interventions are being proposed for implementation here what are your thoughts?

Probes for each recommendation: In terms of feasibility, barriers, needed resources, man power, funds, government role/input?

Also, can you tell me if you have started anything similar already in this hospital? (Discuss each recommendation with the probes one after the other)

- Increase antibiotic resistance awareness in the hospital environment
- Monitoring antibiotic use and consumption /Audits
- Informed education/training for prescribers
- Provide/Implement the guidelines
- Source for rapid diagnostic kits
- Conduct local studies
- Stock effective and cheaper generics

Please add any intervention you think will be beneficial in this system that has not been discussed above.

Probes will be used to shed more light on feasibility, staff requirements, barriers, funding, policy back up, government input etc. (if not covered in the discussion).

Okay let's talk about the recommendations that can be put in place over time to improve use and prescribing of antibiotics.

(Use same probes from above for each recommendation)

- Improving lab services
- Restricted pharmacy dispensing
- Implement health insurance schemes for vulnerable patients sub groups

Are there any other recommendations you think will be helpful if implemented over time?

Appendix XII: Participant informed consent forms

LONDON'S GLOBAL UNIVERSITY UCL

Informed Consent Form

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Project Title: Antibiotic use and prescribing patterns in Niger Delta Region of Nigeria

Researcher: Eneyi Edith Kpokiri

Thank you for your interest in taking part in this research.

If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you sign this consent form. You will be given a copy of this Consent Form to keep and refer to at any time.

Participant's Statement

I agree that:

- I have read the notes written above and the Information Sheet and understand what the study involves.
- I understand that if I decide at any time that I no longer wish to take part in this project, I can notify the researchers involved and withdraw immediately.
- I understand that my participation will be taped/video recorded and I consent to use of this material as part of the project.
- I understand that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.
- I agree that the research project named above has been explained to me to my satisfaction and I agree to take part in this study.

Signature: ……………………… Date: ………………………….

Appendix XIII: Coding frame designed for prescribers' interviews

Property from topic guide	Open Codes	Transcript extracts	Participants
What are your thoughts on antibiotic prescribing in Nigerian hospitals?	Poor practices, Irrational prescribing, Empirical prescribing, Abuse, misuse, resistance, poor labs, relatively good,	➢ ***"Most doctors don't have any empirical evidence before prescribing antibiotics"*** ➢ ***"I think there is a lot of abuse of antibiotics"*** ➢ ***"Some of the lab investigations are not readily available"*** ➢ ***"They prescribe the wrong antibiotics without any prior MCS tests"*** ➢ ***"I would say antibiotics prescribing in our setting is relatively good"***	PRB 001, PRB 007, PRB 002, PRB 008, PRB 012
What factors do you think might have led to these prescribing practices	Clinicians Attitude, Laid down Practices, Local settings, training,	➢ ***"I think one of the main reasons is the lab results not being available"*** ➢ ***"I think the major factor is lack of knowledge and core understanding"***	PRB 001, PRB 007, PRB 004 PRB 005,

	Lack of knowledge, workload, poor labs, delayed results, Drug costs and availability, patient pressure	➢ ***"Cost and availability of the required drugs, antibiotics are prescribed just because they are not expensive and are readily available"*** ➢ ***"Some patient perceptions are that if they don't get antibiotics when they have a fever, they won't get better so some practitioners tend to give antibiotics when there is no indication"***	PRB 002
Have any interventions been put in place to help with antibiotic prescribing?	Formulary list Empirical research Antibiotic guidelines Antibiotic use Policy document	➢ ***"About 2 months ago we designed a new formulary list for the hospital"*** ➢ ***"I did a research work on surgical wound infections, from there we developed policies on how antibiotics should be used"*** ➢ ***"We have also had some trainings"***	PRB 014, PRB 012 PRB 003, PRB 002

Appendix XIV: Ethical approval letters

RESEARCH AND ETHICS COMMITTEE

NIGER DELTA UNIVERSITY TEACHING HOSPITAL, OKOLOBIRI

CLEARANCE CERTIFICATE

Application form number: **NDUTH/ REC/ 0007/ 2015**.

Project Title: ***A Survey of Antibiotic use and Prescribing Patterns in Niger Delta region of Nigeria and Developing Strategies to reduce Antibiotics Resistance.***

Investigators: **Kpokiri Eneyi Edith**.

Department/Institution: **Practice & Policy, University College London.**

Date considered: **9th September, 2015.**

Decision of the committee: **Approved**.

Chairman: Professor Olu Osinowo Signature & Date [redacted]........

DECLARATION BY INVESTIGATOR(S)

Protocol number:

To be completed in duplicate, and one copy returned to the Secretary, Research and Ethics Committee, Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State.

I/we fully understand the conditions under which I am/we are authorised to conduct the above-mentioned research and I/we guarantee that I/we will ensure compliance with these conditions. Should any departure be contemplated from the research procedure as approved, I/we undertake to resubmit the protocol to the Research and Ethics Committee.

Signature [redacted]... Date......09/09/15......

FEDERAL MEDICAL CENTRE
P.M.B. 502
YENAGOA

OFFICE OF THE HEAD OF CLINICAL SERVICES

INTERNAL MEMO

To	HOD – Pharmacy Department
From	Head of Clinical Services.
Date	16th September, 2015.
Subject	Re: A survey of antibiotic use and prescribing patterns in Niger Delta Region of Nigeria, and developing strategies to reduce antibiotic resistance.

The bearer, **Kpokiri Eneyi Edith** is a PhD student of School of Pharmacy, University College London. She has been granted approval to carry out a research work on the topic stated above.

Kindly assist her with the necessary data for her research work.

Thank you.

[redacted]

DR. P. P. F. NUMBERE
Head of Clinical Services.

BAYELSA STATE HOSPITALS MANAGEMENT BOARD

P.M.B. 41, YENAGOA, BAYELSA STATE.

Your Ref:

Our Ref: BSHMB/ADM/426/VOL.I/104

Date: 3rd February, 2016

Eneyi Kpokiri
Department of Practice & Policy
University College London
School Of Pharmacy
29-39 Brunswick Square
London, WCIN 1 AX
United Kingdom.

APPROVAL TO CONDUCT A STUDY ON ANTIBIOTIC USE AND PRESCRIBING PATTERNS

I am directed to refer to the above subject matter and to inform you that approval has been given to your application to **Conduct a Study on Antibiotic use and Prescribing Patterns.**

I am further directed to inform you that you should indicate the facilities you intend to use for the study.

Thanks for your usual cooperation, please.

[redacted]

Kalaowei Okponipere
For: Chief Medical Director

APPENDIX XV: Courses attended

Selected courses attended	Points	Dates
BMA Board of Science Antimicrobial Symposium		2018-05-17
LSE Africa Summit		2018-04-20
Research Day		2018-04-21
ULLA Summer School, KU Leuven, Belgium		2017-07-08
Humanitarian Aid Network, conference Brighton		2017-04-17
International Forum on Quality And Safety in Healthcare		2017-04-28
Introduction to qualitative data analysis		2017-02-02
Introduction to qualitative methods of data collection		2016-05-22
Research Day		2016-09-23
UCL GRAD school Residential Programme 8-10 July 2015	6	2015-07-08
Research Day	2	2015-04-24
Searching Medical Databases 17 Feb 2015	1	2015-02-17 12:30:00
Hugh Kearns - The Seven Secrets of highly successful research students 26 Jan 2015	1	2015-01-26 09:30:00
Marking Scripts (per term)	3	2014-12-05
Reading a Scientific Paper	1	2014-11-07
Publishing in High Profile Journals	1	2014-11-07
EndNote: Using bibliographic referencing software	1	2014-10-31
Overview of Library Resources for Graduates 28 Oct 2014Please book one session only	1	2014-10-28 14:15:00
PhD Induction Programme for School of Life and Medical Sciences (SLMS) 6-8 Oct 2014	5	2014-10-06 09:00:00
Research Day All PhD students are required to attend	2	2014-09-19
Total points obtained for the session 2014/2015	24	

APPENDIX XVI: Antibiotic policy document

SUBJECT	**POLICY DOCUMENT FOR IMPLEMENTATION OF ANTIBIOTIC STEWARDSHIP PROGRAMME**
AUTHOR	**ENEYI KPOKIRI**
COUNTRY	**NIGERIA**
LOCATION /SETTING	**NIGER DELTA REGION / GOVERNMENT HOSPITALS**
EFFECTIVE DATE	**November 2018**
VERSION	**1.0**

BACKGROUND

Antimicrobial resistance (AMR) is a major concern in global health today. Its impact is severe in developing countries where the burdens of infectious diseases are much higher. Optimising antibiotic prescribing in hospitals can reduce the threat of antimicrobial resistance. Studies from developed countries suggest that antibiotic stewardship can improve antibiotic prescribing; however, these interventions are not directly applicable to low and middle-income countries due to differences in the settings and healthcare structure. Research conducted in a low and middle-income healthcare setting has generated useful data on necessary steps to implement a feasible antibiotic stewardship programme in the local hospital settings. This policy document is therefore written as an output of the study results.

AIM

The primary aim of this hospital antibiotic policy is to minimize morbidity and mortality due to antibiotic-resistant infections; and to preserve the effectiveness of antibiotic drugs in the treatment and prevention of infectious diseases.

SCOPE

This policy is essentially for prophylaxis, empirical and definitive antibiotic therapy and it applies to all who prescribe, dispense and administer antibiotics within the hospitals.

POLICY

The WHO has recommended institutional policies for improving antibiotics use. This is a policy document outlining steps to be taken in the implementation of an Antibiotic Stewardship Programme (ASP) for hospitals in LMICs. The aim is to optimise treatment of infections through appropriate use of antibiotics while reducing the related adverse effects. This policy aligns with the recommendations in the WHO global policy package to combat antimicrobial resistance. The basic elements are similar such as education for prescribers, monitoring and surveillance, documentation and data reporting, however the strategies to do these in LMIC settings will defer.

PROCEDURE

Set up an ASP Team

a). **Leadership-** Appointment of an Infectious Disease (ID) Physician who will be committed to champion and support safe and appropriate use of antibiotics in the hospital.

b). **Membership**- Appoint other members of the ASP team. This will consist of a pharmacy consultant, medical microbiology/laboratory staff, nursing director, medical records representative.

Responsibility

a). This team will be responsible for stewardship activities in the hospital and as a team, they will:

- Develop an ASP mission statement they will work with.
- Review infectious disease cases and monitor the antibiotic use patterns on a regular basis.
- Monitor the patterns of antibiotic resistant organisms in the local hospital (MRSA, VRE. ESBL, CRE etc.) And other common infectious disease cases such as *Clostridium difficile* infections.
- Review the antibiograms to obtain the hospitals' bacterial sensitivity patterns.
- Generate reports on antibiotic consumption including the number of antibiotics prescribed, the drug, the class, dose and duration of therapy.
- Document the outcome of antibiotic therapy where possible.
- Collect and review the relevant data for clinical and cost efficacy and for feedback.

Drug Expertise

a). The pharmacist director will be directly involved with routine procurement of antibiotics drugs in line with the patterns of use, ensuring no stock-out for commonly prescribed antibiotics and all in the EML

b). Ensure availability of good quality lower priced generics

c). Provide a regular and updated formulary list of all available antibiotics for prescribers

d). Review all prescriptions and orders for antibiotic drugs for appropriateness before approval for dispensing

Surveillance/monitoring

a). Request for clinical diagnostic tests as required in cases of suspected infections to guide appropriate choice of antibiotic therapy.

b). Initiate an antibiotic review process for all antibiotics prescribed in the hospital. This will prompt clinicians to review the need for ongoing antibiotic therapy when diagnostics test results become available and the clinical picture is much clearer.

c). Laboratory representative will devise a method for flagging off cases of multidrug-resistant organisms (MDRO's). This will be documented alongside antibiograms and used to generate hospital specific antibiotic resistance patterns to guide future empirical treatments.

Reporting

a). The ASP team will delegate members to carry out routine audits of the current practice with antibiotics and report findings to enable improvements to practice.

iii. A minimum of two antibiotic prescribing audits will be conducted every year (6 monthly)

iv. Suggested audit targets are outlined below:

- 90-100% of antibiotics prescribed are clinically warranted
- 90-100% of antibiotics use is documented in the patient's notes
- 90-100% of antibiotics a prescribing is in accordance with local guidelines
- 90-100% of antibiotics prescribed are prescribed at the correct dose
- 90-100% of antibiotics prescribed are prescribed via the most appropriate route with intravenous to oral switch following local guidance
- 90-100% of antibiotics prescribed which require blood levels are monitored appropriately
- 0-10% of antibiotics are prescribed for longer than is necessary
- 90-100% of patients and their prescription charts are reviewed daily by the clinical team
- 90-100% of health care workers have an annual infection control update including antibiotics prescribing

b). The ASP will conduct local research on antibiotics use and patterns of antibiotic resistance/sensitivity. The findings when reported will be used to inform development of local and hospital specific guidelines.

Feedback/ Education

a). Feedback results from audits and local research conducted in form of presentations in clinical meetings and ground rounds highlighting areas of good practice and areas where improvements are still needed.

b). ASP team to organise routine seminars and training on rational use of antibiotics, inviting experts in the area and learning from best practices.

THE ROLE OF HEALTHCARE PROVIDERS

1. Attend relevant training and educational courses on antibiotic use and resistance.
2. Comply with policies, guidelines and other outlined clinical best practices.

ROLE OF HOSPITAL MANAGEMENT

1. To reinforce AMR sensitisation and increase awareness of antibiotic resistance within the hospital environment using billboards, posters in public places and hand leaflets in consulting rooms.
2. Setup the ASP team and other committee with which the ASP team will liaise such as the Drugs and therapeutics committee, infection control group, research and ethics committee etc.
3. Implement a restricted antibiotic list to control prescribing of certain class of antibiotics
4. Implement hospital intranet to support electronic prescribing and documentation
5. Support pharmacists to review and intervene in prescription orders to reduce amount of inappropriate antibiotic prescribing
6. Recruit sufficient personnel needed to function in the different roles as outline in the ASP procedures.

ROLE OF GOVERNMENT

1. Increase healthcare financing by increase the funds allocated to healthcare in the annual national budgets.
2. Provision of healthcare insurance for all citizens.
3. Co-ordinate and organise national programmes on antibiotic resistance to increase awareness at the national level.
4. Update and disseminate national policies and guideline for safe and appropriate use of antibiotic medicines.

REVIEW OF POLICY:

This policy will be reviewed annually and updated according to current medical knowledge, clinical practice and the local circumstances.

DISSEMINATION OF DOCUMENT:

- State Ministry of Health
- Medical directors of hospitals
- Heads of units
- Drug procurement teams/Pharmacy head
- Head of Nursing and Laboratory services

REFERENCES:

1. Centre for Disease Control and Prevention. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available From: http://www.cdc.gov/getsmart/ healthcare/pdfs/core-elements.pdf. [Accessed 17 August 2018].
2. Centers for Disease Control and Prevention. CDC Recommends all nursing homes implement Core Elements to improve antibiotic use. [www.cdc.gov]. [Accessed 17 August 2018]
3. Medscape, expert commentary, Dr. Nimalie Stone, CDC. 21 September 2015.
4. World Health Organization. Step-by-Step Approach for Development and Implementation of Hospital Antibiotic Policy and Standard Treatment Guidelines 2011; World Health Organization: Geneva, Switzerland, 2011. [Accessed 17 August 2018]