FEDERAL MINISTRY OF AGRICULTURE AND RURAL DEVELOPMENT
FEDERAL MINISTRY OF ENVIRONMENT
FEDERAL MINISTRY OF HEALTH

Antimicrobial Use and Resistance in Nigeria

SITUATION ANALYSIS AND RECOMMENDATIONS

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Foreword

Globally, antimicrobial resistance (AMR) has become a well-recognised public health threat in the recent years and interventions to reduce its burden have been launched worldwide. Like many countries, Nigeria is no exception to the challenges faced due to AMR. The emergence of multidrug-resistant organisms that have led to increased mortality and economic burden has increased almost exponentially. Thus, the prudent use of antimicrobial drugs cannot be more strongly emphasised than now. Nigeria, being the most populated country in West Africa has to take the lead in tackling antimicrobial resistance using the 'One Health' approach, which acknowledges the links among humans, animals and the environment, as the corner stone of its plan.

Poverty remains the major contributor to the worsening health status of Nigerians,with majority of the population surviving on or under $3.10 per day. Access to basic health services also vary especially in rural areas due topoor access to information leading to underutilisation of services and further health inequalities. Primary health care (PHC) services are the cornerstone of Nigerian health system but the problem of poor funding has led to the persistence of user fees as a method of health financing thus increasing Out-Of–Pocket (OOP) expenses and exacerbating poverty. Health financing initiatives should be introduced to reduce the impact on the health status of Nigerians.

Prescription monitoring is poorly conducted and prescription only medicines (POM) including antimicrobials are routinely sold Over-The-Counter (OTC) in pharmacies and by patent proprietary medicines vendors (PPMVs). This has been exercabated by the lack of confidence in the public health sector due to drug shortages and poor medicine accessibility. Individuals are therefore driven to utilise the private health care options and other access points to medicines. The government's effort should be focused on equipping the public health facilities and improving access to services.

As regulations are loosely enforced with regards to the sale of POMs OTC, it is difficult to control overuse of antimicrobials in general. An important component of good clinical practice that promotes the efficacy of therapy is the rational use of

antimicrobials. It will be prudent to implement quality-monitoring and regulation of drugs while engagingclinicians (inboth public & private health sectors), pharmacists and PPMVs on the importance of the rational use of antimicrobials.

This situation analysis report is based on the current situation in Nigeria and recommendations are made for immediate and long-term goals. Where we go from here depends on good leadership, multidisciplinary approach, enforcement of regulations and public education on the importance of tackling the growing AMR problem. All effort should be aimed at reducing the misuse of antimicrobials and promoting the development of novel treatment options to sustain the health of Nigerians and the world in the future.

CHIEF **AUDU INNOCENT OGBEH**, OFR
Honourable Minister of Agriculture and Rural Development

ALHAJI **IBRAHIM USMAN JIBRIL**
Honourable Minister of Environment

PROFESSOR **ISAAC F. ADEWOLE**
FAS, FSPSP, FRCOG, DSc (Hons)
Honourable Minister of Health

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A full list of organisations contributing to this work is provided after the references.

Chikwe Ihekweazu

DR **CHIKWE IHEKWEAZU**
National Cordinator /Chief Executive Officer,
Nigeria Centre for Disease Control (NCDC)

Abbreviations and Acronyms

AGOA	Africa Growth and Opportunity Act
AIDS	Acquired Immunedeficiency Syndrome
AJOL	African Journals Online
AMR	Antimicrobial Resistance
ASV	Anthrax Spore Vaccine
BCG	Bacilli Calmette Guerin
BQV	Black Quarter Vaccine
BSI	Blood Stream Infection
BSL	Biosafety Level
BV	Brucellosis Vaccine
CAUTI	Catheter-associated Urinary Tract Infection
CBHI	Community-Based Health Insurance
CBPP	Contagious Bovine Pleuro-pneumonia
CBPPV	Contagious Bovine Pleuro-pneumonia Vaccine
CD	Community Dialogue
CDC	Centers for Disease Control
CFR	Case-Fatality Rate
CGS	Conditional Grants Scheme
CHEWs	Community Health Extension Worker
CHW	Community Health Worker
CI	Confidence Interval
CIB	Community Information Board
CLSI	Clinical and Laboratory Standards Institute
CVLC	Community Viewing and Listening Centres
CONS	Coagulase negative*Staphylococcus*
CRE	Carbapenem-Resistant Enterobacteriaceae
CSM	Cerebrospinal meningitis
Hep.B-Hib	Hepatitis B *Haemophilusinfluenzae* B

DPT	Diphtheria, Pertussis, Tetanus
ECDC	European Centre for Disease Control
ECOWAS	Economic Community of West African States
EDL	Essential Drugs List
EPI	Expanded Programme on Immunisation
ESBL	Extended-Spectrum Beta-Lactamase
EU	European Union
FAO	Food and Agriculture Organisation
FCT	Federal Capital Territory
FCV	Fowl Cholera Vaccine
FMD	Foreign Market Development Programme
FMEnv	Federal Ministry of Environment
FMoH	Federal Ministry of Health
FTV	Fowl Typhoid Vaccine
GAVI	Global Alliance for Vaccines and Immunisation
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
GPEI	Global Polio Eradication Initiative
GSM	Global System for Mobile
HCAI	Health Care Associated Infection
HCW	Health Care Workers
HCW	Health Care Waste
HCWM	Health Care Waste Management
HCWMP	National Health Care Waste Policy Management
HIV	Human Immunodeficiency Virus
HPAI	Highly Pathogenic Avian Influenza
HSRP	Health Sector Reform Programme
HSS	Health System Strengthening

HSV	Hemorrhagic Septicemia Vaccine
IFRC	International Federation of the Red Cross
IMR	Infant Mortality Rate
IPC	Infection Prevention And Control
IPDs	Immunisation Plus Days
ISS	Immunisation System Strengthening
KG	Kilogram
LFN	Laws of the Federation of Nigeria
LGAs	Local Government Areas
LMICs	Low to Middle Income Countries
MDCN	Medical and Dental Council of Nigeria
MDGs	Millennium Development Goals
MDR TB	Multi Drug Resistant Tuberculosis
MG	Milligramme
MLSCN	Medical Laboratory Science Council of Nigeria
MMR	Maternal Mortality Ratio
MRL	Maximum Residue Level
MRSA	Methicillin-Resistant *Staphylococcus Aureus*
MSS	Midwives Service Scheme
AFDAC	National Agency for Food and Drugs Administration and Control
NCDC	Nigeria Centre for Disease Control
NDHS	Nigeria Demographic and Health Survey
NDP	National Drug Policy
NESREA	National Environmental Standards, Regulation& Enforcement Agency
N	Nigerian Naira
NHCWMP	National Health care Waste Management Strategic Plan
NHIS	National Health Insurance Scheme
NHPP	National Health Promotion Policy

NIDs	National Immunisation Days
NIPCP	National Infection Prevention and Control Programme
NMCN	Nursing and Midwifery Council of Nigeria
NPHCDA	National Primary Health Care Development Agency
NPHCDF	National Primary Health Care Development Fund
NPI	National Programme on Immunisation
NQAP	National Policy on Quality Assurance for Medicines and other Health Products
NTS	Non-Typhoidal *Salmonella*
NVRI	National Veterinary Research Institute
OIE	World Organisation for Animal Health
OOP	Out-of-Pocket
OPV	Oral Polio Vaccine
OR	Odds Ratio
ORT	Oral Rehydration Therapy
OTC	Over-The-Counter
PCN	Pharmacists Council of Nigeria
PCV	Pneumococcal Conjugate Vaccine
PHC	Primary Health Care
PLC	Public Limited Company
PMG- MAN	Pharmaceutical Manufacturing Group of the Manufacturers' Association of Nigeria
PMS	Patent Medicine Sellers
POMs	Prescription-only Medicines
PPM	Patent and Proprietary Medicine
PPMVs	Patent Propriety Medicine Vendors
PPR	Peste des Petits Ruminants
PQM	Promoting the Quality of Medicines
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta- Analyses
PTF	Petroleum Trust Fund

SOPs	Standard Operating Procedures
Spp.	Species
SSI	Surgical Site Infection
SBA	Skilled Birth Attendant
SDGs	Sustainable Development Goals
SIAs	Supplementary Immunisation Activities
STG	Standard Treatment Guidelines
TB	Tuberculosis
TFD	Theatre for Development
TT	Tetanus Toxin
UK	United Kingdom
UNAIDS	United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Emergency Fund
$	United States Dollar
USP	United States Pharmacopeia
USP	Universal Safety Precaution
UTIs	Urinary Tract Infections
VCN	Veterinary Council of Nigeria
VRE	Vancomycin Resistant Enterococci
WaSH	Water, Sanitation and Hygiene
WHA	World Health Assembly
WHO	World Health Organisation
WHS	Ward Health System
WTO	World Trade Organisation

Executive Summary

Preamble

Nigeria has a multifactorial health system and a large but young population. The major causes of morbidity and mortality are communicable diseases, and these are generally managed using antimicrobial drugs whose usefulness is being threatened by antimicrobial resitance. AMR threatens all countries in different ways and to varying extents. This document lays out the situation in Nigeria where much of the disease burden comes from Acquired Immunedeficiency Syndrome (AIDS), tuberculosis (TB) and malaria. In children less than 5 years of age, malaria, pneumonia, diarrhoea and meningitis are among the leading causes of death. Antimicrobials are a cornerstone of disease management in Nigeria and there is a pressing need to discover how best to conserve them.

This situation analysis was performed by the Nigeria Centre for Disease Control in collaboration with the Federal Ministries of Health; Agriculture and Rural Development, and Environment as well as the the Global Antibiotic Resistance Partnership (GARP) project. GARP is an initiative of the Center for Disease Dynamics, Economics & Policy (CDDEP), which establishes resistance related policy development capacity and policy analysis in selected low- and middle-income countries.

The Scope and Extent of Antimicrobial Resistance in Nigeria

In Nigeria, tuberculosis, respiratory infections and diarrhoeal disease are leading causes of infectious disease morbidity and mortality. Nigeria also suffers considerable burden from systemic infections including Human Immunodeficiency Virus (HIV), malaria, bacteremia and meningitis. There are, as yet, no available studies outlining the full burden of AMR and its health and economic impact on Nigerians. However these data are available from elsewhere and Nigeria-specific data demonstrates that AMR rates of many disease-causing organisms are untenably high in Nigeria.

Community-acquired Infections in Humans

The most common bacterial infections are community-acquired diarrhoeal diseases, respiratory, urinary tract and invasive infections. Among organisms causing diarrhoeal disease, including the life-threatening childhood diarrhoeas that are an important contributor to Nigeria's excessive infant mortality rate, resistance is rife. There is widespread antimicrobial resistance among enteric Escherichia coli in Nigeria particularly to penicillins, aminoglycosides, cephalosporins, chloramphenicol, tetracyclines and cotrimoxazole. Resistance patterns among Shigella and non-typhoidal Salmonella are just as high and appear to be increasing. In North-West Nigeria, resistance rates of over ninety per cent were reported for Shigella- the cause of dystentery, each to ampicillin, fluoroquinolones, chloramphenicol and cotrimoxazole. These are the currently recommended options for treating the disease.

As reported by the Cholera Regional Platform, Nigeria in 2014 had 35,996 cases of cholera, which represented about 39 per cent of all cases in the region, making her the most affected country by cholera in west and central Africa. A cause for extreme concern was the rise of cholera case-fatality rate (CFR) to 4.76%, as at the end of April 2015- 2,108 cholera cases, with 97 deaths.The systematic review of literature for this situation analysis revealed that resistance was predominantly documented to trimethoprim/ sulphamethoxazole, sulfonamides and nalidixic acid, again obliterating most of the options for antimicrobial-based containment of outbreak cholera. Many countries are moving towards vaccine-based strategies but these are yet to be applied in Nigeria.

A systematic review in Nigeria found marked resistance to all drugs commonly prescribed for urinary tract infections in the country. There are high rates of resistance to ceftriaxone, ampicillin and cotrimoxazole. Most organisms demonstrated 100% resistance to ampicillin and cotrimoxazole which have long been used as first line drugs in the treatment of UTI. Among the first line drugs, Nitrofurantoin hadthe lowest resistance levels with resistance rates as low as 6.5% in E.coli and less than

100% Proteus, Klebsiella and Enterobacter. However, ciprofloxacin and gentamicin had the lowest rates of resistance compared to the other drugs. The documentation of problematic antimicrobial resistant organisms such as carbapenem-resistant enterobacteriaceae (CRE), vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase-producing (ESBL) Gram negative rods is alarming in a country where antibacterial alternatives are not available in the event of resistance to the last-line drugs.

Bloodstream infections are difficult and expensive to treat and often fatal. Few studies on bloodstream infections were available for review, presumably because there is limited capacity for blood culture country-wide. Among Gram positive bacteria recovered from such infections Staphylococcus species showed variable degrees of resistance to commonly used classes of drugs such as the aminoglycosides and fluoroquinolones. Resistance to ciprofloxacin ranged between 0% in Osun State to 73.4% in Edo State. Staphylococcus epidermidis isolates from two States in the Northeastern and Northwestern zones were all resistant to cefuroxime while Staphylococcus aureus showed less resistance ranging between 0% and 60.5% at the same centres. Resistance of Staphylococcus species to chloramphenicol was high in all studies. In a study done in Oyo State, the Gram negative causes of bloodstream infections were ofthe Enterobacteriaceae, and they were highly susceptible to most antimicrobials used in the study. Interestingly all the Gram negative bacilli in that study were 100% sensitive to amikacin, ciprofloxacin, ceftazidime and cefotaxime. However, E. coli were 100% resistant to amoxicillin/clavulanate and chloramphenicol and this resistance pattern has been recorded in other parts of the countries.

Available studies on the resistance rates of central-nervous system pathogens revealed that 20% of all Neisseriae meningitidis isolates were resistant to chloramphenicol, while 30.8% were resistant to Penicillin G. None of the isolates were found to be resistant to ceftriaxone.For this reason,costly third generation cephalosporins such as

ceftriaxone are still the recommended choice of drug for the treatment of meningitis in Nigeria. A meta-analysis of studies in Nigeria revealed that resistance rates of Haemophilus influenzae to penicillin G, chloramphenicol, ceftriaxone were 66.7%, 23.5%, and 4.5% respectively. Streptococcus pneumoniae-one of the most common causes of non-epidemic meningitis, had penicillin G, chloramphenicol, and ceftriaxone resistance rates of 45.2%, 10.3% and 1.7% respectively. Ceftriaxone, augmentin, and amoxycillin had comparable low rates of resistance ranging from 18.2 to 24.3%, suggesting other beta lactams other that penicillin may still be useful in the treatment of pneumococcal pneumonia. Septrin resistance rate was the highest, and this differs from what has been found in other countries. Resistance-averting pneumococcal conjugate vaccines are yet to be rolled out nationally in Nigeria.

Health Care-Associated Infections (HCAIs)

Antimicrobials are used intensively in health care institutions, which house individuals who, due to infirmities, are more susceptible to disease. Health care-associated infections are drivers of the resistant pandemic and can seed resistant organisms into the community where they become widespread. The risk of acquisition of HCAI is 2-20 times higher in developing countries such as Nigeria. Common examples of HCAIs are blood stream infections, surgical site infections and urinary tract infections. Surveillance studies have found that blood stream infections can be episodic and can also be catheter associated. Staphylococcus aureus was the most common cause of blood stream infection in adults whilst Klebsiella spp was predominant among neonates. Surgical site infections were seen following Caesarean sections and orthopaedic manoeuvres. Resistant organisms such as ESBL-producing Enterobacter spp, Methicillin-resistant Staphylococcus aureus and carbapenem-resistant Acinetobacter spp were also isolated. Health care-associated urinary tract infection occurred in patients with prolonged hospitalisation especially in intensive care unit while Catheter-associated urinary tract infection (CAUTI) was seen in urologic conditions such as prostatic enlargement. AMR was noticed in some identified

organisms however, patterns of the resistance were not explicitly described.

Bacterial Resistance in Animals and the Environment

Systematic review of Nigerian literature revealed that resistant bacteria are commonly recovered from livestock including cattle, sheep, goats, camels, pigs and poultry. Also, Correspondingly high levels of resistant organisms was seen from foods such as meats, dairy and vegetables. While it is conceivable that resistant organisms in domestic animals could have been acquired from human and other sources, the high levels of antimicrobial residues in Nigerian meats and the low recovery of resistant organisms from wildlife point to antimicrobial use in agricultural and veterinary practices as the principal driver of resistance.

Resistant bacteria have also been recovered from presumed potable, natural and waste water sites. They have been found in soils , aquaculture sites as well as elsewhere in the environment.

The above summary of the systematic review of literature illustrates that AMR is highly prevalent in the country and there is an urgent need for coordinated national response to AMR in the country. As resistance is pervasive in humans, animals and the environment, a One Health approach, which acknowledges the connections among humans, animals and the environment, to resistance containment is Nigeria's best option.

Drivers of Antimicrobial Resistance in Nigeria

Although National Health Policies are in place to ensure quality health for all Nigerians, the scale of this challenge is large and the funding and political will needed to meet it are short. Thus OOP spending for health care services in Nigeria is among the highest in the world. The budgetary allocation for health is still below the 15% agreed to by the Nigerian government in the 2001 Abuja declaration by African Union countries. Primary health care, the bedrock of the national health system, is insufficiently equipped to meet most Nigerian's needs. Hospitals are under-

provisioned and overstretched. The poor tend to use informal sector providers, many of whom provide lower quality services.

The health care system can only be as strong as its workforce. Currently, physicians, nurses, pharmacists, laboratory technologists and other health workers are in short supply nationally, as well as analytical scientists involved in medicine quality assurance. Many but not all the curricula for these professionals contain some mention of AMR and all would benefit from curricula revisions that treat the topic more explicitly. Continuing education for practicing professionals on AMR is also desirable. The same inputs are also necessary for the veterinary curriculum.

According to Nigeria's legislation, antimicrobials and other antibacterial should only be dispensed with prescription. However, a combination of factors ranging from a shortage of licensed prescribers and medicines in some areas, to proliferation of under-regulated patent medicine vendors and hawkers in others,means that Nigeria suffers severe access problems whilst simultaneously facing a crisis of irrational drug use. Drug misuse extends to the agricultural sector where antimicrobials are liberally used therapeutically and for growth promotion. All of these drug-use problems can exacerbate resistance and infectious disease management.

The quality of antimicrobials is key to ensuring that when antimicrobials are used appropriately, patients receive the appropriate regimen. Quality of pharmaceuticals and resistance-averting health-care tools such as vaccines and diagnosticsdepends on the robustness and security of their supply chain. Nigeria has well-founded mechanism for procuring and disseminating health care products but is prone to stock-outs, distribution challenges and invasion by substandard products from unsanctioned sources.

Much antimicrobial use and misuse is driven by patients, farmers and the general populace who demand antimicrobials for real or presumed infections and procure them from unsanctioned sources even when they are not prescribed. Awareness of AMR is low among Nigerians in general, even among the health professionals.

Resistance is accelerated by selection pressure from inappropriate antimicrobial use while the spread of resistant organisms from one person to another is promoted by poor infection prevention and control. A balance must be maintained where antimicrobials are optimally available but with limited access to unwarranted use. Our current situation analysis reveals that loss of effective antimicrobials due to resistance is already evident in Nigeria. In some cases, resistance rates are untenably high. Resistance trends can be slowed or reversed with appropriate activities and commitment. There is need to enhance infection prevention and control measures such as vaccination, antimicrobial stewardship programmes and to limit non-therapeutic use of antimicrobials in livestock and poultry.

Recommendations

This situation analysis was essential to get a baseline of where the country is regarding the policies, use and challenges for achieving optimal antimicrobial use and conservation in Nigeria. Following this an analysis of the strengths, weaknesses, opportunities and threats (SWOTs) was carried out for achieving a clear strategy for developing a National Action Plan. These recommendations are focused on a one-health approach for achieving the goals.

Nigeria urgently needs a national policy on AMR. Nigeria also needs to better implement and regulate policies related to health care delivery. These include but are not limited to the National drug policy, whihc needs a review following a timely review of the standard treatment guidelines (STG) that is responsive to the generated surveillance data. Nigerian medicines and diagnostics supply chains need to be strengthened and secured. The introduction of a robust track and trace technology system should be explored as a solution to the gap in knowledge of the drug distribution system for monitoring access and use of antimicrobials.

The constitution of a national Infection Prevention and Control (IPC) coordinating body with the mission of providing national and health care facility specific

guidelines for IPC is imperative. Hospital administrators should initiate and sustain functional IPC committee -in all health care facilities, with clear budgetary allocation. The IPC surveillance capacity should be improved with greater collaboration between stakeholders, thus promoting data sharing among institutions. IPC training at facility level is essential, and should be designed to suit different cadres of health care professionals and provide a clear career path for professionals in IPC. Furthermore, the surveillance of prevalent subtypes of some bacteria needs to be enhanced to support vaccination programmes. There is need to explore measures to improve biosecurity by small farm holders and at the market level.

A high level advocacy is required for all stakeholders to create extensive awareness on AMR. It is fundamental to build mediacapacity on appropriate reporting on AMR. There needs to be dedicated communication platforms for creating awareness by improvingexisting tools using culturally accepted channels. AMR needs to be incorporated into all professional curricula and in continuing professional development.

Research and Development (R&D) capacity should be developed across all sectors. This will bolstermore studies on the financial consequences of AMR in the country as well as its impact on achieving the Sustainable development goals (SDGs) amongst others. Furthermore, the capacity for production of human vaccines should be developed.

1 Health and Economic Context

1.1 GEOGRAPHIC & DEMOGRAPHIC CONTEXT

Nigeria is a federation of 36 States that is the most populous country on the African continent. She has an estimated population of 182 million people, expected to rise to over 200 million by the year 2025.[1,2] There are about 374 identifiable ethnic groups in Nigeria with the Igbo, Hausa, and Yoruba as the major groups and languages spoken[3]. The official language is English. The country has different religions including Christianity, Islam and traditional African religion.

Nigeria's population is predominantly young, as is typical of countries with high fertility rates. The national median age is 17.2 years and the proportion of children under age 15 is around 46%, while the proportion of individuals aged 65 and older is 4%.[3,4] The literacy rate for persons 15 years and older in 2015 was 60%[5]. Disparities in literacy level exist based on geography and sex: over 77% of women are literate in urban areas whereas only 36% are in the rural areas.[3] Overall, only 70% of males aged 6 years and above have ever attended school, compared with 58% of females.[3] Table 1.1 depicts an overview of the key demographic, socioeconomic and health indicators in Nigeria.

Table 1.1: Demographic, Socioeconomic and Health Indicators in Nigeria

INDICATORS	FIGURE	SOURCE
Demographic		
Total population	182,201,962	World Bank 2016
Annual population growth rate (%)	2.6	World Bank 2016
Proportion of population in rural areas (%)	52	World Bank 2016
Crude birth rate (births per 1,000 women)	39	World Bank 2016
Crude death rate (deaths per 1,000 pop.)	13	World Bank 2016
Life expectancy at birth (years)	54	National Bureau of Statistics 2014
Socioeconomic		
Gross national income, purchasing power parity, per capita (current $)	5810	World Bank 2016
Health expenditure per capita (current $)	118	World Bank 2016
Out-of-pocket health expenditure (% of total expenditure on health)	72	World Bank 2016
Adult literacy rate, both sexes 15 years and above (%)	60	World Bank 2016
Female literacy rate, adult 15-49 years (%)	53	Nigeria Demographic and Health Survey 2013
Health		
HIV prevalence, adults 15-49 (%)	3.1	NACA 2015
Annual TB Incidence (all cases/100,000)	322	Nigeria Strategic Plan for Tuberculosis Control 2015

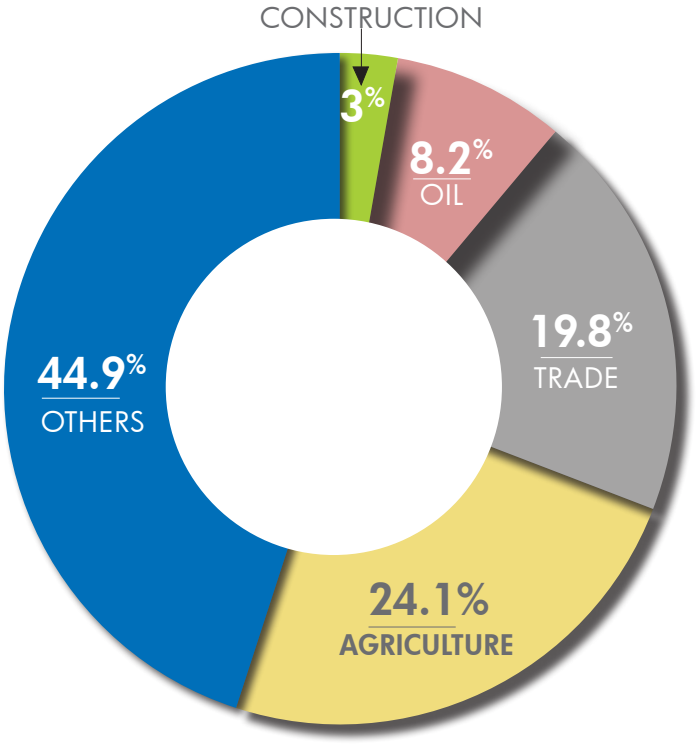
INDICATORS	FIGURE	SOURCE
Health cont'd		
Malaria parasite prevalence,children 6-59 months (%)	27	Nigeria Malaria Indicator Survey 2015
Total fertility rate (per woman) 2006	5.5	Nigeria Demographic and Health Survey 2013
Maternal mortality ratio (per 100,000 live births)	576	Nigeria Demographic and Health Survey 2013
Neonatal mortality rate (per 1,000 live births)	37	Nigeria Demographic and Health Survey 2013
Post-neonatal mortality rate (per 1,000 live births)	31	Nigeria Demographic and Health Survey 2013
Infant mortality rate (per 1,000 live births)	69	Nigeria Demographic and Health Survey 2013
Child mortality rate (per 1,000 live births)	64	Nigeria Demographic and Health Survey 2013
Under-5 mortality rate (per 1,000 live births)	128	Nigeria Demographic and Health Survey 2013

1.2 ECONOMIC CONTEXT

1.2.1 The Role of Economy on Health

In 2015, Nigeria's Gross Domestic Product was $481bn with an annual growth rate of 2.7%.[5] The major sources of revenue are oil, gas and agriculture. Agriculture was the mainstay of Nigeria's economy before the discovery of oil in 1956 and over time, petroleum exports have become the main source of the country's foreign exchange earnings.[6] In 2016, the third quarter report of the National Bureau of Statistics Stated that the contribution of agriculture to the total GDP was 24.1% while the oil sector was 8.2% (Figure 1.1).[7]

Poverty remains one of the major contributors to the worsening health status of Nigerians which has been on the decline over the decade. [8] About 76% of the population lives on $1.90 a day or less and the poverty gap at national poverty lines is 17%. [9] Economic inequalities exist between rural- urban areas and geopolitical zones.



(SOURCE: NATIONAL BUREAU OF STATISTICS) [7]

Figure 1.1: Contribution to the National Gross Domestic Product (%) by Sectors in Nigeria as at the 3rd Quarter of 2016

1.2.2 Health Financing

Revenue for financing the health sector is collected from both pooled and unpooled sources. The pooled sources come from budgetary allocation and direct and indirect taxation (Government Health Expenditure). However, the unpooled sources (private expenditure) contribute over 70% of total health expenditure.[10]

The private sector of the health system continues to grow and it has played a significant role in health care financing for at least the last 15 years.[11] In 2014, private sector expenditure accounted for over 70% of the total health expenditure.[12] Data analysis from 1999-2002 showed that private households' OOP payments accounted for 90–94% of private payments , while private prepaid and risk pooling constituted only 2.4–6.7% with minimal changes between 2012 to 2014.[12,13] OOP spending comprises health-care expenses individuals pay that are not reimbursed by a health insurance company, and its rate in Nigeria is regarded as one of the highest in the world. In about 4% of households in Nigeria more than half of the total household expenditures is spent on health care while 12% spend more than a quarter.[14] OOP spending for health care increased when Nigeria adopted the Bamako Initiative which enboldened the introduction of user fees in the health sector as a strategy of financing government health services.[15]

The Nigerian government established the National Health Insurance Scheme (NHIS) under Act 35 of 1999 and it became operational in 2005 with the aim of improving access to health care and reducing the financial burden of OOP spending for health care services on its citizens.[16] However, the optimal coverage has not been achieved.[17-20]

The estimated annual average official development assistance inflow for 1999 and 2007 was $2.3 and $4.7 per capita, respectively.[21] These figures are way below

the Sub-Saharan African average of $28 per capita.[22] In 2003, it was estimated that development aid contributed N27bn (4% of total health expenditure) to health care financing in Nigeria.In 2004, this increased by 29% to N36bn (4.6% of total health expenditure). Sadly, in 2005 it increased by only 1% to N36.3bn (4% of total health expenditure). International assistance to the Nigerian health sector has been on the increase, however it suffices for only a small proportion of the total public health expenditure.[12, 24]

The Nigerian health system is anchored on Primary Health Care (PHC).[24] Howbeit, poorfunding has been a persistent problem hence the Basic Health Care Provision Fund was introduced to address this gap in the 2014 National Health Act. This fund is allotted for provision of basic minimum package of health services through the National Health Insurance Scheme (NHIS) (50%) in eligible primary or secondary health care facilities; essential drugs (20%); provision and maintenance of facilities, equipment, and transport (15%); development of Human Resources for Primary Health Care (10%); and emergency medical treatment (5%).[25]

The Federal Government's allocation to health increased dramatically from N154.6bn (5.38%) in 2009 to N282.7bn (5.95%) in 2012.[14] It saw a decline from N264.4bn (5.63%) in 2014 to N250bn (4.13%) in 2016. Nevertheless, the budgetary allocation for health is still below the 15% signed by the Nigerian government in the Abuja declaration.[26] The recent advocacy for the implementation of the National Health Act 2014 will no doubt increase universal health coverage and more spending for health care as it includes the mandatory provision of 1% of Annual Consolidated Revenue Fund of the Government for Health care Financing.[27]

1.3 HEALTH CONTEXT

1.3.1 Health Indicators

Life expectancy at birth in Nigeria was estimated at 54 years in 2013.[28] The major causes of mortality and morbidity are communicable diseases, with HIV, malaria and tuberculosis as significant contributors [29] Nigeria's infant mortality rate is 69 per 1,000 live births while the under-five mortality rate is 128 per 1,000 live births.[29] The major causes of newborn mortality are asphyxia 27%, preterm birth 25% and infection 22%, accounting for over half of all neonatal deaths.[8] The causes of death for children less than 5 years include malnutrition 53%, neonatal tetanus 26%, malaria 24%, pneumonia 20%, diarrhoeal 16%, measles 6% and others 1%.[8] Despite the high infant and child mortality rates, it is very noteworthy that the rates have decreased over the years.[30]

1.4 HEALTH POLICY

The National Health Policy was formulated in 1988 and the revised plan launched in September 2004. The objective of the Revised National Health Policy was to strengthen the national health system so as to provide effective, efficient, quality, accessible, and affordable health services thus improving the health status of Nigerians whilst achieving health-related Millennium Development Goals (MDGs).[30] Roles and responsibilities of different tiers of government, including non-governmental organisations, were clearly defined. The policy's overall long term goal is to ensure a functional referral system through which the citizens will be afforded adequate access to primary, secondary, and tertiary health care services .[30]

Other national health policies include

1. The National Drug Policy (NDP), was adopted in 1990 and later revised in 2005. The revision was informed by identified lapses including poor political will and the absence of a well-structured monitoring system The objectives include providing adequate supplies of effective, affordable, safe and good quality

drugs,ensuringtheir rational use, and increasing local production of essential drugs.[31]

In addition, the Standard Treatment Guidelines (STG) 2008 is an important tool for the attainment of comprehensive and effective health care delivery services thereby achieving the goals of the National Drug Policy.

2. Health sector Reform Programme (HSRP) (2003-2007), was developed to kick start the health sector reform.
3. National Strategic Health Investment Plan (2007-2008), was developed to succeed the HSRP and serves as a strategic tool in the health development agenda aimed at achieving health-related MDGs.
4. National Strategic Health Development Plan (2010-2015), was developed to strengthen and sustain health care delivery system which will ultimately improve the health status of Nigerians
5. National Policy on Quality Assurance for Medicines and other Health Products (NQAP): The Federal Ministry of Health, and its development partners, such as USAID/Nigeria, United State Pharmacopeia/Promoting the Quality of Medicine (USP/PQM) and others developed the NQAP. The policy clearly spells out measures for assuring the quality of products and services offered by the national health and pharmaceutical sectors, and securing the supply chain thus hindering the free flow of falsified or substandard medicines and other health products [32]

   This policy is timely and particularly important as it limits unwholesome manufacturing practices in the pharmaceutical industries. These practices significantly contribute to the creation of antimicrobial resistant strains.[10]

6. National Health care Waste Policy: To create an enabling environment that contributes to effective and efficient health care waste management practices with minimal harmful environmental impact.The goal of the policy is to integrate the management National Policy on Management of chemicals for the protection of human and animal health and the environment.

7. Sustainable Development Goals (SDGs)[33] Following her participation in the endorsement of the United Nations' Millennium Declaration in 2000, Nigeria adopted the eight measurable-time-bound Millennium Development Goals (MDGs). The MDGs were set to be achieved by 2015 hence the need for a post MDG agenda to sustain gains made. Sustainable Development Goals (SDGs) is a comprehensive, ambitious and transformational development agenda document with outcomes that has 17 goals and 169 targets.

Despite progress on some MDG indicators, many of the goals and targets have not been met. However, the country registered multiple success stories such as reaching the threshold of eradicating polio, the implementation of a largely successful Conditional Grants Scheme (CGS) and mobilizing community utilisation of health facilities through the village health workers scheme.

1.5 NIGERIA'S LEGAL FRAMEWORK FOR ANTIMICROBIALS AND RESISTANCE CONTROL

1.5.1 Laws/Regulations Governing Medicine Use in Human and Animals

1. Drugs and related products (registration) Decree No. 19 of 1993: This decree prohibits the manufacture, importation, exportation, advertisement, sale or distribution of unregistered drugs, drug products, cosmetics or medical. It also stipulates the procedure for applying for registration of a drug product,

conditions under which certificates of registration and clinical trials can be suspended or cancelled and penalties for contravention amongst others.

2. Poisons and Pharmacy Act, Cap 366 of 1990: This Act provides varying regulations and controls for the different categories of drugs and poisons, from compounding through the intermedate steps to dispensing[34]

3. Food and Drugs Act Cap 150 of 1990: This Act prohibits the availability of some specified drugs or the sale of certain drugs,foods, cosmetics or devices for the treatment of certain diseases. It also prohibits unhealthy practices such as unhygienic manufacture of foods and drugs, misleading packaging, labeling, and advertising. It authorises theappointment of food and drug inspection officers and analysts. [34]

4. Counterfeit and Fake Drugs (miscellaneous provisions) Act, Cap 73 of 1990: This Act prohibits the production, importation, manufacture, sale and distribution of any counterfeit, adulterated, banned or fake drugs. It also prohibits the unauthorised sell of drugs in an open market.[34]

5. The National Essential Drugs List (EDL): This was initiated to streamline the drugs in the health care system thereby enhancing the quality of health care services in the country and ensuring good drug supply management in all public health facilities. The sixth review in 2015 was primarily directed at ensuring that the medicines in the Standard Treatment Guidelines and the Essential. Medicines List are harmonized taking into consideration the new antimalarial drug policy as well as practices current in other vertical programmes including those for mycobacterial infections, HIV/AIDS, and other special services.[35]

1.5.2 Laws Establishing Councils and Regulatory Agencies

1. The Pharmacists Council of Nigeria (PCN): All aspects of educating, training and practising of pharmacy is regulated and controlled by PCN. It also regulates the Pharmacy Technicians and Patent and Proprietary Medicine Vendors, in Nigeria.[34]

2. The Medical and Dental Council of Nigeria (MDCN): MDCN is a Federal Government Agency established by act cap 221(now Cap M8) of 1990. Its responsibility is to ensure best health care delivery by regulating the practice of medicine, dentistry and alternative medicine in Nigeria.[36]

3. The Nursing and Midwifery Council of Nigeria Act Cap No 143 Laws of the Federation of Nigeria 2004 mandated the Council to regulate and regularly review the standards of Nursing and Midwifery Education and Practice in Nigeria ensuring that the changing health needs of the society are met.[37]

4. The Medical Laboratory Science Council of Nigeria (MLSCN) act 11 of 2003: This brought about the creation of MLSCN. MLSCN is charged with the mandate of regulating the training of medical laboratory scientists, technicians and assistants and medical laboratory services. It also registers and licenses medical-laboratory practitioners and -laboratories and monitors and certifies laboratory quality and test kits and reagent. [38]

5. The National Agency for Food and Drugs Administration and Control (NAFDAC) Law: Decree 15 of 1993 established the National Agency for Food and Drugs Administration and Control (NAFDAC) as amended by decree 20 of 1999. The Governing Council of NAFDAC) is empowered to make regulations and guidelines that govern the importation, licensing, labeling and usage of drugs (including antimicrobials for humans and animals) by sections 5 and 30 of the National Agency for Food and Drug Administration and Control Act Cap NI

Laws of the Federation of Nigeria (LFN) 2004. Within the agency, a Directorate of Veterinary and Allied Products has been created to cater for veterinary medicinal products.

Even though there are several laws and regulations, enforcement of these laws is a serious challenge to the agencies charged with these tasks. Some of the challenges include illegal importation of antimicrobials, off the counter sales without veterinary prescription, treatment by unqualified personnel/producers and lack of adherence to products guidelines.

6. Veterinary Surgeons Act CAP V3 LFN 2004 (as amended): It is the legislation governing the regulation of veterinary practice. This provides the authority for the Veterinary Statutory Body to set standards for registration of veterinarians and to regulate their conduct. This does not cover registration and regulation of veterinary para-professionals for now, however this is being pursued in the next amendment in line with World Organisation for Animal Health (OIE) requirement.

7. Animal Disease Control Act 1988: This act provides regulation for the control and prevention of animal diseases, with the objective of preventing the introduction and spread of infectious and contagious diseases among animals, hatcheries and poultries in Nigeria. It is currently being reviewed to specifically address emerging issues and areas that are obsolete.

8. The Veterinary Surgeons Act Cap V3 LFN, 2004 as amended established the Veterinary Council of Nigeria (VCN) to regulate the standard of training and practice of the Veterinary profession in the country. It is to set standards for registration of veterinarians and to regulate their conduct. It issues annual practicing license to registered veterinarians as well as registers and licenses (annually) veterinary practicing premises. This does not cover registration and

regulation of veterinary para-professionals for now, however this is being pursued in the next amendment in line with World Organisation for Animal Health (OIE) requirements.

9. Meat Law (1968): All slaughterhouses must be registered with the Director of Veterinary Services of each State. Slaughtering outside a registered abbatoir is illegal. Animals to be slaughtered are supposed to be rest in the lairage at least 24 hours before slaughtering during which ante-mortem inspection such as disease screening is done. Post mortem inspection is compulsory.

10. Nigerian Veterinary Formulary: This was first published in 2007 and is the compendium of essential veterinary drugs, biologics and chemical pesticides. The veterinary drugs and biologics are for the protection of the health and welfare of animals. The agents are for the prevention, control and diagnosis of disease.

1.5.3 Laws/Regulations Governing Environment

1. National Environmental Sanitation Policy: The National Environmental Sanitation Policy was developed in 2005 by the Federal Ministry of Environment. The purpose of the policy is to promote public health and welfare, improve quality of life and ensure a sustainable environment through the principles and practices that will effect healthful and hygienic conditions in the environment.

2. Harmful Waste (Special Criminal Provision) Act Cap H1LFN 2004: This act prohibits anyone without lawful authority to carry, transport, import or sell any harmful waste.

3. National Environmental Standards and Regulation and Enforcement Agency (NESREA) Act no 11, 2007 was set up to enforce compliance laws, guidelines, policies and standards on environmental matters in the country

4. S.I.15 Management of Solid and Hazardous Wastes Regulation of 1991 regulates the proper treatment of solid and hazardous waste, provision of hazardous waste disposal facilities and ascertains that such facilities meet up to standard in all areas like contingency planning, emergency procedures e.t.c. Part 12 of this regulation provides for tracking of wastes from their point of generation to their final disposal with specific details regarding Health care Waste.
5. S.I.8 National Effluent Limitation of 1991 which makes compulsory the provision of effulent treatment system and the installationof anti-pollution equipment in industries. It also sets the maximum effluent limits allowed for discharge.
6. S.I. 9 National Pollution Abatement industries and facilities generating wastes of 1991 deals with the release of toxic substances. It restricts the release of toxic substances and ensures the permissible pollution limits are not exceeded by stipulating and monitoring pollution control measuresin industries and facilities generating such waste.
7. Environmental Health Officers (Registration and licensing) Act 11 of 2002: To secure and monitor the environment, minimising health hazards and threats the Environmental Health Officers Registration Council of Nigeria was established with the mission regulating Environmental Health profession in Nigeria.[39]
8. National Environmental Health Officers Practices Regulations (2007) Revised Edition (2016)
9. National Environmental (Sanitation and Waste Control) Regulations 2009
10. National Environmental (Pollution Abatement in Chemicals, Pharmaceuticals, soaps and detergent Manufacturing industries) Regulations 2009
11. National Environmental (Pollution Abatement in Food, Beverages and Tobacco Sector) Regulations 2009

1.6 ORGANISATION & DISTRIBUTION OF SERVICES

Nigeria has both orthodox and traditional health care delivery systems, which operate in a somewhat pluratistic health care milleu. Orthodox health care services are provided by both the private and public sectors in the country. The public health service has three levels: primary, secondary and tertiary levels.In 2013, it was estimated that 34,423 health facilities existed in Nigeria.of which 11,395 (33%) were private health facilities and 23,028 (67%) government health facilities. Primary, secondary and tertiary health facilities accounted for 88.2%; 11.6% and 0.2% respectively.[40]

The primary health facilities- health centers and clinics, dispensaries, and health posts are the communities' entry way into the nation's health care system. They typically provide general preventive, curative, promotive, and pre-referral care[2]. Secondary health care facilities include general hospitals, and theyprovidegeneral and specialised medical services including surgery, paediatrics, obstetrics and gynaecology[2]. These facilities serve as referral centers for primary health care facilities. Tertiary facilities provide the highest level of health care in the country and these include specialist/teaching hospitals and Federal Medical Centres.[2]

The Local Government Areas (LGAs) also have Medical Officers of Health who oversee both clinical and public health activities with the support of other health care workers.[41] The State Ministries of Health are overseen by State Commissioners of Health while the Minister of Health is responsible for activities in the tertiary health care institutions.[2,56]. The Minister of Health meets yearly with State Commissioners of Health during the 'National Council on Health' meeting.[41]Information garnered from the meeting serves as a guide to the Government for the development,implementation and administrationof national health guidelines and National Health Policy enabling the organisation, delivery, and distribution of health services. In addition, some parastatals such as the

National Primary Health Care Development Agency (NPHCDA) are currently engaged in primary health care services development and provision.[41]

About 60% of the public primary health care facilities are in the northern zones of the country; these primary centers provide the minimum of health services.[8]The average number of hospital beds in the public sector is 9.2/10,000 population which is more than the average number of beds in sub-Saharan Africa overall (about 5.6).[2] However, across the six geopolitical zones, differences have been observed in the availabilty of hospital beds ranging from 4.3 to 12.1 beds. [2] Regarding primary care, the public sector has only 1.6 facilities per 10,000 people which is low. Slightly more than 6% of all public-sector facilities reported having a laboratory and this varies substantially across the zones.[2]

1.6.1 Human Health Workforce

Table 1.2 shows the number of accredited health training institutions as well as the geopolitical zonal distribution in Nigeria. It shows that schools of nursing and midwifery had the highest number of schools which translates to the nursing and midwifery profession producing the highest number of category of the health workforce. There are more training institutions in the southern part than the northern part of the country. All health workers have their various regulatory bodies, charged with the responsibility of regulating training and conduct of practice as well as keeping data of all practicing health workers. All health workers are expected by law to register annually with their various regulatory bodies. Registered health workforce profile as at December 2012, released by the FMoH in 2013, showed there were 65,759 medical doctors, 249,566 nurses and midwives, 16, 979 pharmacists, 19,225 rmedical laboratory scientists, 1849 pharmacy technicians, as well as 71,396 Junior and Senior Community Health Extension Workers in Nigeria.

Table 1.2: Zonal distribution of health training institutions in Nigeria as at December 2012 in Nigeria

INSTITUTION	TOTAL	SOUTH EAST	SOUTH SOUTH	SOUTH WEST	NORTH CENTRAL	NORTH EAST	NORTH WEST
Accredited Medical School	27	6	9	6	2	1	3
Approved School of Nursing	76	15	16	17	11	6	11
Approved School of Midwifery	67	14	14	14	9	4	12
Accredited Medical Laboratory Science School	15	4	5	3	1	1	1
School of Pharmacy	17	2	6	4	1	2	2
School of Pharmacy Technician	24	4	5	5	3	0	7
Community Health Officers School	14	1	4	3	2	1	3
Dental Technology	4	2	0	2	0	0	0
Schools of Environmental Health	43	6	8	10	8	4	7

Furthermore, the distribution of nurses and midwives per 100,000 population was highest, followed by the distribution of doctors. Though there are more schools of environmental health than medical schools, the distribution of Environmental Health Officers is much lower than that of medical doctors as shown in Table 1.3.

Details of other categories of health workers are shown in Table 1.3.

Table 1.3: Health worker per 100,000 population as at December 2012 in Nigeria

HEALTH OCCUPATIONAL CATEGORIES	NUMBER	HW/100,000 POPULATION
Medical Doctors	65,759	38.9
Nurses and Midwives	249,566	148.0
Dentists	3,129	1.9
Dental Technologist	730	0.4
Dental Therapists	3,253	1.9
Pharmacists	16,979	10.0
Medical Laboratory Scientists	19,225	11.3
Medical Laboratory technicians	8,202	4.8
Medical Laboratory Assistants	11,067	6.5
Community Health Officers	5,986	3.5
Community Health Extension Workers	42,938	25.3
Junior Community Health Extension Officers	28,458	16.8
Environmental Health Officers	6,542	3.9

All these health workers are required to pay annual practicing licensing fees. However these registers need to be updated to exclude health workers that have died, migrated out of the country or out of the profession.[41] The uneven distribution of health workers is evident by cadre areas as physician specialists are more in the urban region while community health workers are in the rural region.[41]

Table 1.4: Zonal distribution of health services in the public sector per 10000 population, Nigeria 2008

	INDICATOR		
GEOPOLITICAL ZONE	**PUBLIC SECTOR HOSPITAL BEDS (PER 10,000 PEOPLE)**	**PUBLIC SECTOR PRIMARY CARE FACILITIES (PER 10,000 PEOPLE)**	**% OF PUBLIC SECTOR FACILITIES THAT CURRENTLY HAVE A LABORATORY**
South east	12.1	1.2	8.3
South south	11.6	1.1	1.8
North central	8.6	2.4	4.2
South west	8.5	1.4	9.3
North east	10.3	2	6.2
North west	4.3	1.5	6.6
National	9.2	1.6	6.1
*n**	*32*	*32*	*27*

**Number of States reporting on this indicator*

Reasons for uneven distribution of health workers in the country include economic differences across the zones. [51] Attractive pay and better working conditions are more common in the urban areas compared with the rural areas.[36] Other reasons are non-pensionable appointment to health workers, socio-economic and geographical difficulties.41,42 Migration of health staff out of the country also contributes greatly to uneven distibution of health workforce in the country. Since 2009, Nigeria has been losing an average of 700 doctors annually to Europe, America, Australia and South Africa.[36] About 2,600 nurses migrated to UK while

2,050 migrated to USA in 2005 alone.[41] In 2006, the largest increase in health workforce was seen in the category of doctors (16.5%), with a 2.3% attrition rate while the lowest increase in workforce number and attrition rate was noticed among laboratorians.[41]

1.6.2 Workforce in Agriculture

Nigeria has ten University veterinary faculties across the country out of which nine are accredited for the training of veterinarians.[43] The Veterinary Council of Nigeria has also established the College of Veterinary Surgeons and it offers membership and fellowship diplomas. VCN also conducts continuing education programmes. In addition there are Faculties and Colleges of Agriculture as well as Schools of Veterinary Medical Laboratory for training of aquatic and terrestrial animal practititoners.[44]

A total of 7,688 veterinarians are registered with the Veterinary Council of Nigeria. About 2,000 of these are in the public sector with the remaining in the private sector. Veterinary laboratorians are mainly at the National Veterinary Research Institute (NVRI), laboratories within the Veterinary Faculties and private veterinary laboratories. Other categories within the workforce are the veterinary para-professionals, agricultural scientists and support staff within other agricultural sub-sectors – animal husbandry, crop and aquatic animals.[44]

1.7 ACCESS TO MEDICINES

The Essential Drugs Programme was initiated in 1988, and it developed the the first National Essential Drug List (EDL) forthe country that same year.[34] All drugs to be procured by the public health facilities were derived from the EDL. The Bamako initiative which is aimed at strengthening PHCs by ensuring sustainable quality drug

supply systems was re-invigorated in all the LGAs in 1998 under the Petroleum Trust Fund (PTF).[8] These initiatives were not fully effective due to poor commitment to the establishment of cost effective procurement systems for health commodities.[8] This has resulted in drug stock outs, loss of confidence and decreased utilisation of public sector health facilities.[8] Drug stock outs in public sector health facilities and opening hours that are not client friendly act as push factors that have promoted care seeking from pharmacies and patent propriety medicine vendors (PPMVs).[2] Thus, nearly 80% of the Nigerian population utilises the services in the private health sector.[2]

The heterogeneous nature of the private health sector in Nigeria allows for proliferation of registered and unregistered care providers including individual medicine sellers, patent and proprietary medicine vendors (PPMVs). Approximately 38% of health facilities in Nigeria are owned by the private sector.[45] This sector provides 75% and 25% of the primary and secondary care respectively.[46]

A 2004 study in Benue State found one PPMV per 3,250 persons compared with one primary care health facility per 10,000 persons in that State.[46] According to the National Demographic and Health Survey report in 2013, 55% of children with fever for whom advice or treatment was sought received this from the private sector with 'chemists'/Patent Medicine Sellers (PMS) playing an important role (46%)[3]. However, only 11% had blood taken from a finger or heel for testing, even though 33% took antimalarial drugs. While there are no significant differences between the urban wealthy and rural poor in the utilisation of private health sector services, the poor are more likely to use informal sector providers who usually provide lower but cheaper quality services but are more accessible for reasons of cost and geographical distribution.[2]

In Nigeria, the sale of prescription-only medicines (POMs) Over-The-Counter (OTC)

is unlawful.[47] Pharmacies are licensed to dispense POMs only against a valid prescription.[48]This is however not what operates in many pharmaceutical stores, as PPMVs act as de-facto service providers providing drugs such as antimicrobials to communities even though they are only licensed to sell over-the-counter drugs.

Sadly there is paucity of evidence regarding the sale of antimicrobials without prescription in Nigeria.[49] Private pharmacies offer advice on commonhealth symptoms or problems and are often seen as the convenient 'first point of call' in many communities where they are present[50] Issues with availability of drugs such as antimicrobials in the public sector has resulted in the proliferation of PPMVs and drug hawkers compoundingthe problem of irrational drug use[9]. Quality monitoring and regulation enforcement on private health sector providers by the government or professional association is limited.[2]

1.8 ACCESS TO HEALTH CARE

Poor access to information and services has resulted to underutilisation and limited coverage of basic health care service. In Nigeria, OOP health expenditure constitutes 71% of total expenditure on health, limiting equitable access to quality health care.[51] The National Health Insurance Scheme has limited coverage and is mainly employer-driven even though the programme is gradually being extended to State and local government.In 2013, it covered the health insurance of only 1% of women and 2% of men aged 15 to 49 years.[30]

Impediments to accessing health care in Nigeria include inadequate information, financial barriers, and lack of access to transport.[30] This was evident in the NDHS 2013, where 33% of mothers reported that they did not give birth at a health facility because there was no time to reach the facility, 29% felt it was not necessary, while others reported distance from the facility (13%) or cost (8%) as the main hindering factor.[30]

The Nigerian Government has initiated interventions to improveaccess to quality health services through the introduction of Midwives Service Scheme (MSS 2009-2013) and Ward Health System (WHS). The objective of MSS was to facilitate an increase in the coverage of Skilled Birth Attendance while that of WHS was to synchronize PHC services across electoral wards with the construction of model PHC facilities in underserved areas.

1.8.1 Access to Health Care in Aquatic and Terrestrial Animal Sector

Veterinary services consist of both the public and private sectors. The public sector veterinarians are at the Federal/State levels, universities, research institutes, colleges of agriculture while the private sector veterinarians are in various service areas including aquatic and terrestrial animal; pharmaceutical, laboratory and consultancy services provision as well as animal production and input supplies.

There is an interface between the public and private especially in the areas of surveillance, disease diagnosis and vaccination. The sanitary mandate ensures veterinarians provideveterinary services especially in the rural areas. Veterinary health care services are available at the primary, secondary and tertiary levels in addition to the private facilities.

1.9 LABORATORY CAPACITY

In 2013, a situation analysis of Nigerian Medical Laboratories was conducted to obtain baseline information on the State of the laboratories in the country. Medical and health laboratories were selected from all six geo-political zones, and at each tier of Nigerian health system (primary, secondary, and tertiary) and private sectors. A total of 366 laboratories were assessed; public (211) and private (155) laboratories. Bacteriology and Viral/Bacterial Serology represented 40-50% and virology, mycobacteriology, toxicology, and immunology under 25%. There were no

significant differences in disciplinary focus between private and public laboratories.

Some laboratories were registered through the FMoH [Private 44.0%, Public 47.0%]; significantly fewer laboratories maintained copies of the certificates of registration ($p< 0.001$). Public laboratories in particular demonstrated the greatest deficiencies in this area ($p< 0.001$; Private 29.4%, Public 10.1%). Very few laboratories [Private 17.1%, Public 12.1%] indicated they were either accredited or preparing for accreditation. 5.7% & 7.3% participated in surveillance networks of epidemic prone and other none communicable diseases respectively. Overall, public laboratories are more likely to participate in networks than private ones.

Table 1.5: Characteristics of public and private laboratories in Nigeria

CHARACTERISTICS	LABORATORY TYPE	
	PUBLIC (%)	PRIVATE (%)
Funding stream		
Government funded	65.9	22.1
User funded	58.9	69.5
Private donors	18.0	12.3
Infrastructure property		
Adequate ventilation	45.0	59.7
Appropriate space	35.8	35.3
Regular monitoring of environmental controls	11.4	8.6
Designated areas for processes	19.6	22.7
Formal back up facility in case of power failure	22.8	28.3

CHARACTERISTICS CONT'D	LABORATORY TYPE	
	PUBLIC (%)	PRIVATE (%)
Quality Management System		
Quality Assurance & Quality Control		
Availability of quality manuals/policies and procedures	7.1	6.9
Participation in quality improvement activities	9.4	8.6
Internal or External Audits	4.8 -9.3	8.3 – 7.9
Documents and records		
System in place to control and retain laboratory documents and records	14.3	16.2
Standard Operating Procedures (SOPs)	14.0	16.5
Laboratory SOPs regular review	13.5	10.4
A defined policy for the retention of SOPs	19.4	20.6
Biosecurity		
Laboratories having documented policies concerning the management of laboratory bio-risk and safety	4.4	5.3
Defined roles and responsibilities related to bio-risk management	6.6	2.4
Biosafety	Public	Private
A documented safety manual or SOP available for laboratory staff available	8.4	8.3
Safety orientation or induction programme	16.7	9.9
Documented disinfection and cleaning procedures	15.3	12.3

Overall, 11.6% of all laboratories indicated funding from other sources not included in the options provided. This included subsidies from the hospital management and doctors, or the National Health Insurance System (NHIS). 61.2% of all public and

private laboratories surveyed indicated that testing prices were regulated. The mean number of technical personnel varied greatly amongst public and private facilities.67% of the laboratories did not have sufficient qualified personnel to perform the assigned laboratory tasks and differences were negligible between private and public laboratories. Other features of the laboratories are outlined in Table 1.5.

40.3% of private and 31.1% of public laboratories indicated use of a laboratory information system. 12.2% of all public and private laboratories had a documented code of conduct or confidentiality agreement available [Private 13.7%, Public 11%]. 40% were reported to handle laboratory-testing results in confidential manner [Private 43.7%, Public 37.2%]; Public laboratories when compared to private laboratories were more likely to publish research findings in peer-reviewed journals, seminars, and/or other national and international conferences.

BOX 1: SWOT ANALYSIS OF HEALTH AND ECONOMIC CONTEXT IN NIGERIA	
STRENGTHS	• Highly skilled health professionals • Availability of national policy on traditional medicine use and vaccination use guideline • Availability of Standard Treatment Guideline (STG) • Existence of specific disease surveillance like HIV, tuberculosis etc. • Availability of government insurance scheme for the population • National health policy • Established disease surveillance notification structure at NCDC • Existing institutional regulatory mechanisms • Existing health care referral system • Dedicated and highly educated workforce (at the tertiary and private health care levels)

BOX 1: SWOT ANALYSIS OF HEALTH AND ECONOMIC CONTEXT IN NIGERIA CONT'D	
STRENGTHS CONT'D	• Strong collaborations with public health care laboratories and the MOH • Notable collaborations with local and international organisations offering opportunities for laboratory training, funding, and research activities • Involvement of laboratory staff in relevant annual conferences and meetings • Participation of laboratory staff in hospital and institutional management meetings • Back-up power sources (generators, UPS) in place to address issue of frequent power outages • Adequately ventilated (AC/windows) and appropriately organized laboratory facilities at all levels except the primary level)
WEAKNESSES	• Poor political will to allocate appropriate financing on health • Low health workers to population ratio • Government health care financing still below 15% • High propensity for corruption in health care fund management • High OOP expenses • Limited studies on economic impact of AMR • Lack of standardisation and poor implementation of policies • Lack of current updated review of the STG • Lack of standard diagnostics centres • Limited number of accredited training institutions • Lack of coordinated National disease surveillance • Lack of antimicrobial stewardship in both private and public sectors • Poor government insurance coverage • Underfunded regulatory agencies • Lack of implementation of treatment protocols according to levels of care • Weak primary health care systems

BOX 1: SWOT ANALYSIS OF HEALTH AND ECONOMIC CONTEXT IN NIGERIA CONT'D	
WEAKNESSES CONT'D	• Economic inequality and poverty line • Lack of abortion practice policy • Maldistribution of health care workforce • Minimal activity to determine effectiveness of partnership efforts • Limited or no system wide review commitment of policy leaders, system partners and performance standards • Insufficient system to promote registration and/or certification of public and private labs • Lack of resources for training, continuing education, recruitment and retention, funding, and training for equipment maintenance, calibration and repair, responsibilities and instructions in national preparedness and response to public health emergencies & surveillance networks • Insufficient workforce & undefined roles of staffing • Poor Public health research agenda establishment and dissemination • Research and development not prioritized • Limited or no review of effectiveness of the laboratory quality management system and maintenance of performance • Frequent power-outages impacting the quality of laboratory services • Poor communication system
OPPORTUNITIES	• Improved international interest in AMR • More contribution from non-oil sources GDP • The Government's commitment to research development and integration of traditional medcine into the nation's health care system would reduce reliance on antimicrobials use

BOX 1: SWOT ANALYSIS OF HEALTH AND ECONOMIC CONTEXT IN NIGERIA CONT'D	
OPPORTUNITIES CONT'D	• Using HMO provider audits to institute antimicrobial education and stewardship in private practice providers • Leverage existing surveillance system to build AMR surveillance system • Leverage and improve on existing health policies • engage accredited laboratories in vertical programmes • World bank supported $90m REDDISE (Regional Disease Surveillance) fund using the one health approach • One health approach coordination in place
THREATS	• Recession • Insurgency • Health workers attrition in the rural areas • Non interest of health care practitioners to practice in rural areas • Poor enforcement on regulations against quackery and PPMVs • Weak Pharmacovigilance system • One federation account • Corruption

2 Burden of Disease and Antimicrobial Resistance

2.1 NATIONAL BURDEN OF DISEASE

Communicable diseases along with maternal, perinatal and nutritional conditions in Nigeria accounted for an estimated 67% of all mortality in 2008.[52] Major causes of infectious disease morbidity and mortality in the country include sepsis, tuberculosis, malaria, HIV, respiratory infections, meningitis, and diarrhoeal diseases. Nigeria has the second largest number of people living with HIV/AIDS worldwide, representing 9% of the global burden of the disease. HIV prevalence from 2000-09 was relatively constant. In 2012, the sero-prevalence rate of HIV in Nigeria of persons aged 15-49 years was 3.1%. However, the period 2001-2008 saw a consistent and gradual decrease in the prevalence of the disease with the prevalence of 6% in 2001 compared to 4.2% in 2008.[53,54]

Six countries accounted for 60% of new cases of malaria: India, Indonesia, China, Nigeria, Pakistan and South Africa. Although the number of deaths due to malaria from 2001-2011 fell slightly, the total number of confirmed malaria cases was on the rise for the same.[55] In 2009, the number of reported pertussis cases (whooping cough) was 11,281 while that of Cholera was 13,691.[55] Tuberculosis incidence rate and mortality estimates are usually high, however when data for co-morbid cases with HIV was excluded for the period of 1990-2012, there was a slight reduction in the estimates.[56]

In addition results of tuberculosis prevalence survey conducted in Nigeria in 2012 showed a burden which was more than twice the WHO estimated burden for the same year. Moreover, the point estimates of TB prevalence rates of smear-positive

and bacteriologically-confirmed cases were 318 and 524 per 100,000 population (aged 15 years and above) respectively.[57]

According to WHO estimates, Nigeria is presently among the 27 high MDR-TB burden countries as the problem of the emerging drug resistant TB has become more pronounced. MDR-TB prevalence is currently at 3.1% and 10.1% among new and retreatment cases respectively. Considering the high case notifications and the epidemiologic significance of occurrence of MDR-TB strains, it is imperative that a true and accurate determination of the MDR-TB burden and the pattern of anti-TB mono- and poly drug resistances in Nigeria be done to inform proper case management and overall planning of TB control activities. [58]

The burden of zoonoses in Nigeria is difficult to quantify due to diversity of sources and lack of surveillance. However, a recent survey on ***Salmonella*** bactereamia among children in central and northwest Nigeria, 2008-2015 indicated that 20.7-23.6% of the ***Salmonella*** bactereamia cases were due to Non-Typhoidal Salmonella with up to 45% and 39% of the isolates being ***Salmonella Typhimurium*** and ***S. Enteritidis*** respectively.[59] This is consistent with the report of high prevalence of Salmonella in commercial poultry farms (43.6%) in Nigeria.[60] Other zoonotic diseases also occur with varying prevalence depending on production systems with seroprevalences of brucellosis varying from 0.2-80.0%, a large serosurvey put the prevalence at 26.3% in northern Nigeria.[61] Zoonotic pathogens were more described from foods of animal origin than from other sources. Carriage and shedding of zoonotic pathogens contaminates the environment and eventually enters the food chain during processing and post processing procedures. Existing reports are likely underestimating the exact burden of zoonoses since there is limited surveillance for zoonoses in humans in Nigeria.[62] Furthermore, the proportion of the national burden of disease linked to the environment is about 29%.[63]

Systematic Search Methods

The infectious disease burden that derives from AMR was qualitatively assessed through a series of systematic reviews using the preferred reporting system for systematic review and meta-analysis (PRISMA Statement) as outlined by Moher et al.[64] Medline,Pubmed, Google Scholar, Embasse, Cochrane and AJOL literature databases were searched and the searches were supplemented with articles from Nigerian experts that were solicited and curated by NCDC. An example protocol is outlined in the appendices and the results will be published as separate studies after peer review.

2.2 BACTERIAL DISEASE AND ANTIMICROBIAL RESISTANCE IN HUMANS

2.2.1 Enteric pathogens

Nigeria's diarrhoea prevalence is rate is one of the worst in sub-Saharan Africa. it is 18.8% and notably highly than the continetal average of 16%. Diarrhoea accounts for over 16% of all child deaths in Nigeria. An estimated 150,000 deaths amongst children under five occur annually due to this disease and this is associated with poor personal and community sanitation and hygiene practices.[65,66] Failure to control the spread of diarrhoeal pathogens both resistant and non-resistant ones due to unclean water, poor sanitation, coupled with malnutrition has greatly worsened the burden of diarrhoeal disease.[67]

About 60% of the eligible articles reviewed for *E. coli*, *Shigella* and non-typhoidal *Salmonella* were published from 2010, and only three articles (10%) were published earlier than 2005. Most of the articles (83%) are studies from Southern Nigeria with South-West and South-South accounting for 52% and 40% of the Southern studies respectively (Table 4.1). The few studies from Northern Nigeria were reported only from Kano, Kaduna and Federal Capital Territory (FCT).

2.2.1.1 Escherichia coli

Diarrhoeagenic ***Escherichia coli*** strains are associated with acute and persistent diarrhoea leading to huge morbidity and mortality with children under 5 years as the most vulnerable group.[68, 69]There is wide spread antimicrobial resistance among faecal ***E.coli*** in Nigeria particularly to penicillins, aminoglycosides, chloramphenicol, tetracyclines and cotrimoxazole. [59,60]

Studies carried out in Edo State, South-South of Nigeria among under five hospitalised children showed resistance rates of 79-100% to penicillins.[70, 71]The same studies also revealed high rates of plasmid-mediated tetracycline resistance at 68-80%. Enabulele et al in Edo State also reported a high prevalence of plasmid-mediated quinolone resistance among HIV patients.[72] In the same region, studies carried out among children admitted for diarrhoea in Rivers State reported resistance rates of 90-100% and 76-100% to ampicillin and cotrimoxazole, respectively.[73,74] Absolute resistance was reported by the same studies to gentamicin and chloramphenicol. High resistance rates of 73%, 68% and 75% to ampicillin, gentamicin and tetracyclines respectively were also reported among hospital patients in Cross Rivers State.[75]

A report of a study carried out in Kano, North-West of Nigeria revealed high antimicrobial resistance rates to ampicillin, nalixidic acid and chloramphenicol (93%, 89% and 78% respectively).[76] A multi-regional study involving five of the six geo-political zones of Nigeria also reported high antimicrobial resistance among the ***E.coli*** isolates to penicillins, cephalosporins, streptomycin, chloramphenicol, tetracyclines and cotrimoxazole.[77]There are no current standard treatment guidelines for the treatment of diarrhoeagenic ***E.coli*** in Nigeria.[78]

2.2.1.2 Non-typhoidal Salmonella

In Nigeria, non-typhoidal ***Salmonella*** (NTS) species have shown varying resistance rates to antimicrobials from one State of the country to another; these rates include ampicillin (50-100%), amoxicillin (0-90%), gentamicin (0-89%), ciprofloxacin (0-30%), ofloxacin (0-20%), nalixidic acid (0-100%), chloramphenicol (36-100%), cotrimoxazole (0-100%) and tetracycline (0-100%). Resistance in NTS appears to be increasing, penicillin resistance as high as 100% was reported from Lagos and Osun both in South-West ern Nigeria.[79,80] The same studies reported similarly high resistance rates to gentamicin (89% and 50% respectively) and nalixidic acid (33% and 100% respectively), low resistance was however reported to newer generation quinolones. Another study from Lagos reported high resistance to third generation cephalosporins with ESBL-production rate of over 45% among NTS isolates. Fashae et al, 2010 in Oyo State reported high rates of resistance to penicillin, cotrimoxazole, chloramphenicol and tetracycline (59%, 54%, 36% and 31% respectively.[81] Similarly, Oluduro et al reported high antimicrobial resistance from a study carried out on apparently healthy people in Ekiti State.[82]

Studies on isolates from children under five years of age from South-South Nigeria, reported 100%reistance penicillin and cotrimoxazole and 30% resistance both gentamicin and ciprofloxacin.[70, 73] High levels of antimicrobial resistance were also reported in South-Eastern Nigeria, where NTS serovars showed high resistance to amoxicillin, chloramphenicol and cotrimoxazole (90%, 58% and 47% respectively).[83] However, relatively low resistance to fluoroquinolones and gentamicin was observed in the study.

In Katsina State, 100% of isolates were resistant to ampicillin and chloramphenicol while respective resistance rates in Kano were 83% and 56%.[76,84] A multicentre study carried out on hospitalised patients under five years old in Northern Nigeria also reported very high levels of resistance to several antimicrobials except fluoroquinolones.[59]

Treatment of NTS infections in Nigeria is currently by administration of ceftriaxone. Higher doses may be used in severe infection. Oral/intravenous doses of ciprofloxacin may also be used.

2.2.1.3 Shigella species

Shigellosis is endemic throughout the world particularly in developing countries where communities are devastated by poverty, war, poor sanitation, poor hygiene, and shortage of water supplies.[85] Epidemiological reports revealed that shigellosis is responsible for approximately 165 million cases annually, of which 163 million (98.8%) are in developingcountries where it contributes to about 1.1 million deaths.[86,87] It commonly affects the under five age group because theyhave low immunity and lack previous exposures.[88]Over the last few decades, ***Shigella*** species have become increasingly resistant to the most readily available and inexpensive antimicrobials.[89] This has led to therapeutic difficulties with associated increased morbidity and mortality. This problem is aggravated in developing countries where indiscriminate use of antimicrobial agents is common.[67]

In Nigeria, three different studies from Edo State on under five years children reported 100% resistance to penicillins,44-100% resistance to gentamicin, 68-70% resistance to tetracyclines and 44-58% resistance to the quinolones.[70, 71, 90] Studies from the same region found high rates of plasmid-mediated

quinolone resistance among isolates from HIV patients.[74] A study of isolates from hospitalised children in Rivers State showed high resistance of *Shigella* spp to ampicillin, gentamicin, streptomycin, chloramphenicol and cotrimoxazole (100%, 86%, 100%, 100%, and 100% respectively).[74] Another report from the Rivers State on under five hospitalised children showed high resistance to ampicillins and tetracyclines (68% and 100% respectively), there was however no resistance to fluoroquinolones.[73]

In South-West Nigeria, Iwalokun et al reported high resistance rates to ampicillin (90%), chloramphenicol (77%), tetracycline (79%) and cotrimoxazole (86%). Similarly high resistance was reported among patients in Osun State;[72, 80] and healthy people in Ekiti State.[82] Furthermore, a report from Enugu, South-East Nigeria, showed high resistance of Shigella spp to ampicillin (68%), chloramphenicol (57%) and cotrimoxazole (43%); and low resistance to fluoroquinolones.[83] In Kano, North-West Nigeria, resistance rates of over 90 per cent were reported each to ampicillin, fluoroquinolones, chloramphenicol and cotrimoxazole.[76]

Recommended mode of management is oral rehydration therapy as antibacterial drugs are usually not necessary. However, appropriate systemic antimicrobials are required when systemic infections occur. These include amoxicillin, cotrimoxazole, ciprofloxacin, or azithromycin.[78]

2.2.1.4 Vibrio cholerae

Vibrio cholerae is associated with a severe acute watery diarrhoea that causes a clinical condition called Cholera.[91]Nigeria has experienced recurrent outbreaks of cholera since the 2010 cholera epidemic which recorded 41,787 cases and 1,716 deaths.Compared to other West and Central African countries, Nigeria

was reported as the most cholera affected country in 2014 by Cholera Regional Platform after it experienced cholera outbreak in the same year. Although the outbreak spread to neighbouring countries, Nigeria's confirmed cases (35,996) in 2014 represented about 39 per cent of all cholera cases in the region. A cause for extreme concern was the rise of cholera CFR rate to 4.76%, as at the end of April 2015 – 2,108 cholera cases, with 97 deaths.[92]

All five studies reviewed, reported serogroup O1 as being responsible for outbreak while one of the studies in addition reported some non-O1/non O139 serogroup isolates. There were no serogroup O139 in any of the reports. Three studies reported the El Tor biotype, one study reported the existence of the El Tor and the atypical El Tor biotype while one study did not biotype their isolates. The Inaba and Ogawa serotypes were reported seperately in two studies while the other three studies did not report on the serotype of their isolates.

Most of the studies reported resistance to trimethoprim/sulphamethoxazole and sulfonamide. Other resistance documented in varying percentages include streptomycin, nalidixic acid, spectinomycin , cloxacillin and penicillin G, chloramphenicol and ampicillin.Isolates were generally sensitive to tetracycline, florfenicol, ofloxacin and erythromycin.

The treatment guideline for cholera is Oral Rehydration Therapy (ORT). However, tetracycline, doxycycline, erythromycin or double doses of cotrimoxazole are treatment options in severe infection and chemoprophylaxis in outbreak situation. All reviewed studies found high levels of resistance to these cotrimoxazole and fluoroquinolones (Figure 2.1 and 2.2). Vaccine-based strategies for outbreak containment are recommended internationally.[93]

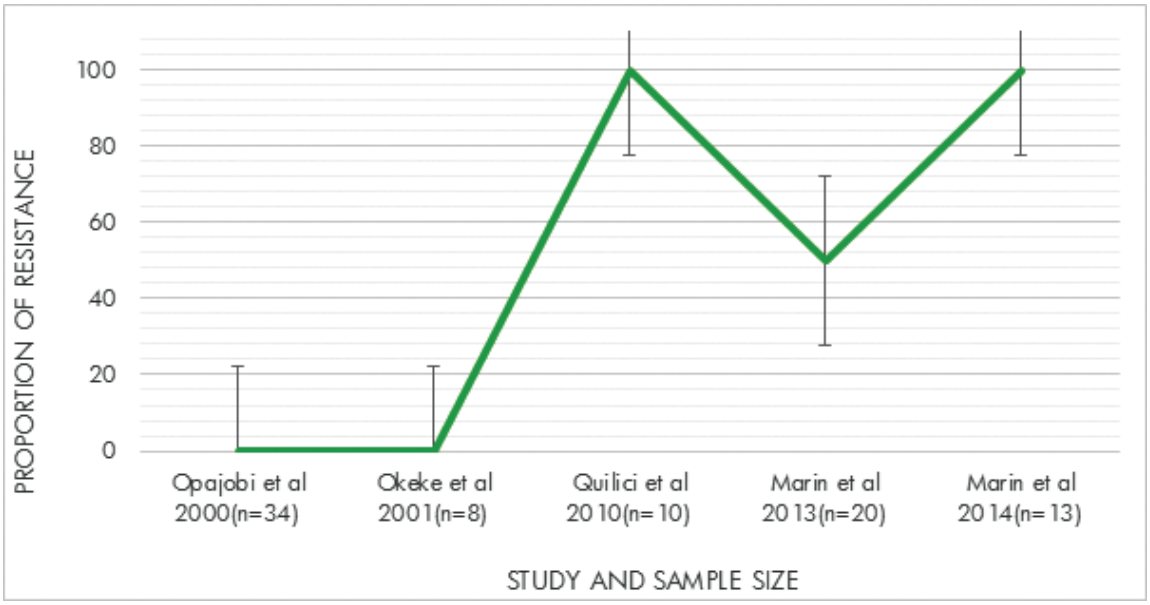


Figure 2.1: Vibrio cholerae resistance to fluoroquinolones in Nigeria

Figure 2.2: Vibrio cholerae resistance to co-trimozaxole in Nigeria

2.2.2 Urinary Tract Infections

Urinary tract infections (UTIs) are globally prevalent affecting people of all ages, race and sex, although they are more common in women. Many UTIs are asymptomatic and/or self-limiting however, antimicrobials may be required in some cases. Infections caused by drug resistant organisms poses a major health risk to patients, as such, resistant organisms are associated with higher morbidity and mortality.

The 63 reviewed research articles on UTI were conducted in 26 of the 36 States including Abuja with Edo State having the highest number of studies (8:12.7%) followed by Oyo (7; 11.1%), then Bayelsa and Osun States (5; 7.9%). Geopolitical zones which had less representation were North-East and North-West with 2 States each namely Borno and Adamawa; and Kaduna and Kano respectively.

The most common organisms causing UTI were *E. coli* (61.6%), *Staphylococcus* in 10 studies (16.7%) and *Klebsiella* species in 5 studies (8.3%).The common organisms causing resistant infections of the urinary tract as reported in 34 of the reviewed articles were Pseudomonas in 7 studies (28.6%) , E. coliin 6 (17.6%) and *Klebsiella* in 4 (11.8.%), *Enterobacter* and *Staphylococcus* in 3 studies each; (8.8%), *Proteus*, *Enterococcus* and *Streptococcus* species in 1 study each (4. 5%).Other uncommon organisms reported to cause resistantinfections were *Citrobacter* and *Salmonella* species. The three most common causes of UTIs (*E. coli, Staphylococcus* and *Klebsiella*) in this review are listed by the WHO as organisms of concern with regards to AMR.[1] However, Pseudomonas species which did not feature among the common causes of UTI in the country, was found to be the 2nd most common cause of drug resistant UTI and most common cause of MDR UTI.[56]

There was marked resistance to all drugs commonly prescribed for UTI in the country.[74]

Resistance rates were highest for ampicillin and cotrimoxazole. Most organisms demonstrated 100% resistance to both drugs,[89] which have been long used as first line drugs in the treatment of UTI. Nitrofurantoin showed the lowest resistance levels among the first line drugs with resistance rates as low as 6.5% in ***E.coli*** and less than 100% in ***Proteus, Klebsiella*** and Enterobacter.10 Studies carried out in South-West Nigeria revealed ***E. coli*** resistance ranges of 48-96%, 46-68%, 68-97% and 70-90% to ampicillin, chloramphenicol, tetracyclines and cotrimoxazole respectively.[69, 94-96] High levels of resistance to third generation cephalosporins was reported among pregnant women in Oyo State and the isolates were predominantly ESBL- producers.[97] Studies from Ekiti and Ogun States also reported high resistance rates of 64 % and 91% as well as 90% and 85% to third generation cephalosporins and gentamicin respectively.[82, 94]Similarly, high resistance rate to streptomycin was reported by Odetoyin et al in Osun State.[95] High resistance to ciprofloxacin was reported in hospital isolates in Ogun and Oyo (80% and 81% respectively).[94, 97]

The review shows high rates of resistance to ceftriaxone which is increasingly being used to treat sepsis and most bacterial infections. However ciprofloxacin and gentamicin had the lowest rates of resistance compared to the other drugs even though appreciable resistance was demonstrated. The occurrence of CRE, VRE and ESBL-producing Gram negative rods though documented in few studies is alarming because of the method of spread of resistance genes among bacteria. There is urgent need for surveillance on AMR in urinary tract pathogens.

2.2.3 Blood Stream Infections

Bacteraemia means transient or continuous presence of bacteria in the blood stream. Sepsis means systemic responses to disseminated microorganism throughout the body with accompanying organ dysfunction.[98, 99] Blood stream infection (BSI) is

present when an organism associated with disease is cultured from the blood of patient. The presence of demonstrable blood culture positive result is requisite in any definition of BSI.[100]

Lack of appropriate antimicrobial stewardship and AMR surveillance in Africa has dulled the perception of the full impact of AMR in this region.[101] Despite the similar trend of increasing AMR, just like in other places, there are no accurate data on extent, pattern, and trend in Nigeria. This paucity of data is due to absence of quality-assured microbiology laboratories, poor record keeping culture and absence of AMR surveillance in the past decades. Although there are pockets of researchers working on AMR, there is lack of national coordination and reporting system on antimicrobial use and resistance. Various AMR surveillance activities are institution based and lack national oversight and relevance. Therefore, a systematic review to assess the antimicrobial resistance pattern as it relates to BSI in Nigeria was conducted.

Eighteen articles were selected for qualitative synthesis for this review according to the aforementioned criteria. Majority of the studies were carried out on neonates. Prevalence of positive blood cultures ranged between 3.9% and 55.5%.[81, 102]

2.2.3.1 Gram Positive Isolates

Resistance of ***Staphylococcus aureus*** to ampicillin ranged between 0 to 95.6% with the least resistance in Oyo State and the greatest resistance in Cross River State.[103, 104] Similarly, the coagulase negative staphylococci (CONS) showed 100% resistance to ampicillin in Kano and Borno, both in the North-East and North-West of Nigeria.[105, 106]

The ***Staphylococcus*** species showed variable degrees of resistance to the aminoglycosides. However, there was less resistance to amikacin than to

gentamicin in studies in which both antimicrobials were tested[107, 108]. Resistance to the quinolones was also variable with resistance to ciprofloxacin ranging between 0% in Osun State and 73.4% in Edo State.[102, 109]

Staphylococcus epidermidis isolates from two States in the North-Eastern and North-Western zones were all resistant to cefuroxime while *S.aureus* showed less resistance of 0% and 60.5% at the same centre.[105, 106] Resistance of *Staphylococcus* species to chloramphenicol was high in all studies.

Most of the studies did not mention the methicillin sensitivity of the *Staphylococcus* species. The isolates were assumed to be methicillin sensitive unless otherwise stated. In Oyo State, the MRSA isolates were highly resistant to gentamicin but 100% sensitive to amikacin, ciprofloxacin and chloramphenicol.[104]

Among the *enterococci*, *Enterococcus faecalis* showed a very good sensitivity to the antimicrobials tested including gentamicin, ampicillin, cefuroxime and ceftriaxone.[102, 110] However, there was high resistance to ampicillin and cefuroxime in Kano State.[105] In a study in which the *Enterococci* were not speciated, there were high levels of resistance to ampicillin, gentamicin, amikacin, ciprofloxacin, cefuroxime and ceftazidime.[104]

2.2.3.2 Gram Negative Isolates

The enterobacteriaceae were highly susceptible to most antimicrobials in the study done in Oyo State.[104]All the Gram-negative bacilli in that study were 100% sensitive to amikacin, ciprofloxacin, ceftazidime and cefotaxime. However, *E. coli* were 100% resistant to amoxicillin/clavulanate and chlorampheicol. In addition, some other unnamed gram negative bacilli were 100% resistant to ampicillin and chloramphenicol. The above findings are in contrast to those of another study which was conducted in Edo State in which the gram negative bacilli were all

highly resistant to the antimicrobials tested.[109] All Pseudomonas isolates showed little resistance to the quinolones (0 - 14.7%)[102, 105, 111-113]except for isolates from Edo State which were highly resistant (90%) to the quinolones.[109]

2.2.4 Salmonella Typhi and Non-typhoidal Salmonella (NTS)

Seven of the studies discussed resistance among *Salmonella* species.[59, 81, 106, 111, 114-116] In a study of BSI among adult HIV patients, all isolates *S. Enteritidis* and *S. Typhimurium* were resistant to ampicillin but were all sensitive to amoxicillin/clavulanate, gentamicin, amikacin, ceftazidime and cefotaxime.[115] Another study in Oyo State which was based solely on *Salmonella* species showed 100% sensitivity of *Salmonella* Typhi and NTS to gentamicin and cefotaxime.All isolates were also sensitive to ciprofloxacin except for 8% of the *S. Enteritidis* which were resistant to quinolones. Similar to the study earlier described, isolates of *S. Enteritidis* and *S. Typhimurium* were highly resistant to ampicillin. They were also highly resistant to chloramphenicol.[81] Other studies showed variable resistance of *Salmonella* species to the antimicrobials tested.[59, 106, 111, 114, 116]

Treatment of NTS infections in Nigeria is currently by administration of ceftriaxone (intramuscular or intravenous injection). Higher doses may be used in severe infection. Oral/intravenous doses of ciprofloxacin may also be used. However, it must be administered with caution because of complications like diarrhoea, nausea, vomiting, abdominal discomfort, headache.[78]

2.2.5 Meningitis and Pneumonia

Meningitis and pneumonia are responsible for considerable morbidity and in Nigeria.[98] The pathogens responsible for causing most cases of meningitis in Nigeria are *Neisseria meningitidis, Haemophilus influenzae*, and *Streptococcus pneumoniae*. *S. pneumoniae* is also the most important cause of community

acquired pneumonia.[98, 99]

Five meningitis studies were found to be eligible for systematic review.[117-121] Twenty per cent of all ***N. meningitidis*** isolates were resistant to chloramphenicol, while 30.8% were resistant to Penicillin G. None of the isolates were found to be resistant to ceftriaxone (Table 2.1). With regards to H.influenzae,resistance rates for penicillin G, chloramphenicol, ceftriaxone were found to be 66.7%, 23.5%, and 4.5% respectively. Penicillin G, chloramphenicol, and ceftriaxone resistance rates for ***S.pneumoniaewere*** found to be 45.2%, 10.3% and 1.7% respectively.

The lowest resistance rates for pathogens causing meningitis were seen with ceftriaxone. None of the N.meningitidis isolates were found to be resistant to ceftriaxone. This is in keeping with most studies that show that resistance to ceftriaxone is rare.[101] Ceftriaxone resistance in ***H.influenzae*** and ***Streptococcus*** pneumoniae were also found to be low. It is for this reason that third generation cephalosporins such as ceftriaxone are still recommended asthe choice drug for meningtitis treatment.[64] Resistance to chloramphenicol, which is used in epidemic meningitis, was also found to be low among the three pathogens. Resistance rates were highest with penicillin G.

Three pneumonia articles were found to be eligible for systematic review.[9,10,11] Resistant rates for antimicrobials commonly used to treat pneumonia such as ceftriaxone; erythromycin, penicillin G, and augmentin, were found to be 18.2%, 29.8%, 62.7% and 18.9% respectively (Table 2.2). Penicillin resistance in ***S. pneumoniae*** has been of global concern.[81, 102] This review found that 62.7% of all pneumonia associated ***S. pneumoniae*** isolates were resistant to penicillin G. This is high, and is comparable to what has been observed globally.[110] Ceftriaxone, augmentin, and amoxycillin had comparable low rates of resistance ranging from

18.2% to 24.3%, suggesting other beta lactams other that penicillin may still be useful in the treatment of pneumococcal pneumonia. Septrin resistance rate was the highest, and this differs from what has been found in other countries.[103]

Table 2.1: Antimicrobial resistance rates in meningitis isolates in Nigeria

ANTIBIOTICS	NO OF ISOLATES TESTED (N)	NO OF RESISTANT ISOLATES (N)	RESISTANCE RATES (%)
Neisseria meningitidis			
Penicillin G	13	4	30.8
Chloramphenicol	35	7	20.0
Ceftriaxone	54	0	0.0
Haemophilus influenzae			
Penicillin G	42	28	66.7
Chloramphenicol	51	12	23.5
Ceftriaxone	44	2	4.5
Streptococcus pneumoniae			
Penicillin G	62	28	45.2
Chloramphenicol	68	7	10.3
Ceftriaxone	60	1	1.7

Resistance rates in pathogen causing meningitis and pneumonia vary widely in Nigeria. Antibacterial agents such as ceftriaxone and chloramphenicol will remain useful in the treatment of meningitis in Nigeria for the foreseeable future. The finding

of a high number penicillin-resistant S. pneumoniae isolates is of great concern, more so because penicillin resistance has been linked to worsened clinical outcomes in patients with invasive pneumococcal diseases .[122] Fortunately, drugs with low rates of resistance are available as alternative treatment.Apart from supportive measures, treatment of meningitis is by the use of co-amoxiclavulanate, benzyl-penicillin or cefuroxime.[78]

Table 2.2: Streptococcus pneumoniae antimicrobial resistance rates (Pneumonia isolates) in Nigeria

ANTIMICROBIALS	NO OF ISOLATES TESTED (N)	NO OF RESISTANT ISOLATES (N)	RESISTANCE RATES (%)
Ceftriaxone	220	40	18.2
Ofloxacin	181	62	34.3
Erythromycin	84	25	29.8
Penicillin G	59	37	62.7
Gentamicin	90	76	84.4
Septrin	212	197	92.9
Amoxicillin- Clavulanate	206	39	18.9
Amoxycillin	202	49	24.3

2.2.6 Health care-Associated Infections

Health care-associated infection (HCAI) previously called nosocomial or hospital-acquired infection has been in the spot light of hospital infection control policies since early 1800s. They are infections acquired in hospital or health care service units, that appear 48 hours or more after hospital admission, and occupational infections among staff.[123, 124] Health care-associated infections are major cause of preventable morbidity and mortality in developing countries where infection rates are relatively higher due to poor infection control practices, lack of supervision, overcrowding in hospitals and inappropriate use of limited resources.[125] HCAIs prolong the duration of hospitalisation, increase cost of health care and contribute to the emergence of multidrug-resistant microorganisms.[125-127] These multidrug-resistant organisms from HCAIs could seed into the communities and become widespread. Generally, 7% of people in developed and 10% of people in developing countries will acquire at least one HCAI in their lifetime.[128] However, the risk of acquisition of HCAI is 2- 20 times higher in developing countries such as Nigeria and despite extensive surveillance of HCAI in the developed countries, no health care setting can yet claim to be totally free of this burden.[129]

The majority (i.e., over two-thirds) of the reviewed articles were from the South-Western region of the country: Osun, Lagos, Oyo, and Ogun States. Two of the reviewed articles focused on clinical specimens sent to the microbiology laboratory for routine analysis[130-132] with clinical isolates coming from in-patients admitted during time of study that met the criteria. Meanwhile, majority based their categorisation on specific organisms isolated.[131-136] and the other reviewed articles were centred on specific HCAI.[130, 137-140] Only 5 studies[131, 141-145] covered HCAI in its entirety and conducted full surveillance of the different types enumerated by previous published protocols.[146, 147] Phenotypic method was mostly utilised for the identification the microorganisms in the laboratory according to Clinical Laboratory Standards Institute

guideline (CLSI).[130, 148, 149.]

Surveillance on blood stream infection (BSI) in the health care system was done in nine of the reviewed articles[131, 143] and confirmed with blood culture. The range of BSI prevalence in the reviewed articles was 6.6%-49%.[141, 143] Blood stream infection in some individuals was episodic and were also catheter associated. Moreover, *S. aureus* was the most common cause of blood stream infection in adults.[141] However, *Klebsiella* spp was identified in neonates as the commonest cause of BSI.[144] Diverse organisms were seen implicated in BSI which include: *S. aureus*, *Pseudomonas* spp, *Klebsiella* spp, *E. coli*, *Proteus* spp, *Enterobacter* spp, *Acinetobacter* spp.[130, 135, 138, 144] Resistant organisms such as ESBL-producing *Enterobacter* spp (Extended- spectrum beta-lactamases), Methicillin resistant *Staphylococcus aureus* and carbapenem resistant *Acinetobacter* spp were also isolated.[133-135] This buttresses the the occurrence of AMR in the hospital setting.[150]

Surveillance for surgical site infection (SSI) was common among the reviewed articles. Wound swabs and wound biopsies were specimens taken for microbiological investigation. Surgical site infections have been seen following Caesarean Sections138 or orthopaedic manoeuvres[130, 138, 141] and organisms most isolated include: *S. aureus*, *Pseudomonas* spp, *Klebsiella* spp, *Proteus* spp, *Citrobacter* spp, and *E. coli.* Similar antimicrobial resistant organisms as seen in BSI were also identified in SSI. The range of SSI prevalence in the reviewed articles was 9.1%-70.6%.[134, 138]

In this systematic review, health care-associated urinary tract infection occurred in patients with prolonged hospitalisation especially in intensive care unit[141] while catheter-associated urinary tract infection (CAUTI) was seen in urologic conditions such as prostatic enlargement.[140] Although, catheter tip was used as specimen for laboratory investigation in some reports[140] of CAUTI which could however increase false positive laboratory cultures in diagnosing CAUTI.[151] The range of UTI prevalence

in the reviewed articles was 3.4%-88.5%[23,27]. Common organisms isolated from health care-associated urinary tract infection include: *Klebsiella* spp, *Pseudomonas* spp, *E. coli*, *S. aureus*, *Proteus mirabilis*, *Candida albican*s, CoNS, *Acinetobacter baumanii*. AMR was noticed in some identified organisms however, patterns of the resistance were not explicitly described.[140]

Only a few studies in this review included health care-associated pneumonia in their surveillance scope. Surveillance on ventilator-associated pneumonia was rarely done among the reviewed articles.[141] The range of health care-associated pneumonia prevalence in the reviewed articles was (1-86%).[135, 143] Microorganisms such as *Klebsiella* spp, ESBL-producing *Enterobacter* spp, MRSA were identified as pathogens causing health care-associated pneumonia. Other health care-associated infections studied in this systematic review included: gastroenteritis, skin and soft tissue infection (e.g. decubitus ulcer).

2.3 BURDEN OF DISEASE IN LIVESTOCK

Livestock are plagued by many diseases caused by different pathogens, however diseases of economic and public health importance include:- Highly Pathogenic Avian Influenza (HPAI), Contagious Bovine Pleuro-pneumonia (CBPP), Peste des Petits Ruminants (PPR), Foot and Mouth disease (FMD), Rabies, Tuberculosis, Anthrax, Brucellosis, Newcastle and Infectious Bursal (Gumboro) diseases. Some of these diseases are transboundary in nature hence limiting trade . There are control programmes for HPAI, CBPP, PPR and Rabies. Apart from HPAI, the control programme for the other diseases is mainly annual vaccinations. Nigeria has keyed into the PPR Global Control and Eradication Programme with the expected goal of eradicating PPR by 2023. Other global disease control programmes that Nigeria will participate in are for FMD and Rabies.

2.3.1 Antimicrobial Residue in Food of Animal Origin and Animal Feed

The health and welfare of animals is safeguarded by the use of veterinary drugs, biologics and pesticide chemicals. Often, antimicrobial residues (either the parent coumpound or its metabolite) are excreted into the environment by animals after exposure to antimicrobials either for growth or therapeutic reasons.

Drugs are the most frequently detected chemical residues in food of animal origin, and majority of these are antimicrobials commonly used in veterinary practice in Nigeria.[152] Drug and pesticide residue affects the quality of meat such as palatability and aroma. It also raises public health and economic concern. Drug residues in foods of animal origin threaten human health by being acutely or cumulatively allergenic, organotoxic, mutagenic, teratogenic or carcinogenic. For these reasons and more African livestock is denied entry into the European and American livestock markets.. The indiscriminate use of antimicrobials for the prevention and treatment of bacterial infection in animals is a common practice as in other developing countries. [153, 154] A greater proportion of cattle in Nigeria are reared by the nomadic herdsmen who administer chemotherapeutic agents without veterinary prescription.[155] When such laymen use these drugs, correct dosage is unlikely to be administered and the drug withdrawal periods are usually not observed. One of the common antimicrobials widely used in livestock is tetracycline.[156, 157]

2.3.2 Antimicrobial Residue in Animal Feed

In livestock management, the use of antimicrobials for therapeutic and prophylactic purposes is common and this is often administered in form of medicated feedstuffs. Medicated feedstuffs are basically mixtures animal feed and veterinary medicinal products. Medicated feedstuffs are usually authorised for the animal species which the feed is administrated to and contains high antimicrobial concentrations depending on its intended aim and the physiological-health State of the animals. Human error, improper production, handling and storage practices can lead to the

unintentional contamination of antimicrobial negative feeds with antimicrobials. For example during the production of medicated feedstuff, a little proportion may be left in production line or storage tanks leading to the cross-contamination of next batches of antimicrobial negative feed.

2.3.3 Risks of Unintentional Presence of Antimicrobials in Feed

Several potential risks arise from cross-contamination of antimicrobial negative feeds, both to animals and to consumers:

- Unexpected antimicrobials in feedstuff could interact with other medical agents administered to animals. Therefore, a therapeutic failure might be observed with associated economic losses for the producer as well as the farmer.
- It could create an ideal scenario for the induction and transfer of antimicrobial-resistance mechanisms making antimicrobials ineffective against animal pathologies and could reduce effectiveness of human medical treatments.
- Affords opportunity for antimicrobials to enter the human food chain (through eggs, milk, meat, etc.) especially when drug withdrawal periods are not followed.

2.3.4 The Public Health Importance of Antimicrobial Residues in Foods

The long-term effects of antimicrobials on humans here is not fully known, however it is known that they can provoke strong allergic reactions in sensitive people. However, only a few cases of hypersensitivity have been reported as a result of exposure to residues in meat. Anaphylactic reactions to penicillin in pork and beef have been described and in one case, anaphylaxis was possibly caused by streptomycin residues. Angioneurotic edema and tightness in the chest may also be caused by penicillin residues in meat.

Antimicrobial use causal factor to the rise of AMR, which in turn challenges treatment of human infections. Hence, antimicrobials used in humans is prohibited for use in

animals. The increasing use of antimicrobials veterinary health is paralled by an increase of resitant bacteria in animal. Resistant bacteria then spread among groups of animals, including fish, or to the local environment (i.e., local soil, air, and water) through the spreading of manure or through contaminated foods to humans. Although correct cooking procedure kills bacteria, contamination can occur through improper handling before cooking. Many of the antimicrobial-resistant ***E.coli*** strains that cause urinary tract and bloodstream infections in humans appear likely to have originated from contaminated retail meat. Antimicrobial residues in milk that is used to produce fermented products can interfere with the fermentation process by affecting growth of the desired lactic acid bacteria while selecting for resistant pathogens present in the milk posing a potential health hazard and financial loss. This is one of the reasons why the sale of milk from cows treated for mastitis is prohibited in many countries and measures a put in place to routinely test milk for the presence of antimicrobial residues. Disruption of normal human intestinal flora may be caused by the effect of drug residues food of animal origin consumed by humans.

The presence of veterinary drug residues in food products are a global health concern. The occurrence of contamination of edible animal products by antimicrobial and pesticide residues beyond the FAO/WHO permissible level is high in developing countries. The adverse health effects of drug residues and drug resistance could be worsened by the unchecked misuse and abuse of drugs . Moreso, the lack of appropriate legislation to control the quality and distribution of veterinary pharmaceuticals and phytosanitary products in Nigeria market, will aggravate the health risk posed by drug residues should liberalisation of the veterinary profession be allowed.

2.3.5 Resistance in Isolates from Animals

Food-producing animals are linked to humans via the food chain and the shared environment thus a one health approach to understanding how to control the AMR

threat becomes apparent[158, 159]. Food animals may be exposed to antimicrobials used in veterinary practice or for growth promotion. Depending on the nature, quantity and timing of antimicrobial administration, the possibility exists that antimicrobial residues will be present in meats at the time of sale or consumption, potentially allowing for resistance selection from and through the food chain.

2.3.6 Antimicrobial Resistance Studies

Using diverse phenotypic or genotypic methods, 48 studies tested resistance of a wide range of isolates to a total of 55 antimicrobials belonging to different classes and generations. In almost all instances, resistant organisms were recovered from livestock (cattle, goats, pigs, sheep, camels and chickens) and from foods (dairy, vegetables and meats). The AMR reported from livestock and food are most likely anthropogenic since a study of wild bats uncovered very low recovery of resistant organisms.[160] One study recovered amoxicillin resistant organisms from tap and bagged water.[161] Resistance was also detected in isolates from polluted water, waste and dump sites, cow manure and abbatoir effluent as well as from Naira currency notes and cell phones; 67% of Vibrio from aquaculture samples were MDR.[162]

2.4 THE BURDEN OF AMR IN THE NIGERIAN ENVIRONMENT

The protocol for the systematic review of antimicrobial resistance and residues in wildlife, livestock, aquaculture, food and the environment, was similar to those performed for human pathogens but used a broader range of databases (Pub Med, Google Scholar, Cabdirect, Medline, Embase, Cochrane and African Journals Online).

Recently, the natural environment emerged as an important contributor to the global burden of AMR with the environment recognised as the origin of some antimicrobial

resistance genes of clinical and public health interest.[163] Inadequate treatment of wastewater from drug manufacturers, and effluents from agriculture and aquaculture are major drivers of resistance in the environment. However, not much is known about burden of resistance in the Nigerian environment, probably because resistance is still viewed largely from the lens of clinical medicine and not as an ecological problem. More importantly, as found in other sectors, existing information on resistance in Nigerian environment are products of individual studies with no coordinated efforts to address this important subject.

This notwithstanding, recent studies have identified untreated wastewater from hospitals, pharmaceutical industries, domestic and aquaculture sources;[164-166] water, soil and waste from poultry farms;[167-169] wastewater from abattoir[170] and leachates from municipal solid waste dumpsites[171, 172] as important contributors of antimicrobial resistant bacteria to the Nigerian environment. Further, metagenomic analysis showed that contamination of the Nigerian aquatic ecosystems with antimicrobial resistance genes is about four orders of magnitude higher than levels reported for highly contaminated aquatic ecosystems in other part of the world.[172] In addition, recent studies of the microbial quality of raw and treated drinking water in South-Western Nigeria indicated the presence of pathogenic and non-pathogenic bacteria that exhibited multidrug resistance.[173-175] In most of these studies, the reported bacteria species carried antimicrobial resistance genes of global clinical and/or public health interest.

BOX 2: SWOT ANALYSIS OF BACTERIAL RESISTANCE AND ANTIMICROBIAL USE IN NIGERIA BASED ON A ONE–HEALTH APPROACH	
STRENGTHS	• Existence of potential infrastructure for laboratory surveillance for bacterial resistance • Potential human resources • Availability of institutions for AMR monitoring • Presence of training institutions on AMR • Leverage the Integrated Disease Surveillance and Response platform • Presence of AMR standing committees in few institutions
WEAKNESSES	• Availability of an old legislation/national policy on antimicrobial use (not in use) • No national committee on AMR • No AMR survey/surveillance system • Poor awareness on AMR • Lack of national reference laboratory for AMR testing • Non-availability of quality-assured microbiology laboratories • Outdated Standard Treatment Guidelines (STG) • Lack of coordination and comprehensive national reports on antimicrobials use • No document on isolates from animal/environmental component
OPPORTUNITIES	• Leverage Health reform agenda • Multi-stakeholders commitments • Availability of alternatives to antimicrobials e.g. probiotics, vaccines etc • Potential for multi-centre surveys for generalizability • Existing National Action Plans in other countries

BOX 2: SWOT ANALYSIS OF BACTERIAL RESISTANCE AND ANTIMICROBIAL USE IN NIGERIA BASED ON A ONE–HEALTH APPROACH CONT'D	
THREATS	• Increasing prevalence of MDR strain • Increased morbidity and mortality rate • Lack of financial resources • Diminishing antimicrobial development
RECOMMENDATIONS	1. Develop national action policy on AMR at both national and institutional level 2. Promote R&D 3. Timely review of STD 4. Encourage diagnostic laboratories to enroll in step-wise accreditation process 5. Incorporate AMR into various professional curricula 6. Promote data sharing among institutions

3 Supply Chain and Implications for Antimicrobial Access and Appropriate Use

3.1 SIZE OF THE PHARMACEUTICAL MARKET IN NIGERIA

The estimated population of the Economic Community of West African States (ECOWAS) sub-region is 600 million which represents a huge potential market for the pharmaceutical sector. Nigeria provides 60 per cent of the health products consumed in the sub-region.[176] Varying estimates of the size of the pharmaceutical market in Nigeria exist. The Pharmaceutical Manufacturing Group of the Manufacturers' Association of Nigeria (PMG- MAN) in 2009 estimated the size of the pharmaceuticals and health care products market to be in excess of $2bn annually. The estimate for prescription of ethical pharmaceuticals was $500m, that of Over-The-Counter (OTC) pharmaceuticals was about $900m while the market for biological products (including vaccines, insulin, interferon, etc.) was about $100m. The Business Intelligence Services estimated the pharmaceutical market in Nigeria in 2009 at $600m with the largest share of $418m attributedto generic medicines, followed by Over-The-Counter (OTC) products at $121m then patented products at $6m.[176] Unfortunately, no information could be found on how much of this market share is attributed to antimicrobial agents.

3.2 ANTIMICROBIAL USE IN LIVESTOCK

One of the missions of the World Organisation for Animal Health (OIE) is to ensure prudent use of antimicrobials in animals through application of the OIE standards set in the Terrestrial Animal Health Code (Chapter 6.9) and the

Aquatic Animal Health Code (Chapter 6.2). In pursuance of this, the OIE in 2013 had a global conference themed 'Responsible and Prudent Use of Antimicrobial Agents for Animals: International Solidarity to Fight Against Antimicrobial Resistance'. Recommendations were made by participants to the OIE and Member countries for implementation.[177] One of the recommendations was to establish a global database with the aim of collecting and harmonizing quantitative data on the use of antimicrobial use in animals. This was to be effected from 2013 and it includes the baseline data and reporting. Thus Nigeria submitted the baseline data reported on data for 2014 and 2015. The various classes of antimicrobials used in food animals and their quantities in 2014 and 2015 are in Table 3.1 below:[178]

Table 3.1.: Quantity of antimicrobials and other drugs sold/used in animals in Nigeria 2014-2015

		QUANTITY (KG)	
S/N	ANTIMICROBIAL	JUN – DEC, 2014	JAN – DEC, 2015
1	Aggregated antimicrobials	188,339	190,219
2	Tetracyclines	8,147	168,880
3	Fluoroquinolones	5,115	3,146
4	Macrolides	3,349	9,798
5	Sulfonamides	1,060	687
6	Polypeptides	459	142,333
7	Amphenicol	268	658
8	Penicillins	193	-
9	Aminoglycosides	46	131
10	Glycopeptides	24	40
	Total	**207,000**	**515,892**

These quantities are from what has been imported through the authorization agency and does not include other procurement sources. There is need to know the quantities used in specific species of food animals and the possible route of administration. This will entail advocacy and training of the stakeholders in the drug use chain (pharmaceutical manufacturers, wholesalers/retailers, veterinary/ veterinary para-professionals and farmers).

3.3 PHARMACEUTICAL REGISTRATION, LICENSING AND INSPECTION

3.3.1 Regulatory framework: Responsible institutions and Laws

The National Agency for Food and Drug Administration and Control (NAFDAC) and the Pharmacists Council of Nigeria (PCN) are the two main government institutions responsible for regulating different aspects of the pharmaceutical supply chain in Nigeria. The Federal Ministry of Health gives policy directions for the sector.

NAFDAC was established by Decree No.15 of 1993 (now Act Cap N1 Laws of the Federal Republic of Nigeria 2004) with the mandate to regulate and control the use, sale, importation, exportation, manufacture and distributionof food, drugs, cosmetics, medical devices, packaged water and chemicals. The NAFDAC Act provides legal backing for the Agency to conduct its regulatory functions including the registration/licensing of all regulated products before marketing such products in Nigeria; inspection and investigation of relevant manufacturing facilities within and outside the country to ascertain their Good Manufacturing Practice (GMP) status towards certification of the sites and their products; quality control of products meant for import and export; regulation of products; labeling; promotion and public education; post marketing surveillance of registered products to ensure maintenance of quality and safety, and compilation of standard specifications

and guidelines.[179] The Agency develops guidelines and standard operating procedures (SOPs) to guide both the regulators and the regulated on appropriate implementation of aspects of the law.

Other laws relevant to the supply chain and AMR surveillance that give NAFDAC and PCN the legal backing for their work include:

1. Counterfeit and Fake Drugs and Unwholesome Processed Foods (Miscellaneous Provisions) Decree No. 25 of 1999 now Act Cap 62 LFN
2. Drugs and Related Products (Registration), Decree No. 19 of 1993
3. Food and Drugs Act, 1976
4. Food and Drugs (Amendment) Decree No.21 of 1999

While NAFDAC regulates the product related aspects of the pharmaceutical sector, the Pharmacists Council of Nigeria (PCN) established by Decree No.91 of 1992 now ACT cap P17 LFN 2004 is responsible for regulating the practice aspects including registration and training of pharmacists and development of basic pharmacy curricula for degree programmes and mandatory continuing education programmes. It also regulates all premises where pharmaceutical services are rendered.[179] This include Inspection and registration of pharmaceutical retail, wholesale, drug warehouses/importation and manufacturing premises to ensure compliance with GMP.

3.3.2 Current Capacity to Regulate and Enforce Regulations

Registration records from the Pharmacists Council of Nigeria (PCN) reveals that in 2016 there were 164 registered drug manufacturing facilities, 1,304 drug distributors, 554 drug importers, 3,769 retail pharmacies and 56,974 PPMV stores.

Additionally, 21,892 pharmacists and 3,172 pharmacy technicians were registered as at 31st of December 2016. The council has a staff strength of 277.

A query of the NAFDAC registered drugs database showed that in 2016, out of 45,552 registered drugs with valid registration licenses, 11,013 were antimicrobials. These figures give an idea of the enormous task before the agency, first in evaluating the products before registration and secondly to monitor them post registration. As at 31st December 2015, NAFDAC had a workforce of 2,236 staff distributed across its formations nationwide. The Agency has 13 directorates; 6 zonal offices that coordinate the activities of the State offices; 37 State offices including the FCT; as well as laboratories in five zones of the country.[180] These officers and offices have the responsibility of monitoring all regulated products under the Agency's purview.

The large number of products, practitioners and premises (registered and unregistered) that need to be regulated, the high level of fake and counterfeit medicines in the pharmaceutical sector, the chaotic drug distribution system, the weak infrastructure, the weak enforcement power and lack of cooperation from other law enforcement agencies, the inadequate human resource capacity and capability, the inadequate funding, the over-reliance on imported pharmaceuticals, and the inadequate facilities for quality control make it difficult for regulators to effectively regulate and control the pharmaceutical sector. The regulatory sector is further faced with the problem of poor motivation and low retention of staff.[176, 181]

In addition, PMG-MAN has instituted a self-regulatory mechanism where annual Good Manufacturing Practices (GMP) audits of its members is undertaken by experienced auditors. In companies where lapses are identified, Corrective and Preventive Actions (CAPAs) are imposed and such members are paired through a mentoring processs, with companies that are recognised to have strong capacity in GMP this assists them in correcting the lapses and implementing the CAPAs. The

auditors engaged are often persons with experience in regulatory issues through previous work with WHO or NAFDAC.

3.4 IMPORTATION AND LOCAL PRODUCTION OF MEDICINES: FORMAL DRUG SALES

The pharmaceutical industry in Nigeria is vibrant with over 120 pharmaceutical manufacturers and a predominantly indigenous ownership. The sector employs about 500,000 persons in the manufacturing and distributing chain with the vast majority of the jobs attributed to the distribution chain. Capacity utilisation of local manufacturing facilities is at about 40 per cent with adequate capacity for production of certain categories of medicines to meet demand at national and sub regional levels. Many of the companies produce liquid preparations, tablets, capsules, ointments, lotions, creams and ophthalmic preparations.[176]

Currently the indigenous manufacturing companies have 25 per cent of the national market share while the remaining 75 per cent is filled by imports from other countries particularly Asian countries. Currently, four indigenous manufacturing companies have obtained satisfactory status for the World Health Organisation (WHO) Good Manufacturing Practices (GMP), which is a step towards WHO prequalification for some of their products. These companies are Swiss Pharmaceutical Limited, May and Baker, Evans Medical PLC and Chi Pharmaceuticals.[180] This will enable them to take part in international tenders to supply some of the most widely used medicines in Nigeria such as antimalarial medicines.

3.4.1 Quantity of Drugs Sold and Consumed

Information on actual medicine consumption in Nigeria is hard to obtain however, the volume of medicines manufactured locally and those imported into the country may be used as a proxy. A survey by Federal Ministry of Health in 2008 showed

that antimicrobials/antibacterials had 15% of the market share of the various therapeutic classes of medicines locally produced in Nigeria. Out of 49 local drug manufacturers reviewed, 15 were found to be manufacturing ampicillin/cloxacillin capsules producing a total of 1.2 billion capsules and 3 manufactured 7.9 million grams of the powder. Two companies manufactured 180 million amoxicillin capsules and 5 manufactured 188 million grams of the powder. Four companies produced 193.6 million ampicillin capsules and 4 manufactured 367 million grams of the powder for suspension.[176]

3.4.2 Informal Drug Sales

In 2010, it was estimated that there were over 10,000 unregistered patent and proprietary medicine (PPM) stores in Nigeria. Most of these stores are in areas where full-fledged pharmacies do not exist particularly rural areas, villages and poor communities.[176] These stores often sell drugs that are outside the list of medicines approved for them. In addition, there are also several itinerant drug sellers that go about hawking unapproved and often poor quality medicines to the public including antimicrobial agents.

3.5 USED PHARMACEUTICAL CHEMICALS/ HEALTH CARE WASTE (PHARMACEUTICAL WASTE)

Health care waste (HCW) as defined by WHO includes any health care by-product such as sharp and non sharp used medical devices , body parts radioactive materials etc Poor management of HCW exposes health care workers, waste handlers, dustbin scavengers and the community to infections, toxic effects and injuries.

The responsibility for the development of chemicals management, regulation and health care waste regulations rests primarily with the Federal Ministry of

Environment (FMEnv) in collaboration with the Federal Ministry of Health (FMoH). In this light, the FMEnv in collaboration with FMoH developed the following policy documents

1. National Health Care Waste Policy Management (HCWMP) 2013
2. National Health Care Waste Management Strategic Plan (NHCWMP) 2013
3. National Health Care Waste Management Guidelines 2013
4. National Policy on Chemicals Management
5. National Environmental Sanitation Policy

It is estimated that between 10%-25% of health care waste from medical institutions are hazardous in nature. The National Inventory of HCW in Nigeria is shown below in Table 3.2. The teaching hospitals had the highest amount of waste per bed – 0.98kg/bed/day followed by federal hospitals with 0.62kg/be/day. This may be a reflection of the level of care. Private hospitals had a low amount of waste - 0.18kg/bed/day. This may be a reflection of inadequate records or lack of awareness.

*Table 3.2: Average Volume of Health care Waste (Kg) Generated per Bed/Day in Nigeria**

ZONE	FEDERAL HOSPITAL	TEACHING HOSPITAL	SPECIALIST HOSPITAL	STATE/GEN HOSPITAL	PRIVATE	TOTAL	AVERAGE
North Central	0.39	0.55	0.15	1.46	0.42	2.97	0.59
North East	0.62	2.87	-	-	0.08	3.57	0.71
South South	1.23	0.08	0.11	0.19	-	1.61	0.32
South East	0.50	-	0.49	0.57	0.57	2.13	0.43
South West	-	1.8	0.04	0.00	0.03	1.87	0.37
North West	0.99	0.58	0.28	0.56	-	2.41	0.48
TOTAL	3.73	5.88	1.07	2.78	1.10		
AVERAGE	0.62	0.98	0.18	0.46	0.18		

**Source: National Health care Waste Management Strategic Plan (2013-2017); Federal Ministry of Environment, 2013*

3.6 PROCUREMENT & DISTRIBUTION

Procurement is a key challenge in the supply of human and animal medicines in Nigeria and, as is the case with distribution, procurement of medicines is fragmented and involves many organisations. In the public sector, there is a national procurement policy and a dedicated procurement department. The idea is to involve all actors and pull together all procurement resources to enjoy pooled procurement benefits. However, this needs to be improved upon.[176]

Distribution of medicines in Nigeria is chaotic and involves many different bodies, organisations and stakeholders. Some major manufacturers contract private logistics organisations to distribute their medicines and some international development partners use the services of courier companies to deliver medicines to benefitting outlets.[176]

Manufacturers and importers have their own distribution channels for distributing drugs in the private sector and they sell to wholesalers, retailers, hospitals and clinics. This results in medicines being sold in unregistered and unlicensed premises and, in many cases, by non-pharmacists.[176]

In the public sector, medicine supplies are currently distributed through three different warehouses, the Central Medical Stores, the Federal Medical Stores and the State Medical Stores. The Government (including Federal, State and Local Government Areas) supplies pharmaceutical products to its various health institutions. In addition, the Federal Government supplies drugs to tertiary health care institutions (University Teaching Hospitals) and Federal Medical Centres located in all the 36 States. State Governments are responsible for providing health care products to State hospitals as well as offering technical support to the Local Government Areas (LGAs).[176]

Several efforts have been made over the years to streamline procurement and distribution practices in Nigeria. The 2005 National Drug Policy has the goals of ensuring sustained availablity of adequate supplies of drugs and ensure that the supplied drugs are effective, affordable, safe and of good quality; to ensure the rational use of such drugs; and to stimulate increased local production of essential drugs, is one such effort.[182]Public sector institutions are mandated to procure medicines on the essential medicine list.

The reality regarding supplies of medicines in Nigeria remains such that those who are not trained and registered as pharmacists are actively involved in supplying pharmaceuticals, using unregistered premises. The ongoing efforts through the National Drug Distribution Guidelines to streamline the distribution system and restrict drug distribution to pharmacists through specially designated centres such as Mega Drug Distribution Centres, State Drug Distribution Centres and coordinated wholesale centres is commendable. This will promote rational drug use and strengthen the ability of regulators to effectively regulate the sector.

3.7 SUPPLY CHAIN & IMPLICATION FOR ANTIMICROBIALS ACCESS AND APPROPRIATE USE IN AGRICULTURE

Veterinary products (antimicrobials and biologics) are produced locally and also imported. There are several pharmaceutical companies that manufacture veterinary drugs locally while the National Veterinary Research Institute (NVRI) produces bacterial and viral vaccines locally. The bacteria vaccines for the immunisation of livestock against bacteria diseases of public health and economic importance are: Contagious Bovine Pleuropneumonia CBPPV), Anthrax (ASV), Brucella (BV), Black Quarter (BQV), Hemorrhagic Septicemia (HSV), Fowl Cholera (FCV), Fowl Typhoid (FTV) and Hanta Vac. However, the production from NVRI does not meet the total requirement for the livestock sector and this is supplemented through importation. The Federal Government does not purchase drugs for supply, though State veterinary services that run the drug revolving scheme have stores where drugs are bought and kept for supply to their veterinary clinics. Most manufacturers and importers of veterinary drugs have distributors who sell to retailers, who in turn sell to animal health care providers and farmers/producers.

For vaccines NVRI has a new policy to sell only to registered veterinary outlets and veterinarians. In reality, any end user can purchase from a retail outlet. The implication of this is that non-professionals as well as farmers have unfettered access to veterinary drugs and vaccines often not following the manufacturer's instructions, and this invariably leads to abuses that cause resistance.[183]

Rational use of medicines requires that 'patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate duration, and at the lowest cost to them and their community'.[184]

3.8 ANTIMICROBIAL USE IN HUMANS IN NIGERIA

An important component of good clinical practice that promotes the efficacy of therapy is the rational use of antimicrobials.[185] Similarly, antimicrobial abuse and misuse usually arise when drugs are not matched to the right patient at the right time, or are inappropriately taken by the patient or not used with the right capabilities in place.[186] This can lead to longer disease duration, increased risk of disease-related complications or even death.[187, 188]

The total global antibiotic consumption grew between 2000 and 2010 by over 30%, based on data from 71 countries. Greater increases were recorded in Low to Middle Income Countries (LMICs)[4]. A WHO report found that in LMICs (including those in sub-saharan Africa), 40% of antimicrobials prescribed were in insufficient doses.[189]

In many countries, 80% of antimicrobials used occurred within the community.[190] Findings from a field test on rational drug use in 12 developing countries showed that Nigeria had the highest average numbers of drugs prescribed to patients per encounter (3.8 drugs/encounter) and third highest percentage of antimicrobial prescriptions (48%).[191] Combined with increased use of antimicrobials in agriculture, overuse/misuse of antimicrobials is a key driver for emergence of drug resistant pathogens contributing to the rising AMR rates.[101]

A systematic review was conducted on rational and irrational antimicrobial use among humans in Nigeria with the aim of describing the quantitative indicators of rational antimicrobial use and identifying factors influencing use of antimicrobials. Eleven reviewed articles published between 2004 and 2015 were used formed the basis of the situation analysis of antimicrobial use in Nigeria (Table 21). Most studies were conducted in health facilities and represented all parts of the country except the North. The studies looked mainly at prescribing patterns of health care providers and dispensing without a prescription. None of the studies assessed

the social acceptability of taking antimicrobials without prescriptions, prescribing according to clinical guidelines, the impact of excessive pharmaceutical promotion/economic incentives, effect of consultation/patient-dispenser interaction time, effect of diagnostic support services, or the effect of regulatory mechanisms on antimicrobial use and prescribing.

Findings from indicators of irrational antimicrobial use shown in two studies highlighted the use of antimicrobials without prescription. About 46.7% and 71.1% of children ≤5 years were given unprescribed antimicrobials for diarrhoea treatment and sore throat cases respectively.[17,18]Another study found that proportion of adults that used antimicrobials after a doctor's prescription was 68.3% while only 42% completed the recommended antimicrobial course.[192]

Regarding prescription behaviour, four articles reported that the percentage of antimicrobials prescribed per patient encountered ranged from 26.8% among persons ≥15 years to 71.1% in children <5 years.[193-195]Another study documented that 49.4% of patients in the NHIS clinic were prescribed antimicrobials compared with 33.6% in the general outpatient clinic.[196] It was also reported from three studies that the proportional contribution of antimicrobials prescription of all medicines in children under 5 years ranged from 13.0% to 53.7%. [193, 195, 197]

Unnecessary prescription of antimicrobials by medical doctors was also reported, with 56.4% prescribers providing antimicrobial empirically to children <5 years visiting four clinics on account of pharyngitis in one study.[198] Underuse of antimicrobials is also important when considering irrational use of antimicrobials; 25.5% of house officers were not confident prescribing antimicrobials to patients.

The commonest antimicrobial used or prescribed were the penicillin group of antimicrobials ranging from 25% to 71.2%.[192-195, 198] A study on the use of

unprescribed antimicrobials for treatment of diarrhoea in children reported that 71.4% of mothers gave their wards Metronidazole while the commonest antimicrobial given to children with respiratory tract infection was Cotrimoxazole (53.1%) in another study.[199, 200] The commonest antimicrobials prescribed to children in a public health facility was Cephalexin (31.1%).[197]

Seven of the eligible studies described potential influential factors driving the irrational use of antimicrobials in Nigeria. Regarding medicine use behaviour, two studies (18%) reported Over-The-Counter (OTC) supply as a factor influencing access to unprescribed antimicrobials for 28.6% to 42.4% of mothers with children <5years.[199, 200] Patients' demand for antimicrobials was also highlighted as a factor predisposing Nigerian communities to antimicrobial overuse in one study. Approximately 57.2% of caregivers of children ≤5 years presenting with a sore throat at a health centre demanded for antimicrobials from the prescribers.[198]

Generally, caregivers were not satisfied with a doctor that did not prescribe an antimicrobial for their child's sore-throat and Stated that they would change their doctors if an antimicrobial was not prescribed.[198] Sociodemographic factors such as lower education level of caregivers, older age of caregivers and being an older child also contribute to higher chances of antimicrobial use or prescription among children <5 years.[197-200] Factors contributing to poor adherence to antimicrobial treatment included financial incapability to purchase full dose, long duration of treatment and side effects experienced.[192] Furthermore, the unfinished doses of antimicrobials were kept for future use, thrown into refuse or sewage and or given to other persons with similar complaints.[192]

One of the reported factors influencing prescription behaviour was health insurance status of patient; those with National Health Insurance were more likely to have antimicrobials prescribed[23]. Prescribers' characteristics were also important factors

influencing access to unnecessary antimicrobial prescriptions. Prescribers with longer years of practice, non-specialised and older aged were more likely to give antimicrobials empirically to children while doctors with shorter years of practice were not confident prescribing antimicrobials to patients without supervision.[198, 201]

BOX 3: SWOT ANALYSIS OF SUPPLY CHAIN AND IMPLICATIONS FOR ANTIMICROBIAL ACCESS AND APPROPRIATE USE IN NIGERIA

Pharmaceutical market

STRENGTHS	WEAKNESSES	OPPORTUNITIES	THREATS
• Huge population and large market for pharmaceuticals		• Room for growth in capacity utilisation	

Pharmaceutical registration, licensing and inspection

STRENGTHS	WEAKNESSES	OPPORTUNITIES	THREATS
• Availability of the two regulatory bodies with appropriate legal frame work • Availability of data on registered practitioners, regulators and premises	• Low capacity to regulate large numbers of products. • Inadequate human resource • Weak infrastructure • Weak enforcement • Lack of cooperation from other law enforcement agencies • Poor motivation and low retention of staff, • Overreliance on imported pharmaceuticals	• Training of more pharmacists and regulators on rational use of medicines • Engage more professionals • Need to improve on data management	• High level of fake and counterfeit medicines in circulation • Unregistered practitioners • Smuggling of unregistered medicines

BOX 3: SWOT ANALYSIS OF SUPPLY CHAIN AND IMPLICATIONS FOR ANTIMICROBIAL ACCESS AND APPROPRIATE USE IN NIGERIA CONT'D

Pharmaceutical registration, licensing and inspection

STRENGTHS	WEAKNESSES	OPPORTUNITIES	THREATS
• Predominantly indigenous pharmaceutical manufacturers • Obtaining acceptable level of compliance with WHO Good Manufacturing Practices (GMP) guidelines for some indigenous drug manufacturing companies	• Inadequate number of pharmaceutical manufacturers • Very low capacity to meet local anti microbial medicine demand	• Obtain WHO pre qualification for drug manufacturing companies in Nigeria • Establishing dedicated manufacturing facilities for anti microbials with potential to ensure better management of pharmaceutical waste	• Chaotic drug distribution system in the private sector • Inadequate facility for quality control • Poor management of waste from pharmaceutical processes • Inadequate funding

Procurement and distribution

STRENGTHS	WEAKNESSES	OPPORTUNITIES	THREATS
• Establishment of national procurement policy and a dedicated procurement department • Streamlined drug distribution system in the public sector • Availability of a national drug policy (though due for review)	• Lack of information on actual medicine consumed in the country	• Setting up of more mega and State drug distribution centers in some States • Pooled Procurement process for procuring good antimicrobial products • Review and implementation of national drug policy	• Poor waste management of expired pharmaceutical • Lack of community pharmacies in rural areas • Sale of prescription medicines by PPMVs • Non qualification of courier services used in the delivering thermo labile medicines and diagnostics

BOX 3: SWOT ANALYSIS OF SUPPLY CHAIN AND IMPLICATIONS FOR ANTIMICROBIAL ACCESS AND APPROPRIATE USE IN NIGERIA CONT'D

GAPS	RECOMMENDATIONS
1. Large population suffering from infectious and non-infectious diseases – there is need for statistics (from group B) to show extent of the problem 2. Need for data on Antimicrobial supply chain in animals 3. Need for data on pharmaceutical waste management (including waste from production processes and expired products/chemicals) – to be provided by Federal Ministry of Environment	1. There is need to cite the correct Act in addition to the decree when referring to laws in the document. 2. Carry out more recent survey on drug utilisation to provide up-to-date data on drug utilisation particularly with respect to antimicrobials 3. Review and implementation of national drug policy 4. The need to introduce track and trace technology in the drug distribution system 5. There is need to create extensive awareness among health care providers and the general public on rational use of medicines

4 Infection Prevention and Control, Vaccination and Biosecurity

Infection Prevention and Control (IPC) is a simple but crucial intervention to reduce demand for antimicrobials by preventing infections from occurring in the first place, and stopping them fom spreading when they do.[202] infection prevention measures including Water, Sanitation and Hygiene (WaSH) services can slow the development and restrict the spread of difficult to treat antimicrobial-resistant infections.making them the 'best buy' for shifting the demand curve for antimicrobials.[202]

Vaccines are among the most impactful and cost-effective public health interventions available today. Diseases prevented by vaccines, such as pneumonia, meningitis, and measles constitute about a quarter of the 800,000 child deaths in Nigeria. Vaccination is also one of the alternatives to use of antimicrobials in animals. In addition to protecting health and saving lives, vaccines also provide economic benefit both in humans and animals.[202]

4.1 INFECTION PREVENTION AND CONTROL (IPC) CAPACITY IN NIGERIA

Infection Prevention and Control (IPC) has been a neglected area in many health care facilities despite many policies related to IPC in Nigeria. The emergence of multidrug resistant organisms has put further strain on the health care facilities. Their spread to other patients and health care workers (HCW) within health care facilities and the community has been linked to the absence or breakdown of IPC activities. This has become even more frightening with the spread of extensively multidrug resistant tuberculosis and other 'super bugs.[203] Transmission

of highly resistant bacteria from patient to patient within the hospital environment amplifies the problem of AMR and may result in the infection of patients who are yet to receive antimicrobials. The key element in minimising such horizontal transmission of infection within hospitals is careful adherence to infection prevention and control (IPC) guidelines. Every infection prevented is one that needs no treatment.[204]

Infection Prevention and Control programmes around a set of core components outlined by the World Health Organisation (WHO).[205] They include:

1. Infection control programme
2. Guidelines
3. Training
4. Surveillance
5. Multimodal strategies for implementing IPC
6. Monitoring and evaluation
7. Workload, staffing and bed occupancy
8. Built environment, equipment and materials for IPC

These core components for IPC programmes are essential as the allow countries to develop national action plans for combating AMR.[205] This situational analysis reviewed the Infection Prevention and Control as well as vaccination and biosecurity situation in Nigeria and recommend the framework within which these activities can be inculcated into the AMR National action plan.

The National Policy for Infection Prevention and Control 2013[206] lays out the institutional framework for IPC in Nigeria. It States the roles and responsibilities of

4.2 ORGANISATIONAL FRAMEWORK FOR THE IMPLEMENTATION OF IPC

the Federal, State and Local tiers of government; the health facilities and the communities. It stipulates that the Federal Ministry of Health provides leadership by instituting a National Infection Prevention and Control Programme (NIPCP) domiciled in the Department of Public Health of the FMoH to coordinate national activities related to IPC with a management unit and a designated Programme Officer. Same applies at both State and Local Government levels. At the health facility level, the chief medical directors/medical directors are to be responsible for IPC and are to establish an IPC Committee which shall adopt the implementation of the National IPC policy in the facility.

Infection control programmes survive and are sustained where there is strong administrative support. Administrative support signifies political support and sets the stage for ownership of the programme both at national and health care facility level. The implementation of the national IPC programme as stipulated in the policy is very poor. Thus far, Nigeria only has the policy and strategy but no guideline though there are many programme specific guidelines.

The current IPC policy is also mainly focused on HIV/AIDs. There is need for a more encompassing policy which covers all components of IPC and addresses AMR.

4.3 HUMAN CAPACITY DEVELOPMENT FOR IPC AND WaSH SERVICES

A fundamental requirement for effective AMR IPC practices is an educated workforce. The WHO core components recommend that the national IPC programme support education and training of health workforce as one of its core function to reduce the risk of Health care-associated infections (HCAIs). Human capacity for IPC in Nigeria for both human, animal and

environmental health services remains a problem both in quantity and quality. There is a dearth of IPC professionals due to a lack of professional training opportunities in Nigeria. Furthermore, there is no accredited IPC training centre in the country. Gaps also exist in the training of veterinary para-professionals especially for fishery and wildlife.

4.4 SURVEILLANCE OF HEALTH CARE ASSOCIATED INFECTIONS (HCAI)

Surveillance of HCAI is critical to inform and guide IPC strategies. It is the backbone of a good infection control programme, but little has been done in Nigeria due to a non-functional infection prevention and control programme.[207] Every surveillance system depends on good quality data which includes the appropriate application of case definitions and good microbiological laboratory procedures. The latter is necessary for the identification of aetiological agents and AMR patterns.The current situation in the country is that some tertiary centres have established surveillance activities and others have not. Furthermore, there is no formal framework for collaboration among surveillance programmes nation-wide. This laspe in national frame seriously hampers efforts to track emerging resistance challenges.

4.5 KNOWLEDGE AND PRACTICE OF IPC BY HEALTH WORKERS

Studies on knowledge of IPC among health workers in tertiary hospitals in Nigeria on different components of IPC showed that 90% of health workers studied in the in South-West and 95% in South-East Nigeria had good knowledge.[208, 209] Another study in Nigeria found that of the 290 studies 66% identified lack of appropriate or adequate resources to practice standard precautions, 52% mentioned lack of regular training on infection control, 38.9% revealed lack of an infection prevention and control committee and 34% reported excess workload as the major challenges preventing routine practice of standard precautions.[210]

A study carried out prior to introduction of the national policy on IPC showed poor IPC practices with regards to TB infection prevention mainly due to failure in administrative measures (providing necessary equipment and logistics for IPC) among other factors.[211] Two years after the introduction of the national policy on IPC, a study to assess hand hygiene practices among health workers in a semi-urban tertiary hospital in South-Western part of Nigeria revealed that hand hygiene practice as observed was still low and that health care workers pay attention to hand hygiene when it appears there is a direct observable threat to their health.[208, 212] In another study carried out among doctors and nurses in a tertiary hospital in Benin City regarding their practices of universal safety precaution (USP) against HIV infection, it revealed poor adherence to USP among both categories of health workers attributed mainly due to lack of IPC materials.[213]

In health care waste management, it has been identified that poor practices regarding written waste policy, poster and guidelines for waste management, waste segregation, storing, treatment and recycling exist.[214] A survey conducted in 2016 to assess IPC and health care waste management in selected LGAs in Akwa Ibom, Cross River and Rivers States found that: National policy on IPC were not implemented in almost all the health facilities across the three States. The proportion of health facilities with job aids for injection safety ranged from 14% (Rivers State) to 18% (Akwa Ibom State). Most health facilities did not have an annual work plan for HCWM; only 5% of facilities in Akwa Ibom and 7% in Cross River had an annual work plan. Almost all the health facilities did not have an annual budgetary provision for HCWM. The assessment also found that the proportion of health facilities with hand-washing facilities and soap near toilets was low and present in only 20.5% of facilities in Akwa Ibom State.[215]

4.6 VACCINATION IN NIGERIA

4.6.1 Vaccination in humans

Vaccine-preventable deaths, due to causes such as pneumonia, diarrhoea, and measles, account for about 40% of all deaths in Nigeria's under-five year old children.[217] Scaling up coverage of five vaccines (Hib, pneumococcal, measles, pertussis, rotavirus) to 90% is proposed to avert economic loss of $17bn over the next ten years.[216]

The Expanded Programme on Immunisation (EPI), which was initiated in 1979, has the objective of providing immunisation services to reduce the burden from vaccine-preventable diseases thus creates the entry point for primary health care delivery in communities in Nigeria. The establishment of the National Programme on Immunisation (NPI) in1996 bolstered national commitment and ownership of the EPI. Table 4.1 lists the vaccines used.

Other vaccinations outside the routine schedule [218]

- Yellow fever vaccine -for those traveling outside the country irrespective of age, 0.5ml is given subcutaneously every 10 years
- Meningitis vaccines – administered for preventive campaigns, during outbreaks or when visiting endemic countries.
- Meningitis A vaccines-administered to 1-29 year olds in a total of 25 States as part of a preventive mass campaign. This campaign is phased over three years, the first phase started in in November 2011.

Recent advances in Nigeria immunisation scheme (National Programme on Immunisation) include the doubling DTP3 coverage (29% to 69%) between 2000 and 2010, and the introduction of two new vaccines (Men AfriVac and Pentavalent). In late 2011, Nigeria conducted a mass campaign to deliver a new meningitis

vaccine. Also in 2012, she launched the Saving One Million Lives Initiative – a scheme for expanding primary health care in Nigeria to significantly reduce mortality by 2015. Nigeria began a three-year, phased rollout of the pentavalent vaccine in 2012, which protects against diphtheria, tetanus, pertussis,hepatitis B, and H.influenza b. In 2014, pneumococcal vaccine was introduced, fotunately rotavirus vaccination is expected to begin in 2017.[216] The Global Alliance for Vaccines and Immunisation (GAVI) support to Nigeria includes vaccine support for Pentavalent, Pneumococcal Conjugate, Yellow Fever, Meningitis A and Measles vaccines; cash support for health system strengthening (HSS); and immunisation system strengthening (ISS).[219]

Nigeria made a remarkable progress against polio via the support of the global polio eradication initiative (GPEI) and other development partners and in 2015, was declared polio endemic free by WHO. Sadly, polio made a comeback in 2016. However, drastic measures are been put in place to ensure its total interruption and eradication. There seems to be increasing coverage of vaccination in Nigeria as evident by the administrative Penta3 coverage of 96% in 2015, which exceeded the set target of 87% for the country for the same year. Factors contributing to poor routine immunisation coverage in Nigeria include weak governance, inadequate funding, vaccine stock-out, poor vaccine distribution and poor staff performance.

4.6.1.1 Immunisation Plus Days (IPDs)[220]

Immunisation Plus Days (IPDs) are a modification of the National Immunisation Days (NIDs) in which routine vaccines and other health interventions are delivered to communities during polio vaccinations. The Strategy delivers a range of antigens (measles and DPT vaccines) administered with the oral polio vaccines plus other child survival interventions such as anti- helminthics, Vitamin A,

distribution of insecticide treated nets etc. It also includes Measles Supplementary Immunisation Activities (SIAs) catch-up campaigns..

4.6.2 Vaccination in animals

Vaccination could be administered for prophylaxis or as a result of disease outbreaks. Vaccination coverage of 70% - 80% over a period of time results in high herd immunity and can lead to control of disease. The NVRI produces viral and bacterial animal vaccines for use locally (Table 4.2) and these could be exported to the sub-region on demand. The bacteria vaccines produced by NVRI include: - Anthrax Spore Vaccine (ASV), Brucellosis Vaccine (BV, Black Quarter Vaccine (BQV), Contagious Bovine Pleuro-pneumonia Vaccine (CBPPV), Fowl Typhoid vaccine (FTV), Fowl Cholera Vaccine (FCV), Hemorrhagic Septicemia Vaccine (HSV) and HantaVac. The amount of vaccines produced in the country is not sufficient for the huge animal population, leading to importation especially for poultry vaccine.There are also no local vaccine production for disease prevention in fish though there are diseases that are preventable by vaccination There is a possible danger of vaccine outbreak in imported vaccines due to delay in cargo clearing and or failures in importerised cold chain. Furthermore, there are challenges with use of vaccines due to storage and maintenance of the cold chain.

NVRI which is a BSL 3 laboratory can be upgraded to produce what is required nationally.[183]

Table 4.1: Routine immunisation of children in Nigeria is carried out using the following vaccines [218]

VACCINE	PERIOD OF VACCINATION
BCG (Bacilli Calmette Guerin)	At birth or as soon as possible after birth
OPV (Oral Polio Vaccine)	At birth and at 6, 10, and 14 weeks of age
Pentavalent	At birth and at 6, 10, and 14 weeks of age
Pneumococcal Conjugate Vaccine (PCV)	6, 10 and 14 weeks of age.
Measles	At 9 months of age
Yellow Fever	At 9 months of age
Vitamin A	At 9 months and 15 months of age

** TT (Tetanus Toxoid) is administered to pregnant women and other women of child bearing age*

Table 4.2: Locally manufactured veterinary vaccines in Nigeria [221]

LOCAL VACCINES	
1. Anti-rabies vaccine	11. New castle Disease vaccine (NDV) 1_2
2. Anthrax rabies	12. NDV (Intraoccular)
3. Black quarter	13. NDV (Komorov)
4. Brucella abortus	14. NDV (Lasota)
5. CBPP	15. PPR
6. Fowl Cholera	16. Fowl Pox
7. Fowl Thyphoid	
8. Hemorrhagic septicaemia	
9. Hantavirus	
10. Gumboro vaccine	

4.7 WATER, SANITATION AND HYGIENE (WaSH)

In line with the targets of the Sustainable Development Goals (SDGs), the right to clean drinking water and sanitation for all remains a priority aspiration. WaSH in health care facilities cannot be over emphasised because it serves to prevent infections and spread of disease thusprotecting staff and patients. Owing to a lack of clean and hygienic water supply in most cities in the country; water and sanitation has been hampered nationwide and thus making infection prevention control a herculean task. The need to improve on sanitation practices remains a key challenge due to lack of working policies and improper waste disposal by residents which often times blocks drainages and water ways. According to the published data by Water Aid Nigeria, only 29% of the Nigeria population have access to basic sanitation, 25% still practice open defecation while 31% lack access to improved water sources.[222] Studies of the microbial quality of raw and treated drinking water in South-West Nigeria indicated the presence of pathogenic and non-pathogenic bacteria that exhibited multidrug resistance genes.[173-175]

4.7.1 Community Level Access to Water

With a population of over 160 million, access to clean and hygienic water supply is abysmally low in Nigeria. Rural community dwellers depend on water supply from rivers and streams. This has no doubt affected the health and wellbeing of people living in the rural areas and has exposed them to high rate of infections. Although there exists State owned Municipal Water Corporations in the country, most residents in the urban areas are however responsible for their water supplies through borehole and motorised Well water. About 11 per cent of all under five deaths occur in Nigeria. The under 5 mortality due to diarrhoeal diseases is alarming. Ten per cent of children under age 5 had diarrhoea while 2 % had bloody diarrhoea. All of this has been attributed to lack of safe water, basic sanitation and hygiene.[223]

4.7.2 Sanitation Services

According to the World Health Organisation (WHO) 'Sanitation generally means provision of facilities and services for the safe disposal of human urine and faeces.' There are different concepts of sanitations and they can be applied at three levels. These could be basic sanitation, on-site sanitation/food sanitation - hygienic measures for ensuring food safety; and environmental sanitation - the control of environmental factors that form links in disease transmission. Subsets of this category are solid waste management, water and wastewater treatment, industrial waste treatment, and noise and pollution control.[224]

About 72 million Nigerians were living without sanitation in 2004.[225.] According to a study by Owoeye and Ayodeji (2013) performed in an urban area in South-West Nigeria, indiscriminate dumping of refuse and delay in evacuation of waste by management authority, were identified as common poor sanitation practices/attitude. The result showed that more than 30% disposed their refuse indiscriminately, out of which 11.7% burnt waste within residential environment thereby causing air pollution. About 21.3% dispose waste in open spaces and 1.7%, dispose waste in drainages due to lack of sanitation service. Liquid wastes are poorly managed. House hold waste water from bathrooms, laundries and kitchens are not properly disposed constituting foul smelling water good for breeding of mosquitoes and other vectors of communicable diseases.[226]

4.8 AVAILABILITY OF ALTERNATIVES TO ANTIMICROBIALS, INCLUDING VACCINES AND OTHERS

The problems caused by antimicrobials resistance demand that renewed and concerted efforts be made for the provision and use of alternatives to antimicrobials that will be effective against pathogenic microorganisms without any fear of developing or heighteningresistance. Some of these alternatives that can be used and made available in Nigeria include vaccines, probiotics, immune-boosting using trace elements/vitamins and some bioactive phytochemicals.[227]

Presently, vaccines offer better promise as a suitable alternative to antimicrobials and could protect at-risk populations during and out of outbreaks.[228] The National Primary Health Care Development Agency (NPHCDA) has been given the mandate to ensure the availability of vaccines and provide extended immunisation coverage especially in children to protect them from vaccine preventable diseases.

Probiotics which are technologically modified extract from life microbes are gradually being included by prescribers in treatment regimens especially for diarrhoea. Similarly, principal immune-boosting trace elements such as selenium and zinc, vitamins such as A, C, D and E can be used as a tool in the fight against AMR in Nigeria.

Traditional healers have long used plants and plant products (phytochemicals) to prevent or cure infectious conditions. Many of these plants have been investigated scientifically for antimicrobial activities and many have shown the ability to inhibit growth of pathogenic bacteria. Several agents appear to have structures and modes of action that are distinct from those of the antimicrobials in current use, suggesting that cross-resistance with agents already in use may be rare or minimal.[227]

Currently, drugs of plant-origin include quinine and Artemesinin for malaria (cinchona tree). Some other plants with medicinal qualities include the Neem tree (*Azadirachta indica*), widely known in Nigeria as 'Dongo Yaro' which have antifungal, antibacterial, anti-oxidant and anti- malarial properties ; *Ocimum gratissimum L.* popularly known as 'scent leaf' is used for treating diarrhoeal diseases;[229] seeds of *Citrus parasidi Macfad* (grape fruit) are effective for treating urinary tract infections that are caused by pathogens resistant to the conventional antimicrobials.[230]

Despite the vast amount of plant-derived medications, Nigerians have not really tapped into the global herbal/natural medicine market. However, the question of standardisation remains a crucial concern and challenge which must be addressed

urgently, if herbal/complementary and herbal/alternative medicine is to take its rightful place in the Nigerian health system or if plant medicines are to generate structural scaffolds for pharmaceuticals.[231]The Nigerian National Institute for Pharmaceutical Research and Development in collaboration with local traditional medicine specialists developed Niprisan, a new drug extracted from indigenous herbs for the prophylactic management of patients with sickle cell disease[232] and could encourage anti-infective discovery along similar lines.

In 2007, Nigeria developed a traditional medicine policy with the aim of facilitating the integration of traditional medicine into the national health system. This will also enhance the country's capacity for delivering herbal and agricultural products to the international markets especially the EU and the US market under the Africa Growth and Opportunity Act (AGOA), ultimately diversifying the export base of the nation's economy.[231]

4.9 BIOSECURITY MEASURES IN FARMS

In agriculture, biosecurity refers to the process of reducing the likelihood of the introduction and spread of pathogens within and between farms. This is achieved by the principles of bio exclusion (preventing infectious agents from entering the farm) and biocontainment (preventing infectious agents from exiting the farm). Activities involved include segregation, traffic control, cleaning, and disinfection.[233] Farm biosecurity helps to prevent the spread of harmful pests and diseases in the farm. It also guards against the exposure to harmful biological agents as measures taken to ensure the security in farms. This protection of farmlands is therefore essential in order to enhance non-contamination of food crops and to prevent unauthorised access to the farms. This measure helps to achieve infection prevention control on the farm and maintain the nutritional value of the food crops. Improved animal production and transport environment, reduced stock density and stress, increased hygiene and

disease control techniques will in turn minimise antimicrobial use as growth promoters or for the treatment of animal diseases.[234]The knowledge and implementation of biosecurity measures is poor in Nigeria as highlighted by a study among pig farmers.[235]

Nigeria exports shrimps to the European Union, in order to meet EU standards it follows the FAO standards for waste water treatment in the fishery industry. This involves use of sedimentation tanks and effluent treatment plants before treated water is discharged into the water body. The effluents it is also screened for gamete, larvae and micro-organisms.[236]

BOX 4: SWOT ANALYSIS OF IPC, VACCINATION AND BIOSECURITY IN NIGERIA	
STRENGTHS	• Existence of policy and strategic framework documents on IPC, policies & guidelines on food safety, animal health, waste management, water and sanitation (WaSH) and on water quality standards • Increasing awareness of Infection control across specialties • Availability of bacterial vaccines e.g. CSM& pentavalent vaccine • High coverage for viral vaccine preventable diseases • Local production of vaccines for animal use • Government funded vaccination for bacterial diseases in animals.
WEAKNESSES	• No national IPC coordinating body providing oversight in health care facilities • Shortage of skilled IPC practitioners • Lack of national guidelines for IPC • Poor availability and quality of water in health care facilities and community

BOX 4: SWOT ANALYSIS OF IPC, VACCINATION AND BIOSECURITY IN NIGERIA CONT'D	
WEAKNESSES CONT'D	• Lack of implementation or enforcement of policies and regulations on food safety and meat hygiene • Poor vaccine coverage in humans and animals • Vaccines known to target resistance are inadequately deployed e.g. Rotavirus, Pneumococcal • Poor adherence to guidelines on animal health by small farm holders and at the market level • Poor waste management and adherence to waste disposal guidelines in farms, hospitals and communities
OPPORTUNITIES	• Inclusion of IPC and hand hygiene in the emergency preparedness plan for epidemics in the country • Training materials, guidelines and tools which are already available on IPC in TB and HIV/ AIDS can be optimised • Annual hand hygiene campaigns (May 5 hand hygiene day , October 15 community hand washing day) • Existent network for polio vaccination can be used for vaccination against bacterial infections • Universal health coverage and SDGs can be utilised to advance implementation of IPC • Existence of national associations for infection prevention and control • Use of solar energy for IPC processes e.g. power generation, decontamination • Availability of global standards for animal health ('biosecurity')
THREATS	• Poor enforcement of legislation and guidelines on IPC, Vaccination and biosecurity • Inter-professional rivalry in concerned sectors • Lack of resources and infrastructure for IPC

BOX 4: SWOT ANALYSIS OF IPC, VACCINATION AND BIOSECURITY IN NIGERIA CONT'D	
THREATS CONT'D	• Hard to reach areas, cultural barriers and Security challenges (e.g. insurgency, threat to life) hinder adequate vaccine coverage • Lack of local production of vaccines for human use

5 Antimicrobial Resistance Awareness and Training

5.1 AMR AWARENESS

Though there is paucity of data on AMR awareness among the general public, human health, animal and environmental professionals, the available evidence indicates that the human-animal-environment tripartite professionals have a broad knowledge of AMR and related areas. However, this has not translated into attitude and practice, due to lack of appropriate or adequate resources for standard precautions (e.g. appropriate hand washing, use personal protective equipment, sharps disposal, appropriate waste disposal), lack of regular training on infection control, poor public visibility, poor enforcement of regulations and excess workload.

5.2 ACCESS TO INFORMATION

5.2.1 General Public

The Government of Nigeria has been implementing the National Health Promotion Policy (NHPP) since 2006. The NHPP envisions a population of Nigerians empowered with correct health information, living healthy lifestyles and who demand quality health services. Existing structures such as the Social Mobilisation Committees at the National, State and LGA levels have been championing nationwide public awareness activities in line with the NHPP.

Though Nigeria has paucity of data on access, use and effects of existing communication channels, available evidence indicates that in spite of the economic and literacy factors that limit many people's access to the mass media, the media still remains the channel with the farthest reach. It has contributed to massive awareness campaign activities that have provided opinion leaders and sometimes, household heads with information and knowledge on appropriate practices. Such information and knowledge trickle down to individuals within the family and

facilitate the adoption of positive behaviours.

However, radio usage is higher compared to television and newspapers. Radio has been used extensively to reach groups in communities with programmes promoting the adoption of healthy habits. The print media, Social and Behavior Change Communication (SBCC) materials such as fact sheets, wristband, billboards, posters, descriptive clothing, and wall paintings are key information channels for opinion leaders, policy makers and the general public.

Emerging opportunities exist with the increase in Nigeria's GSM teledensity as its usage is widespread both in urban and rural areas. Text messages have been used to reach millions of people during information campaigns. The number of GSM lines in Nigeria increased from zero in 2001 to nearly 19 million in 2006. The teledensity calculation since 2006 has been based on a population of 140 million and stood at 107% with the number of active telephones lines of 149.8 million at 2016. A major challenge in this is still the limited access to telephones in some rural communities.[237]

In addition, it is important to note that successful engagement with communities to identify current attitudes, practices and barriers on a health issue and build consensus on key ideal behaviours has been achieved through other channels of communication that involved the use of a pool of knowledgeable and skilled community resource persons. These critical communication channels include interpersonal communication, Community Dialogue (CD), Community Theatre for Development (TFD), Community viewing and listening centres, Community Information Board (CIB). Other communication channels include town announcers, traditional & religious leaders, faith-based organisations, community organisations, civil societies, cooperatives, trade unions and associations.

Thus, in line with the objective of the NHPP, public awareness and understanding

of AMR can only be successful based on the availability of a communication strategy that will guide relevant stakeholders in the use of the existing community communication systems to create and sustain positive healthy behaviours and attitudes that will enhance the adoption of AMR appropriate use and practices.

5.2.2 Professionals And Policy Makers

Existing information dissemination structures amongst professionals and policy makers include training (pre service and in-service), seminars, conferences, meetings and symposiums. Additional structures for AMR information dissemination include National Councils on Health (NCH), Environment (NCE), and Agriculture (NCARD) and professional associations.

5.3 AMR CURRICULA

Teaching curricula varies based on the category of health worker and level of training. Training for each category of health worker is overseen by its own council, such as the Medical and Dental council of Nigeria, Pharmacist Council of Nigeria, Nursing and Midwifery Council of Nigeria and the Medical Laboratory Science Council of Nigeria. University curricula are systematically planned and guided learning experiences with intended learning outcomes which are specific for each course of study in schools. This in turn results in the continuous and willful growth of learners, making them socially competent. Regular review of institutional curricula is important. In Nigeria, the University's senate is responsible for the development and approval of curricula for the courses/programmes offered by it. However, the relevant professional regulatory bodies and the National Universities Commission (NUC) provide 'minimum standards' that must be achieved by the University to obtain and maintain their accreditation status.[66]

A review of the medical school curriculum was conducted between 2011 and

2012, which included a national survey of medical schools. Some of its findings included that though the curricula content was satisfactory, it did not prepare medical students adequately for clinical practice, was not community-oriented and lacked multidisciplinary postings.[238] Thus, in line with current global requirements in medical education, new postings/courses were suggested for inclusion in the 2012 curriculum and one of the suggested new postings was 'Infectious Diseases Posting'.[238] The aim of this posting is to produce medical graduates who understand the epidemiology, pathogenesis, management, prevention and control, laboratory role and socioeconomic implications of infectious diseases.[238] Per the 2012 revised medical curricula for a 4th year medical student, principles and mechanism of antimicrobial resistance was part of the requisite knowledge for passing the laboratory medicine module. The aim of these new courses is to improve the quality of doctors produced and encourage current and future academic staff to develop academic tracks and attract postgraduate research in specialties such as AMR.[238]

For pharmacists, the current undergraduate national curriculum includes a course in pharmaceutical microbiology where students are taught evaluation of antimicrobial activities, bacterial genetics and drug resistance.[239] For medical laboratory scientists, in the final year undergraduates specialise in various disciplines such as chemical pathology, haematology and blood transfusion, histopathology and medical microbiology and parasitology. Only those specialising in medical microbiology and parasitology are taught pharmaceutical microbiology and microbial genetics, which contains principles and mechanisms of bacterial resistance to antimicrobials.[240] For nurses and midwives, undergraduates are taught microbiology containing AMR modules in the third year of the undergraduate training.[241]

From the fourth year of the undergraduate training for veterinary practitioners, AMR is taught in veterinary pharmacology under chemotherapy. This is taught in the

Veterinary Faculties. There is need to review the current curricula in view of the rising global threat of AMR so that it reflects day one competencies for veterinary graduates in this field. AMR issues are also brought up in the VCN Continuing Education classes.[242] In all the above professions, there is a gap in the teaching of AMR in the undergraduate curricula thus requiring further review of the existing curricula.

BOX 5: SWOT ANALYSIS OF AWARENESS ON AMR IN NIGERIA	
STRENGTHS	• Highly skilled health professionals • Regulatory councils for most categories of health, agricultural and environmental workers • There is a curriculum for training of health care workers that can be modified • Political opportunities in Senate and House of representatives • Traditional and herbal medicine practitioners have a policy guiding their activities • There is an IPC policy in the country • There is a guideline for prophylactic use of antimicrobials • There is a standard treatment guideline for human and animal health in the country • There is a waste treatment guideline in Environment
WEAKNESSES	• Some categories e.g. scientific officers (microbiologists, chemists, physicist, biological scientists) have no regulatory bodies • No continuous professional development • No information available from vertical programmes around AMR training for service providers eg TB programme • Currently the document is not updated on curriculum content on AMR from NUC • Lack of knowledge about awareness activities carried out by professional bodies

BOX 5: SWOT ANALYSIS OF AWARENESS ON AMR IN NIGERIA CONT'D	
WEAKNESSES CONT'D	• Poor access to IPC policy guidelines • IPC policy not being adequately implemented • IPC domiciled in Department of Public Health. Poor collaboration with Department of Hospital Services in the Federal Ministry of Health • Teaching and practice by non regulated basic scientists could influence the practice of health professionals • Weak coordination of AMR awareness activities implemented by government and partners • Non existent of one health approach towards AMR awareness • Non adherence to guideline for prophylactic use of antimicrobials • Inadequate adherence to standard treatment guidelines • Poor access to relevant documents on AMR such as policy and guidelines documents. Improve through online availability of working documents • No domestication of World Antimicrobials Awareness week (WHO November) • Poor information dissemination on appropriate use of antimicrobials to the general public • Problem of unskilled prescribers of antimicrobials across the tripartite sectors
OPPORTUNITIES	• Since NUC oversees curriculum of science and other relevant professionals, AMR could be included in the respective curriculum • Grazing reserves being established could be targeted on AMR awareness • Grazing bill could be adapted to include AMR awareness • Political opportunities that can be harnessed to push AMR awareness • Annual conferences, CPD and committees (Live stock Development Committee) in the tripartite sector for advocacy activities

BOX 5: SWOT ANALYSIS OF AWARENESS ON AMR IN NIGERIA CONT'D	

OPPORTUNITIES	• Partners and relevant organisations with interest in AMR activities such as:
	  • awareness
	  • surveys
	  • beliefs
	  • knowledge, attitudes and practices
	  • research and development
	• Forum that could be used for high level advocacy such as Health (NCH), Agriculture (NCA)

THREATS	• Non regulation of AMR activities (awareness, training, etc) by partners such as vertical programmes.

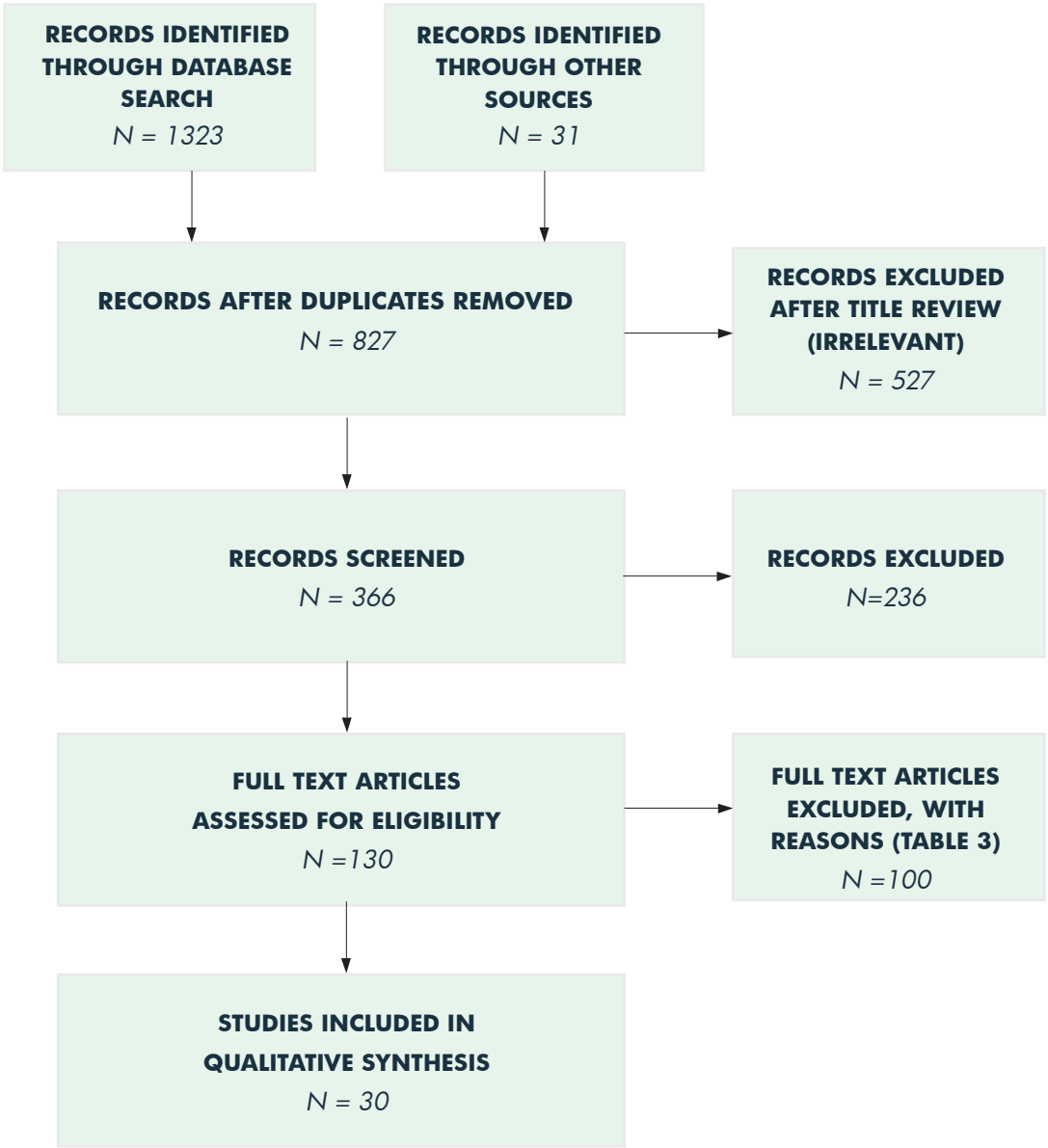
Appendix 1: Systematic Search Process (Example for Diarrhoeal Pathogens)

I.1. SEARCH TERMS USED TO RETRIEVE ARTICLES FROM ELECTRONIC DATA BASES
resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal OR diarrh* AND Escherichia coli AND nigeria AND "2000/01/01"
Nigeria OR resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal OR diarrh* AND Escherichia coli AND "2000/01/01"
resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal AND non typhoidal salmonella AND Nigeria
Nigeria AND resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal AND non typhoidal salmonella
resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal OR diarrh* AND shigella OR shigellosis AND Nigeria AND "2000/01/01"
Nigeria OR resistance OR sensitivity OR susceptibility AND enteric OR faeces OR faecal OR stool OR intestinal OR diarrh* AND shigella OR shigellosis AND "2000/01/01"

1.2. CRITERIA FOR ARTICLE SELECTION
Articles must discuss enteric pathogens from human clinical specimens
Articles should discuss isolates from stool and/or rectal swabs
Articles must contain information about specimen collected in Nigeria
Articles must give information on AMR
Articles must be published from 2000 till date
Articles must be in full text

1.3. REASONS FOR EXCLUSION OF FULL TEXT ARTICLES
Lack of access to full article
No separate antimicrobial records for each of the enteric pathogen
No separate antimicrobial record for stool and blood isolates
Resistance profile of isolates not expressed in quantitative terms
No separation of antimicrobial profile of human and animal pathogens
Case report/ review
Reports on pathogen that are not strictly enteric
Duplicate publication

I.4. PRISMA FLOW CHART OF THE SEARCH PROCESS



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Municipality, Tanzania. Pakistan Journal of Nutrition. 2009;8(3):203-7.

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Contributors

NAME	DESIGNATION/ORGANISATION
Chikwe Ihekweazu	CEO, Nigeria Centre for Disease Control, Abuja
COORDINATORS	
Aaron Oladipo Aboderin	Department of Medical Microbiology and Parasitology, Obafemi Awolowo University/Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Osun
Adebola Tolulope Olayinka	Department of Medical Microbiology, Ahmadu Bello University Teaching Hospital, Zaria, Kaduna/AFENET Nigeria, Haile Selassie, Asokoro, Abuja
Iruka N. Okeke	Global Antibiotic Resistance Partnership (GARP) Nigeria Co-chair and Professor and MRC/DfID African Research Leader Department of Pharmaceutical Microbiology Faculty of Pharmacy University of Ibadan, Ibadan, Oyo State
Obasanya Joshua	Director Prevention and Programmes Coordination, Nigeria Centre for Disease Control, Abuja
CONTRIBUTORS	
Abiodun Egwuenu	Epidemiologist, Nigeria Centre for Disease Control, Abuja
Adeyemi Temitayo Adeyemo	Department of Medical Microbiology and Parasitology, Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Osun State, Nigeria
Aghogho Gbetsere	Federal Ministry of Environment, Abuja
Akeem Alaka	Nigeria Centre for Disease Control, Abuja
Amupitan A.A. Obafemi	Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun
Awosanya Emmanuel	AFENET-Nigeria, Haile Selassie, Asokoro, Abuja
Aroyewun Eunice	Severe Typhoid in Africa Project (Medical Microbiology Department, College of Medicine, University College Hospital, Ibadan, Oyo
Bejide Oyeniyi Stephen	Severe Typhoid in Africa (SETA) Nigeria, University College Hospital, Ibadan, Oyo
'Biodun Ogunniyi	Consultant Epidemiologist, Nigeria Centre for Disease Control, Abuja/ University College Hospital Ibadan
Busayo O. Olayinka	Department of Pharmaceutics & Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Kaduna

NAME	DESIGNATION/ORGANISATION
Chibuzor Eneh	Assistant Director, Emergency Preparedness and Response, Nigeria Centre for Disease Control, Abuja
Comfort Kunak Ogar	Assistant Director. Pharmacovigilance and Post Marketing Surveillance (PV/PMS) Directorate, National Agency for Food and Drug Administration and Control (NAFDAC)
Dooshima Kwange	Disease Surveillance and Reporting, Epidemiology Division, Federal Department of Veterinary and Pest Control Services, Federal Ministry of Agriculture and Rural Development, Abuja
Ekpo Stella Effiong	Pharmaceutical Microbiology, Faculty of Pharmacy, University of Ibadan
Fatima Abba	Pharmacist, Nigeria Centre for Disease Control,Abuja
Frank S. Kudla	Federal Ministry of Environment, Abuja
Folashade Feyisayo Osundina	Ladoke Akintola University of Technology Teaching Hospital, Oshogbo, Osun
Folasade Ogunsola	Provost, College of Medicine, Lagos University Teaching Hospital, Lagos
Folorunso Oludayo Fasina	Emergency Centre for Transboundary Animal Diseases, Food and Agriculture Organisation of the United Nations (FAO), United Nations Complex UN Avenue, Gigiri, Nairobi, Kenya
Garba Sadiq	Nigeria Centre for Disease Control, Abuja
Gbenga Joseph	Chief Pharmacist, Nigeria Centre for disease Control, Abuja
Hadizah Adeoti	University of Ibadan, Oyo
Hamzat Omotayo	World Health Organisation, Nigeria
Helen Adamu, DVM MPH	Center for Clinical Care and Clinical Research Nigeria
Irek Emmanuel O.	Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun
Isiramen Olajide, MPH	Center for Clinical Care and Clinical Research, University of Maryland, Baltimore Nigeria
Joan Ejembi	Department of Medical Microbiology, Ahmadu Bello University Teaching Hospital, Zaria, Kaduna
Khan Mohsin	eHealth Africa

NAME	DESIGNATION/ORGANISATION
Kola Jinadu	Consultant Public Health Physician/Epidemiologist, Nigeria Centre for Disease Control, Abuja
Mabel Aworh Ajumobi	Assistant Director (Veterinary Drugs Monitoring), Department of Veterinary & Pest Control Services, Federal Ministry of Agriculture & Rural Development, Area 11, Garki, Abuja
Musa Garbati	Department of Medicine, Infectious Diseases and Immunology Unit, University of Maiduguri, Maiduguri, Borno
Mercy Niyang, MPH	University of Maryland-Maryland Global Initiative Cooperation, Nigeria
Mohammed Yahaya	Lecturer/Honorary Consultant Clinical Microbiologist, Department of Medical Microbiology, College of Health Sciences, Usmanu Danfodiyo University/Usmanu Danfodiyo University Teaching Hospital, Sokoto
Nurudeen O. Oloso	Department of Production Animal Studies (Epidemiology Section), Faculty of Veterinary Science, University of Pretoria, South Africa
Obadare Temitope Oyewole	Department of Medical Microbiology and Parasitology, Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Nigeria
Ojewuyi Abiodun	Department of Medical Microbiology and Parasitology, OAUTHC. Ile- Ife
Olufemi Abayomi	AFENET-Nigeria, Haile Selassie, Asokoro, Abuja
Oluwatoyin B. Karimu	Chief Pharmacist, Food and Drugs Services Department, Federal Ministry of Health, Abuja
Oluwatoyin Modupe Aiyelotan	AFENET-Nigeria, Haile Selassie, Asokoro, Abuja
Olayinka Habib Raji	Research Associate, Severe Typhoid in Africa (SETA Nigeria) Department of Medical Microbiology and Parasitology, College of Medicine, University of Ibadan, Ibadan, Oyo
Omoniyei Tarelayefa Love	Global Antibiotics Resistance Partnership (GARP) Country Assistant, Ducit Blue Solutions, Abuja
Onyekachi Estelle Mbadiwe	Global Antibiotic Resistance Partnership (GARP) Country Coordinator and Business Director, Ducit Blue Solutions, Abuja
Oyama Enang Enang	World Health Organisation, Nigeria

NAME	DESIGNATION/ORGANISATION
Oyekola Victor Abiri	Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, Osun
Rahab Charles Amaza	Nigeria Centre for Disease Control, Abuja
Peters O. Oladosu	National Institute for Pharmaceutical Research and Development, Abuja
Shamsudin Aliyu	Department of Medical Microbiology, Ahmadu Bello University, Zaria
Shamsudeen Fagbo	Zoonotic Diseases Unit, Preventive Medicine, Ministry of Health, Riyadh Saudi Arabia
Steve Olonilila	Department of Microbiology, Faculty of Life Sciences, Ahmadu Bello University, Zaria, Kaduna
Tochi Joy Okwor	Consultant Public/Occupational Health Physician and IPC Specialist, NICA
Ugochukwu Eze	University of Lagos/Lagos University Teaching Hospital, Lagos
Yonni Apeji	Department of Pharmaceutics & Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria,Kaduna
EXTERNAL REVIEWERS	
Hellen Gelband	Associate Director, Center for Disease Dynamics, Economics & Policy
Kim Faure	CDDEP Southern African Country Coordinator, Centre for Disease Dynamics Economics and Policy
Mirfin M. Mpundu	Executive Director - Ecumenical Pharmaceutical Network, Head - Action on Antibiotic Resistance (ReAct) Africa
Molly Miller-Petrie	Research Associate, Centre for Disease Dynamics Economics & Policy, (CDDEP), Washington DC
EDITOR	
Monu Nwoko El-shama	Department of Pharmaceutical Microbiology, University of Ibadan, Ibadan, Oyo

FEDERAL MINISTRIES OF AGRICULTURE, ENVIRONMENT AND HEALTH

ANTIMICROBIAL USE AND RESISTANCE IN NIGERIA

Situation Analysis and Recommendations

NIGERIA'S NATIONAL AMR COORDINATING BODY:

Nigeria Centre for Disease Control (NCDC)

Plot 801 Ebitu Ukiwe Street, Jabi Abuja,Nigeria

0800-970000-10 (Toll Free Call Centre)

info@ncdc.gov.ng www.facebook.com/nigeria.ncdcgov

@ncdcgov https://www.ncdc.gov.ng