Assessment of Antimicrobial Resistance Surveillance System in Nigeria

Okolie Jovita Obiageli

A thesis submitted in partial fulfilment of the requirements of the University of the West of England, Bristol for the degree of Doctor of Philosophy

College of Health, Science and Society, University of the West of England, Bristol
May, 2024

Acknowledgements

Firstly, I would like to express my deepest gratitude to God Almighty for providing me this opportunity and granting me the capability and grace to successfully complete this study. Without His help, I probably would have given-up at moments of intense pressure, bereavement and overwhelming circumstances.

I am deeply indebted to my husband Ian, and lovely children Harrod and Maia for bearing with me this whole period. For the times I have failed to show up at school events, turned down family invites and suspended holidays just to ensure I meet deadlines. Thank you for your perseverance, this accomplishment is for you.

To my Dad whom has gone to be with the Lord, thank you for stirring the waters of academic pursuits within me. Your encouragement and regard for academic achievements are the building blocks of my academic enthusiasm and aspiration.

To the rest of my family members, my mom Lady Bernadette and siblings, I appreciate you all for absolving me of every blame incurred as a result of my absence, inactivity and non-involvement in family duties and responsibilities.

With the deepest sense of appreciation, I want to thank my director of studies Prof. Emmanuel Adukwu for his immense support. Many times he bent over backwards, worked weekends, on holidays and even in transit to ensure I am making steady progress and keeping up with all progression assessment and milestone requirements. Many thanks for providing your supervisory support in the capacities of both a mentor and coach.

To Dr Sanda Ismail my second supervisor, this research could not have reached a logical conclusion without your thoroughness and in-depth critiquing. Thank you for contributing towards the delivery of this project and for offering a piece of your intellectual nuggets and wealth of experience to this work.

To my research mate Uzo who constantly inspired and cheered me up, you are the best pal and motivator on this research journey. From re-energising me at my low moments to steering my thought process from a point of writer's block to a deluge of ideas. Thanks for always being there for me.

To the College of Health, Science and Society director of postgraduate research, Dr Tim Moss and entire faculty staff, thank you for providing resources to help develop my skills to become a better researcher and for providing a responsive team of graduate administrative staff who are always available to resolve all my queries to ensure uninterrupted assess to my academic engagement.

A final thanks to University of the West of England Bristol for the opportunity of being a scholar and a life-time Alumni of such an academically renowned, multi-ethnic and multi-cultural friendly academic institution.

Abstract

Antimicrobial resistance (AMR) is among the top ten public health threats worldwide. This problem is further compounded by poor surveillance and oftentimes lack of good quality data to enable accurate estimation and description of the magnitude (prevalence and incidence), burden (health and economic) and distribution (geographical areas and population) of AMR globally. Consequent upon this paucity of information, data needed to guide strategic intervention is lacking and thus leading to poor management and investment decisions. The Nigeria National Action Plan (NAP) recognises surveillance as a critical component for the control of AMR. However, the current AMR surveillance system (AMRSS) may not be representing the actual burden of AMR in the country. With the knowledge of this problem, the aim of this research was to evaluate the capacity and sustainability of AMRSS in Nigeria and to provide suggestions to optimise and strengthen the AMRSS effectiveness and efficiency.

Methods

This research utilised a three dimensional study approach to enrich and triangulate data from different sources: 1) a systematic review of twenty-three surveillance systems was conducted to generate an overview of AMR surveillance approaches and methodologies in Africa; 2) a cross-sectional study of 302 laboratories was carried out to assess the technical capacity of laboratories involved in AMR surveillance in Nigeria as well as identify gaps, vulnerabilities and opportunities for improving data quality and performance using surveillance quality indicators (SQIs) and; 3) in-depth qualitative interview which explored perceptions, views, and opinions of 34 stakeholders which was used to access governance areas of NAP implementation as well as gauge active participation, political will and stakeholder engagement which are crucial to AMRSS success and sustainability.

Results

The systematic review highlights a number of methodological and reporting flaws in existing surveillance systems that impact completeness, representativeness, accuracy, validity, reliability and usefulness of data. The cross-sectional study reveals that the weakest and most vulnerable of all SQIs were items related to data recording. Even though the weaknesses and strengths varied among laboratories, the tertiary laboratories reported highest performance levels. Generally, the performance of one indicator influenced the other thus strengthening one indicator will potentially affect overall laboratory performance. Responses from the qualitative interview reveals under-resourcing and poor multi-sectoral engagement as the key themes impacting AMRSS performance and sustainability. It also suggests that some governance domain essential for effective administration of the NAP were not effectively implemented.

Conclusion

The current AMRSS in Nigeria has limited capacity. This alongside other confounders could potentially lead to possible over-representation of resistance in the population. There is urgent need to strengthen the system and this study has helped to provide better insights to the enablers and critical focus areas for improving overall performance and for sustainability of the surveillance system. This will enable the surveillance system to leverage on the technical capacity, strength and opportunities provided by eligible laboratories to optimise data quality for a more robust and representative surveillance.

Table of contents

List of tables

List of figures

List of abbreviations

ACDC	African Centre for Disease Control
AMR	Antimicrobial Resistance
AMRSS	Antimicrobial Resistance Surveillance System
AMU	Antimicrobial Use
AST	Antimicrobial Susceptibility Testing
BSI	Blood Stream Infection
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CASA	Community Associated *Staphylococcus aureus*
CDC	Centre for Disease Control and Prevention
CLSI	Clinical and Laboratory Standard Institute
CONS	Coagulase Negative Staphylococci
CRE	Carbapenem Resistant *Enterobacteria*
DALYs	Disability Adjusted Life Years
DNA	Deoxyribonucleic Acid
EARS	NET European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Control
EDDL	Essential Drug Diagnostic List
EQA	External Quality Assurance
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organisation
FMARD	Federal Ministry of Agriculture and Rural Development
FMoH	Federal Ministry of Health
GAP	Global Action plan
GAP-AMR	Global Action Plan on Antimicrobial resistance
GDP	Gross Domestic Product
GLASS	Global Antimicrobial resistance and use Surveillance System
HCAI	Health Care Associated Infection
HCA-MRSA	Healthcare Associated Methicillin-resistant *Staphylococcus aureus*
IACG	Inter-Agency Coordination Group
ICU	Intensive Care Unit
IDSR	Independent Disease Response Surveillance
IQA	Internal Quality Assurance
KOL	Key Opinion Leaders
LMICs	Low and Medium Income Countries
LoS	Length of Stay
MAAP	Mapping Antimicrobial resistance and Antimicrobial use Partnership
MDR	Multi-Drug Resistance
MESH	Medical Subject Headings
NAC	National Antibiotic Committee
NAP	National Action Plan
NCDC	Nigeria Centre for Disease Control
NTS	Non-*Typhoidal Salmonella*
OIE	Office International des Epizooties
OOP	Out Of Pocket
PHC	Primary Health Centre
PICO	Patient/problem Intervention Comparison and Outcome
PRISMA	Preferential Reporting Items for Systematic Reviews
RLL	Regional Reference Laboratories
SCC	Surveillance Coordinating Centre

SOP	Standard Operating Procedure
SQI	Surveillance Quality Indicator
SS	Surveillance System
SSI	Surgical Site Infection
SWiM	Synthesis Without Meta-analysis
THL	Tertiary Healthcare Laboratories
UN	United Nations
UTI	Urinary Tract Infection
UWE	University of the West of England
VRE	Vancomycin Resistant *Enterobacteriaceae*
WASH	Water Sanitation and Hygiene
WGS	Whole Genome Sequencing
WHA	World Health Assembly
WHO	World Health Organisation
WOAH	World Organisation of Animal Health

List of publications

A section of this thesis has been published in Volume 78, Issue 1 of the Journal of Antimicrobial Chemotherapy under the tittle 'Systematic review of Surveillance Systems for AMR in Africa' (Okolie *et al*., 2022). The article was first received on 8th June, 2022 and accepted on 16th September 2022 after a rigorous peer review process. Interestingly, this article which addresses the very important issue of AMR surveillance in Africa has been cited four times following its publication on 13th October 2022 (as at October 2023), and was included in the best of JAC: a collection of top 10 papers for the BSAC winter conference for impact and citation.

Chapter outline

This thesis is written in manuscript style to complement the research design, methods and objectives as well as facilitate direct reporting of the outcomes from each study as they address various aspects of the research questions. The introductory chapter provides background information; justification of study; problem statement; research questions and objectives; and methodological foundation of study. Chapter 2 highlights global epidemiology of AMR from the literature review conducted in order to give context to the threats of AMR, provide perspectives to the relevance of surveillance and position the research within gaps in current surveillance strategies. Chapter 3 presents a systematic review of surveillance methodologies for AMR in Africa and a summary of the surveillance systems characteristics, features, scope and attributes which was used to assess gaps in the system. Chapter 4 covers a cross-sectional study of laboratories in Nigeria in the scope of capacity for AMR surveillance in order to identify strengths, weaknesses and opportunities for surveillance expansion. In chapter 5, stakeholders' opinion was explored through in-depth qualitative interviews which revealed challenges of effective AMR surveillance implementation in Nigeria. Chapter 6 contains a surveillance enhancement toolkit developed to address the problems, gaps, challenges and concerns highlighted from this research by proposing a combination of strategies that could be cost effective to implement whilst at the same time optimising efficiency.

Each study chapter includes a method, result, discussion on the significant findings as well as study limitations/strength and recommendations. In Chapter 7, the thesis concludes with a recap of the key findings from all the studies and relates them to the initial research aim, objectives and questions proposed at project inception. It also provides a number of recommendations for future research and policy implementation to enhance AMR surveillance in Nigeria and other LMICs.

Chapter 1: Introduction

1.1 Background

1.1.1 Antimicrobial resistance

Antimicrobial resistance (AMR) is a process in which antimicrobial agents become less effective at targeting microorganisms. This means that infections caused by resistant organisms may fail to respond to antimicrobial drugs (World Health Organisation, 2014). A situation that threatens the successful treatment of an ever-increasing and ever-evolving range of infections and thus recognised as one of the top 10 public health problems in the 21st century (World Health Organisation, 2020; OIE, 2018). The former United Kingdom's Chief Medical Officer, Dame Sally Davies, stated at the 2019 United Nation's Interagency Coordination Group on AMR that 'We are in an arm race against microbes'. This means that if we do not take action to slow down AMR, it could lead to microorganisms winning a major battle in their fight against humans (UN-IACG, 2016).

The processes leading to the development of AMR are multifaceted but the major drivers remain over reliance on antimicrobials for treatment and prevention of infectious diseases and the use of antimicrobials outside human medicine (OIE, 2018). The later plays significant role in the rapid development and spread of AMR in the population (ECDC, 2018; World Health Organisation, 2016). About two decades ago, it was estimated that 54 billion standard units of antibiotics were consumed globally, and this figure increased by 36% in the following 10 years thus creating the preconditions of a public health crisis (Valavanidis, 2017; Ling *et al.,* 2015; Van Boeckel *et al.,* 2014). A recent 2021 global estimate of antibiotic consumption published by Oxford University records a cumulative increase of 46% from the figure recorded in the year 2000 (Browne *et al.,* 2021).

Infectious diseases have been a source of major public health crisis, population mortality and morbidity and global economic loss (Ball *et al.,* 2018; Oloso *et al.,* 2018). These public health

crisis easily overwhelm health systems and oftentimes measures to limit them culminate in more antimicrobial dosing and consumption (Ball *et al.,* 2018; Valavanidis, 2017). Regrettably, consequences of actions undertaken to minimise fatalities from public health events have resulted in greater crises from drug resistance (O'Neill, 2014). The emergence of drug-resistant microorganisms results in poor prognosis and treatment outcome, prolonged hospital stay and consequently, increased healthcare spending, and deaths (Shaikh *et al.,* 2015). Tackling the threats of AMR to population health and economy through appropriate surveillance and control policies is considered a key priority to health agencies and systems globally (Ragheb *et al.*, 2019; World Bank, 2016).

According to World Bank (2016), economic burden of infectious disease from AMR could push an additional 24 million individuals into extreme poverty and lead to a fall of between 1.1% and 3.8% in global gross domestic production (GDP) by 2050. A review commissioned by the Wellcome Trust on the global crisis of rising drug resistance concluded that AMR causes more than 700,000 deaths yearly and this number is expected to rise in the coming years if AMR is not addressed (O'Neill, 2014). Another systematic analysis of global burden of AMR estimated about 4.95 million deaths associated with bacterial AMR occurred in 2019, including 1.27 million deaths attributable to bacterial AMR. Findings from this analysis also estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27.3 deaths per 100 000 (Murray *et al.,* 2022). Shallcross *et al.* (2015) asserted that the health and economic threats arising from AMR in human, livestock, and environment needs to be approached systematically and collectively through multi-sectoral (One Health) approach and more importantly prioritising the development of newer molecular classes of antimicrobial agents.

1.1.2 Antimicrobial development: The chase, the race and the decline

Antimicrobial drugs have brought about profound health benefits in infectious disease management by making previously difficult to treat infections now easily treatable using simple treatment regimen (Ferri *et al.*, 2017). This simplified and effective approach to infectious disease management encouraged antimicrobial seeking and usage unlike the pre-penicillin era where complex and daunting techniques such as bloodletting (which is based on ancient medical theory), topical iodine, mercury, bromine and chemotherapy were used. Apart from the complications and side effects of these earlier techniques, their therapeutic effects were not near as good as modern antimicrobials at treating infections (Aminov, 2010; Powers, 2004). The concerns around these unsafe approaches to treating infections coupled with poor patient compliance heightened the anticipation of a game-changing revolutionary breakthrough in treatment of infections.

The chase for the development of antimicrobials dates back to 1904 when Ehrlich began seeking for cure against syphilis, a sexually transmitted disease that was endemic for decades and almost incurable at that time. In 1910, Ehrlich successfully synthesised hundreds of organoarsenic derivatives of a highly toxic drug 'atoxyl' which showed significant promise for the treatment of patients with syphilis (Aminov, 2010). This drug was later developed and marketed under the trade name salvarsan for treating syphilis. Despite the side effects associated with this drug, it remained the frequently prescribed drug of choice for syphilis until the arrival of penicillin in the 1940s (Aminov, 2010; Hudzicki, 2009).

The journey to penicillin began in 1928 when Alexander Fleming noticed mould growing on a Petri-dish of *Staphylococcus* bacteria. He observed that the mould produced some self-defence chemical that seemed to be preventing the bacteria around it from growing (Acuña, 2003; Abraham and Chain 1988). He also observed that the chemical could kill bacteria. Twelve years later and after series of trials, scientists succeeded in the purification of the active substance from the mould which they named penicillin (Acuña, 2003). This scientific breakthrough

transformed medicine worldwide and set up the stage for future paradigms in drug discovery research**.** The following decades saw the development of new classes of antimicrobial drugs which ushered in the golden era of antibiotics. Between 1950 and 1970, research into antimicrobial development peaked which resulted in a number of new antibiotics, some of which made their way up to the patient's bedside (Owens, 2008; Powers, 2004). This era was sadly followed by a gradual decline in the synthesis and discovery of new classes of antibiotics. Consequent upon this decline in discovery and development of novel antimicrobials, drug resistant pathogens began to evolve (Iskandar *et al.,* 2022).

By the end of the 19th century, bacteria have become resistant to the original penicillin and nearly the full array of contemporary antibiotics and the need for research into the development of new antibiotics to contain resistance had become significant (Iskandar *et al.,* 2022). Since no new drug discovery happened after the golden era, the mainstream approach for the development of new drugs to combat emerging and re-emerging resistance has been the modification of existing antibiotics (Chastre, 2008). These formularies were either derivatives of existing antibiotics or approved for use in combination with existing antibiotics. They are not new treatments in the true sense of new antibiotics with new mechanisms of action as they follow same pathway and act through the same target site which the resistant pathogens are able to bypass.

The innovation gap is widening between the introductions of new molecular classes of antibiotics: the fluoroquinolones in 1962 and the oxazolidinone linezolid in 2000 (Walsh, 2003). This calls for renewed commitment to novel approaches in the discovery of antimicrobial molecules and therapeutics to tackle resistant pathogens as modification of existing classes of antimicrobials is no longer enough to contain AMR which is developing at a faster pace (Poole, 2014; Walsh, 2003).

1.1.3 Antimicrobial agents: Definition and classification

Antimicrobials are naturally-occurring, semi-synthetic and synthetic compounds with selective antimicrobial activity that can be administered orally, parenterally or topically and are used in human and veterinary medicine to treat and prevent diseases (Ferri *et al.,* 2017). They are generally used to suppress the growth of, or destroy micro-organisms including bacteria, viruses, fungi and parasites. The World Organisation for Animal Health (WOAH) and Food and Agriculture Organisation (FAO) expanded the scope of antimicrobial agents to include any substance that exerts antimicrobial activities on disease causing microbes with no or minimal damage to the host (OIE, 2018; World Health Organisation, 2014).

Antimicrobials act against all microbial varieties and thus can be specifically classified according to the microorganisms they act against (antibacterials act against bacteria; antivirals act against viruses; antifungals act against fungi; antiparasitics act against parasites etc.). They can also be classified by functionality (microbicidal for a group of antimicrobial agents capable of killing the microbes or microbiostatic for the antimicrobials that merely inhibit their growth (Xiong *et al.,* 2018; Wintersdorff *et al.*, 2016; Giedraitienė *et al.*, 2011). Broadly, there are four main classes of antimicrobials based on the type of microorganism they exert their antimicrobial activity upon which includes; antibacterial, antiviral, anti-fungal and anti-parasitic (Xiong *et al.,* 2018; World Health Organisation, 2016).

1.1.3.1 Antibacterial drugs

Antibacterials are a group of drugs that can kill or inhibit growth of bacteria and are used to treat infections of bacterial origin (Browne *et al.,* 2021; Bryskier, 2005) . Their functionality is linked to or due to their pharmacodynamics and chemical structures (Driscoll *et al.,* 2007). Antibacterials are the most prescribed and used of all the classes of antimicrobial agents (US-CDC, 2019). Physicians rely hugely on antibacterials to manage a range of medical conditions including immune-compromised individuals and patients receiving organ transplants who could easily develop life threatening complications from bacterial infections in the absence of

antibacterial treatment (Hidron *et al.*, 2008). The use of antibacterials as prophylaxis in post-surgical procedures which carries high risks of developing sepsis, and their frequent use in management of commonly occurring infectious diseases have saved millions of lives (Ghose, 2013). These factors justify the high demand of antibacterials and the consequent rise in bacteria resistance to frequently used antibacterial agents (Grünewald and Ruf, 2016). The ever-growing lists of antibacterial resistant pathogens is of great concern as this has expanded to now include resistance to some third-line drugs such as vancomycin and those in the carbapenems group. Other drug resistant bacteria pathogen of concern includes: Methicillin-resistant *Staphylococcus aureus* (MRSA), Carbapenem-resistant *Acinetobacter*, *Clostridioides difficile* (*C. difficile*), Carbapenem-resistant *Enterobacterales*, Drug-resistant *Neisseria gonorrhoeae*, Vancomycin-resistant *Enterococcus* (VRE), Multidrug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*), Erythromycin-resistant Group A *Streptococcus*, and Clindamycin-resistant Group B *Streptococcus*. The problem of antibiotic resistance requires increased efforts towards identifying new antibacterial agents that will be effective against pathogens with the highest resistance to frequently prescribed antibacterial agents. Potential approaches for this will involve expanded sampling and continuous surveillance to gain a comprehensive understanding of antibiotic resistance and microbial physiology (Essack *et al.*, 2017; World Health Organisation, 2014).

1.1.3.2 Antifungal drugs

Antifungals are used to destroy or prevent fungal growth. Clinically, they are used to combat diseases such as athletes' foot, ringworm, thrush and a list of other infections (McManus and Shah, 2019; Dismukes, 2000). Apart from their use in clinical medicine, antifungal agents have other applications in household products for the control of molds and fungicides for agricultural use (Ghannoum and Rice, 1999). Like bacteria, fungi can develop resistance. The downside

here unlike antibacterials is that antifungal drugs are limited in variety, therefore antifungal resistance can severely limit treatment options.

The development of a broad armamentarium of antifungal agents is made difficult due to the intricacies in finding molecular targets for antifungal activity without causing damage to the human host. This is because at the molecular level, the ultrastructure of fungal organisms and human cells are similar. Given that fungi are eukaryotes like their human hosts, the availability of agents that can be safely exploited for fungi management is thus limited (Espinel-Ingroff, 2019). These unique molecular features of fungi in addition to the extended use of antifungals outside human medicine is encouraging fungi resistance to the already limited treatment options. Persistent use of antifungals in agricultural domain is contributing to resistance in people exposed to those fungicides and thus, making antifungal resistance another clinical threat after antibacterial resistance (Cokol *et al.*, 2011). Although antifungal resistance is developing at a slower pace than antibacterial resistance, timely interventions are urgently needed in the area of development of new drugs to start containing this problem (Kathiravan *et al.*, 2012; Cokol *et al.*, 2011).

1.1.3.3 Antiviral drugs

Antiviral drugs are a class of medications used for the prevention, treatment or management of viral infections (Cani *et al.*, 2019). Viral infections are quite common, some of which are self-limiting (*i.e.* they can resolve without treatment). This phenomena leaves the need for prescription of antiviral drugs oftentimes for more serious viral infection like retrovirus infections, including HIV, and influenza (Ferguson *et al.*, 2005). Resistance to antiviral drugs were not considered a public health threat until after the 2009 swine flu pandemic when the seasonal H1N1 virus developed resistance to oseltamivir. This raised concerns over antiviral resistance from influenza virus strains which can rapidly spread within the community and is capable of posing huge public health threats (De Clercq and Li, 2016; Razonable, 2011). Due

to the transmissibility pattern and contagiousness of some viral infections, and its associated life threatening consequences, surveillance and phenotypic susceptibility testing to quickly identify emerging antiviral resistance threats needs to be prioritised (Cani *et al.,* 2019).

1.1.3.4 Antiparasitic drugs

Antiparasitic agents are a group of drugs used to combat infectious diseases caused by parasites such as leishmaniasis, malaria, chagas disease and many others. Some notable parasites include: nematodes, cestodes, trematodes, and protozoa (Gelband and Delahoy, 2014). Parasitic diseases stands amongst the most prevalent and severe diseases globally (Kappagoda *et al.,* 2011). Parasites have also developed clever mechanisms to evade the immune system suppression thus making the control of parasitic diseases increasingly challenging without vaccines. Vaccines have been recommended for prevention of certain parasites like helminths which are endemic in Low-Medium-Income Countries (LMICs), but since vaccines are not available yet, treatment rely mainly on antiparasitic agents (Fruci and Poole, 2016; Pal *et al.*, 2015). Treatment of parasite infection is further compounded by resistance occasioned by scarcity of newer range of drugs. The available antiparasitics have been overused in communities and in mass control programs, a practice that fuels resistance.

Resistance of *Plasmodium falciparium* (the most virulent species of malaria causing parasites) to chloroquine and sulfadoxine-pyrimethamine has been recorded as early as 1955. *Plasmodium falciparium* is equally beginning to develop resistance to artemisinin-based combination therapy (ACTs), a newer formulation that was developed to mitigate resistance to chloroquine. Similarly, resistance to a range of anthelminthic (a group of antiparasitics used for treatment of intestinal worm infestation) has been recorded to frequently prescribed drugs like metronidazole and albendazole (Woodward, 2013). The ability of parasitic infection to develop and spread resistance within rural communities is high due to poor living condition and availability of carrier vectors in those settings. This situation makes parasite infection a

bigger threat to health in low income settings as well as to global health (Kapoor *et al.,* 2017; Van Hoek *et al.,* 2011).

Like other microorganisms, parasites will continue to evolve and develop resistance. However, this natural process may be slowed down by adoption of strict quarantine measures, sustainable use of available antiparasitic agents and drug combination strategy. These approaches in addition to surveillance informed treatment guidelines will ensure antiparasitic drugs remain effective for as long as possible (Kappagoda *et al.,* 2011).

1.1.4 Mechanisms of antimicrobial resistance

Alexander Fleming was among the first who cautioned about potential bacteria resistance to penicillin if used inappropriately. In his 1945 Nobel lecture, he said "There is a danger in antibacterial under-dosing and that exposing the microbes to non-lethal quantities of the drug will make them develop resistance" (Alexander 1945, p.93). In a later review on the development of antimicrobials, World Bank (2016), Galimand *et al.* (2003) and Gootz (1990) again reported that antimicrobials have safety and efficacy advantages but must be used appropriately to avoid reversal to pre-antimicrobial era. Sadly, a century after that novel scientific breakthrough in antimicrobial discovery, overuse and misuse are now rendering these drugs less effective through a chain of mechanism driven by reduced drug sensitivity and selective pressure.

As shown in figure 1.1, AMR occurs through natural evolutionary selection processes where certain microorganisms continuously thrive in the presence of antimicrobial agents, thus obtaining a selective advantage (Ragheb *et al.,* 2019). These processes involve genetic mutations in the deoxyribonucleic acid (DNA) of these microorganisms which confer resistance by triggering various mechanisms including the production of enzymes. These enzymes in effect destroy antimicrobial agents by rendering them inactive. The acquisition of this drug inactivating capability and other intrinsic abilities suggest that AMR has long been

established (Lin *et al.*, 2016; Uchil *et al.*, 2014; Yigit *et al.*, 2011). As one or more organisms mutate and become resistant, treatment with antimicrobial will only be able to destroy the non-resistant organisms, thus creating an environment for resistant pathogens to multiply and populate the human body.

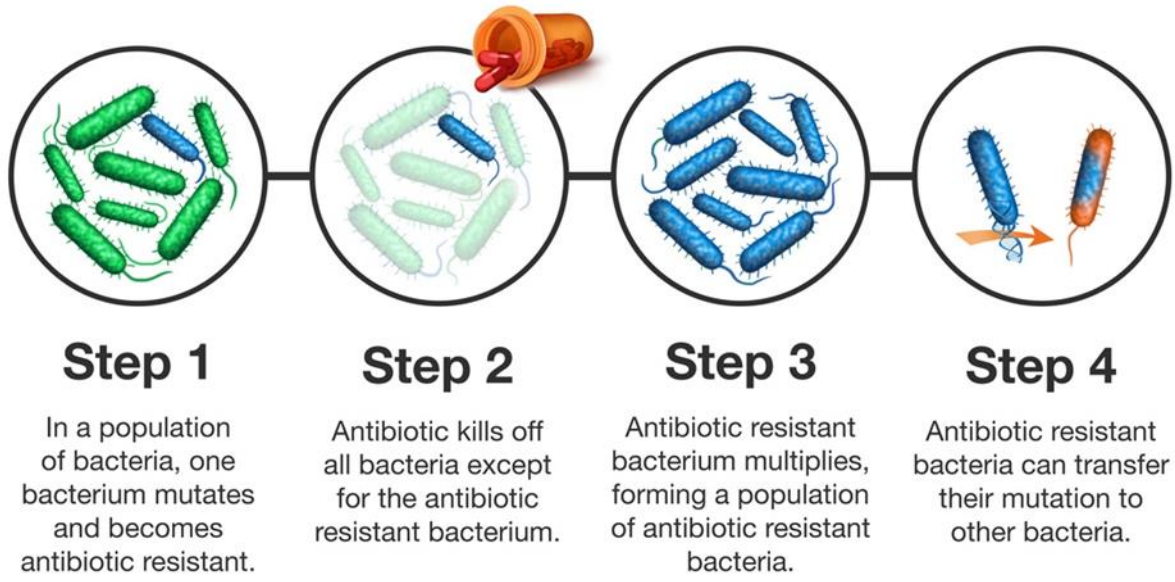


Figure 1.1 Process of resistance development, Source: https://www.acne.org/the-dangers-and-ineffectiveness-of-antibiotics-for-acne

Antimicrobials are developed to exert their action in diverse ways including: inhibition of cell wall synthesis, inhibition of protein synthesis, inhibition of nuclei acid synthesis, inhibition of folate synthesis, and depolarisation of cell membrane (Mann, 2005). This wide range of mechanisms for exerting antimicrobial action is expected to provide better control over microorganism drug resistance but this is beginning to fail due to improper stewardship of antimicrobial agents. Antimicrobial misuse has helped microorganisms develop mechanisms that enable them bypass the therapeutic effect of drugs through: reduced cell wall permeability; modifying a drug target; inactivating a drug; and acquiring efflux pump (Galimand *et al.*, 2003). Figure 1.2 shows overview of antibiotic targets and the established bacteria AMR mechanisms to counter the drugs therapeutic efficacy. These mechanisms of resistance are

mediated through intrinsic (innate) or extrinsic (acquired) attributes of microorganisms (Høiby *et al.*, 2010).

Intrinsic resistance is described as the inherent characteristic of an organism which makes them naturally resistant to a certain antimicrobial drug or a family of antimicrobial agents (Reygaert, 2018; Tenover, 2006). This type of resistance is predictable because it is consistent with a particular group, genus, or species (Rawat and Nair, 2010). Reduced cell wall permeability and acquisition of efflux pump are the two major mechanisms for mediating intrinsic resistance (Shaikh *et al.*, 2015; Poole, 2014).

1.1.4.1 Reduced cell wall permeability

This is an intrinsic mechanism used by certain bacteria pathogen to block penetration of antimicrobial agents that are formulated to penetrate their cell and alter intracellular processes (Xiong *et al.*, 2018; Reygaert, 2018). This type of resistance is common among Gram negative bacteria that possess an extra outer cell membrane which confer on them a tight barrier. This tight barrier prevents large molecules of drug from penetrating their cell and exert antimicrobial activities on them (Pisoschi *et al.*, 2018; Van Hoek *et al.*, 2011). Typical of this type of resistance is the resistance of Gram-negative bacteria to vancomycin (a glycopeptide antibacterial drug). This is consequent upon the large size of the molecules of this group of agents which are too big to penetrate the extra outer cell wall of these Gram negative bacteria (Poole, 2014). Apart from acquisition of extra outer membrane, Gram negative bacteria as well as some Gram positive bacteria have structures called porins. These porins act as pores through which molecules can pass through into the membrane of the cell. A decrease in the number of porins and mutations can change the selectivity of the porin channel which excludes certain antibiotics from penetrating into the bacteria cell (Haque *et al.*, 2012; Patel, 2005).

1.1.4.2 Acquisition of efflux pump

This is another pathway of innate resistance by which certain microbes resist penetration of antibiotics (Freire-Moran *et al.*, 2011). The function of the efflux pump mechanisms serves to rid the bacterial cell of toxic substances or antibiotics (Rawat and Nair, 2010; Nicolau and Oliver, 2010). Efflux mechanisms could also offer resistance to similar class of antibiotic or a set of unrelated antimicrobials, which results in multi-drug resistance (MDRs) (Akinyemi and Fakorede, 2018; Gutiérrez *et al.*, 2007).

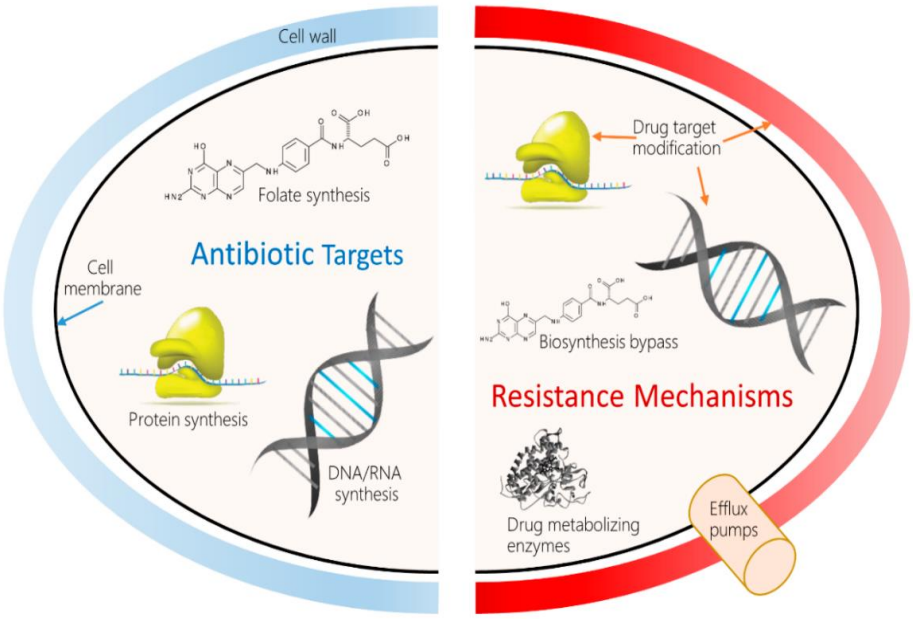


Figure 1.2 showing antimicrobial drug target sites and molecular mechanisms of AMR. Left: the most common classes of antibiotics currently in use inhibits bacterial growth by impeding the biosynthesis of peptidoglycan, a main constituent of cell wall; disrupting the bacterial cell membrane; and inhibiting DNA replication, gene transcription and translation, and folate biosynthesis. Right: Corresponding mechanism of resistance developed by bacteria to resist these attacks, such as pumping the antibiotic out of the cell, inactivating the drug using specialized enzymes, modifying the target structures to prevent interference, and bypassing the affected metabolic pathway. Source https://www.mdpi.com/1422-0067/21/4/1363

Extrinsic or acquired resistance is mediated by changes in an organism's natural genetic makeup through altered cellular morphology and function (Toro *et al.*, 2011). The genetic changes resulting from acquired resistance are typically caused by gene mutation and/or acquisition of genes from other organisms via gene transfer (Tran-Dien *et al.*, 2018; Giedraitiene *et al.*, 2011). Unlike intrinsic resistance, acquired resistance is harder to track as

each new outbreak or isolate may have acquired resistance to a different spectrum of antibiotics. (Marston *et al.*, 2016; Freire-Moran *et al.*, 2011). Antimicrobial drug inactivation and modifying a drug target are the two mechanisms for acquired resistance.

1.1.4.3 Antimicrobial drug inactivation

This is the most frequently studied type of resistance (Reygaert, 2018). This resistance is achieved using enzymes produced by the microorganism to inactivate the antimicrobial agent (Roberts and Schwarz, 2017). The development of enzymes that specifically inactivate antibiotics is one of the first resistance mechanisms observed in bacteria (Zervosen *et al.*, 2012). It is an effective technique used by microorganisms to withstand the action of several types of antibiotics (Rousham *et al.*, 2018). Notable amongst this type are the enzymes that mediate β-lactam ring hydrolysis. The production of plasmid-mediated resistance to β-lactamases has contributed to the research into development of new parenteral antibiotics that can withstand hydrolysis of β-lactamases (Thu Trang *et al.*, 2013; Yigit *et al.*, 2011). This form of resistance prevents penetration of b-lactams antibiotics (penicillins, cephalosporins, carbapenems and monobactams) which constitutes a broad range of commonly used agents in clinical practice (Dheda *et al.*, 2017; Hawkey and Jones, 2009).

1.1.4.4 Drug target modification

Resistance through target modification aids microorganisms to evade therapeutic action of drugs by altering the shape or size of the binding target of the antibacterial agent through chromosomal mutation. This form of resistance reduces antibiotic's binding affinity to the target sites of the microorganism. The inability of this binding to occur inhibits the microbicidal or microbiostatic actions of the antimicrobial agent (Rousham *et al.*, 2018; Uchil *et al.*, 2014). Across the various types of resistance mechanism, one fundamental factor responsible for developing each form of these resistance is over exposure to antimicrobial agents (Kapoor *et al.*, 2017; Van Hoek *et al.*, 2011). Many years of improper use of antimicrobials in human and

veterinary medicine, animal husbandry, and livestock have culminated in unremitting selective pressure and increase in the development of resistance in microbial communities.

1.1.5 Factors accelerating antimicrobial Resistance

The acquisition of antimicrobial resistance is a natural evolutionary response to antimicrobial treatment, but the One health linkages shown in figure 1.3 contribute to exacerbate the issue (Laxminarayan *et al.,* 2016; 2015). Tacconelli *et al*. (2018) documented that broad and intertwined mechanisms encompassing social, economic and environmental dimensions are increasing the prevalence of antimicrobial-resistant microorganisms at a societal level, arising mainly from human overuse, use in animal production and environmental pollution.

1.1.5.1 Misuse and overuse

Antimicrobials are among the most commonly prescribed drugs in human medicine (Mendelson *et al.,* 2016). Incidentally up to 50% of all antimicrobials given are not needed and this irrational use of antimicrobial medications is considered to be a major driver for antimicrobial resistance in human (Mendelson *et al.,* 2016; Holmes *et al.,* 2016). In low income settings where healthcare delivery largely depends on informal providers, the overall amount of antimicrobial prescription is at the lowest which suggests huge over the counter buying (World Health Organisation, 2014). Kariuki *et al*. (2018) identified prescribers and dispensers' factor as a driver of antimicrobial misuse in settings where patients pay out of pocket for healthcare. Prescribers and dispensers in such settings are often profit-driven and ever-willing to sell antimicrobials over the counter as quick fix for mild to moderate illness which are often self-limiting. In high income settings, despite guidelines and stewardship programmes to promote prudent use of antimicrobials, over prescribing arising from physicians' inability to manage patient pressure in primary care settings remain an important driver of AMR. (Fouz *et al.,* 2020). Antimicrobial misuse is also influenced by health system policies and regulatory framework (Fouz *et al.,* 2020). As suggested by Sulis *et al*. (2020) an effective way to balance

therapeutic choice and collateral damage is by auditing prescribing and dispensing practices using external standard procedures. In addition, Thandar *et al.* (2020) recommended the development and publishing of national guidelines for treatment algorithms to foster appropriate use of antimicrobials, encourage educational support and also enforce professional registration as mandatory requirements for prescribers.

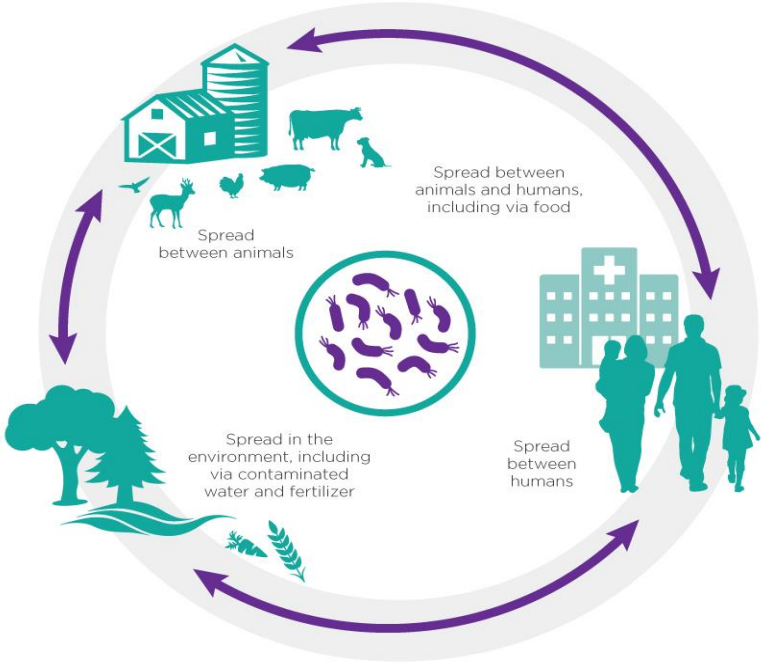


Figure 1.3 Showing One health linkages (human health, animal health, and the environment) to the issue of AMR. In a continuous circle, it shows how AMR is spread between: 1) humans 2) animals and humans including via food 3) animals 4) the environment, including via contaminated water and fertilizers. Source: A Pan-Canadian framework for action https://www.canada.ca/content/dam/hc-sc/images/services/publications/drugs-health-products/tackling-antimicrobial-resistance-use-pan-canadian-framework-action/fig2-eng.jpg

1.1.5.2 Agricultural use of antimicrobials

Farming processes with antimicrobial suboptimum management is posing challenge to effective control of AMR. More antimicrobials are used in veterinary medicine, food production and in meat-producing animals than in humans (Ragheb *et al.*, 2019; Rinsky *et al.*, 2013). Studies have shown that evolution of antimicrobial resistance is in part, as a result of the selective pressure exerted by antimicrobial use outside of human medicine (Yam *et al.*, 2019). The connection between the use of antimicrobial growth promoters in farm animals and

the transmission of antimicrobial-resistant pathogens from animals to humans have been reported as far back as 1960s (Dung *et al.,* 2020). Excessive use of antimicrobials in food animals is driving resistance at an alarming rate. An estimated 131,109 tons of antimicrobials were used in food animals in 2013 and this figure is projected to rise to 200,235 tons by 2030 (Ragheb *et al.,* 2019; Rinsky *et al.,* 2013). Antimicrobial resistance in animal cultivation is now well established and affects zoonotic pathogens such as *Salmonella* serovars and *Campylobacter* spp more (Fouz *et al.,* 2020). Antimicrobial resistant bacteria originating in animals can be transmitted to humans through the environment, food products, and/or by direct contact (Spoor *et al.,* 2013).

The observed and anticipated risks from continuous use of antimicrobials in animal cultivation, coupled with facts from the Swann's landmark study regarding use of antimicrobials in meat producing animals gave rise to the European prohibition on the use of antimicrobials for the advancement of animals growth (Mendelson *et al.,* 2016; Laxminarayan *et al.,* 2015). This prohibition did not take effect as the use of antimicrobials for promoting growth in meat producing animals continued until 2006 when it came into full effect. However, outside the European Union, including the United States, the use of antimicrobials in poultry farming still exists. In the United States specifically, antibiotic use in turkey farming is reported to be about 9 times as high as the quantity used in United Kingdom, and US chickens are given twice as much antibiotics as in the United Kingdom (Singer *et al.,* 2023; Tiseo *et al.,* 2020; ASOA, 2020). Information on antimicrobial use in farm animals is limited from developing countries. However, estimates suggest that uncontrolled use of antimicrobials in food animals is a serious concern (Laxminarayan *et al.,* 2016; 2015).

A three year retrospective survey of antibiotic usage in livestock production in South Western Nigeria showed that tetracyclines, fluoroquinolones and beta-lactams/aminoglycosides constitutes (33.6%), (26.5%) and (20.4%) of the majority of antibiotics used over 3 years

(Adesokan *et al.*, 2015). Another survey of antimicrobial use in poultry farms in Nigeria provides additional evidence that the poultry production environment in the country represents an important reservoir of antibiotic resistance genes which poses potential public health risk to human populations (Njoga *et al.*, 2021; Joshua *et al.*, 2018).

As already established, drug resistant pathogens can pass to humans through the food chain. A Danish study of commercially sold pork found 40% of the pork meat contained methicillin-resistant *Staphylococcus aureus* (MRSA) which can easily be passed to human either by handling or consumption of this meat (Poole, 2014). The transfer of ESBL and AmpC-β-lactamase genes on plasmids and *E-coli* clones from livestock to humans through the food chain is driving resistance in human and also a growing public health concern (Holmes *et al.*, 2016). Apart from the food chain route, antimicrobial resistance can pass from livestock to human through direct contact, this is common amongst livestock keepers who dwell in same setting with these farm animals. This type of antimicrobial resistance extends to both commensals and opportunistic pathogens (Mendelson *et al.*, 2016).

1.1.5.3 Poor environmental waste management

Resistance arising from poor waste management and contaminants from the pharmaceutical industry is also driving resistance in the environment (Chee-Sanford *et al.*, 2009). Antimicrobial resistant pathogens have also been recovered from pre-treatment and post-treatment processes of waste material. Antimicrobial-resistant pathogens have also been discovered from surface and ground water. The driver of resistant pathogens through waterways arises from disposal of pharmaceutical waste containing active ingredients from manufacturing plants into river/waterways or surrounding soil. This process favours the selection of resistant organisms and serves as channels for transmitting antimicrobial resistant pathogen to the environment (Diene and Rolain, 2013). Absence of regulation and/or lack of

enforcements of regulations regarding disposal of pharmaceutical waste into rivers or the environment are encouraging this threatening act in developing countries.

The universal emergence, survival and transmission of antimicrobial-resistant pathogens by humans, animals and the environment is hugely affected by poor access to clean water, open drainage networks, differences in health-care infection-control procedures, insufficient availability of antimicrobials and diagnostics in many LMICs (Silva *et al.*, 2020). Although some of these issues exist in high-resource environments, in low and middle-income countries, they are particularly important drivers of antimicrobial resistance (Mishra *et al.*, 2020). Antimicrobial resistance is clearly driven via complex channels all of which combine to complicate containment efforts. This means that for any AMR containment strategy to be successful, knowledge of antimicrobial use pattern and drivers, and how these affect resistance development must be considered a pre-requisite in designing solutions to the problem of AMR (Wellington *et al.*, 2013)**.**

1.1.6 Transmission of resistant pathogens

Resistant pathogens can easily be transmitted via a variety of routes though rate of transmission can be impacted by factors like setting (Pendleton *et al.*, 2013). Healthcare facilities and resource-deficient communities where infection prevention and control practices are not observed serve as reservoir for AMR. Broadly, transmission of AMR can be viewed from a triad perspective (Gerrard, 2016; Otter *et al.*, 2011).

1.1.6.1 Health care facilities

Health care facilities serves as important breeding ground where resistant bacteria thrive and having many sick people in close proximity to each other supports spread of resistant strains (Weiner *et al.*, 2016). The risk is even higher for hospitalised patients, who are exposed to additional risk factors. Poor hygiene practices also enables the spread of resistant bacteria through sharing of materials or work tools among health care workers (Otter *et al.*, 2011).

Other factors that facilitate spread of resistant pathogens include insufficient sanitation, crowded wards and few isolation rooms (Chalmers *et al.,* 2014; Allegranzi and Pittet, 2009). Resistant pathogens can spread from one person to another through direct contacts or surface (such as a doorknob) contamination and transmitted to another person who touches the surface (Pendleton *et al.,* 2013).

1.1.6.2 Easy travel routes

Globalisation has further enabled spread of infectious diseases across the world as millions of people traveling across borders have the potential of carrying resistant pathogens (Pendleton *et al.,* 2013). Many studies have demonstrated that a large proportion of international travelers acquire drug resistant pathogen during visits in areas with a high prevalence of resistant strains (Yam *et al.,* 2019; World Health Organisation, 2014; Spoor *et al.*, 2013). Bengtsson-Palme *et al.* (2018) documented that animals for food production and vegetables are equally transported across borders, and bacteria pathogens follow along route of transportation. According to Chang *et al.* (2015) these routes of transmission contributes to the complexity of antimicrobial resistance and buttresses the fact that AMR is a global issue since resistant pathogens can successfully spread to other parts of the world.

1.1.6.3 Animals to humans

Resistant pathogens can be transmitted from animals to humans and vice versa (Weese and van Duijkeren, 2010). Animals inhabiting resistant pathogens can transfer them to humans by close contact in the case of animals kept as pets or raised for food (Muloi *et al.*, 2018; Economou and Gousia, 2015). Farmers, livestock keepers and veterinarians are at risk of getting infected by resistant bacteria due to their association with livestock (Ludden *et al.*, 2019). Farmers and their families have been found to be colonised with the same resistant bacteria as their animals, which is capable of spreading further in the community (Economou and Gousia, 2015). Antimicrobials used to treat and prevent infections in animals as well as those used for growth

promotion are exactly the same antimicrobials used in humans (Brown *et al.*, 2017; Spoor *et al.*, 2013). Due to repeated treatment, these animals become colonised with antibiotic resistant bacteria and subsequently spread these resistant strains to other animals and humans (Arenas *et al.*, 2017). During slaughter or when processing meat from animals which can comprise those harboring resistant pathogens and those that are not, these resistant pathogens can potentially be picked up by other non-harboring product and the transmission chain goes on (Bortolaia *et al.,* 2016). Eating food contaminated with resistant bacteria may cause an infection or colonisation of the gut with resistant strains (Hong *et al.*, 2013).

As resistant bacteria are frequently detected in humans, environment and livestock meat product, studies have tried to examine the difference or similarities of the resistant pathogen identified in human and those identified in animals to help determine the rate of cross transmission (Ludden *et al.*, 2019; Olonitola *et al.,* 2015b). Some studies have identified significant similarities between the antibiotic resistance genes found in meat and those found in humans (Lupindu *et al.*, 2015). Proper cooking and handling of food is encouraged to help break this chain of infection in addition to surveillance and monitoring for new resistance (Mathew *et al.,* 2007).

1.1.7 Global AMR policies and strategies

In recognition of the rising health and economic threats from AMR, the 68th World Health Assembly (WHA) in May 2015 endorsed the Global Action Plan on Antimicrobial Resistance (GAP-AMR) which outlines five objectives. The goal of the GAP is to provide a coordinated, coherent, comprehensive and harmonised agenda for the control of AMR at national, regional and global levels. The tripartite collaboration between the United Nations (UN), Organisation for Food and Agriculture (FAO) and the World Health Organisation (WHO) was also initiated with support from countries, private sector, academics and civil society Organisations to address the economic and social challenges posed by AMR (Essack *et al.*, 2017; World Bank,

2016; World Health Organisation, 2016; World Health Organisation, 2015). To ensure the sustainability of livestock production and the protection of terrestrial and aquatic animals from acquiring antimicrobial resistance, the FAO and World Organisation for Animal Health (WOAH) enforced effective antimicrobial use in animals (FAO, OIE and WHO, 2016). Despite these global AMR tackling efforts, it was recognised that robust AMR surveillance information needed to enhance these global containment strategies is lacking. This called for AMR surveillance to be prioritised and the launch of the Global Antimicrobial Resistance and Use Surveillance System (GLASS). GLASS was charged with the responsibility of ensuring global representation of AMR data through provision of standardised AMR surveillance approach and aggregation of surveillance data from participating countries (World Health Organisation, 2016).

Uptake of GLASS from low-and-medium-income countries (LMICs) have been regarded as poor (Fonjungo *et al.*, 2018). Consequently, good quality and representative data on the global burden of AMR is lacking. This to a large extent is owning to the underrepresentation of surveillance information across regions as most AMR surveillance data comes from high income countries (ASLM-MAAP, 2018). In Africa, understanding the impact and magnitude of AMR is greatly challenged by poor continent-wide surveillance data (Ndihokubwayo *et al.*, 2013). Perovic and Schultsz (2018) identified lack of laboratory infrastructure as one of the possible bottlenecks to AMR surveillance in Africa. Due to the gaps in existing AMR data, the global status of AMR is regarded as skewed, exaggerated and quite tentative (De Kraker, Stewardson, and Harbarth, 2016; World Health Organisation, 2014). Undoubtedly, low-quality surveillance data means soaring rates of AMR which is difficult to track and map without real-time data. Since data from AMR surveillance is required to drive containment efforts, these gaps in data representation impacts intervention efforts and thus undermines the ability to

identify emerging trends/threats, monitor impact of interventions, estimate the burden of AMR and provide data needed for research (Seale *et al.*, 2017).

Antimicrobial drugs are considered integral in infectious disease management due to their ability to prevent or kill disease causing microorganisms (Ferri *et al.*, 2017). Therefore, to ensure continuity of successful treatment and prevention of infectious diseases, antimicrobials must be used in a responsible way to remain effective. To achieve this goal, it is important for countries to intensify efforts towards prioritising AMR surveillance and develop a national action plan (NAP) that will guide implementation of established containment strategies (OIE, 2018; World Health Organisation, 2014).

1.1.7.1 The Nigeria action plan

In response to the WHO call for the development of National Action Plan (NAP) at national levels, Nigeria established an AMR technical working group (TWG) to assess the magnitude of AMR in the country. The assessment observed that the risk posed by AMR to essential medicines and its safety makes AMR an issue of national priority for Nigeria. It further highlighted challenges across all levels of governance, such as; lack of AMR diagnostics and antimicrobial use (AMU) reporting structures (Nigeria Centre for Disease Control, 2017). The outcome of this assessment informed the development of a national action plan which focused on the WHO-GAP five strategic areas: 1) improving awareness and understanding of antimicrobial resistance through effective communication, education and training; 2) strengthening the knowledge and evidence base through surveillance and research; 3) reducing the incidence of infection through effective sanitation, hygiene and prevention measures; 4) optimising the use of antimicrobial medicines in human and animal health; and 5) preparing the economic case for sustainable investment in new medicines, diagnostic tools, vaccines and other interventions (Nigeria Centre for Disease Control, 2017). Following the NAP development and implementation, laboratory-based surveillance of AMR commenced at

designated sentinel sites in line with WHO-GLASS recommendations (Anzaku *et al.*, 2018; Oloso *et al.*, 2018; Nigeria Centre for Disease Control, 2017). Despite this containment effort, AMR still poses challenge to effective management of infections due to considerable gaps in our understanding of AMR, including the magnitude of drug-resistant infections in the country (Mohammed *et al.*, 2018).

An earlier review of Nigeria surveillance system by Ayukekbong *et al*. (2017) highlighted that the surveillance approach adopted by the system creates the need for a process to evaluate the effectiveness of this approach and other AMR related projects in order to ensure measurable progress of containment efforts. Notably, AMR surveillance in Nigeria at present involves tertiary healthcare settings only. Whilst this is not unusual, the suitability of this approach with reference to the country's unique characteristics and challenges need to be assessed. As noted by Iskander *et al*. (2021) there is no 'One size-fits-all' approach to surveillance and as such, surveillance methodology must be tailored to specific location needs. This can only be achieved by understanding the particularities of each country and aligning them to regional, national and international containment goals. Through continuous assessment and reassessment of surveillance systems, gaps are identified and addressed for greater surveillance efficiency and sustainability **(**Fleming Fund-Nigeria, 2019).

1.2 Problem statement

AMR has been increasing steadily over the years and is now a major public health problem worldwide (World Health Organisation, 2016). This problem has the capacity to overwhelm health systems and lead to unprecedented health and economic crisis. Deaths arising from AMR is projected to reach a record number of 10 million yearly by 2050 with LMICs to bear about 40% burden of these deaths (O'Neill, 2016; O'Neil, 2014). These statistics are not surprising particularly from LMICs due to poor public health practices and poor living condition in these settings. In many developing countries including Nigeria, the spread of

infectious diseases from poor 'water, sanitation and hygiene' (WASH) practices is a source of growing concern due to the inter-sectional and cross-sectional dimensions of AMR and WASH as well as dumping of inadequately treated waste from the pharmaceutical industry into water ways (Nadimpalli *et al.,* 2020; Anzuka *et al.,* 2018). The Interagency Coordination Group report on AMR indicated that the spread of infectious pathogens through unsafe water contributes to gastrointestinal diseases which increases even further the demand for antimicrobial treatment and selective pressure (UN-IACG, 2016). A combination of other factors including: shortage of licensed prescribers, poor access to quality medicines, proliferation of under-regulated patent medicine vendors, drug markets and hawkers, means that Nigeria suffers severe access problems whilst simultaneously facing a crisis of irrational drug use. These challenges are also complicated by out of pocket (OOP) spending for healthcare services which encourage patients to patronise cheaper and unlicensed care providers, many of which offer substandard level of care (Laxminarayan *et al.,* 2015). Drug misuse also extends to the agricultural sector where antimicrobials are liberally used therapeutically for growth promotion (Adebowale et al., 2023). The armamentarium of problems confronting Nigeria healthcare system strongly correlates with factors that accelerate antimicrobial misuse which has been implicated as a major driver of AMR (Nasir *et al.*, 2015). It suffice to say that in view of these challenges and other contributing factors, that AMR is a problem in Nigeria that requires concerted effort towards tackling it.

1.3 Justification of study

Antimicrobial resistance has global impact but the burden of AMR will largely be borne by LMICs due to unavailability of reliable surveillance data to manage the situation. All age-related death rate attributable to resistance is estimated to be highest in Sub-Saharan Africa at 1.27 deaths per 100 000 (Murray *et al.,* 2022; O'neil, 2014). Remarkably, 85.2% of the poorest

countries and 39.6% of the world's LMICs are in the region of Africa including Nigeria, and this justifies the regional focus of this study (World Bank, 2022).

There is a growing body of literature raising concerns about grossly exaggerated and tentative global estimates of AMR and the impacts of under or over estimation on control policies and strategies, thus highlighting the need to improve quality of data. Despite these concerns, most research continue to focus on morphological, prevalence and incident cases with no studies investigating surveillance methodologies in the context of AMR thus limiting the evidence required to provide targeted support for surveillance system strengthening.

The WHO recognises good quality surveillance data as critical in optimising AMR containment efforts. Despite indicators showing that AMR is a problem in Nigeria, nationwide estimate on burden of AMR is still lacking (NCDCAMRS, 2017). Adequate surveillance information needed to inform containment efforts are not available (Shankar, 2016). Although a surveillance plan is in place as part of the national action plan, Oloso *et al.* (2018) reported that the toolkits adopted by Nigeria to tackle and monitor AMR has not been properly examined for their effectiveness. In their review, they opined that independent studies are needed to evaluate the implementation and effectiveness of the surveillance system post implementation. The surveillance protocols have not been assessed for gaps in data reporting, testing approach, capacity of reporting laboratories, compliance with the WHO standards and key surveillance performance indicators. This paucity of information regarding surveillance attributes and performance makes it difficult to understand how AMR surveillance is functioning and thus negates the ability of containment efforts which relies on surveillance outcome for improvement.

An earlier scoping report of AMR surveillance systems in four African countries including Nigeria further highlighted the need to strengthen AMR surveillance in the country (Dacombe *et al*., 2016). The report also revealed the importance of AMR surveillance as key to

progressing towards AMR containment and indicated that a participatory, systematic needs assessment and joint planning will be required to fully understand how a practicable surveillance system for AMR could be established in Nigeria.

Given the clinical, social and economic impact of AMR and challenges of gathering high quality patient-level data needed for more accurate estimation of resistance, urgent research into Nigeria surveillance system is required (Dunachie *et al.*, 2020; Bernabé *et al.*, 2017; De Kraker, Stewardson, and Harbarth, 2016). Thus, a clear research agenda highlighting the most important current knowledge gaps in AMR surveillance in Nigeria needs to be defined to guide the direction of these research efforts. In this manner, new data that are important to understanding and combating the problem can be utilised in developing future containment initiatives (Ndihokubwayo *et al.*, 2013).

It is in line with these knowledge gaps, coupled with the overall need to improve and strengthen future capacity building for more realistic AMR surveillance that this study was formed. Findings from this study will supplement surveillance efforts by identifying gaps in the current surveillance systems, and provide evidence-based approach for mitigating these gaps as steps for advancing towards applying systematic approach in conducting surveillance particularly in resource constrained regions.

1.4 Research aim

The aim of this research is to examine the capacity and sustainability of antimicrobial resistance (AMR) surveillance and containment strategies in Nigeria.

1.4.1 Research objectives

1. To systematically assess the effectiveness of designs and reporting methodologies for routine surveillance of AMR pathogens in Africa.

2. To conduct a situational analysis of AMR surveillance systems in Nigeria, post establishment of the National Action Plan of 2017.

3. To develop a solution toolkit for effective AMR surveillance in Nigeria.

1.4.2 Research questions

1. What are the gaps in AMR surveillance designs and reporting methodology in Africa?
2. To what extent is Nigeria implementing the surveillance component of its National Action Plan on AMR?
3. What strategies are currently being used for AMR surveillance in Nigeria?
4. How efficient and effective are these strategies in tackling AMR?

1.5 Epistemological foundations of research methodology

The theories of ontology and epistemology have long existed before their use in social sciences to justify methods and methodology of research leading to knowledge (Guba, 1990; Kuhn, 1996). The ontological underpinning of pragmatism aligns naturally with my position as a researcher which holds that there are in fact many different ways of interpreting the world and conducting research to investigate reality and that combination of different approaches may provide a broader understanding of the phenomena being investigated (Crotty, 1998). Pragmatism involves research designs to be based on what will work best in finding answer thus allowing pragmatic researchers to explore innovative and dynamic ways to finding solutions (Scotland, 2012).

Having considered other methodological approaches, I recognise that the best and most logical way to answer the research questions was to use a combination of methods to align with the research objectives thus involving qualitative (interpretive) and quantitative (positivist) avenues (Tucker *et al.,* 2020). Whilst positivist holds that things must be measurable, interpretive agrees for knowledge to be developed through reflection (Smith *et al.,* 2012; Smith, 2004). The quantitative avenue measured relationship within and between variables examined in the study (objective position) whereas the qualitative attempts to find the causal relationship through engaging with respondents (subjective position).

Although it is widely agreed that quantitative and qualitative research methods address different but complementary aspects of research and they can be combined, but it then becomes necessary to probe beneath the surface of the technical level deep to the ontological nuances and epistemological underpinnings. In justification of this method, I have relied on dialectical pluralism which embraces differences in everyday realm of inquiry as the structure for the selected interpretivist and positivist paradigms (Johnson *et al.*, 2014).

1.6 Ethics application

In compliance with the requirements of the conduct of good research practice, ethical approval was sought as part of the preliminary process for this study. An application was made to the Faculty Research Ethical Committee at University of the West of England stating the protocol and declaration of interests where applicable. After careful assessment by the committee, ethical approval was granted on 2nd October, 2020 with the reference number UWE REC REF No: HAS.20.05.180. A copy of the approval is provided in appendix A1.

Chapter 2 Literature review

2.1 Introduction

Responding to complex public health issues like antimicrobial resistance (AMR) requires excellent understanding of its root causes and containment challenges. As the previous chapter explained, microorganisms have developed mechanisms that helps them survive therapeutic effects of drugs and how human actions continue to drive the transmission and spread of resistant pathogens, thus making AMR containment a global issue. In this chapter, a literature search and review of the global epidemiology of AMR is reported to give context to the magnitude, burden and threats of AMR. The chapter then proceeds to review the role of surveillance in AMR containment and the several approaches that are relevant to the containment of AMR. This provides a rich perspective to surveillance scope, attributes and challenges in order to give more context to global and local gaps in current surveillance and AMR containment strategies.

2.2 Global epidemiology of antimicrobial resistance

Antimicrobial resistance is recognised as a concerning global issue. Epidemiological data needed to combat this problem is scarce especially from low-and medium-income countries where surveillance activities are either poor or completely absent (Essack *et al.*, 2017; World Bank, 2016; World Health Organisation, 2014). Available data from active surveillance systems were assessed to provide the regional and global distribution of AMR.

Latest data on invasive bacteria isolates reported by the European Antimicrobial Resistance Surveillance Network (EARS-NET) shows that 96.6% of the twenty-nine European Union/European Economic Area (EU/EEA) countries reported varying degrees of resistance for all eight bacterial isolates under surveillance (*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter species, Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecalis and Enterococcus faecium*). Greece was the only country that

did not report any case of *S. pneumoniae* (EARS-NET, 2022). Overall, the most commonly reported bacterial species in 2021 was *E. coli* (39.4%), followed by *S. aureus* (22.1%), *K. pneumoniae* (11.9%), *E. faecalis* (8.8%), *P. aeruginosa* (6.1%), *E. faecium* (6.2%), *S. pneumoniae* (2.5%), and *Acinetobacter* spp. (3.0%) (EARS-NET, 2022). This report shows increase in the number of reported cases for all pathogens from previous year (2020). The largest increases were observed for *Acinetobacter* spp. (+43%), followed by *E. faecium* (+21%) and *E. faecalis* (+14%), with smaller increases for *S. aureus* (+9.4%), *P. aeruginosa* (+8.2%), *K. pneumoniae* (+8.1%), *S. pneumoniae* (+4.3%), and for the most frequently reported pathogen - i.e. *E. coli* (+2.8%) (EARS-NET, 2022). More than half (53.1%) of *E. coli* isolates, a third (34.3%) of *K. pneumoniae* and a fifth (18.7%) of *P. aeruginosa* isolates reported from the EU/EAA were resistant to at least one antimicrobial group under regular surveillance. Generally, among the antimicrobial groups being monitored, resistance to the carbapenem group was higher in *K. pneumoniae* and *P. aeruginosa* compared to *E. coli. K. pneumonia* resistant to cabapenem continues to increase from +8% in 2019, to +31% in 2020 and a further +20% in 2021 (EARS-NET, 2022; EARS-NET, 2018).

The most striking observation from the 2022 report was the 43% increase in the number of reported cases of *Acinetobacter* species. More worrying is the average resistant rate of *Acinetobacter* spp. to each of the three antimicrobial groups (carbapenems, fluoroquinolones and aminoglycosides) which has more than double (+121%) in 2021. These findings indicate that the situation of *Acinetobacter* spp. in the EU/EEA has deteriorated for the second year in a row (EARS-NET, 2022; EARS-NET, 2018; European Centre for Disease Prevention and Control, 2018). On *S. pneumoniae,* there was an observed decrease in the number of reported cases in 2020 (2.6%) compared to 2019 (5.3%) but the latest report shows that *S. pneumoniae* resistance in the region appeared stable (2.5%) with no significant increase in number of cases (EARS-NET, 2022; Anon, 2019). For *S. aureus*, there has been a sustained decline in the

percentage of methicillin-resistance (MRSA) from 19.6% in 2014 to 16.9% in 2017. This trend has been slightly altered in the following years with the latest report showing an increase of +9.4% from the 2020 report. Despite showing either a significantly decreasing trend or no significant trend, MRSA remains an important pathogen in the EU/EEA as the levels of MRSA were still high in several countries (EARS-NET, 2022; European Centre for Disease Prevention and Control, 2018; Monnet, 2016). Also significant is vancomycin-resistant *Enterococcus faecium* in EU/EEA which has increased from 10.5% in 2015 to 17.3% in 2018 (EARS-NET, 2022; GLASS-Report, 2019; EARS-NET, 2018).

In Asia, review of surveillance data from Asian Network for Immune Pathogen Surveillance (ANSORP) recorded high prevalence rates of *S. pneumoniae* resistance to beta-lactam and the macrolides, particularly erythromycin to which greater than 70% of clinical isolates collected showed full resistant (Kang and Song, 2013). The average resistance rate of *S. pneumoniae* to erythromycin across Asia was 72.7%: 96.4% in China, Taiwan (84.9%) and Vietnam (80.7%) (Kim *et al.*, 2017; Zhao *et al.*, 2017). World Health Organisation (2018) and GLASS-Report (2019) documented 59.3% multidrug resistance (MDR) among *S. pneumoniae* isolates and over 50% of methicillin resistant *Staphylococcus aureus* (MRSA). MRSA has been implicated as the leading cause of hospital acquired infections in the Asian region, including infections such as pneumoniae, surgical site infections (SSIs) and bloodstream infections (BSIs). Zhao *et al*. (2017) observed that *S. aureus* infections caused by MRSA accounted for 25.5% of community associated *S. aureus* (CASA) and 67.4% of health care associated (HCA) infections. Across the region of Asia, varying degree of HCA-MRSA infections were reported: India (22.6%), Philippines (38.1%), Korea (77.6%), Vietnam (74.1%), and Sri Lanka reported highest rate (86.5%) (Kang and Song 2013). For penicillin resistant, prevalence rate of 57.7% was seen in non-meningeal isolates which is beyond previous penicillin resistant rate by 4.6%

(Kim *et al.*, 2017, 2012). In China and South Korea, 2.2% and 0.3% of the total (4.6%) non-meningeal isolates collected showed full resistance to penicillin (Lai *et al*., 2014).

ANSORP study also reported widespread resistance of *S. aureus* from hospital acquired pneumoniae (HAP) to frequently prescribed antimicrobials in the region, including: oxacillin (82.1%), ciprofloxacin (78.2%), clindamycin (64.2%), erythromycin (76.5%) and tetracycline (70.9%) (Zhao *et al.*, 2017; Kang and Song, 2013; Kim *et al.*, 2012). *Pseudomonas aeruginosa* resistance to carbapenem is observed to be high and extremely prevalent in Asian countries (Yong *et al.*, 2014; Lee *et al.*, 2011; Lee *et al.*, 2010). Hospital acquired *P. aeruginosa* resistance to ceftazidime, cefepime, piperacillin-tazobactam, imipenem and ciprofloxacin were reported at 34.7%, 27.7%, 36.9%, 27.2% and 30.1% respectively (Chung *et al.*, 2011). Also imipenem resistant *Acinetobacter* spp associated with hospital acquired pneumoniae was found in the region at varying degrees: Malaysia (86.7%), Thailand (81.4%), India (85.7%) and China (58.9%) (Chung *et al.*, 2011). Indian surveillance report from the study for monitoring antimicrobial resistance trends (SMART) revealed high level of resistance to extended spectrum beta lactamase (ESBL) in *E. coli*, *K. pneumoniae*, and *Klebsiella oxytoca* at 79.0%, 69.4%, and 100% respectively (Lu *et al.*, 2012). Among Enterobacteriaceae isolates, Korea regions had ESBL positivity of 22.4% in *K. pneumoniae* and 10.2% in E. coli isolates (Ko, 2019). In Taiwanese intensive care units (ICU), the prevalence of *Enterobacteriaceae* isolates with ESBL were 26% in *K. pneumoniae*, 14% in *E. coli*, and 13% in *Proteus mirabilis* (Jean *et al.*, 2009).

In the Asia-Pacific region, the prevalence of carbapenem-resistant *Enterobacteriaceae* (CRE) was still low (0.6%) according to an earlier report (Xu *et al.*, 2015). Currently, growing trend have been observed with a prevalence rate between 24.7% and 29.8% in genus such as *E. coli, Klebsiella* spp, and *Enterobacter*. *Klebsiella pneumoniae* resistance to carbapenem, a third line antibiotics was the most common CRE recorded (45.9%) of the strains isolated (Becker *et al.*,

2018; Xu *et al.*, 2015). *Klebsiella pneumoniae* is a major cause of hospital-acquired infections (HAIs) or Healthcare acquired infections (HCAIs) such as pneumoniae, bloodstream infections, and infections in newborns and intensive-care unit patients (Vuotto *et al.*, 2014; Kontopoulou *et al.*, 2010). Holt *et al.* (2015) reported that the spread of carbapenem resistant *K. pneumoniae* is rapidly making treatment of infections caused by this strain ineffective and difficult. Similar to *K. pneumoniae*, *Escherichia coli* is the second CRE equally showing widespread resistance at 21.9% (Becker *et al.*, 2018; Xu *et al.*, 2015).

More worrying is resistance to Colistin, a last treatment option for life-threatening infections caused by *Enterobacteriaceae* (i.e. *E.coli*, *Klebsiella*) which are resistant to carbapenems has recently been detected in this region and several countries and regions, thus making infections caused by this bacteria untreatable (World Health Organisation, 2020; Van Duin *et al.*, 2018; Brown *et al.*, 2017). Fluoroquinolones resistant gonorrhea is yet another source of growing concern in this region and globally (World Health Organisation, 2016; Holt *et al.*, 2015). Recent data reported from 73 countries shows that the total number of gonorrhoea isolates examined for susceptibility to different antimicrobials increased from 12,895 for cefixime in 2017 to 15,876 in 2018 and resistant to ciprofloxacin increased from 25,505 in 2017 to 27,251 in 2018 (GASP, 2021). Due to the widespread of drug resistant gonococcal pathogens, the WHO guidelines for treatment of gonorrhea now excludes the use of quinolones (Kristinsson and Georgsson, 2015; Ma *et al.*, 2015). Resistance to first-line drugs used to treat infections caused by *Staphylococcus aureus*, a common cause of severe infections in health facilities and the community is highly prevalent in this region (Brown *et al.*, 2017; Dheda *et al.*, 2017; World Health Organisation, 2016). Globally, evidence shows that persons with methicillin-resistant *Staphylococcus aureus* (MRSA) are 64% more likely to die from this infection compared to those with the non-resistant form of the infection (World Health Organisation, 2018).

In Africa, Tadesse *et al.* (2017) noted that data concerning the true extent of the problem of AMR in the region is limited because surveillance of drug resistance exists only in few countries. Bernabé *et al.* (2017) also documented that precise and dependable data on AMR in Africa is scarce. Despite the endorsement of Integrated Disease Surveillance and Response (IDSR) by the WHO African member states to strengthen networks of public health laboratories, and contribute to elective monitoring of antimicrobial resistance, implementation of IDSR suffered serious setback (Essack *et al.*, 2017). A recent external quality assessment of public health laboratories in Africa revealed weakness in antimicrobial susceptibility testing capacity in many countries (Fleming Fund-Nigeria, 2019). Regardless of the paucity of accurate data, a review of some surveillance data conducted between 2008 to 2009, revealed that 78% of *Shigella* isolates recovered from a multiple centre study were found to be resistant to the first line drugs used to treat this condition (UNAS, 2015). Out of 137 isolates of *N. meningitidis* recovered between 2000 and 2006 from 18 Africa countries, 2% of the isolates displayed reduced susceptibility to penicillin, ceftriaxone and chloramphenicol (UNAS, 2015).

A systematic review on the resistant profile of 13 Gram negative and 5 Gram positive bacteria to 37 antibiotics across African countries showed penicillin resistant *S. pneumoniae* in 14 studies and amoxicillin resistant *H. influenzae* isolates were seen in 18 studies. Overall, resistance of *E. coli* to amoxicillin, trimethoprim and gentamicin was 88.1%, 80.7% and 29.8% (Picot *et al.*, 2014; Anagaw *et al.*, 2013). Ciprofloxacin resistance in *S. Typhi* was rare, though resistance in other *Salmonella* species has been documented (Akinyemi *et al.*, 2018; Obaro *et al.*, 2015; Okoro *et al.*, 2012). No documented ceftriaxone resistance in *N. gonorrhoeae* had been reported, though the resistance to quinolone was 37.5% (GLASS-Report, 2019). Clark *et al.* (2016), Perdigão-Neto *et al.* (2014), and Liakopoulos *et al.* (2013) noted that carbapenem resistance was common in *Acinetobacter* spp. and *P. aeruginosa* but low in Enterobacteriaceae,

though recent literature has suggested increased resistance especially in hospital transmitted isolates (Keith and Pamer, 2019; Mustafa *et al.*, 2016). There are no active regional AMR surveillance systems in Africa, majority of AMR surveillance in Africa are conducted at individual or institutional level (Tadesse *et al.*, 2017).

2.2.1 Magnitude of antimicrobial resistance in Nigeria

More than ever, actions, policies and conversations geared towards AMR containment is beginning to receive the attention of stakeholders and key opinion leaders. In order to better plan intervention strategies, the magnitude and epidemiological data of infectious diseases from AMR is required but this has been difficult to estimate due to suboptimum nationwide surveillance data. Available data are estimated from collection of small studies carried out by institutions or private research groups. These studies vary greatly in scope, setting, sampling and methodology which impacts data aggregation and are insufficient to support surveillance or intervention plans (Fleming Fund, 2019; Fleming Fund-Nigeria, 2019). Despite limitation of data, AMR burden estimate which utilised 471 million individual records or isolates covering 7,585 study centres showed there were 64,500 deaths attributable to AMR and 263,400 deaths associated with AMR in 2019 (GRAM-IHME, 2020). A collection of other small scale studies on prevalence of antimicrobial resistance across Nigeria also shows spread of resistant pathogens across the region.

In Central and North-West Nigeria, a multicenter study of *Salmonella* bacteremia conducted between 2008-2015 among children under five years indicated that 20.7 (23.6%) of the *Salmonella* bacteremia cases were due to non-typhoidal *Salmonella* (Obaro *et al.*, 2015). Obaro *et al.* (2015) also reported that the non-typhoidal *Salmonella* (NTS) species identified showed varying resistance to the following antimicrobials agents: ampicillin (50-100%), amoxicillin (0-90%), gentamicin (089%), ciprofloxacin (0-30%), ofloxacin (0-20%), nalixidic acid (0-100%), chloramphenicol (36-100%), cotrimoxazole (0-100%) and tetracycline (0-100%). In

South-West Nigeria, a retrospective study carried out by Fashae *et al*. (2010a) to determine the prevalence and antibiotic resistance rates in *Salmonella serovars* from humans beginning from 2004 through to 2007 observed high rates of resistance to penicillin (59%), cotrimoxazole (54%), chloramphenicol (36%) and tetracycline (31%). A similar study by Oluduro and Famurewa (2007) to determine the rate of drug-resistant *Salmonella serovars* using samples collected from apparently healthy people in Ekiti state also documented 100% *Salmonella* resistance to penicillin and cotrimoxazole. In South-Eastern Nigeria, isolates recovered from patients admitted to three large teaching hospitals located in this zone showed resistance of non-typhoidal *Salmonella serovars* to amoxicillin, chloramphenicol and cotrimoxazole at 90%, 58% and 47% respectively. In North-West Nigeria, NTS had 100% resistance to ampicillin and chloramphenicol (Obaro *et al.*, 2015).

There are also collection of reports on *Shigella spp.* Studies on resistance rate of *Shigella* to frequently used treatment in South-South Nigeria, revealed over 50% resistance across penicillin, gentamicin, tetracyclines and quinolones (Imade and Eghafona, 2015; Egbule, 2014; Akortha and Egbule, 2008). In South-West Nigeria, there is equally high resistance of *Shigella* to ampicillin (90%), chloramphenicol (77%), tetracycline (79%) and cotrimoxazole (86%) (Abdu *et al.*, 2013). Additionally, a report from South-East Nigeria, showed high resistance of *Shigella* to ampicillin (68%), chloramphenicol (57%) and cotrimoxazole (43%) with lower resistance to fluoroquinolones (Imade and Eghafona, 2015; Egbule, 2014). In North-West Nigeria, *Shigella spp* showed resistance of over 90% to ampicillin, fluoroquinolones, chloramphenicol and cotrimoxazole (Abdullahi *et al.,* 2010)

A literature review of diarrheagenic *Escherichia coli* resistance to available treatment showed varying degrees of resistance: (79-100%) penicillin, (68-80%) for tetracycline and (76-100%) to ampicillin and cotrimoxazole (Duru and Umoren, 2014; Yah *et al.,* 2006). A review of studies on resistance of diarrhoeagenic *Escherichia coli* strains in South-South Nigeria found

complete resistance of diarrheagenic *Escherichia coli* strains to gentamicin and chloramphenicol (Duru and Umoren, 2014; Akortha and Egbule, 2008). *E. coli* isolates from hospitalized patients in the North-West of Nigeria were resistant to ampicillin, gentamicin and tetracyclines at 73%, 68% and 75% respectively (Akinjogunla *et al.*, 2009). A multi-regional study across five geo-political zones in the country also confirms high antimicrobial resistance of *E.coli* isolates to penicillin, cephalosporin, streptomycin, chloramphenicol, tetracycline and cotrimoxazole (Nsofor, 2013).

A review of isolates collected from patients with urinary tract infections (UTI) showed complete resistance to ampicillin and cotrimoxazole (Ashkenazi *et al.*, 2003). Amongst the first line UTI drugs, Nitrofurantoin showed the least resistance with a rate of 6.5% in *E.coli* and less than 100% in *Proteus*, *Klebsiella* and *Enterobacter* (Mokuolu *et al.*, 2002). In South-West Nigeria, *E. coli* resistance rate ranged from 48-96% to ampicillin, 46-68% to chloramphenicol, 68-97% to tetracyclines and 70-90% to cotrimoxazole (Odetoyin *et al.*, 2016; Olowe *et al.*, 2014; Okeke *et al.*, 2000). UTI isolates from a clinical study in Oyo State showed highest resistance to third generation cephalosporins and lowest resistance to ciprofloxacin. Although resistance rates to ciprofloxacin were low compared to the other drugs, considerable resistance was established (Fortini *et al.*, 2015). The carbapenem resistance *enterobacteriaceae*, vancomycin resistance *enterococcus* (VRE) and extended spectrum beta-lactamase (ESBL) producing Gram negative rods have also been established and growing at an alarming rate in the country. Taiwo and Aderounmu (2009) documented *Klebsiella* spp, *Pseudomonas* spp, *E. coli*, *S. aureus*, *Proteus mirabilis*, *Candida albicans*, coagulase-negative *staphylococci* (CoNS), and *A. baumanii* as most resistant isolates from health care-associated urinary tract infection in Nigeria. Microorganisms such as *Klebsiella* spp, ESBL-producing *Enterobacter* spp, and MRSA were also identified as pathogens causing health care-associated pneumonia according to the situational analysis reported by Nigeria Center for Disease Control AMR

Symposium (NCDCAMRS, 2017).

Amongst blood stream bacterial infections (BSI) in Nigeria, *Staphylococcus aureus* recorded resistance ranging from 0-95.6% to ampicillin (Akindolire *et al.*, 2016; Meremikwu *et al.*, 2005). Coagulase negative *staphylococci* showed 100% resistance to ampicillin in North-West and North-East region of the country (Pius *et al.*, 2016; Nwankwo *et al.*, 2011). *Staphylococcus spp* showed variable degrees of resistance to the aminoglycosides, with least resistance to amikacin (Akindolire *et al.*, 2016; Adeyemi *et al.*, 2010). Data regarding MRSA in blood stream infection is still scare, though some studies had reported resistance rate of 23-40% (Akindolire *et al.*, 2016). *Enterococci* isolates recovered from blood stream infections in Nigeria showed low resistance rate to gentamicin, ampicillin, cefuroxime and ceftriaxone, except in Kano State where high resistance to ampicillin and cefuroxime were documented (Nwankwo *et al.*, 2011; Taiwo *et al.*, 2008). There are no robust studies on blood stream infection (BSI) but few records from health care settings have demonstrated high resistance rate to most antimicrobials used in regular clinical case management including amoxicillin/clavulanate and chloramphenicol (Yusuf and Airauhi, 2015; Afolabi *et al.*, 2011). Studies have revealed that *S. aureus* was the most common cause of blood stream infections in adults, while *Klebsiella spp* was identified in neonates (Iwuafor *et al.*, 2016; Osinupebi *et al.*, 2013). Commonly implicated organisms in blood stream infections includes *S. aureus*, *Pseudomonas* spp, *Klebsiella* spp, *E. coli*, *Proteus* spp, *Enterobacter* spp, and *Acinetobacter* spp (Uzochukwu *et al.*, 2015; Nwadike, Ojide and Kalu, 2014; Jido and Garba, 2012; Oni *et al.*, 2006). Resistant organisms like ESBL-producing *Enterobacter* spp, Methicillin resistant *Staphylococcus aureus* and carbapenem resistant *Acinetobacter* spp have also been implicated (Nwadike, Ojide and Kalu, 2014; Taiwo *et al.*, 2005; Aibinu *et al.*, 2003). A comprehensive and systematic surveillance is highly recommended to promote standardised collection,

analysis and sharing of findings for appropriate containment strategies and to influence design of future intervention framework.

2.3 Burden of Antimicrobial resistance

There is considerable variability in the current estimation of the burden of AMR due to limited and unreliable data, particularly from LMICs (O'Rourke *et al.*, 2020; Kırmusaoğlu *et al.*, 2019). These discrepancies do not only lead to inaccurate evaluation of interventions but also inform poor investment decisions. Studies have shown that to be able to accurately estimate the burden of AMR, a multidimensional approach encompassing the different perspectives of this problem has to be considered. Broadly, the burden of AMR can be viewed from three different perspectives: Patient perspective, Healthcare perspective, and Economic perspective.

2.3.1 Patient perspective

The criteria for estimating the burden of AMR from patient perspective is based on mortality and morbidity rates. A global review of studies estimating the patient burden of AMR shows that, 95% (177/187) focused on mortality burden, whereas 5% (10/187) focused on morbidity burden. Result from studies on morbidity shows that AMR has significant impact on outcomes such as disability-adjusted life-years (DALYs); recurring infections or development of secondary infections; clinical failure and time to stability (Xiong *et al.*, 2018; Wintersdorff *et al.*, 2016; Giedraitienė *et al.*, 2011). Antimicrobial resistance is equally associated with higher mortality rate as infection with resistant microorganisms will double the chances of developing a serious health issue and triple the chances of death. Data shows that attributable mortality to AMR is about 33,000 in Europe and over 35,000 in USA (Amann *et al.*, 2019; Ragheb *et al.*, 2019). Much more attributable deaths are expected in Africa as shown in figure 2.1 due to higher incidence of infectious diseases, poorly functioning health structures and unregulated antimicrobial sales (Sauvage and Terrak, 2016; Zervosen *et al.*, 2012). Statistics shows that death from AMR alone could surpass deaths from HIV, tuberculosis, malaria, cancer, accident

and other major causes of deaths worldwide. Despite the difficulty of obtaining accurate data particularly from LMICs, AMR associated deaths is estimation to reach 10 million yearly by 2050, which makes AMR a serious global threat (Chokshi *et al.*, 2019; O'Neill, 2016).

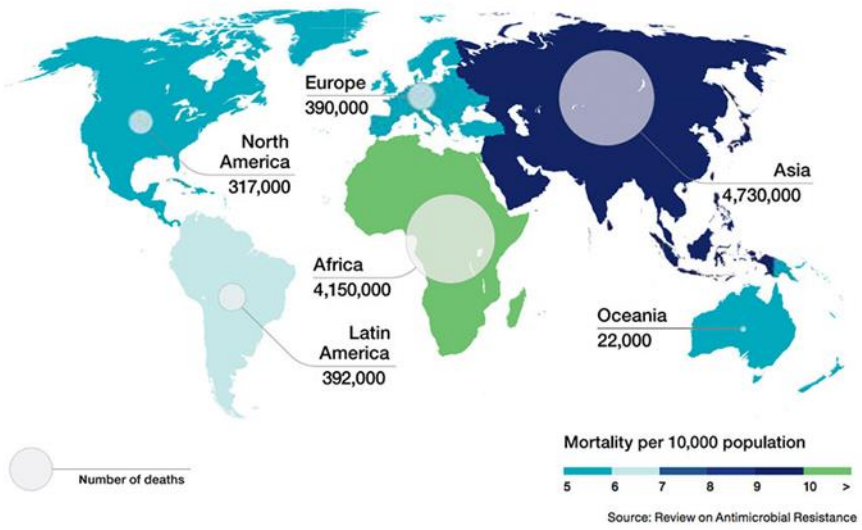


Figure 2.1 Deaths attributable to AMR annually by 2050 showing mortality per 10,000 population to be highest in Africa. Source: Review on antimicrobial resistance from public health post, extracted from; https://www.getdoc.com/wp-content/uploads/2020/09/antibiotic-resistance-community-world.jpg

2.3.2 Healthcare perspective

Estimating the burden of AMR from healthcare perspective incorporates the payer and provider perspectives. Indicators like length of stay (LoS) due to AMR, and the need for more expensive second and third line treatment alternatives put more pressure on patients and health systems spending on healthcare (Caniça *et al.*, 2019; Tenover, 2006). According to a CDC report, AMR could cost an additional $2 billion every year towards hospital bill for treating patients with resistant infections. In addition to monetary costs, AMR creates burden on health systems through secondary impacts (Reygaert, 2018; Kulshreshtha *et al.*, 2017).

2.3.3 Economic perspective

In measuring economic impact of antimicrobial resistance, monetary cost is considered the main outcome, this is followed by GDP and productivity loss (Ait Ouakrim *et al.*, 2020). The

economic impact of AMR is projected to be worse than the financial crisis of 2008 and would hit LMICs more (Ait Ouakrim *et al.,* 2020; Naylor *et al.*, 2018). Poorer countries could lose up to 5% of their GDP towards extra spending on healthcare which is estimated to reach $1 trillion a year by 2030. More so, an estimated costs of over $14 billion to $3 trillion loss in GDP attributable to AMR is estimated to occur by 2050 (World Health Oorganisation, 2014). In addition to the direct impact of AMR on health budget and GDP, antimicrobial resistance has a major influence on labour through the loss of productivity caused by sickness and death. The implication of AMR on health, society and economy is such that it cannot be neglected (US-CDC, 2019; Figueiredo *et al.*, 2015).

2.4 Containment strategies for antimicrobial resistance worldwide.

Strategies for containment of antimicrobial resistance seek to address broadly the economic and health impacts of antimicrobial resistance at national and global levels (O'Neill, 2014; World Health Oorganisation, 2014). The AMR containment framework consists of interventions aimed at slowing down the emergence and spread of antimicrobial-resistant microorganisms through five core strategies: 1) Reducing disease burden and the spread of infection, 2) Improving use of antimicrobials, 3) Strengthening health systems and their surveillance capabilities, 4) Enforcing regulations and legislation and 5) Encouraging the development of new antimicrobial drugs and vaccines (World Health Organisation, 2015).

2.4.1 Reducing disease burden and the spread of infection through education

On the strategies targeted at reducing disease burden and the spread of infection, Rogers, Jones and Hoffman (2018) opined that education of patients and the general community on the appropriate measures to prevent infection such as good hygiene, vector control, immunisation and other preventive measures can support AMR containment. Ayukekbong *et al.* (2017) and Thandar *et al*. (2020) recommended enforcement of infection prevention and control policies at hospital and healthcare setting. The challenges to this strategy are ubiquitous. Challenges

arising from patient compliance, environmental contamination, over-crowded living conditions and poverty makes implementing this policy difficult in communities. In healthcare settings, the struggle to get clinicians to perform hand hygiene knows no geographical boundaries. In resource limited settings, the challenge is even greater with competing pressures arising from understaffing and suboptimal infrastructure (Dramowski *et al.,* 2022).

2.4.2 Antimicrobial stewardship

In terms of prudent use of antimicrobials, there has been strong advocacy for antimicrobial stewardship as strategy for AMR containment. Ayukekbong, Ntemgwa and Atabe (2017) reported that AMR can be contained by educating communities on appropriate health seeking behavior, use of antimicrobial alternatives and discouragement of self-initiation of treatment. Marvasi *et al.* (2021) also echoed the above containment strategies for antimicrobial resistance, by proposing the education of antimicrobial agent prescribers and dispensers on the importance of appropriate antimicrobial use for treatment and prevention of disease. In Nigeria as well as in other LMICs, implementing any AMR containment policy that is patient and prescriber-driven can be daunting without strict monitoring and enforcement strategies (Dramowski *et al.,* 2022). Gaps along the pharmaceutical supply chain and regulatory failure allows proliferation of unregulated medicine vendors which aids unrestricted access to antimicrobials (Ogundeji *et al*., 2019). Additionally, the healthcare policy in Nigeria where over 90% of the citizens pay out of pocket for medicare, plus lack of social health protection would continue to encourage people to patronage unregulated healthcare providers (including traditional health practitioners) who offer cheaper and oftentimes substandard healthcare services. These factors have undeniable far reaching impacts on antimicrobial access and usage in the community, and as far as these factors exists, misuse of antimicrobials will continue to occur and resistance will keep soaring thus creating specific need for continuous surveillance (Ogundare *et al*., 2022; Ogundeji *et al*., 2019).

In hospital settings, Kakkar *et al.* (2017) also recommended in addition to infection control and stewardship programmes, establishment of effective hospital therapeutics committees with the responsibility for overseeing antimicrobial use in hospitals. Anzaku *et al.* (2020) also supports the call for the development and regular updated guidelines for antimicrobial treatment, antimicrobial prophylaxis, and hospital antimicrobial formularies. Waele *et al.* (2018) opined that antimicrobial usage, including the quantity and patterns of use should be monitored. These strategies have been observed to be effective at tackling misuse of antimicrobials but Anzaku *et al.* (2020), Saeed *et al.* (2017) and Shallcross *et al.* (2015) mentioned that challenges of implementing antimicrobial stewardship and treatment guidelines in LMICs are numerous. Challenges arising from antimicrobial seeking behaviour amongst patients, gap in public health capacity, inadequate manpower and resources within the hospital setting are some bottlenecks in the execution of these strategies. In some LMICs, antimicrobial stewardship policies are not in place, and where they exist like in the case of Nigeria, there is poor compliance and enforcement (Mohammed *et al.*, 2018; Nasir *et al.*, 2015).

2.4.3 Strengthening health systems and their surveillance capabilities

Surveillance forms an integral part of the AMR containment continuum which is why the World Health Assembly recommends prioritisation of antimicrobial resistance surveillance by national governments. Governments, non-governmental organisations, professional societies and international agencies are encouraged to support the establishment of networks, trained staff and adequate infrastructures that can undertake epidemiologically valid surveillance of antimicrobial resistance and antimicrobial use to provide information for optimal containment of resistance (US-CDC, 2019; Fleming-Fund, 2019; World Health Organisation, 2018; Saeed *et al.*, 2017). Additionally, development of reference laboratories to coordinate effective epidemiological surveillance of antimicrobial resistance in the community, hospitals and other

health care facilities should form a major part of the national strategy for AMR containment (Kariuki *et al.*, 2018; World Health Organisation 2018; Pius *et al.*, 2016).

2.4.4 Enforcing regulations and legislation

The use of treatment guidelines as an alternative measure is also impacted by lack of quality data to inform review of essential drug lists. This lack of quality data leads to the use of substandard treatment guidelines that are not sufficient for the local situation which, contributes to antimicrobial selective pressure and resistance. Establishment of an Essential Drugs and Diagnostic List (EDDL) consistent with the national strategy and ensuring accessibility and quality of these drugs and diagnostics is also one of the ways to systematically contain AMR (Marston *et al.*, 2016; Liakopoulos *et al.*, 2013). These strategies seek to optimise treatment regimens with regard to safety, efficacy and the risk of selecting resistant organisms. Since antimicrobial stewardship cannot be completely implemented yet and misuse of antimicrobials cannot be completely eradicated, good quality surveillance data is therefore needed to continuously update treatment guidelines to ensure safety of patients. In other words, in the absence of reliable surveillance information, some of these AMR containment strategies cannot be completely achieved (Fonjungo *et al.*, 2018).

Another containment strategy for AMR is to implement stricter policy for use of antimicrobials outside human medicine by ensuring obligatory prescriptions for all antimicrobials used for disease control in food animals. Thandar *et al*. (2020) recommended establishment of an effective registration scheme for dispensing outlets by making antimicrobials available to those with prescription-only and dispensed on the advice of a trained health care professional. In Nigeria, the use of antimicrobials in food animal production is uncontrollable. Several poultry farms operate illegally and liberally use antimicrobials therapeutically for growth promotion. This factor in addition to availability of unlicensed prescribers makes assess to antimicrobials without prescription relatively easy to obtain. Even amongst licensed prescribers, over the

counter sale of antimicrobials without prescription is still high (Mendelson *et al.*, 2016). There are policies and legislatures to contain irrational use of antimicrobial agents such as the Food and Drug Act, Cap 150 (1990) which prohibits sale of antimicrobials without prescription. However, monitoring and enforcing this policy is challenged by profit driven drug merchants operating across rural and urban Nigeria (Oloso *et al.,* 2018). These factors contribute to exacerbate resistance and complicate infectious disease management thereby creating a need for active surveillance to help contain and manage these problems (Kariuki *et al.,* 2018; Laxminarayan *et al.,* 2016).

2.4.5 Encouraging the development of new antimicrobial drugs and vaccines

The development of newer antimicrobial drugs is yet another way to tackle resistance but this has been largely slow due to lack of interest by pharmaceutical companies. Since 2017, only 12 antibiotics have been approved for therapeutic use, 10 of which belongs to existing classes with established mechanisms of resistance (Sun *et al.,* 2022; Tacconelli *et al.,* 2018). Boyd, Teng & Frei (2021) encouraged cooperation between industry, government bodies and academic institutions in the search for new drugs and vaccines. Sun *et al.* (2022) and Gray & Wenzel (2020) listed drug development programmes as a critical containment process for AMR. Jackson *et al*. (2018) also encouraged national, regional and global health authorities to seek innovative partnerships with the pharmaceutical industry to improve access to newer essential drugs. Establishment of international database of potential research funding agencies with an interest in antimicrobial development will encourage new research into development of novel antimicrobials (Sun *et al.,* 2022; Ragheb *et al.,* 2019; Caniça *et al.,* 2019).

Other strategies such as enforcing regulations and granting marketing authorisations to antimicrobials that meet international standards of quality, safety and efficacy is being hindered by illegal drug smugglers in many LMICs including Nigeria (Adamu *et al.,* 2020; Amann *et al.,* 2019). Isabel *et al.* (2021) and World Bank (2016) also advised government and national

drug regulating bodies to identify and eliminate economic incentives that encourage inappropriate antimicrobial use. With recourse to the enormous challenges mitigating against successful implementation of some of these strategies and the health threat associated with uncontrollable assess to antimicrobials, surveillance is thus needed to consolidate viable interventions.

2.5 The scope of surveillance: components, dimensions and approaches

Surveillance is widely regarded as a practice applied to public health for detection and control of disease and/or for monitoring public health events. The former CDC Chief Epidemiologist, Alexander Langmuir established the concept of surveillance as a separate activity from control or epidemiological research through his Epidemic Intelligence Service in the 1950s (Langmuir, 1980). His definition provided the systematic components of surveillance as an ongoing, 'systematic', data collection, (mortality, morbidity and other relevant data), data analysis, interpretation and dissemination of information to stakeholders and policy makers (Nsubuga *et al.*, 2006). To achieve this purpose, the surveillance modality and approach must be informed by its objective (s).

In the context of AMR, the main objectives of surveillance include to track changes in microbial populations, permit the early detection of resistant strains of public health importance, support the prompt notification and investigation of outbreaks, provide local evidence for empirical treatment, and assess the impact of resistance containment interventions including stewardship. In addition to surveillance objectives, the approach to surveillance is influenced by other factors such as the relative public health importance of the condition which is determined by criteria such as expected numbers of cases, severity of the infectious disease as measured by its mortality rate and case-fatality ratio, medical costs of the infections, and preventability (US-CDC, 2019; Fleming-Fund, 2019; World Health Organisation, 2018).

Surveillance differs in approach and modalities and can be adapted or adopted in accordance with local needs and following a systematic needs assessment (GLASS-Report, 2019; Jee *et al.*, 2018). According to WHO description, surveillance can be comprehensive (involving the entire population at risk of infection) or sentinel (involving a limited catchment area as indicator for the rest of the population); continuous (on-going), periodic (collected over a limited periods of time) or episodic (for diseases that are predictably seasonal). Surveillance activities can either be active (where reports are sought from the primary data collector on a regular basis) or passive (where reports are awaited and no attempt is made to seek reports actively from the primary data collector) (World Health Organisation, 2018). Surveillance activities can further be characterised as routine (the regular systematic collection of a specified data set); or enhanced (the collection of additional data about cases reported under routine surveillance). In terms of approach, there is an extensive body of literature on strategies for identifying AMR. Generally, there are two main approaches to identifying AMR: case-finding (based on prospective surveillance of targeted pathogens from priority specimens routinely sent to the laboratory for clinical investigation) and case-based (this approach is based on data from all patient specimens who present with signs and symptoms that meets the case definition) (US-CDC, 2019; Fleming-Fund, 2019; World Health Organisation, 2018). These distinctions are crucial for the standardisation on the composition and activities of surveillance networks and more importantly to guide collection of quality data (Saeed *et al.*, 2017).

Appropriate strategies for surveillance of antimicrobial resistance should match identified health system structure, resources, available technical capacity for testing, and be sustainable. In some instance, a combination of complementary approaches is often desirable for robust data collection (GLASS-Report, 2019; Jee *et al.*, 2018). In line with this, the Global Antimicrobial Resistance and Use Surveillance System (GLASS) approach promotes a shift from surveillance based solely on laboratory data to an approach that includes epidemiological,

clinical, and population-level data (World Health Organisation, 2015). In resource limited settings, sentinel surveillance based on case finding using routinely generated data from the laboratories is the commonly used approach. This approach has limitations in its ability to define specificity in the epidemiology of infection due to poor collection of population-level and clinical data particularly in settings where routine microbiological testing is underutilised. In these settings, only patients who fail empiric treatment are more likely to be sampled for microbiological diagnosis (Jee *et al.*, 2018; Saeed *et al.*, 2017). Consequently, AMR is over estimated as the denominator for determining the actual case number is pooled from patient population whose infections are most likely caused by resistant pathogen (World Health Organisation, 2015). A potential concern for AMR surveillance based on routine microbiology is the representativeness of data for the target population. Incidentally, many LMICs adopts this method of surveillance which may not likely be suitable in settings where access to healthcare services vary by location, population and hierarchical healthcare system (US-CDC, 2019). On the other hand, case-based surveillance using patients with specific conditions as the unit of surveillance provides clearly defined numerators (e.g. urinary tract infection) and denominators (e.g. patients with community or hospital acquired infection, patients with a specific condition or patients that have received a specific clinical procedure) with clinical relevance and more comparable at the local, national and international level. This approach, though laborious and cost intensive to implement and sustain in LMICs provides a more comprehensive picture of patterns in resistance by patient characteristics (Ryu *et al.*, 2019).

The dimensions of surveillance have expanded rapidly in recent years and to ensure that all surveillance systems activities (from data input to output) are of high quality and fit for purpose, they should be regularly assessed using the established evaluation criteria (PHE, 2017). The capacity of the surveillance system to accurately describe patterns of diseases that

represent the target population as closely as possible is central. Therefore relevant evaluations of these systems are crucial to improving their performance and efficiency.

2.5.1 Surveillance: a critical element for efficient AMR control

Surveillance is the cornerstone for effective tackling of AMR. Reliable data from surveillance helps to evaluate resistance status and the spread of AMR as well as provide early warning to local, national, and worldwide containment networks (GLASS-Report, 2019; Jee *et al.*, 2018). Surveillance is an evidence-based tool in disease monitoring by informing strategy to tackle most of the world's devastating diseases. Global surveillance exists for tuberculosis, HIV, malaria and influenza, which has been helpful in monitoring drug resistant strains and informed modification of interventions for these infectious diseases (World Health Organisation, 2016; World Bank, 2016).

The usefulness of surveillance is recognised by the WHO which necessitated the launch of the Global Antimicrobial Resistance and Use Surveillance System (GLASS) with the main focus to provide standardised methods for collection, analysis, and sharing of AMR data amongst participating countries (GLASS-Report, 2019). Prior to GLASS launch, the existence of territorial-level surveillance systems including the European Center for Disease Prevention and Control (ECDC), European Antimicrobial Resistance Surveillance Network (EARS-Net), the WHO's Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) and the Latin American Network for Antimicrobial Resistance Surveillance (ReLavra) affirms to the importance of surveillance in AMR containment (European Centre for Disease Prevention and Control, 2018; World Health Organisation, 2018). Clearly, the role of surveillance in public health disease management and containment of AMR in particular cannot be over emphasised.

Surveillance when conducted appropriately can provide invaluable insight to treatment options for disease management. Particularly in the case of AMR, surveillance data serves to: firstly

direct clinical decision in certain emergency situations where administration of antimicrobial is urgently needed while awaiting sensitivity/susceptibility test result (Holmes *et al.*, 2016). According to Hindler and Stelling (2007), immediate empirical treatment starting with broad spectrum antimicrobial agent is often initiated in clinical settings where severe infection is suspected but the presence of AMR could potentially limit the chances of achieving therapeutic potency if the antimicrobial agent is not carefully selected. In this situation, valuable surveillance could inform treatment guideline by providing data relating to the degree of resistance among the priority pathogen to a range of antimicrobial agents within the local setting. This will enable prescribers to make informed decision in choosing the antibiotics in urgent situation while antimicrobial susceptibility testing is being awaited.

Secondly, AMR surveillance is valuable for global public health practice since it describes the patterns and trends of resistant (World Health Organisation, 2015). ESPAUR-UK (2019) report indicated that AMR surveillance information can be used to profile geographic and territorial patterns in AMR-related infections at various settings. This helps to make enquiries into specific elements forming resistance patterns and to monitor the potential effect of interventions. Surveillance also measures the degree of danger from various resistant pathogens at various settings and therefore provides information for possible intervention activity to forestall uncontrollable spread (Oloso *et al.*, 2018; OIE, 2018; Vuitton *et al.*, 2015).

Thirdly, AMR surveillance gives epidemiological information to estimate the health and economic impact of AMR and the adequacy of control measures in human health, animal health, food chain and the environment (Cox *et al.*, 2017). For surveillance data to provide the required information needed to make important public health decisions, Perovic and Schultsz (2018) opined that it is important to gather data on the resistance profile of pathogens as a whole, including those associated with human health, environment, food chain and animals. The framework must also incorporate epidemiological, clinical, and population level data

(Dacombe *et al.*, 2016). The GLASS report indicates that any surveillance system that fulfils these purposes, should be able to provide reasonable data to drive local, national and regional policy for AMR control and provide an evidence base for AMR action plans and promotion (World Health Organisation, 2018). In Nigeria as well as other LMICs, it is not clear what sort of surveillance information is collected and the completeness of these information which further impacts measuring efficiency of AMR intervention and AMR-associated disease burden.

2.5.2 AMR surveillance in Africa: activities, programs and plans

Despite supports in forms of funding and capacity training, AMR surveillance in Africa is still under performing (Amann *et al.*, 2019; Opintan *et al.*, 2015). Surveillance for antimicrobial resistance is a global responsibility and within the African region efforts are being made towards generating reliable surveillance information. The Africa Center for Disease Control (ACDC) is positioned to support policies that aim to help address issues of AMR specific to Africa. Surveillance activities are also facilitated by ACDC's Regional Collaborating Centers (RCCs), non-governmental organisation (NGOs), existing AMR surveillance networks, the WHO tripartite body, Food and Agriculture Organisation (FAO), the World Organisation for Animal Health (WOAH), the Inter-African Bureau for Animal Resources (AU-IBAR), and the African Union Pan-African Veterinary Vaccine Center (AU-PANVAC) (ACDC, 2017). ACDC also collaborates with Ministries of Agriculture, veterinary and environmental health to encourage information and specimen sharing, as well as new discoveries (Amukele, 2017). As an organisation that receives institutional authority from the African Union, ACDC is well situated to advance continent-wide policies and promotes inter-government partnership through WHO, FAO, WOAH and other non-governmental organisation (Nkengasong, 2017).

In addition to activities of ACDC, the Anti-Microbial Resistance Surveillance Network (AMRSNET) was inaugurated with the responsibilities to: improve surveillance of AMR

among humans and animals, delay the rising of AMR in the African continent, limit transmission of AMR and mitigate harm among patients infected with AMR pathogens. AMRSNET also serves as a public health surveillance institution and an essential facilitator for AMR surveillance and control in Africa by supplementing existing activities of the WHO, Ministries of Health and non-governmental organisations responsible for AMR related roles (Clift, 2019). This network developed the scope of infectious pathogens across human and animal health sectors and also categorised resistant pathogen based on burden of disease, prevalence, trends and feasibility of interventions (ACDC, 2017).

There is also support from charities towards advancing AMR surveillance in Africa. One of such support is the Fleming Fund provided for LMICs to help tackle AMR. This fund supports country programmes and human resource development through fellowship programs with an Africa wide project, Mapping Antimicrobial Resistance and Antimicrobial Use Partnership (MAAP). Some countries benefitting from this grant include; Senegal, Sierra Leone, Ghana, Nigeria, Eswatini, Malawi, Kenya, Tanzania, Uganda, Zambia and Zimbabwe (Fleming-Fund, 2019). With support from this funding and help from the Norwegian Agency for Development and Cooperation (NORAD), Malawi started a surveillance program which has enabled public health laboratories to co-ordinate AMR data collection and strengthening of their surveillance capacity by developing human resources and infrastructures (Norad-Malawi, 2016).

The United State Center for Disease Control (US-CDC) and the Kenya Ministry of Health (MoH) through their National Public Health Laboratory Services (NPHLS) have set up laboratory based national antimicrobial resistance surveillance (US-CDC, 2018). The MoH and the National Microbiology Reference Laboratory (NMRL) coordinate national antimicrobial resistance surveillance methodologies across participating laboratories, health institutions, research organisation and the academia (Ministry of Health, 2017; FAO, 2017). The Ministry of Health is also directly coordinating AMR surveillance at four sites. This is the first national

antimicrobial resistance surveillance program undertaken by Kenya's administration and it is expected to provide a better understanding of the impact of antimicrobial resistance organisms in Kenya (US-CDC, 2019; Ministry of Health, 2017).

The US-CDC is also working with the Senegal national laboratories directorate to reinforce antimicrobial resistance surveillance by developing AMR surveillance protocol and redesigning the antimicrobial resistance reporting framework (US-CDC, 2018). This has helped to improve data quality and allow laboratories to check for patterns of resistance by accessing information from other laboratories (ACDC, 2017). The US-CDC also worked with partners in Senegal to set up a National Antibiotics Committee (NAC) and is supporting the NAC to develop national guidelines on the proper utilisation of antimicrobial agents and training of health-care workers on proper antibiotic utilisation (US-CDC, 2017).

The WHO on the other hand also serves as the lead implementer for the Global Action Plan through its provincial and country offices by working legitimately with national and regional governments to create and execute national AMR activity (World Health Organisation, 2017). Research and academic centers are also carrying out inquest towards evaluating status of AMR and how best to possibly decrease transmission (ACDC, 2017).

There are policies and interventions in place to support AMR surveillance in the region including Nigeria yet, it is not clear the extent to which these policies and plans have translated into actions as we still do not understand how surveillance systems are operating and the burden of AMR in the region. For these reasons, robust information needed to send early warnings for appropriate healthcare interventions and AMR containment is lacking (Bernabé *et al*., 2017). An assessment carried out to determine how African countries are implementing their antimicrobial resistance surveillance shows that, surveillance is completely absent in some countries (GLASS-Report, 2019). In countries where surveillance is present, they are not conducted in a systematic manner and thus lacks the capacity to inform public health

interventions (Arnold *et al.*, 2018). Pessoa-Silva (2018) proposed a thorough review of regional surveillance framework and methodologies to help identify the gaps in surveillance data reporting and how best these gaps can be managed.

2.5.3 Limitation of current data on AMR surveillance

The goal of a surveillance programme is to collect data needed to monitor progress, and measure the impact of actions taken to control AMR, but the future of achieving this global goal is looking bleak as current data on AMR appears to be exaggerated and tentative (Orubu *et al.*, 2020). Schnall *et al.* (2019), in their review had mentioned that the figure of 700,000 annual deaths from resistant infections often cited in literature suffers from methodological limitations and statistical uncertainty. This is because available data on AMR is largely reported from developed countries with limited data to establish the situation in LMICs. In Africa, surveillance data are not systematically collected and not frequently shared with or recognised by national bodies. This lack of systematic approach to the conduct of surveillance limits the usability of data to influence national actions (Iskandar *et al.*, 2021).

The 13th WHO-GLASS high level meeting drew global attention to the growing concerns of poor surveillance information and under reporting of important indicators needed to understand the situation of AMR at regional and global levels. The absence of this information impacts on the validity and reliability of data which consequently limit its use. Another factor limiting usability of microbiological results is underutilisation of databases that support ease of data retrieval for clinical and epidemiological purpose as well as their preservation (Plüddemann *et al.*, 2015). These shortcomings have implications on the timeliness attribute of surveillance systems as poor data management could lead to delay in information sharing coupled with higher risk of data loss. It will be beneficial also to understand how data is being managed in Nigeria as this can greatly impact on the integrity and completeness of information.

Another limitation of available data on AMR is the absence of internal and external quality assurance. ASLM-MAAP (2018) and Dacombe *et al.* (2016) reported that monitoring of the quality of results must be ensured as well as performance of quality assurance on appropriate diagnostic tests including those of microbial identification and antimicrobial susceptibility tests (AST) of key pathogens. It is not clear in majority of the surveillance reports whether or not external quality assurance (EQA) was performed and the steps undertaken to complete the necessary quality checks. The trustworthiness of surveillance reports can be severely impacted if they are not quality assured and where there is lack of transparency in reporting the process of EQA undertaken.

Lastly, the lack of frequent quality assessment of laboratories limits trustworthiness of data. Since data for tackling AMR are largely generated from the laboratory, understanding the laboratory capacity for collecting reliable data is important, particularly those participating in AMR surveillance. This will help to evaluate the various components of the laboratory including qualification of technical laboratory staff, equipment maintenance, reagents and media source and antimicrobial susceptibility testing (AST) and reporting in a bid to unify and benchmark data reporting standard. WHO-AMR (2017), LSHTM (2016) and Dacombe *et al.* (2016) advised building adequate capacity for diagnostic laboratories as a strategic plan for AMR containment. Therefore, to ensure adequate control of AMR, processes leading to the generation of the data must be thoroughly assessed from the perspective of the primary data collectors. According to World Health Organisation (2015), any laboratory indicated for surveillance purposes should at least meet the minimum laboratory requirements as stated by the regulating board and have the capacity to submit data to a coordinating system. In many LMICs including Nigeria, the capacity of the laboratories participating in surveillance is not well understood at both national and regional levels. In this manner, transparency in reporting,

reliability and quality assurance can be enhanced and consequently improve trust, reliability and usability.

2.6 Summary of the literature review

The foundation to the significance of surveillance in the containment of AMR has been laid in this chapter as well as issues around the limitation and accuracy of current data. The collection of studies presented here evidences that AMR is a global threat, but completeness of information and poor data quality remain constraints to data utilisation. As viewed by modern research, incomplete data is seem as empty, void and often useless as they lead to wrong conclusions and insufficient knowledge of the problem. Clearly, there is genuine need to be more systematic in the conduct of AMR surveillance to facilitate generation of quality, valid and representative data. Since sources of data completeness issue differ from system to system, assessment of surveillance system attributes and their alignment with systematic surveillance methodology will help highlight important parameters that impact data quality and usefulness.

Chapter 3 Systematic review of surveillance systems for antimicrobial resistance in Africa

3.1 Introduction

As the preceding chapter emphasised, burden estimates of antimicrobial resistance (AMR) suffers from methodological limitation and statistical uncertainty which impacts usability of data. To further investigate the foundations of data quality issues along the stream of surveillance activities, this chapter evaluated the surveillance systems for AMR in Africa. Specifically, it examined reported surveillance data with the aim of identifying frequently missing or underreported parameters. Beyond the assessment of individual surveillance system attributes, regional surveillance situation was assessed for homogeneity of surveillance methodology necessary for optimising data aggregation at regional level. The outcome of this study have been published in peer-reviewed journal and gives perspective to the flaws in current surveillance data reporting protocol and other potential source of bias.

3.2 Background

Today's widely accepted definition of public health surveillance is: the ongoing systematic collection, analysis, interpretation and feedback of outcome-specific data for use in the planning, implementation, and evaluation of public health practice and action (Nsubuga *et al.,* 2006). Surveillance is an invaluable tool for monitoring trends, patterns as well as effects of therapeutic and policy interventions in AMR and hence regarded as a key containment strategy for AMR (Aenishaenslin *et al.*, 2019; Bancroft, 2019; Calba *et al.,* 2015). Considering the complex process of acquiring AMR which involves an interplay of human, animal and environmental domains, a reliable surveillance scheme that collects data on resistant pathogens across these domains is needed to guide treatment and prescribing pattern, detect the emergence of AMR threats, evaluate trends, as well as assess impact of interventions (Ashraf *et al.,* 2019; Chatterjee *et al.,* 2018; Adeniji, 2018). This requires that surveillance activities must be

continuous and conducted in a systematic manner in order to provide good quality data needed for tackling this problem particularly in low and medium income countries (LMICs).

Poor or lack of surveillance activities in many LMICs creates a situation that impairs AMR containment efforts (Ndihokubwayo *et al.*, 2013). In Africa, understanding the full extent of AMR and its impact is hampered by poor continent-wide AMR surveillance data (Adeniji, 2018). Country data, when available, are not routinely collected and not frequently shared with or recognised by national bodies which limits their ability to influence national actions (Iskandar *et al.*, 2021). There are also overall difficulties in navigating AMR surveillance in Africa, in the robustness of information required to send early warnings for appropriate healthcare intervention and in the resources and leadership needed for effective surveillance (Bernabé *et al*., 2017). In recognition of this negligence, the 68th World Health Assembly (WHA) endorsed a Global Action Plan (GAP) in 2014 to tackle AMR with an overarching goal to draw national and global attention to AMR (World Health Organisation, 2015). The GAP proposed a set of objectives of which the first two focus on awareness and understanding of AMR through surveillance and research.

Despite the GAP policy recommendation for development of national action plans (NAPs) and continuous surveillance of priority pathogens at national and regional levels, a desktop analysis carried out to assess uptake of this policy in the African region revealed that only two countries had NAPs for AMR and none had any form of national surveillance (Essack *et al.*, 2017). With the rising spread of AMR, routine surveillance must be prioritised especially in LMICs and in Africa where the burden of AMR is anticipated to be the highest (Bernabé *et al.*, 2017; O' Neil, 2014).

Although current evidence from the World Health Organisation (2018) early implementation report indicates increasing surveillance in African region in response to rising threat from AMR

and in compliance to the WHO recommendations, these surveillance systems have not been mapped and their methods of collecting and reporting surveillance data have not been assessed for adequate collection of parameters to help estimate burden of disease caused by AMR. These parameters are crucial for identifying patterns of resistance, patient needs, instituting treatment guidelines, and monitoring the effectiveness of containment efforts. Surveillance system assessment is important as surveillance generally are often characterised by heterogeneity in scope, objectives, methodology and reporting across different geographical locations despite efforts for harmonisation (Calba *et al.*, 2015). Although characteristics that are important to one system may be less important to another, it is recommended that emphasis be placed on harmonisation of surveillance approach particularly at a regional level (ECDC, 2014). Hence, ensuring that the elements required for driving containment efforts are captured and correlated with demographic data for the patient populations from whom the pathogens were isolated from forms the bases for reliable data and a key priority for surveillance systems.

Information on surveillance systems in Africa are generally lacking thus, one system cannot leverage on the success of another for surveillance improvement. In addition, without understanding the differences in surveillance methodologies and data collection processes, making recommendations, monitoring the effectiveness of surveillance system and estimating morbidity and mortality figures at a regional level can be grossly hampered. The Global Antimicrobial Resistance and Use Surveillance System (GLASS) exists to bridge these gaps by highlighting important parameters that will ensure data-driven action on AMR and also serves as a global platform for aggregation of surveillance data. To current knowledge, it is not clear whether these systems provide appropriate descriptions of methodology and quality assessment of data which are crucial to the adequate interpretation of surveillance information. With the view of informing future capacity building in AMR surveillance in Africa, the

overarching goal of this study is to systematically review approaches to AMR surveillance, identify gaps in data reporting and compliance with GLASS and GAP recommendations.

3.2.1 Research question

What are the gaps in AMR surveillance designs and reporting methodology in Africa?

3.3 Method

This was a desk based research which utilised a systematic review method of evidence synthesis which are designed to distill evidence from a variety of studies including published and unpublished literature in a reproducible manner (Wilson, 2016). Due to the rigor and transparency involved in the conduct of systematic reviews, they are regarded as a high quality unbiased method of providing evidence for practice and policy-making and identifying gaps in research (Sobieraj & Baker, 2021; Aromataris *et al.,* 2015). Since the aim of evidence synthesis is to identify and synthesise all available evidence regarding a research objective including peer and non-peer (grey literature) reviewed, Hopewell *et al*. (2007) argues that a systematic review is not complete if it does not include records from grey sources. Grey literatures though produced outside commercial/academic publishers, represents a valuable body of information that is crucial when synthesising and analysing all available evidence (Adams *et al.,* 2016; Papas and Williams, 2011). To ensure this review exhausted available information sources, grey literatures were also included. This inclusion further reduces the impact of publication bias which is associated with systematic reviews utilising only published papers (Benzies *et al.,* 2006).

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA 2020) reporting checklist (Page *et al.,* 2021). The PRISMA statement was first published in 2009 by Liberati *et al*. (2009) as an evidence-based guideline designed by experts to address an ongoing lack of well documented and transparent review reporting methods in published research papers. An update to this guideline was published in 2020 in

response to the advances in systematic review methodology and terminology. The 2020 PRISMA checklist utilised for this study contains a 27-item reporting checklist to help researchers identify, select, appraise and synthesise studies as well as to optimise the quality of reporting. The systematic review is complemented by Synthesis Without Meta-analysis (SWiM) guidelines (Campbell *et al.*, 2020). The 9-item SWiM guideline was developed to guide clear reporting in reviews of interventions in which alternative synthesis methods to meta-analysis of effect estimates are used. This systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) on 31 July, 2020 under protocol CRD42020192165. A copy of the published protocol is available on https://www.crd.york.ac.uk/prospero/#searchadvanced using the protocol number above as the search word.

3.3.1 Rationale for review method

The choice for this method of review was made on the bases of what is most relevant to answer the research question and meet the acceptable standard for critical and quality appraisal. The overarching goal of this study includes implications for policy recommendation and to increase the strength of recommendation for policy and practice, a research method which reflects rigour, transparency and regarded as gold standard in terms of evidence synthesis was selected. Being that systematic reviews are widely recognised as high quality source of evidence, it was considered most appropriate for the research objective. This is in contrast to scoping reviews which provide an overview or map of available evidence, less likely to assess quality of studies and sometimes act as precursor to a systematic review. Typically, risk of bias assessment is not included in a scoping review thus, limiting its potential to provide concrete guidance for policy or practice recommendation (Munn *et al.,* 2018).

3.3.2 Eligibility criteria

Eligibility was limited to surveillance systems in 47 countries under the WHO-African region. AMR surveillance system in this review is defined as a structured and systematic process that collects data on the prevalence or incidence cases of AMR, performed continuously or periodically, with a defined methodology and specified performance indicators which can be used to monitor progress. Checklist of included countries and surveillance systems is available in appendix A2

3.3.3 Inclusion criteria

Surveillance systems in any of the 47 African countries with identifiable and available methodology, scope and design. Also included are systems endorsed by institutions; regional, national or transnational health organisations; scientific societies; and academic bodies. To further meet the inclusion criteria, the system must be providing data on periodic basis and reporting surveillance data for at least six months on at least one of the following GLASS priority pathogen isolates from human sources (*Acinetobacter spp., Escherichia coli, Neisseria gonorrhoeae, Salmonella spp., Klebsiella pneumoniae, Shigella spp., Staphylococcus aureus, Streptococcus pneumoniae*) (Report, 2014). To be eligible for inclusion, the surveillance system must be based on one of the following surveillance approaches: Active, Passive, Laboratory-based, Population-sentinel, Targeted population-based surveillance for specific pathogen, Sector-specific, Integrated One-Health approach, and Community-based. As the review is focused on surveillance of pathogens isolated from humans, articles reporting AMR in both adult, geriatric and pediatric patient populations were all included. To meet the general inclusion criteria, literature must be written in English language, on one or more of the WHO African countries, report at least one of the review outcomes (surveillance system attributes, surveillance scope, surveillance method, GLASS activity and NAP implementation) and be of relevance to the primary objective of this review.

3.3.4 Exclusion criteria

This review excluded surveillance activities and systems from animals, environment and food; studies on epidemiologic, morphological or cellular analysis; systems that are inactive; articles on antimicrobial susceptibility or sensitivity pattern; studies related to aggregate resistance rates or total bacteria isolates; articles reporting surveillance of tuberculosis, malaria and human immunodeficiency virus; surveillance beyond Africa and non-English publications. Also excluded were articles without available full texts. All publications were individually reviewed and those not meeting the pre-defined inclusion criteria were excluded from the final articles for analysis.

3.3.5 Information sources

Information was sourced from the following five electronic databases (Cochrane, PubMed, EMBASE, Scopus and AJOL). All databases were systematically searched from inception and all articles on AMR surveillance systems from all types of patient populations, published up until December 2021, and written in English language were identified and retrieved. A comprehensive grey literature search was also conducted to identify institutional, regional, national or transnational literature or prints on surveillance systems and country self-assessment questionnaire for AMR in Africa. The grey literature databases searched include: google scholar; websites of WHO, institutes of public health, countries and ministries; Africa Centre for Disease Control and Prevention (ACDC), African Society for Laboratory Medicine (ASLM), and National Centre's for Disease Control (NCDC) (Searched between November and December 2021). Lastly, a secondary search of the bibliography of each of the retrieved article meeting the inclusion criteria were manually checked for additional eligible documents which could have been missed during the database and grey literature search.

3.3.6 Search strategy

The search strategy was developed by the researcher with assistance of faculty librarians at the University of the West of England, Bristol, United Kingdom. Search terms were derived from the Population Intervention Comparison Outcome (PICO) elements shown in appendix A3 (Aslam & Emmanuel, 2010; Richardson *et al.*, 1995). Corresponding subject related synonyms for each keyword were identified and used to build the search strings. The search strategy that was used for database search is available in appendix A4. The search string was primarily developed on PubMed with applicable Boolean operators before translating to other databases using database specific controlled vocabulary. The Boolean operator "OR" was applied between keywords to connect all the synonyms and broaden search result, while "AND" was used to narrow the result by searching for articles with combination of all the keywords. The use of wildcat (*) for "truncation" of root words was also applied. The Medical Subject Heading (MeSH terms) was equally used to help narrow down results and locate studies relevant to research domain were necessary. Filters were applied across database to retrieve articles in English language only, this is due to cost and time involved in procuring translating software or hiring professional translators. Limits were also applied to retrieve articles on human population. For the grey literature search, the websites of all organisations and countries meeting the inclusion criteria were searched using the internal website search function to locate relevant materials. In addition, google was searched for each country utilising the following combination of keywords in English to extract relevant data from publicly available resources: 'antimicrobial resistance' AND/OR 'national action plan' AND/OR 'surveillance systems' AND 'country'.

3.3.7 Selection Process

A total of 4302 articles were retrieved and downloaded into a comma-separated values (CSV) file before exporting to DistillerSR v2 software for screening. DistillerSR (DSR) is a web-based systematic review software developed by evidence partners which follows an intuitive

5-step process and allows for: uploading references, creating screening forms, assigning reviewers, monitoring project progress, and exporting data. The software was set up to assign unique reference ID to each uploaded article for ease of de-duplication, full-text retrieval and reference tracking. The imported documents were first checked for duplicates and identified duplicates were quarantined before commencement of screening using the software work-flow which was setup to perform level 1 to 5 screening. The embedded screening form for each level was adapted to reflect the study specifics. A two-step initial selection process involving: level 1 (rapid title) screening of all the retrieved documents and exclusion of non-relevant documents; and level 2 (detailed abstracts) screening against defined inclusion criteria for all relevant documents was performed. A sample copy of the adapted screening form used for title and abstract screening is provided in appendix A5. All selected articles included after level 2 screening were thoroughly assessed before progressing to level 3. The full text of potentially eligible documents were obtained and assessed for reporting relevant outcome (Country progress, GLASS participation and surveillance system attributes) and documents not meeting the general eligibility criteria were excluded.

3.3.8 Data Collection Process

The embedded data extraction tool in the DSR was adapted to the specifics of the review and was used to manually extract all required data. The tool extracted information on NAP progress, GLASS participation, and surveillance system on country by country basis. The data extraction form that was designed and used for country and surveillance system data collection is available in appendix A6 and A7. The data collected for each country included: surveillance field (human only), NAP development, NAP project timelines, surveillance approach, surveillance activity, establishment of a reference laboratory and GLASS enrolment. For the surveillance systems, data on testing method, sources of data, reporting standard, frequency of reporting, provision of External Quality Assurance (EQA), targeted population,

representativeness, standardisation of procedures, and pathogen type were collected. Surveillance systems were generally grouped under: national, transnational, regional or institutional. Data were aggregated at the level of countries and surveillance systems.

3.3.9 Outcomes

The main outcomes for this review are based on the surveillance system attributes as outlined in the Centre for Disease Control and Prevention guidelines for evaluating public health surveillance systems which includes; data quality, sensitivity, representativeness, acceptability, efficiency, effectiveness and timeliness (Lee *et al.*, 2014; Centres for Disease Control, 1988). Due to limitation of data, this review outcome focused on representativeness, data quality and timeliness. In addition, NAP development and implementation, GLASS enrolment and surveillance reporting were reported as secondary outcomes.

3.3.10 Intervention

Surveillance is the only intervention for this study and it was classified according to 1) Approach which includes: laboratory based, sentinel, population-based, sector-specific surveillance, Integrated One Health approach and Community-based surveillance and 2) Category which includes: National, Sub-national, Transnational, Regional or Institutional.

3.3.11 Risk of bias

All literatures meeting the inclusion criteria were grouped under two categories (Peer reviewed and non-peer reviewed/grey literature) to facilitate appropriate quality checks/critical appraisal. Critical appraisal is the process of carefully and systematically examining research to judge its trustworthiness, relevance and value in a particular context (Burls, 2009). A study characteristics/identifier form provided in appendix A8 was used to categorise the literature into study types. All grey literature including: national, regional, transnational, organisational, assessments, evaluation or policy reports were appraised using the AACODS checklist which

provides five criteria for critiquing grey literature and checks for (Authority, Accuracy, Coverage, Objectivity, Date, Significance) (Tyndall, 2010). For all questions, a 'yes' is assigned if the study meets all the criteria; 'partly' if the study largely meets the criterion but differs in some important aspect; 'no' if the study deviates substantively from the criterion; 'unclear' if the report provides insufficient information to judge whether the study complies with the criterion and 'NA' (not applicable)' if the criterion is not relevant in a particular instance. This critical evaluation was undertaken to ascertain the quality of information retrieved from this source. This is particularly important as grey literatures do not usually receive the same quality checks as peer reviewed published work. A copy of AACODS checklist used for appraising the grey literature is provided in appendix A9.

For peer review articles, the Joanna Briggs Institute (JBI) checklist for systematic review was used to assess the methodological quality of all systematic reviews included in this study. Responses ranging from yes, no, unclear or not applicable were assigned to individual questions in accordance to evidence presented in the study (JBI, 2020). Lastly, the JBI checklist for qualitative research was also used to assess literature that included qualitative and mixed method studies (Lockwood, Munn and Porritt, 2015; Pluye and Hong, 2014). These checklists were generally used to assess the methodological quality and rigors of relevant studies and to determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis. A copy of the JBI checklist used for appraising the systematic reviews and qualitative studies is provided in appendix A10 and A11 respectively**.**

All included surveillance systems were assessed using the basis of surveillance systems attributes recommended in the European Centre for Disease Prevention and Control (ECDC, 2014) guidelines for evaluating public health surveillance systems and checks for: representativeness, data quality and timelines. Detailed table of included publication/documents, the individual study characteristics and critical appraisal tool used is

presented in table 3.1. Links to access each of the publication/documents included in the final analysis is provided in appendix A12.

3.3.12 Data analysis

Data synthesis involved collating and summarising results in tabular form to reflect country progress on the development and implementation of national action plans, AMR surveillance activities, and characteristics of each surveillance system which includes: type of surveillance activities, isolate source, patient population and quality assessments. Frequency of distributions expressed as percentage (%) was calculated for each variable and displayed graphically. Analysis was stratified by country, surveillance system and attributes. The review followed the Synthesis Without Meta-analysis (SWiM) guidelines for the synthesis and reporting of findings extracted from included studies (Campbell *et al.*, 2020).

3.4 Results

3.4.1 Description of study selection

Of the initial 4304 records retrieved from electronic database and grey literature search, 667 duplicates were identified and quarantined by the DSR. The remaining 3637 records passed through two-level screening for title and abstract, after which a further 3561 articles were excluded for not meeting the inclusion criteria. These were articles on AMR surveillance in animals and environment; studies on surveillance for HIV, tuberculosis and malaria; studies on susceptibility/sensitivity pattern, studies on characterisation of infection; morphological studies and studies on burden of AMR. Only the full texts of 76 records which met the eligibility criteria were retrieved and fully reviewed. An additional 49 records were removed after full text review for not reporting at least one of the review outcome which includes; country progress, surveillance system attribute, surveillance scope, surveillance method or any specified performance indicators which can be used to monitor progress. A further 5 records were identified after secondary search of reference tables of included articles. A total of 32

Table 3.1: List of included studies (characteristics and critical appraisal)

S/N	Authors (date)	Title	Study design	Main objective	Setting	Quality assessment tool used
1	Seale et al., 2017	Supporting surveillance capacity for antimicrobial resistance: Laboratory capacity strengthening for drug resistance infection in low and middle income countries	Desk-based analysis Focus group discussion Observational	To map and compare existing models and surveillance systems for AMR, to examine what worked and what did not work.	Ethiopia, Malawi	JBI
2	Jimah & Ogunseitan 2020	National action plan on antimicrobial resistance: stakeholders analysis on implementation in Ghana	Qualitative interviews	To better understand stakeholders perspective on the implementation and sustainability of the NAP	Ghana	JBI
3	Hazim et al., 2018	Establishment of a sentinel laboratory based AMR surveillance network in Ethiopia.	Situational analysis	To describe how laboratory-based AMR surveillance was implemented in Ethiopia including challenges and lessons learned to help guide successful AMR surveillance in other settings.	Ethiopia	AACODS
4	WHO (GLASS) 2021	Global Antimicrobial Resistance and use Surveillance report.	Implementation status of national AMR surveillance systems	To describe countries activities in relation to AMR surveillance systems.	AFRO region	AACODS
5	WHO (GLASS) 2020	Global Antimicrobial Resistance and use Surveillance report.	Early implementation summary report	To describe countries activities in relation to AMR surveillance systems.	Cote d'Ivoire, Ethiopia, Gambia, Kenya, Liberia, Madagascar, Mali, Mauritius, Mozambique, Nigeria, South Africa, Uganda, United republic of Tanzania, Zambia, Zimbabwe	AACODS
6	WHO (GLASS) 2019	Global Antimicrobial Resistance and use Surveillance report.	Early implementation summary report	To describe countries activities in relation to AMR surveillance systems.	Ethiopia, Gambia, Kenya, Liberia, Madagascar, Malawi, Mali, Mauritius, Mozambique, Nigeria, South Africa, Uganda, Zambia, Zimbabwe	AACODS

7	WHO (GLASS) 2018	Global Antimicrobial Resistance and use Surveillance report.	Early implementation summary report	To describe countries activities in relation to AMR surveillance systems.	Kenya, Madagascar, Malawi, Mozambique, Nigeria, South-Africa, Uganda, Zambia, Zimbabwe	AACODS
8	WHO 2017-2020	Joint external evaluation (JEE) of International health regulations (IHR) core capabilities	Mission evaluation report	To assess country capacities and capabilities relevant to the 19 technical areas of the JEE and provide data to inform current strengths, areas for improvement and priority actions.	AFRO region	AACODS
9	FAO, OiE and WHO 2021	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	Self-assessment questionnaire	Report of country progress in the implementation of national action plans	AFRO region	AACODS
10	FAO, OiE and WHO 2020	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	Self-assessment questionnaire	Report of country progress in the implementation of national action plans	AFRO region	AACODS
11	FAO, OiE and WHO 2019	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	Self-assessment questionnaire	Report of country progress in the implementation of national action plans	AFRO region	AACODS
12	FAO, OiE and WHO 2018	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	Self-assessment questionnaire	Report of the second round of results of AMR country self-assessment survey	AFRO region	AACODS
13	FAO, OiE and WHO 2017	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	Self-assessment questionnaire	To monitor country progress in the implementation of national action plans	AFRO region	AACODS
14	Ogyu et al., 2020	National action plan to combat AMR: a One-Health approach to assess policy priorities in action plans	Quantitative analysis	To systematically categorize, describe and quantify useful information about AMR policies and content of NAPs.	AFRO region	JBI
15	WHO 2014	Global action plan on antimicrobial resistance	Policy guide	Manual for developing national action plans.	Trans-regional	AACODS
16	NAP 2021	National action plan antimicrobial resistance		Tackling antimicrobial resistance	Eritrea	AACODS

17	NAP 2018	National action plan antimicrobial resistance containment strategy	Strategic plan	Implementation plan	Eswatini	AACODS
18	NAP 2015	The national action plan on antimicrobial resistance	Strategic plan	To address actions needed to be taken in order to combat AMR in the country.	Ethiopia	AACODS
19	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	To summarize the structure for the development and implementation of the NAP	Ghana	AACODS
20	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	A national strategic plan to address AMR in human, animal, crops, food safety and environmental aspects	Kenya	AACODS
21	NAP 2018	The national action plan on antimicrobial resistance	Strategic plan	To address actions needed to be taken in order to combat AMR in the country.	Liberia	AACODS
22	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	A national strategic plan to address AMR in human, animal, crops, food safety and environmental aspects	Malawi	AACODS
23	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	To address actions needed to be taken in order to combat AMR in the country.	Mauritius	AACODS
24	NAP 2017	Namibian antimicrobial resistance action plan	Strategic plan	Action plan for antimicrobial resistance	Namibia	AACODS
25	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	A national strategic plan to address AMR in human, animal, crops, food safety and environmental aspects	Nigeria	AACODS
26	NAP 2020	National action plan on antimicrobial resistance	Strategic plan	Combating antimicrobial resistance	Rwanda	AACODS
27	NAP 2018	National strategic plan for combating antimicrobial resistance	Strategic plan	Tackling antimicrobial resistance	Sierra Leone	AACODS
28	NAP 2014	The national action plan on antimicrobial resistance	Strategic plan	To summarize the structure for the development and implementation of the NAP	South Africa	AACODS
29	NAP 2018	The national action plan on antimicrobial resistance	Strategic plan	To summarize the structure for the development and implementation of the NAP	Uganda	AACODS

30	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	To address actions needed to be taken in order to combat AMR in the country.	United republic of Tanzania	AACODS
31	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	To summarize the structure for the development and implementation of the NAP	Zambia	AACODS
32	NAP 2017	The national action plan on antimicrobial resistance	Strategic plan	A national strategic plan to address AMR in human, animal, crops, food safety and environmental aspects	Zimbabwe	AACODS

articles met the overall inclusion criteria and were considered in this synthesis. Article selection process is summarised in the PRISMA flow chart figure 3.1.

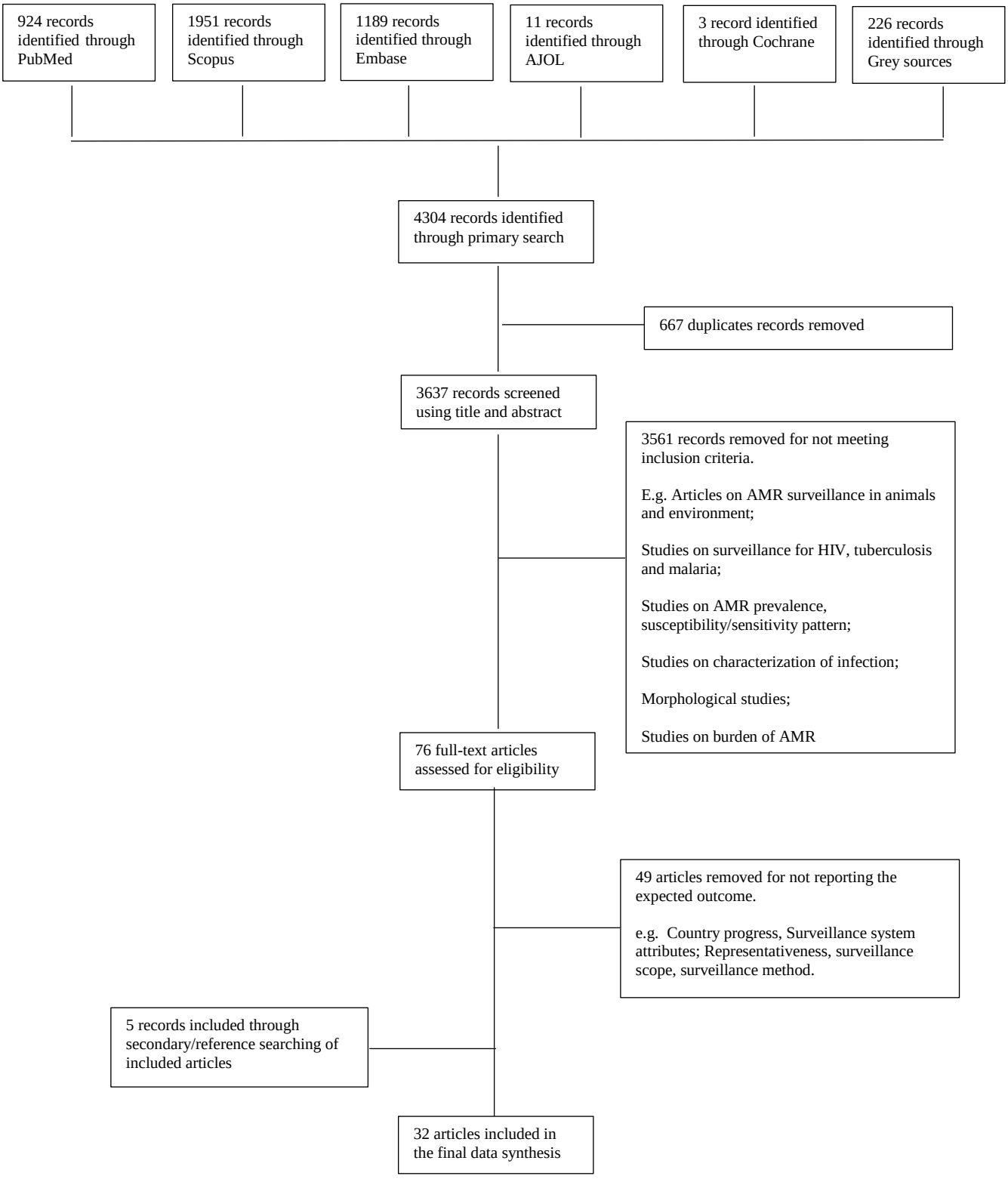


Figure 3.1: PRISMA flow chart showing screening steps of articles retrieved from database and grey literature search

3.4.2 Characteristics of included studies

Of the 32 fully reviewed records, 4 records were published peer reviewed journals and 28 records were retrieved from grey sources. The grey literature records comprised of 4x GLASS reports, 1x Joint External Evaluation (JEE) of International Health Regulations (IHR) core capabilities, 5x The Tripartite Antimicrobial Resistance Country Self-assessment Survey (TrACSS) reports on monitoring progress on addressing AMR, 1x WHO GAP policy guide and 17 NAPs.

3.4.3 National action plans

Data revealed that countries within the region are at various stages with the development and implementation of their NAPs. NAPs development and implementation is progressive albeit gradual. Majority of the African countries have developed a NAP for antimicrobial resistance. Currently, thirty-five (74.5%) countries of the 47 WHO-AFRO region have developed/implemented NAP for AMR, five (10.6%) countries have their action plans undergoing development and in seven (14.9%) countries, no information regarding NAP development status for AMR was reported.

Figure 3.2 shows trends in development and implementation of NAPs over the five years of GAP launch in the region. Of the thirty-five NAPs detected, only nineteen were publicly available. After review against eligibility criteria, only seventeen NAPs met the inclusion criteria. These are national action plans that have been published, are publicly available and written in English. National action plans for the rest of the countries could not be assessed as they were either non-English or not publicly available. Data collected also showed that NAP implementation indicators are not commensurate with NAPs development despite reports of implementation and funding. Indicators such as presence of a National Reference Laboratory (NRL), National Coordinating Centers (NCC), sentinel sites and functional laboratories were

not reported to be operational in all the NAPs reviewed. Of the seventeen NAPs assessed, only thirteen (76.5%) countries reported to have established a NRL. In terms of surveillance activity for AMR, varying levels of activities were recorded: four (23.5%) countries reported having a functioning national AMR surveillance covering common bacterial infections in hospitalised and community patients, with EQA; one (5.9%) country reported conducting surveillance at sentinel sites for some pathogens of public health importance; five (29.4%) countries reported having a national AMR surveillance system that integrates surveillance of AMR across sectors, and generates regular reports covering at least one common indicator; three (17.6%) countries reported AMR data is collated locally for common bacteria, but data collection may not use a standardised approach and lacks national coordination and/or quality management; one (5.9%) country reported presence of laboratories with technical capacity for AMR detection/reporting; one (5.9%) country reported sentinel sites for AMR surveillance have been identified in the human health sector to increase geographical coverage; two (11.8%) country reported no capacity for generating AMR data.

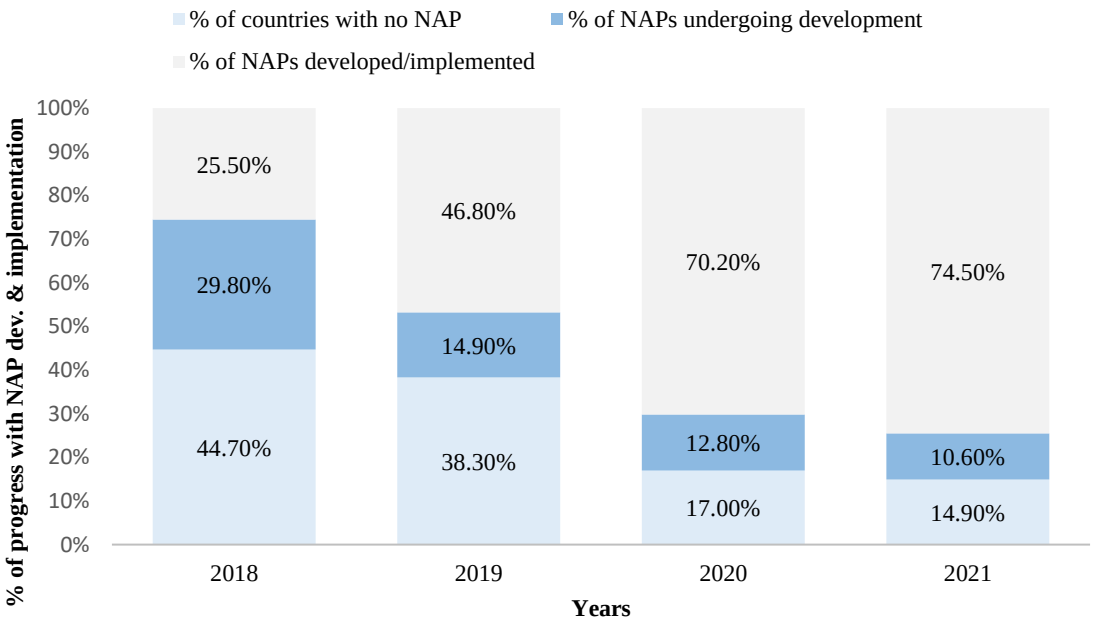


Figure 3.2: Trends in development and implementation of NAPs in the region for the period reviewed

In terms of approach to tackling AMR: ten (58.8%) countries reported using multi-sectoral approach; one (5.9%) country reported use of One-health approach; four (23.5%) countries reported joint working; two (11.8%) countries reported no formal multi-sectoral governance or coordination mechanism on AMR exists. Table 3.2 shows the seventeen NAPs assessed and their implementation indicators in-line with GAP objectives.

3.4.4 Country level surveillance systems for AMR

Thirty (30) surveillance systems were initially detected from the 47 countries in the WHO African region. After review of available information regarding these surveillance systems, six surveillance systems were excluded for not reporting surveillance data, one system was excluded for reporting Antimicrobial Consumption (AMC) surveillance data only. Only twenty-three systems met the inclusion criteria and these are systems in place for routine AMR surveillance and data collection. All systems identified as national surveillance. Table 3.3 shows the general features of these surveillance systems for which data were extracted. Data shows population pool from these surveillance systems are generally from laboratories, hospitals, out-patients and in-patients sources. All systems also reported AMR data collection from patients of all ages though the actual patient ages were not reported. Fourteen (60.9%) system reported frequency of reporting as yearly, four (17.4%) systems reported frequency as pooled, five (21.7%) reported both yearly and pooled. Technical level of data management of the laboratory network in the AMR surveillance systems also vary: five (21.7%) systems reported most laboratories of the network use computers to manage part of their data but important improvements in the system are required; four (17.4%) systems reported some minor improvements are required in some laboratories of the network to improve computerised management of AMR laboratory data; six (26.1%) systems reported Antimicrobial Susceptibility Testing (AST) data are handled manually, or AST data management is not computerised in all laboratories of the network and/or there are problems in the recording of

Table 3.2: Status of national action plans development and implementation indicators in the region

Country	Progress with development of Action plan on AMR	Timeline	Multisector/one health approach	Surveillance activity for AMR	National Reference laboratory	Reporting to GLASS
Eritrea	NAP developed	2021-2025	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.	AMR data is collated locally for common bacteria, but data collection may not use a standardised approach and lacks national coordination and/or quality management.	Not established	No
Eswatini	NAP developed	2021-2025	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.	National AMR surveillance activities for common bacterial infections follow national standards, and a national reference laboratory that participates in external quality assurance	Established	No
Ethiopia	National AMR action plan approved by government that reflects Global Action Plan objectives, with a budgeted operational plan and monitoring arrangements.	2015-2020	Multi-sectoral working group(s) is (are) functional, with clear terms of reference, regular meetings, and funding for working group(s) with activities and reporting/accountability arrangements defined.	There is a functioning national AMR surveillance system covering common bacterial infections in hospitalised and community patients, with external quality assurance, and a national coordinating centre producing reports on AMR.	Established	Yes
Ghana	National AMR action plan has funding sources identified, is being implemented, and has relevant sectors involved with a defined monitoring and evaluation process in place	2017-2021	Joint working on issues including agreement on common objectives.	National AMR surveillance activities for common bacterial infections follow national standards, and a national reference laboratory that participates in external quality assurance.	Established	Yes
Kenya	National AMR action plan approved by government that reflects Global Action Plan objectives, with a budgeted operational plan and monitoring arrangements.	2017-2020	Joint working on issues including agreement on common objectives	There is a functioning national AMR surveillance system covering common bacterial infections in hospitalized and community patients, with external quality assurance, and a national coordinating centre producing reports on AMR.	Established	Yes

Liberia	National AMR action plan has funding sources identified, is being implemented, and has relevant sectors involved with a defined monitoring and evaluation process in place.	2018-2022	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.	AMR data is collated locally for common bacteria, but data collection may not use a standardised approach and lacks national coordination and/or quality management.	Established	Yes
Mauritius	NAP developed	2017-2021	No formal multi-sectoral governance or coordination mechanism on AMR exists	There are laboratories that have the technical capacity for antimicrobial detection/reporting.	Established	Yes
Malawi	NAP developed, approved and launched.	2017-2022	No formal multi-sectoral governance or coordination mechanism on AMR exists	No capacity for generating data (antibiotic susceptibility testing and accompanying clinical and epidemiological data) and reporting on antibiotic resistance.	Not established	No
Namibia	NAP developed	2017-2022	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.	National AMR surveillance activities for common bacterial infections follow national standards, and a national reference laboratory that participates in external quality assurance.	Established	No
Nigeria	National AMR action plan approved by government that reflects Global Action Plan objectives, with a budgeted operational plan and monitoring arrangements.	2017-2022	Multi-sectoral working group(s) is (are) functional, with clear terms of reference, regular meetings, and funding for working group(s) with activities and reporting/accountability arrangements defined	National AMR surveillance activities for common bacterial infections follow national standards, and a national reference laboratory that participates in external quality assurance.	Established	Yes
Rwanda	NAP developed	2020-2024	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership	AMR data is collated locally for common bacteria, but data collection may not use a standardised approach and lacks national coordination and/or quality management.	No information	No
Sierra-Leone	NAP developed	2018-2022	Multi-sectoral working group(s) or coordination committee on AMR established with Government leadership.	No capacity for generating data (antibiotic susceptibility testing and accompanying clinical and	Not established	No

				epidemiological data) and reporting on antibiotic resistance.		
South Africa	NAP developed	2014-2024	Joint working on issues including agreement on common objectives	There is a functioning national AMR surveillance system covering common bacterial infections in hospitalised and community patients, with external quality assurance, and a national coordinating centre producing reports on AMR.	Established	Yes
Uganda	NAP developed	2018-2023	Functional multi-sectoral working group	AMR Surveillance sentinel sites have been identified in the human health sector to increase geographical coverage.	Established	Yes
United Republic of Tanzania	National AMR action plan has funding sources identified, is being implemented, and has relevant sectors involved with a defined monitoring and evaluation process in place.	2017-2022	Joint working on issues including agreement on common objectives.	There is a functioning national AMR surveillance system covering common bacterial infections in hospitalised and community patients, with external quality assurance, and a national coordinating centre producing reports on AMR.	Established	Yes
Zambia	National AMR action plan approved by government that reflects Global Action Plan objectives, with a budgeted operational plan and monitoring arrangements	2017-2027	Multi-sectoral working group(s) is (are) functional, with clear terms of reference, regular meetings, and funding for working group(s) with activities and reporting/accountability arrangements defined	There is a functioning national AMR surveillance system covering common bacterial infections in hospitalised and community patients, with external quality assurance, and a national coordinating centre producing reports on AMR.	Established	Yes
Zimbabwe	NAP developed	2017-2021	One health	Sentinel sites are conducting surveillance of some pathogens of public health importance.	Established	Yes

Table 3.3: General features of antimicrobial resistance (AMR) surveillance systems identified and classified according to study criteria

Country	Surveillance coverage	Focus/scope	Targeted population	Reported age group	Frequency of reporting	Technical level of data management of the laboratory network in the AMR surveillance system	Pathogens reported					
							Acinetobacter spp.	*E. coli*	*K. pneumoniae*	*Salmonella spp.*	*S. aureus*	*S. pneumoniae*
Algeria	National	AMR	Hospitals and out patients	All ages	Yearly	Most laboratories of the network use computers to manage part of their data but important improvements in the system are required	✓	✓	x	x	x	x
Burundi	National	AMR	Hospitals In-out patients	All ages	Pooled	AST data are handled manually, or AST data management is not computerized in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	✓	x	✓	x	x
Cameroon	National	AMR	Hospitals	All ages	Yearly	Not reported	x	✓	x	✓	x	✓
Chad	National	AMR	Hospitals	All ages	Yearly	AST data are handled manually, or AST data management is not computerized in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	x	x	✓	✓	x
Cote d'Ivoire	National	AMR	Hospitals	All ages	Yearly	Most laboratories of the network use computers to manage part of their data but important improvements in the system are required	x	x	x	x	x	x
Ethiopia	National	AMR	Hospitals Out patients	All ages	Yearly/pooled	Some minor improvements are required in some laboratories of the network to improve the computerized management of AMR laboratory data	✓	✓	✓	x	✓	✓
Gabon	National	AMR	Laboratories	All ages	Yearly	Not reported	x	✓	x	x	x	x

Gambia	National	AMR	Hospitals	All ages	Yearly/Pooled	Not reported	x	x	x	✓	x	✓
Ghana	National	AMR	Hospitals	All ages	Yearly	AST data are handled manually, or AST data management is not computerized in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	✓	x	✓	x	x
Kenya	National	AMR	Hospitals Outpatients	All ages	Yearly/Pooled	Some minor improvements are required in some laboratories of the network to improve the computerized management of AMR laboratory data (sample input procedures, sample storage information, computerized transmission of data, etc…)	✓	x	x	✓	x	x
Liberia	National	AMR	Hospitals	All ages	Yearly/pooled	AST data are handled manually, or AST data management is not computerized in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	✓	x	x	x	x
Madagascar	National	AMR	Laboratories	All ages	Yearly	Most laboratories of the network use computers to manage part of their data but important improvements in the system are required	✓	✓	✓	✓	✓	✓
Malawi	National	AMR	In-outpatient facilities	All ages	Pooled	Not reported	✓	✓	✓	✓	✓	✓
Mali	National	AMR	Hospitals Out patients	All ages	Yearly	Some minor improvements are required in some laboratories of the network to improve the computerized management of AMR laboratory data.	✓	✓	✓	✓	✓	✓
Mauritania	National	AMR	Hospitals	All ages	Yearly	Not reported	✓	x	x	x	x	✓
Mauritius	National	AMR	Hospitals	All ages	Pooled	AST data are handled manually, or AST data management is not computerized in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	x	x	x	x	✓
Mozambique	National	AMR	Hospitals	All ages	Pooled	Not reported	✓	✓	✓	✓	✓	✓

Nigeria	National	AMR	Inpatient and outpatient facilities	All ages	Yearly	Not reported	✓	✓	✓	✓	✓	✓
South Africa	National	AMR	Hospitals and outpatient facilities	All ages	Yearly/pooled	Most laboratories of the network use computers to manage part of their data but important improvements in the system are required	✓	✓	✓	✓	✓	✓
Uganda	National	AMR	Hospitals and outpatient	All ages	Yearly	Not reported	x	✓	✓	✓	✓	x
United Republic of Tanzania	National	AMR	Hospitals	All ages	Yearly	Most laboratories of the network use computers to manage part of their data but important improvements in the system are required	x	x	✓	✓	✓	✓
Zambia	National	AMR	Inpatient and outpatient facilities	All ages	Yearly	Some minor improvements are required in some laboratories of the network to improve the computerized management of AMR laboratory data	✓	✓	✓	✓	✓	x
Zimbabwe	National	AMR	Laboratories	All ages	Yearly	AST data are handled manually, or AST data management is not computerised in all laboratories of the network and/or there are problems in the recording of the samples and their traceability along the analysis chain	x	x	✓	✓	x	✓

Not reported (x) Reported pathogen (✓)

the samples and their traceability along the analysis chain; eight (34.8%) systems did not report technical level of data management.

These surveillance systems also features specific characteristics which are reported in table 3.4. The report shows that South-Africa had the highest number of surveillance sites totaling 737 while Gambia and Mozambique had the least with a single site each. Testing methods are consistent across all system. Twenty-two (95.7%) systems reported use of AST standard, only one (4.3%) system reported the use of both AST and Whole Genome Sequencing (WGS). EQA is provided to majority of the NRLs affiliated to these surveillance systems. Of the twenty-three surveillance systems assessed, nineteen (82.6%) systems reported provision of EQA to the NRLs; four (17.4%) system reported no provision of EQA to the NRL. Of the nineteen systems providing EQA to their NRL, only eight (42.1%) systems reported provision of EQA to all other local laboratories performing AST for AMR surveillance; two (10.5%) reported provision of EQA to some laboratories performing AST for AMR surveillance; nine (47.4%) systems do not provide EQA to non-reference laboratories which performs and reports AST for AMR surveillance to national networks. For all the twenty-three surveillance systems that were assessed, record of the use of AST interpretation criteria was available for sixteen systems; among these, the Clinical and Laboratory Standards Institute (CLSI) breakpoint was used in twelve (75%) countries; the European Committee for Antimicrobial Susceptibility Testing (EUCAST) breakpoint was used as reference in one (6.3%) country; in 3 (18.7%) countries, some laboratories use CLSI and others use EUCAST. Only eighteen systems reported level of standardisation and harmonisation of procedures among laboratories included in the AMR surveillance system, the other five systems did not record this information. Of the eighteen systems reporting this indicator: three (16.7%) reported 100% of their laboratories use the same AST guidelines; two (11.1%) system reported between 80% and < 100% of laboratories use the same AST guidelines; four (22.2%) reported between 30% to 79% of

Table 3.4: Characteristics of included surveillance systems for antimicrobial resistance from the region

Country	Primary source of data	Number of surveillance sites	Testing method used	Resistance criteria /reporting standard	Provision of EQA to local laboratories	Provision of EQA to NRL	Data on number of tested patients	Infection origin	Level of the standardization and harmonization of procedures among laboratories included in the AMR surveillance system
Algeria	Hospitals	Not reported	AST standard	Not reported	Not provided	Not provided	Not reported	Not reported	100% of laboratories use the same AST guidelines
Burundi	Hospitals Laboratory	14	AST standard	CLSI	Not provided	Provided	Not reported	Not reported	Not reported
Cameroon	Hospitals	Not reported	AST standard	Not reported	Not provided	Not provided	Not reported	Not reported	No standardized national AST guidelines are in place or Less than 30% laboratories follow the same AST guidelines
Chad	Hospitals	Not reported	AST standard	Not reported	Not provided	Not provided	Not reported	Not reported	No standardized national AST guidelines are in place or Less than 30% laboratories follow the same AST guidelines
Cote d'Ivoire	Laboratory	52	AST standard	Not reported	Not provided	Not provided	Not reported	Not reported	No standardized national AST guidelines are in place or less than 30% laboratories follow the same AST guidelines
Ethiopia	Laboratory	9	AST standard	CLSI	Provided to all labs	Provided	Not reported	Reported	Between 30% to 79% of laboratories follow the same AST guidelines
Gabon	NRL	2	AST standard	Not reported	Not provided	Provided	Not reported	Not reported	Not reported
Gambia	Laboratory	1	AST standard	CLSI	Not provided	Provided	Not reported	Not reported	Not reported
Ghana	laboratory	Not reported	AST standard	Not reported	Provided to some labs	provided	Not reported	Not reported	No standardized national AST guidelines are in place or less than 30% laboratories

									follow the same AST guidelines
Kenya	Laboratory	5	AST standard	CLSI	Provided to all labs	Provided	Not reported	Not reported	Between 80% and < 100% of laboratories use the same AST guidelines
Liberia	Laboratory	3	AST standard	CLSI	Not provided	Provided	Not reported	Not reported	No standardized national AST guidelines are in place or less than 30% laboratories follow the same AST guidelines
Madagascar	Laboratory	9	AST standard	EUCAST /CLSI	Not provided	Provided	Not reported	<70% Reported	Between 30% to 79% of laboratories follow the same AST guidelines
Malawi	Laboratory	14	AST standard	EUCAST	Provided to all labs	Provided	<70% data reported	Not reported	Not reported
Mali	Laboratory	5	AST standard	EUCAST /CLSI	Provided to all labs	Provided	70-100% Reported	Not reported	100% of laboratories use the same AST guidelines
Mauritania	Laboratory	Not reported	AST standard	Not reported	Not provided	Provided	Not reported	Not reported	No standardized national AST guidelines are in place or Less than 30% laboratories follow the same AST guidelines
Mauritius	Laboratory	154	AST standard	CLSI	Not provided	Provided	Not reported	Not reported	No standardized national AST guidelines are in place or Less than 30% laboratories follow the same AST guidelines
Mozambique	Laboratory	1	AST standard	CLSI	Provided to all labs	Provided	70-100% data reported	70-100% data reported	Between 80% and < 100% of laboratories use the same AST guidelines
Nigeria	Laboratory	29	AST standard	CLSI	Provided to some labs	Provided	Data not reported	<70% data reported	No standardized national AST guidelines are in place or less than 30% laboratories follow the same AST guidelines

South Africa	Laboratory	737	AST standard/ WGS	EUCAST and CLSI	Provided to all labs	Provided	70-100% data reported	Not reported	100% of laboratories use the same AST guidelines
Uganda	Laboratory	22	AST standard	CLSI	Provided to all labs	Provided	70-100% reported	Not reported	Between 30% to 79% of laboratories follow the same AST guidelines
United Republic of Tanzania	Laboratory	63	AST standard	CLSI	Provided to all labs	Provided	Not reported	Not reported	No standardized national AST guidelines are in place or less than 30% laboratories follow the same AST guidelines
Zambia	Laboratory	6	AST standard	CLSI	Not provided	Provided	No data reported	No data reported	Between 30% to 79% of laboratories follow the same AST guidelines
Zimbabwe	Hospitals and laboratories	5	AST standard	CLSI	Not provided	Provided	Not reported	Not reported	Not reported

laboratories follow the same AST guidelines; nine (50%) reported no standardised national AST guidelines are in place or less than 30% laboratories follow the same AST guidelines.

3.4.5 Transnational surveillance systems for AMR

In addition to the national surveillance systems, 11 trans-national surveillance systems were also detected. These surveillance systems are supported by government and institutional funding; some pharmaceutical companies including Pfizer, Glaxo Smith Kline (GSK), Merck and co; and other organisations such as Bill and Melinda Gates Foundation (BMGF), WHO, and CDC. These systems collect data on a wide range of pathogens including *Enterococcus spp., Staphylococcus spp., Klebsiella, Acinetobacter spp., Pseudomonas spp.* and *Enterobacter spp.* (the ESKAPE pathogens). Some of these systems have been conducting surveillance before the WHO-GAP and GLASS launch but their operational scopes were not available, hence their exclusion for not meeting the inclusion criteria. Table 3.5 shows features of these surveillance systems that were excluded from the review.

3.4.6 Enrollment and data reporting to Global Antimicrobial Resistance and Use Surveillance System (GLASS)

As shown in figure 3.3, countries are gradually responding to invitation for enrollment and calls for data reporting to GLASS (a network that collects data on global AMR surveillance). Of the 47 African countries that were reviewed, only ten (21.3%) countries were enrolled on the GLASS network as at 2018 report, this number increased to fifteen (31.9%) countries in 2019 and then to nineteen (40.4%) and thirty (63.8%) countries at 2020 and 2021 reports respectively. Following the same trend, surveillance data reporting to GLASS recorded gradual increase at the various call for data submission. Of the 47 African countries that were reviewed, nine (19.1%) countries reported surveillance data during the first call, this number increased to fourteen (29.8%) countries at the second call and then to fifteen (31.9%) countries at both the

third and fourth calls. Similar trend was also observed in the number of surveillance sites in the region. As shown in figure 3.4 surveillance sites increased from only 35 sites in 2018 to

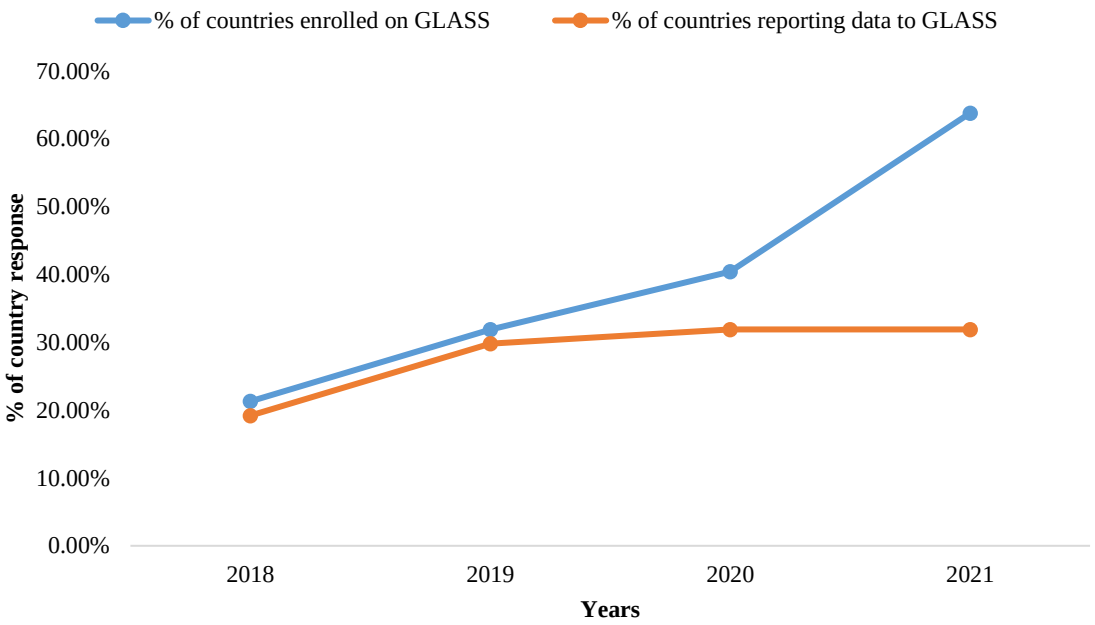


Figure 3.3: Showing percentage of countries enrolled to GLASS and countries reporting surveillance data to GLASS for the period reviewed. The percentage of the respective parameters (enrolled and reporting) were calculated for each year using 47 as the denominator

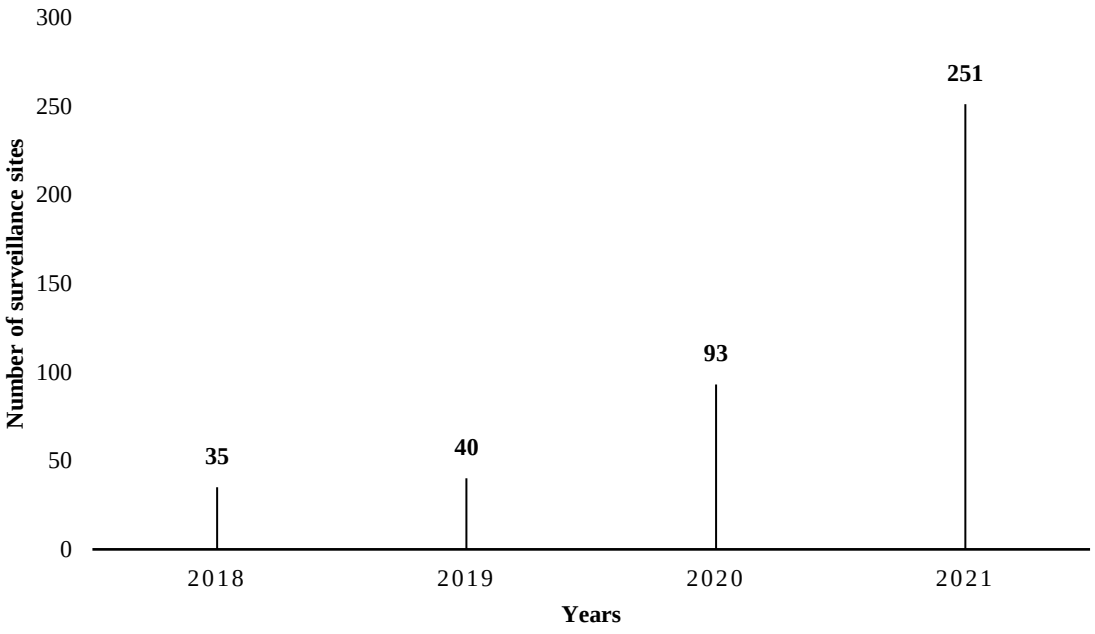


Figure 3.4: Trends in the increase of the number of surveillance sites reporting data to GLASS for the period reviewed

251 sites in 2021. Very importantly, data collected from surveillance systems reporting to GLASS shows some surveillance parameters were either underreported or completely missing. Figure 3.5 shows percentage of systems reporting some of these required surveillance indicators. It shows infection origin as the least reported indicator four (17.4%), whereas pathogen type is the most reported. Only five (21.7%) systems reported information on patient population.

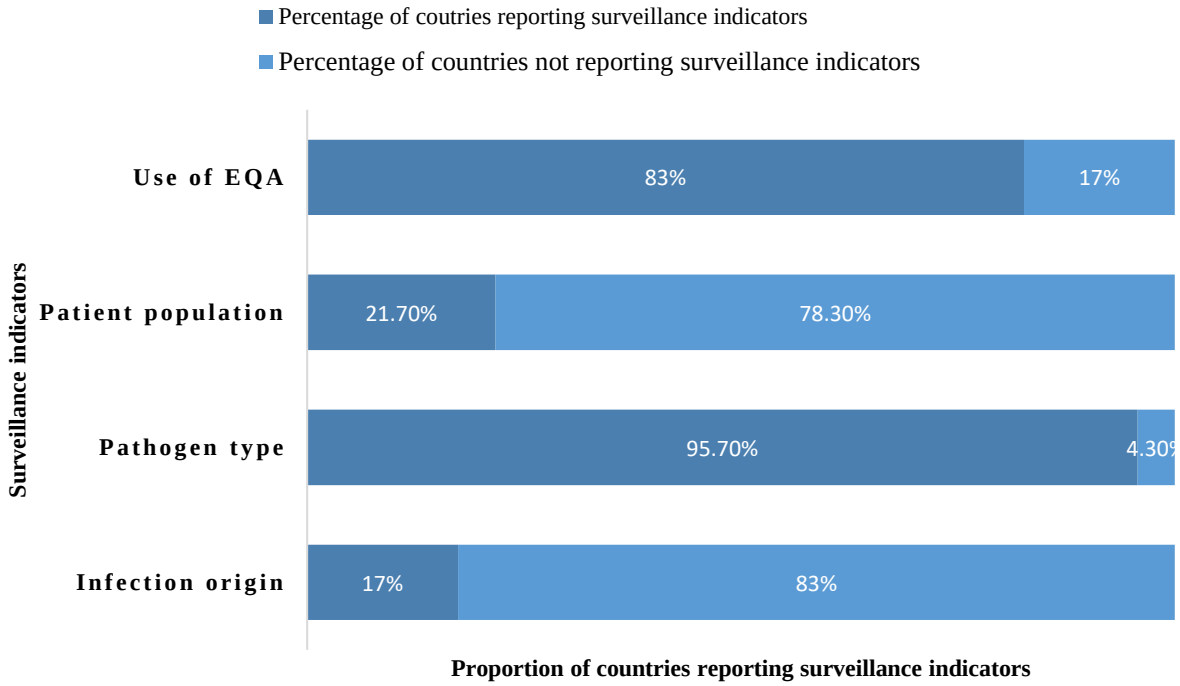


Figure 3.5: Showing percentage of systems reporting important surveillance indicators

Table 3.5: Transnational Surveillance activities identified and classified according to the study criteria (general features and characteristics). These systems were excluded for non-availability of information on operational scope

Surveillance system	Countries	Website	Funding Organisation	Types	Year	Pathogens
Africa CDC Anti-Microbial Resistance Surveillance Network (AMRSNET)	All Africa Countries	https://mail.africacdc.org/about/africa-cdc-antimicrobial-resistance-surveillance-network	Africa Union	Trans-national	2018-ongiong	unselected
Community-Based Surveillance of Antimicrobial Use and Resistance in Resource Constrained Settings Project Group	India, South Africa	https://doi.org/10.1111/j.1365-3156.2010.02695.x	USAID	Pilot project	2010	*Streptococcus pneumoniae, Haemophilus influenzae*
Global Antibiotic Resistance Partnership (GARP)	India, Kenya, Mozambique, Nepal, South Africa, United Republic of Tanzania, Uganda.	https://cddep.org/projects/global-antibiotic-resistance-partnership/	BMGF foundation	Academic	2008-ongoing	Unselected
The Gonococcal Antimicrobial Surveillance Programme (GASP)	WHO regions	https://www.who.int/data/gho/data/themes/topics/who-gonococcal-amr-surveillance-programme-who-gasp	WHO	Trans-regional	1992-ongoin	*Neisseria gonorrhoeae*
International Network for the Study and Prevention of Emerging Antimicrobial Resistance	Cote d'Ivoire, Morocco, Senegal, Tunisia	https://wwwnc.cdc.gov/eid/article/7/2/70-0319_article	Public (CDC)	Academic	1998-2010	*Streptococcus spp., Streptococcus pneumoniae, Staphylococcus spp., Enterobacteriaceae, Neisseria meningitidis, Acinetobacter baumannii, Salmonella Typhi, Haemophilus influenzae, Brucella spp.,Clostridium*
African-German StaphNet consortium	Tanzania, Gabon, Mozambique	https://doi.org/10.2217/fmb.12.126	Public (Deutsche Forschungsgemeinschaf)	Clinical study	2010-ongoing	S.aureus

Survey of Antibiotic Resistance (SOAR)	Democratic Republic of Congo, Senegal, Nigeria, Turkey, Egypt, South Africa, Morocco, Tunisia,	https://www.amrindustryalliance.org/case-study/gsks-survey-of-antibiotic-resistance-soar/	Pharma (GlaxoSmithKline)	Research	2002-ongoing	Streptococcus pneumoniae, Haemophilus influenzae
Community Acquired Bacteremic Syndromes in Young Nigerian Children (CABSYNC)	Nigeria	https://www.unmc.edu/pediatrics/research/ifain/projects/index.html	NIH and Gate Foundation	Academic	2008-ongoing	Unselected but including GLASS pathogens
Community Acquired Pneumonia and Invasive Bacterial Diseases in Young Nigerian Children (CAPIBD)	Nigeria	http://www.ifain.org/projects/capbid/	NIH and Gate Foundation	Academic	2012-2018	Unselected but including GLASS pathogens
Burden for Antimicrobial resistance in Neonates in Developing Societies(BARNARDS)	Nigeria South Africa Rwanda Ethiopia	https://www.ineosoxford.ox.ac.uk/research/barnards	BMGF	Academic	2015-2018	GLASS pathogens
Group for Enteric, Respiratory, and Meningeal Surveillance in South Africa(GERMS-SA)	South Africa	https://www.nicd.ac.za/wp-content/uploads/2019/11/GERMS-SA-AR-2018-Final.pdf	South Africa Government	Government	2003-ongoing	GLASS pathogens

3.5 Discussion

The most important findings from this systematic review of surveillance systems for AMR in Africa are: (a) there is evidence of development and implementation of NAPs (b) majority of the surveillance systems perform AST (c) EQA are not routinely performed across participating laboratories (d) some important surveillance parameters are not recorded (e) information on incidence-based-indicators are generally lacking in all the systems (f) there is no tool for evaluating the effectiveness of surveillance system for AMR. Data collected for this review suggests that surveillance activities for AMR is beginning to gain traction in the region though levels of implementation still varies across the three core components of national AMR surveillance indicators (NCC, NRL, and sentinel surveillance sites). Surveillance expansion in the region is indicative of commitment on the part of governmental agencies and political will towards prioritising policies aimed at addressing AMR. More countries are beginning to respond to AMR surveillance which shows a progressive trend compared to previous reports (Varma *et al.,* 2018; Tadesse *et al*., 2017; Essack *et al.,* 2017). This can be attributed to the recognition of the importance of AMR surveillance by WHO and the recommendations for development and implementation of NAPs for AMR (WHO, FAO, and OIE, 2016). As highlighted in the WHO-GAP on AMR, establishing an efficient AMR surveillance begins with the development of a NAP that reflects the objectives of the GAP (World Health Organisation, 2015). This is reflected in the data collected for this review as all the NAPs are developed in accordance with the GAP objectives. Despite the slow and gradual development, the number of countries with comprehensive NAPs that reflect the objectives of AMR surveillance have increased from only one country in 2014 to thirty-five in 2022. It is understandable that achieving AMR surveillance goes beyond NAP development but largely to implementing these plans and translating them to actual AMR surveillance. Though reports of NAP implementation which is an important step towards establishing surveillance and AMR

containment are available, indicators that serve as evidence of NAP implementation are yet to be actioned in some systems. Whilst it is obvious that countries are yet to implement to the full scale actions that are proportionate to the AMR challenges faced by the region, tools that assess and monitor NAP implementation are required to identify strengths, challenges and gaps.

The region has also recorded increase in the number of national surveillance activities compared to the pre GAP-AMR era where all identified AMR surveillance and related activities in the region were mainly trans-national surveillance. The presence of more AMR focused surveillance systems in the region suggests that countries are beginning to recognise the importance of surveillance as a tool for tackling AMR, though major improvements are needed in the aspects of data collection and reporting protocols particularly as they relate to data quality and data completeness. Review of reporting document shows some important surveillance parameters were missing in some systems and when reported, are not sufficient to establish pattern of infection in the region as they are frequently reported in isolation. There is poor representation of the number of infected patients, clinical infection, infection origin, specimens, sampling setting, population covered and demographic data (gender and age). Data from the reviews shows that important indicators like infection origin is poorly reported. Only 17% of the countries participating in surveillance reported infection origin. There is generally low frequency of systems including indicators like number of infected patients, incidence based and clinical infection. Assessment of the surveillance systems using the European Center for Disease Prevention and Control (ECDC) surveillance system evaluation checklist which assesses for SS attributes showed no system checked all the attribute boxes and there is poor representativeness for majority of the countries. The number of surveillance sites for some countries is not sufficient for national surveillance. While some countries have wide-spread population coverage, others report data from subset of local laboratories and healthcare settings which focuses on one locality thereby limiting data representativeness at a national level.

Data incompleteness hugely undermines the ability of surveillance reports to fulfil the goal of surveillance which is primarily to generate reliable results from which the most effective AMR control measures can be built. Observably, surveillance is expanding in the region but the mere existence of a surveillance system by itself does not guarantee provision of quality and representative data and until these types of data are available, global estimate of the burden of AMR will be largely unreliable and may not inform meaningful action.

There is methodologic homogeneity in the aspect of testing standard which is consistent across all systems, though major differences exists in the uniformity of parameters being collected and reported. When parameters that are reported in one system are not reported in another, it causes controversy in surveillance data reliance and utilisation. More so, with the increasing demand of surveillance data for public reporting, homogeneity of surveillance methods will help to highlight best practices, enable benchmarking and enhance regional aggregation of data (Núñez-Núñez *et al.*, 2018). Interestingly, all identified surveillance systems perform AST standard, and in addition South-Africa also performs WGS. AST is a widely used method to guide clinical decision making for highly resistant pathogens, it is also effective and efficient for tracking resistance of specific pathogens to a wide range of antimicrobial agents and its in-line with WHO testing standards. Despite the popularity of this method of testing, there are concerns around its sensitivity profile and timeliness. Studies have reported that in addition to AST, WGS is another valuable method that systems could consider for AMR surveillance (Vegyari *et al.*, 2020; Nguyen *et al*., 2018; Ellington *et al.*, 2017). WGS offers a paradigm shift in laboratory testing which is different from the traditional techniques involving exposing pathogens to different antibiotics concentration to determine sensitivity plus an added benefit of results availability within the day (Inglis *et al*., 2020). Though this method is unlikely to replace the traditional AST method in the nearest future, with the ever evolving dynamics of

resistant pathogens, a rapid testing technique that delivers quick molecular results will effectively support AMR surveillance.

Another important finding from this review is the absence of EQA in majority of the surveillance sites/laboratories and poor technical level and standardisation of data management. EQA enhances validity of data and helps assure reliability and quality of laboratory results which is the hallmark of a surveillance system (Cole *et al.*, 2019). Lack of quality assurance metrics at the laboratory level also has far reaching impacts on data integrity (Perovic *et al*., 2019). To mitigate these, laboratories must subscribe to a sustainable EQA scheme operating to internationally recognised standards as an important requirement to partake in any form of surveillance. The WHO has outlined some sets of EQA with potentially more adoptable indicators suited for developing systems, but the uptake of this scheme remains largely insignificant. The poor uptake of this quality assurance tool in the region reduces the usefulness of results as reference for clinical and public health information.

Another constraint is the mode of data entry which is not standardised across the WHO AFRO region and the poor-usage of WHONET software for data recording. WHONET is a windows-based database software designed for the management of microbiology data. It provides automated process for categorisation, referencing, retrieval, and analysis of data and supports seamless sharing of surveillance reports. Surprisingly, despite the usefulness of WHONET in surveillance data handling, majority of the systems record surveillance data on computers and on paper which limits data sharing and is unsafe for data preservation. These data management methods impact on timeliness attribute of surveillance system which is assessed by the flow of data across the system from collection, transmission, analysis and reporting. Lack of standardisation of data entry and management; poor quality assessment and accreditation of data sources; and absence of checks on data reporting, analysis and sharing gives rise to duplication and sampling bias which further limit representativeness of data (Ashley *et al.*,

2019). While some systems have wide spread population coverage, others report data from a subset of local laboratories and healthcare settings which focuses on one locality thereby further limiting data representativeness at a national level.

The use of laboratory-based approach for AMR surveillance is consistent across the region. Though laboratory-based surveillance is widely in use and serves as an efficient strategy for capturing trends in resistance over time, some studies argue that this approach limits understanding of the extent to which laboratory results can inform public health policy on AMR (Jayatilleke, 2020; Seale *et al.,* 2017; Schrag *et al.,* 2002). These studies recommend an integrated model which is more informative, lower cost and combines clinical, laboratory and demographic surveillance at sentinel sites. To achieve the most effective surveillance approach for the region, a robust comparative analysis is required to inform best practices that will be cost saving and beneficial to LMICs.

Another notable finding from this review is the evidence of GLASS participation. A review of GLASS early implementation reports, World Health Organisation (2018-2020) shows significant increase in the number of countries that have completed GLASS enrollment from the region as well as the number of countries reporting surveillance data to GLASS. This increasing trend shows significant progress from the level reported in an earlier study and demonstrates improved awareness and acceptance of the importance of sharing valid data in the containment of AMR (Price *et al.,* 2018). Although the increased enrollment and reporting to GLASS is encouraging, it is important to mention that enrollment needs to be commensurate with other indicators of active surveillance including evidence of good quality and representative data, which are systematically collected and reported to GLASS. To inform public health opinion for scientific and monitoring purposes, surveillance data needs to be collected systematically and analysed for trends, prevalence and other relevant information (Sangeda *et al.,* 2020). Currently the quality of reported data differ substantially which impacts

the usefulness of such data. Whilst GLASS serves as a unified network for systematic collection of surveillance data, it also facilitates long-term and sustainable investments by countries and supports the provision of epidemiological and clinical data. It is useful for more countries to enroll on the GLASS network and contribute to robust data needed for global AMR containment in a sustainable and pragmatic way. The region is still trailing behind at this giving that the number of countries reporting surveillance data to GLASS is only a fraction of the number of countries in the region.

3.6 Study limitation

Some information used for this review were retrieved from country self-assessment reports. Self-assessment reports are often characterised by intrinsic limitation such as exaggerated responses, underreporting weakness or overestimating strength. Although the authenticity of such reports were verified, they could be subject to self-reporting bias. Of the 35 NAPs detected, only 17 English and 2 non-English action plans were publicly available and only 23 of these NAPs have translated into surveillance activities. These constraints have limitation on the robustness of data reported in this review.

3.7 Conclusion

Surveillance remains a cornerstone for tackling AMR, and surveillance data serves as a reference point for estimating morbidity and mortality figures. There is general agreement that data collection processes for AMR needs strengthening particularly in the context of developing countries (Sangeda *et al*., 2020). Data collected from the region differ substantially and marred by unreported/underreported parameters which impacts negatively on data integrity. There is a global call for sufficient data to enable full understanding of the magnitude of AMR and to direct policy action. To successfully fill this knowledge gap, data must be reliable, a true representative of the population and collected in a systematic manner. This will not only ensure that development of policies and strategies are informed by the country

situation in an effective way but will also enhance global AMR containment efforts. Although findings from this review show that surveillance is increasingly been implemented in the region, a number of methodological and reporting issues exists that can affect validity, reliability and usefulness of these surveillance findings. For instance in a case where a drug exerts broad-spectrum effects against different types of disease-causing pathogens, it is important to report which disease or infection is more prevalent, the population in which it frequently occurs and their clinical implications. Underreporting these indicators will not only misinform selection of the appropriate group for surveillance, it will also misguide the choice of region or setting and the priority patient population for randomised trials and other therapeutic interventions. With the expansion in number of surveillance systems with varying conceptual framework, there is increasing pressure globally to improve the effectiveness of these systems to accurately describe pattern of diseases (Sangeda *et al.*, 2020). The lack of an evaluation framework that can systematically assess performance of surveillance systems for AMR highlights the need for a toolkit that can specifically evaluate surveillance systems for AMR particularly in the context of developing countries.

3.8 Recommendation

The first step towards strengthening evidence-based data at national and regional level will require developing a unified checklist that outlines key indicators of clinical importance. This is highly recommended in the reporting of surveillance findings alongside implementing effective surveillance research, collaboration between countries and investment in newer techniques.

With the rising trend of multidrug-resistant organisms, there is need for adoption of newer testing techniques that delivers rapid results to replace traditional bacteria culture testing methods which can take several days.

Finally, the collaborative efforts of the European Surveillance of Antimicrobial Surveillance System (EARSS) and the European Surveillance of Antimicrobial Consumption Program (ESAC) has demonstrated that antimicrobial resistance surveillance is enhanced when linked to the monitoring of antimicrobial use practices. This offers an integrated and highly recommended approach to surveillance, though implementing an effective AMR stewardship scheme remains a challenge in the region.

Chapter 4 : Using surveillance quality indicators to identify barriers to data completion and opportunities for improving laboratory performance & reporting in Nigeria: a cross sectional study

4.1 Introduction

Poor quality data does not only impact effectiveness attribute of surveillance systems, it also impedes achievement of overall surveillance objective. As revealed from the previous chapter, significant factors contributing to data completeness and quality issues arise from absence of external quality assurance (EQA), missing epidemiological and patient level information and poor coordination of data amongst others. In view of these challenges, this chapter explore the dynamics of this problem in more detail from the context of primary data collectors (the laboratories) and the possible presence of other confounders. A surveillance quality indicator scale was used to examine relevant components of the laboratory to determine the drivers, vulnerabilities as well as opportunities for mitigating the problem and improving data quality and representativeness.

4.2 Background

Laboratory networks are a core component of all surveillance and health systems (World Health Organisation, 2013). Accurate and timely laboratory information is at the centre of the efficient treatment, management and prevention of infectious and non-infectious diseases (Ghoshal, Vasanth, and Tejan, 2020). Furthermore, many public health interventions/policies rely heavily on data from the laboratories and particularly, at times of serious public health crisis, laboratories are at the very heart of the investigation and response mechanisms (Kay et *al.,* 2021*)*. The difficulties encountered in providing timely laboratory testing during epidemic and pandemics highlights that global health security relies on adequate public health laboratory capacity in all countries (Hamblion *et al.,* 2018). Today's world cannot afford unreliable

laboratory results, wasting precious time, samples, and too often, precious lives (World Health Organisation, 2013).

The Nigeria's 2017 National Action Plan (NAP) highlighted that strengthening knowledge and evidence of antimicrobial resistance through surveillance is a strategic priority for tackling AMR. In actualising this NAP priority, the laboratory plays a central role not only for detecting, confirming, and reporting resistant pathogen to the surveillance network, but also supports global, regional and local containment efforts through provision of other useful information that guides policy action and clinical trials (Kay *et al.*, 2021). To inform meaningful action, the laboratory as part of the surveillance eco-system must guarantee timely, valid, and reliable data as well as correlation of the data with important demographic information (Ng'etichi *et al.*, 2021). Whilst quality assurance of data is important for trustworthiness and usefulness; identifying, recruitment and integration of eligible laboratories into the surveillance system is equally crucial for expansion of laboratory networks and generation of robust data. More importantly, ensuring that the laboratory recruitment is distributed across various levels of healthcare setting will help to ensure that the generated data is not skewed and representative of the population under surveillance (Ndjomou *et al.*, 2021).

According to the WHO, laboratory networks are described as a group of laboratories bonded together for a stated purpose at different levels (World Health Organisation, 2020). This definition further highlights that network of laboratories recruited for surveillance purpose must incorporate laboratories at various levels and geographical settings for the actualisation of surveillance motives (Boeras *et al.*, 2016). This is fundamental as often, public health interventions tend to focus disproportionately on urban geographies which by default excludes rural settings (Corburn, 2017). This is particularly important in Nigeria where healthcare delivery is divided along the lines of hierarchical healthcare organisational structure (tertiary, secondary and primary levels) and geographical locations. Figure 4.1 shows the organisational

and governance structure of Nigeria health system by order of ranking. This dichotomy suggests that laboratory recruitment is likely to be skewed in favour of urban settings and laboratories at the tertiary levels which has the propensity of impacting representativeness of data generated from this sort of system.

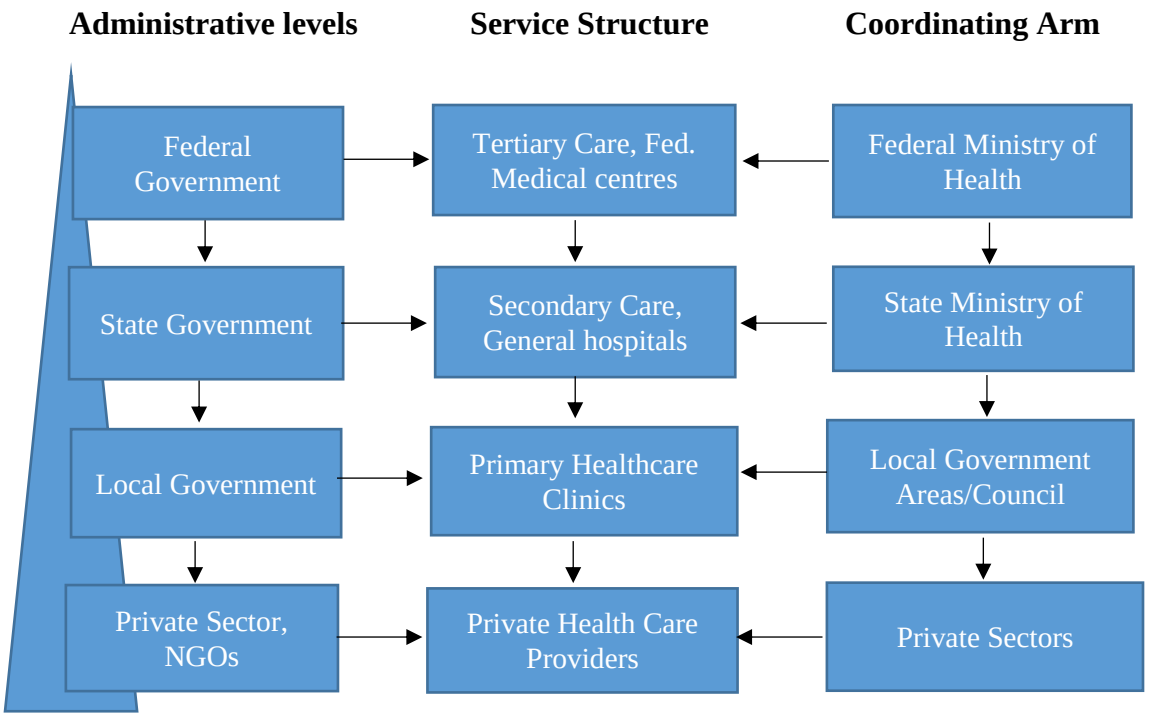


Figure 4.1: Hierarchical organisation of healthcare system and governance structure in Nigeria (a top-bottom approach)

The role of laboratory services and the efforts to strengthen them, for both clinical and public health functions are increasingly recognised (Amin *et al*., 2022). Giving the important role of laboratory in AMR surveillance and response mechanism, laboratory assessment in-line with surveillance objectives of the NAP is crucial for laboratory strengthening and improvement of subsequent laboratory iterations into the surveillance system. More so, laboratory assessment provides invaluable indicators that can be used to assess level of surveillance implementation. (Malania *et al.*, 2021). This assessment should consider all aspects of AMR surveillance activities including: clinical sampling, laboratory testing procedures, specimen sharing, reagents and equipment supplying systems, data management, human resourcing, and

infrastructure (Kan, 2022; World Health Organisation, 2014). It is worthy of mention that laboratory services are functional only if a combination of these elements are adequate and in place (World Health Organisation, 2013). The functionality of the laboratory is also determined by the organisational structure of the laboratories at local, regional and national levels as this impacts flow of surveillance data across time and space (Kan, 2022).

The status of laboratory networks for AMR surveillance in Nigeria has not been assessed post NAP implementation. It is not clear the technical capacity, organisational structure, and hierarchical criteria followed in the recruitment of laboratories, as well as the distribution of laboratories across zones/settings, and whether they align with surveillance system requirements and protocols. This cross sectional study will fill these knowledge gaps and thus: provides a snapshot of representative sample of laboratories at various levels which is useful for assessing surveillance system performance; identify challenges, vulnerabilities, and gaps as well as strengths and enablers within systems which are essential for surveillance systems strengthening; and provide roadmap for equitable laboratory recruitment which is necessary for enhancement and improvement of surveillance system.

This chapter addresses the second objective of this research and will analyse AMR surveillance in the scope of laboratory networks using surveillance system quality indicators to evaluate: technical capacity, representativeness of laboratory recruitment, external and internal quality assessment, overall knowledge, readiness and compliance with the WHO surveillance framework. The outcome of this study will provide national decision-makers a better visualisation of critical focus areas for planning and implementing laboratory capacity improvement and strengthening activities.

4.3 Materials and Methods

4.3.1 Study Design

This study adopted a cross-sectional study design utilising structured questionnaire administered online via Qualtrics^{XM} software (Qualtrics Provo UT, 2020). Cross-sectional

study is a type of observational study that allows data to be collected on the whole sample population at a single point in time (Rezigalla, 2020). This method is often used to describe characteristics that exist in a population and provides a snapshot of the current circumstance or situation under investigation. This is in contrast to longitudinal studies which aim to understand how circumstances or situations has changed over time. Unlike in case-control or cohort studies where participants are selected based on outcome or exposure, participants in this type of study are selected based on particular variables of interest (Gail *et al.*, 2019). This flexibility allowed selection of the appropriate target group using predefined inclusion and exclusion criteria. This method was considered appropriate for this study as it allowed the researcher to assess various levels (tertiary, secondary, primary) of laboratories at the same time whilst collecting specific characteristics which were used to assess laboratory networks and other quality indicators. Particularly, it allowed multiple variables to be investigated at the same time which helped in understanding the recruitment pattern of laboratories for surveillance, the organisational structure of the laboratory system as well as their technical capacities and imbalances in the laboratory systems. Though this type of research method can be used to make inferences about possible relationships between study groups; assess system needs/gaps and inform planning of future research study; and inform allocation of health resources, it is difficult to derive causal relationship from this method (Taur, 2022).

This study was reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (von Elm *et al.*, 2014). STROBE is a 22 item checklist which provides guidance on what should be addressed in articles reporting on the three main observational study designs including cross sectional studies (Lee *et al.*, 2021). The checklist is designed to aid authors in ensuring high quality presentation of the conducted observational study.

4.3.2 Ethics and research governance

In order to meet the ethical standard requirements for the conduct of research projects at the University of the West of England, ethical approval was sought for this study from the Faculty Research Ethics Committees (FRECs). This process ensures compliance with the code of good research practice which involves a clear demonstration of transparency in research protocol and in the participants' recruitment process. As part of the appraisal process, all supporting documents were duly scrutinised. These included: study background, sample of survey questionnaire, copy of official invitation letter for the professional bodies, participants' information sheet, privacy notice detailing how participants' data will be used and consent form. An important ethical consideration is to demonstrate the voluntary nature of participation and to show that participants who wish to withdraw their response from the study would be able to do so. For this purpose, the survey was set-up to randomly generate a unique ID number to allow respondents who wish to withdraw their response to do so at any time by quoting the ID number in an email to the researcher. Data collection followed the general data protection regulation (GDPR) by not collecting personal identifiable data of the respondents. The demographic data collected were those that helped the researcher distinguish between the laboratory affiliations, connections, and locations.

Also, in keeping with ethical requirements in relation to provision of adequate information to participants prior to undertaking the survey, a background section containing summary of the study was included at the beginning of the survey. This part also contained a prefaced statement to alert the participant that by clicking on the submit button at the end of the survey will imply that the participant is consenting to take part in the study in full knowledge of the information provided in the study background. As a final requirement for transparency and good research practice, a formal agreement to participate was obtained from each of the professional bodies to demonstrate that participants were not coerced by the researcher. Evidence of agreement is

shown in appendix A13. Final ethical approval was obtained on 2nd October, 2020 with the reference number UWE REC REF No: HAS.20.05.180. Ethical approval is provided in appendix A1.

4.3.3 Setting

The setting for this study included healthcare facilities across Nigeria without geographical location restriction. This nation-wide approach was adopted on the knowledge that most public health interventions tend to focus disproportionately on urban geographies, so in order to achieve a balanced opinion and to minimise the likelihood of selection bias and misrepresentation, there was no limit to geographical coverage in the survey (Corburn 2017). This is an important consideration for this Nigerian study where policy implementation tends to follow a top-bottom approach due to the hierarchical healthcare organisational structure encompassing tertiary, secondary and primary care coupled with urban and rural diversities. This trend suggests that policies that are implemented at the urban and tertiary levels may not be observed at the lower level care settings. What this means for AMR surveillance is the likelihood of laboratory recruitment and other indicators to be in favour of urban settings thus giving a biased outcome if the study focused on only those settings. To this effect, the setting for this study was mapped by geopolitical zones which is an aggregate of the federated states by region, states, and local councils.

Figure 4.2 shows the geopolitical map of Nigeria. To also ensure this study captures important aspects of laboratory engagement for AMR surveillance and other quality indicators across board, no exclusions were made on the basis of laboratory affiliations (private, government) and tiers (tertiary, secondary and primary). As such, all functional laboratories including dependent (labs connected to healthcare facility); independent (labs not connected to healthcare facility); laboratories affiliated to teaching hospitals; state medical centres; primary health

centres; ministries of health, environment and agriculture; and port health laboratories were eligible for inclusion.

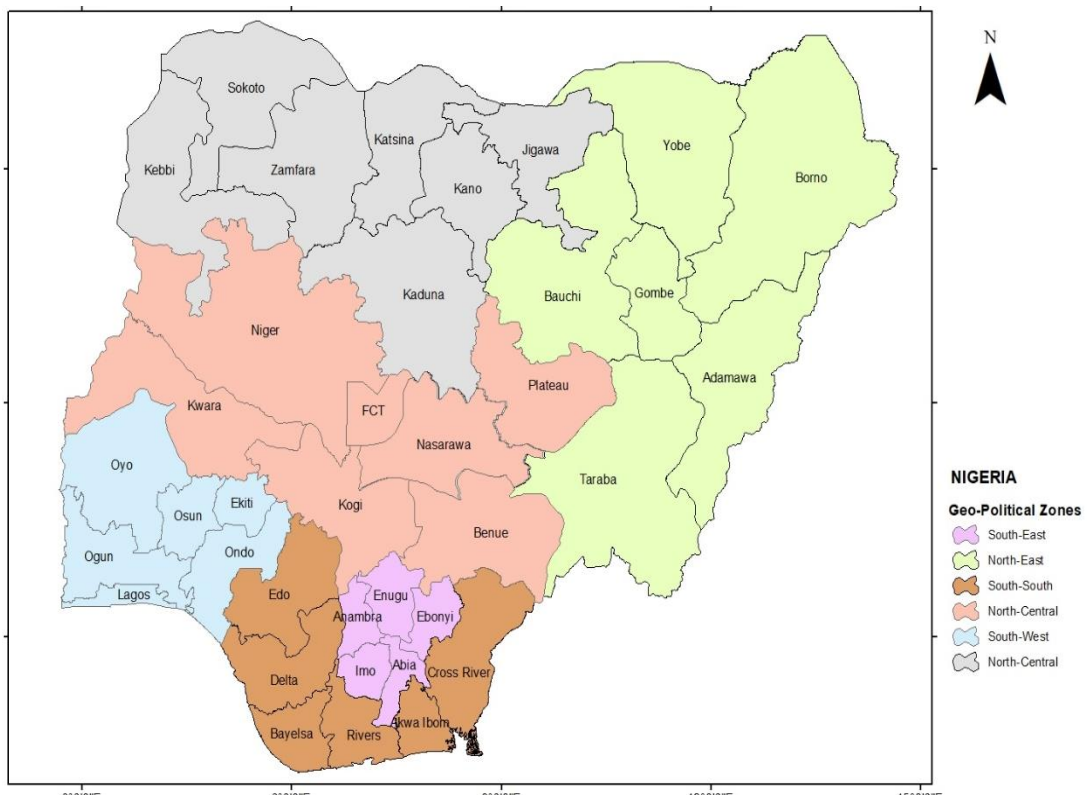


Figure 4.2: Aggregation of the Nigeria states by Geo-political Zones. Source: GRID, eHA Geographic Coordinate System: GCS_Minna. Author: EnvironReview. Available: https://environreview.com.ng/map-of-nigeria-showing-geopolitical-zones/

4.3.4 Study participants and recruitment

The participants for the study were recruited from three professional bodies responsible for laboratory services, laboratory practitioners and regulatory activities across private and government establishments: 1) Association of Medical Laboratory Scientist of Nigeria (AMLSN) is a professional body consisting of registered microbiologists, laboratory scientists, technicians/assistants and epidemiologists working across government and private practices. This organisation operate at national, state and chapter levels and thus have membership at varying levels with experts drawn from a broad range of organisations and sectors 2) Guild of Medical Laboratory Directors (GMLD) is collection of laboratory scientist in private (non-government) practice and consists of directors, managers, and owners of private laboratories.

This body also includes medical laboratory scientists (MLS) in academia and non-governmental organisations 3) Medical Laboratory Science Council of Nigeria (MLSCN) is a statutory regulatory agency. Aside from being a regulatory body, it maintains a register of certified laboratory practitioners and database of registered laboratories. As laboratory services and MLS are components of multidisciplinary healthcare system which cuts across diverse sectors and settings (ministries, hospital, charities), it was not possible to identify and sample all the organisation, units, affiliate institutions and establishment that incorporates laboratory services. For this purpose, a purposive sampling method was used to identify these three key groups that have representation of both practitioners and laboratory practices regardless of status or affiliation. An initial request letter to participate in the study with detailed participants' information sheet (version: v1 10.07.2019) was emailed to the representative of each of the three professional bodies to solicit their member participation. A copy of the invitation letter sent to the professional organisations requesting for their members' participation in the survey is provided in appendix A14. This was followed up with telephone calls and series of correspondence with the contact persons before an agreement to participate was received. Following the agreement to participate, a unique survey link was generated and sent to the respective contact persons of the professional bodies who distributed same to their members via an internal membership email list. The questionnaire was designed for directors, practice managers, senior staff members or a representative of the laboratory. This is to ensure that the survey responses were provided by someone with significant or technical role in the organisation for reliability, accuracy and authenticity of information. The laboratory catchment area/geographical location were also recorded to help examine representativeness.

4.3.5 Dependent and independent variables

A variable in research simply refers to a person, place, thing, or phenomenon that you are trying to measure in some way (Flannelly, Flannelly, and Jankowski, 2014). In order to accurately

describe the outcome of the research, a distinction has to be made between the independent and dependent variable(s) based on the study design (Kunißen, 2019). In experimental research, the ability to manipulate one variable in order to measure its effects on other variables is regularly used to distinguish the independent variable from the rest. Whereas in correlational research where no variable is being manipulated at any point in time, the subject variable (which is the characteristics of the population) is commonly regarded as the independent variable (Moe & Oo, 2020). Since this is an observational study, the distinction between dependent and independent variables was made on the bases of a correlational research. In this case, the characteristics of the population is regarded as the independent variables which include: laboratory affiliation, level of laboratory, geopolitical zone of laboratory and source of samples whereas knowledge, capacity, participation, readiness and recording were regarded as dependent/outcome variables. These variables are of mix characteristics including numerical (continuous, discrete) and categorical (ordinal, nominal, binary) variables which makes up the 49-item questionnaire.

4.3.6 Survey questionnaire

The survey questionnaire was adapted from the WHO questionnaire for assessment of national networks for AMR surveillance (World Health Organisation, 2013) and questionnaire for assessing laboratory capacity by Noreen *et al.* (2017). The survey questionnaire was structured to collect information necessary for the purpose of the study. It focused on laboratory-based questions in relation to antimicrobial resistance surveillance, national action plan implementation and some quality metrics. The final survey questionnaire comprised of 49 questions split into five Surveillance Quality Indicators (SQIs): knowledge of AMR surveillance; laboratory capacity for AMR surveillance; readiness to participate in AMR surveillance; status of AMR surveillance participation; and recording/capturing of important AMR surveillance data. The questionnaire also captured the following demographic variables:

laboratory location by State; catchment area of lab; laboratory affiliation (government, private); laboratory connection (tertiary, secondary, and primary); major source of samples; and respondent's occupational role. All questions had pre-defined answers ranging from single answer, multiple answers, selection list option, and single-line text entry option.

The questionnaire was validated to ensure it contained questions that cover all aspects of the construct being measured. The content validation was carried out by three independent subject experts with knowledge of laboratory surveillance processes and strategies in the context Nigeria. The validation process was in two phases: firstly the full domain of content relevant to the study was defined; in the second phase, specific areas from the domain relevant to the study objectives were sampled and tested to establish that the items are representative of the intended study outcome. The content validity index individual (I-CVA) was utilised to evaluate the relevance of individual item on a 4-Likert scale (from 1=non-relevant to 4= very relevant). Then for each question, the number of experts giving 3 or 4 score (relevant) against those giving 1 or 2 (non-relevant) were counted and the proportion was calculated. All individual experts scoring were in agreement with the order, hence l-CVI score of 1.0 was assigned. This score aligns with Lynn (1986), that where five or fewer experts are involved, all must agree (i.e. l-CVI of 1.0) to overcome problem of chance agreement. To further give inference on comprehensiveness of the whole questionnaire, content validity index scale (S-CVI) was used to evaluate the validity of the overall scale. Again the S-CVA validation showed a universal agreement from all experts.

The survey was piloted across 15 participants with diverse background to help check for validity, ambiguity, language confusion and that respondents understood the questions as well as ensured all commands are active in survey mode and that the survey displays correctly. General feedback from the piloting phase confirmed validity (comprehensiveness and relevance) of the questions in relation to the construct being measured. The feedback also

provided comments which contributed to the final questionnaire look and feel. Specifically, it informed the use of 'force response' command for mandatory questions and 'skip logic' which automatically skips the survey to a different portion of the survey based on the answers provided to the trigger questions (yes/no). The suggestion to re-arrange the survey items in group was also adopted. All questions relating to a specific SQI were grouped under their respective category (e.g. knowledge, readiness) to enhance flow. Some questions which were highlighted to lack clarity where modified to improve understanding which helped participants in their choice of answers. The average survey completion time was determined following the piloting and this information was included in the survey introduction.

4.3.7 Data Collection and management

All data were electronically collected over a period of seven (7) months from December 2020 through July 2021. Completed questionnaires were automatically stored on Qualtrics database until extracted by the researcher. Raw data were extracted from Qualtrics after completion and downloaded into Excel spreadsheet where partially complete responses were deleted. The surveillance quality indicators (knowledge of AMR surveillance; laboratory capacity for AMR surveillance; readiness to participate in AMR surveillance; AMR surveillance participation; and recording/capturing of important AMR surveillance data) were coded and scoring levels assigned before the data entry into data analysis software.

4.3.8 Bias

Sampling bias is common in population based studies including cross-sectional studies (Enzenbach *et al.,* 2019). The presence of sampling bias limits the generalisability of the research outcome and also threatens external validity due to misrepresentation. In order to minimise the occurrence of this type of bias, the researcher defined a target population (using predetermined eligibility criteria) and sampling frame with the list of groups that the sample will be drawn from. These include private and government laboratories; tertiary, secondary and

primary care laboratories as well as laboratories in urban and rural settings. By employing the purposive sampling method, the three professional bodies with varying responsibilities to laboratory services were sampled. These professional bodies have representation across all levels of healthcare and thus helped to ensure all potential respondents within the sample frame have equal chance of participating in the survey.

4.3.9 Sample size

Sample size estimation is important for ethical and methodological reasons (Wang and Ji, 2020). Inappropriate sample size can undermine validity of a study particularly in population based studies where a representative number of the population is sampled (Bolarinwa, 2020). An ideal sample size should not be small (as this may prevent findings from being extrapolated) and, contrary to what one might think should not be excess as increase in accuracy (confidence interval) reduces beyond a certain point, and hence not worth the effort and expense involved in recruiting the extra participants. To strike a statistical balance in participants' recruitment, researchers rely on statistically derived sample size estimation using the appropriate formula for the study design. This will ensure that sample size is representative of the population which gives the study sufficient confidence to infer the statistical analysis results to the wider population. Where the overall size of the population is known, sample size could be calculated using the general population size as reference, but in this case, the actual number of laboratories in Nigeria could not be ascertained. Various authors and resources quote conflicting numbers of laboratories which seems inaccurate and confusing so sample size estimation based on the population size was not possible. Sample size was therefore based on consideration of the model suited for studies involving logistic regression (Bujang *et al.,* 2018).

In effect, the sample size for this study was determined using Event Per Variable (EPV) formulae based on the study objective, the statistical analysis involved, and the type of variables involved (Bujang *et al.,* 2018). EVP utilises the number of event per predictor

variable in a study to determine the ideal sample size. In this case, the researcher decides the number of EVP to assign per independent variable bearing in mind that the higher the number, the larger the sample size and the likelihood to derive statistics that can represent the parameters in the targeted population. In assigning EVP, certain rules apply. The rule of minimum of ten events per variable is generally accepted as methodological quality item in appraising published studies though this is considered a lower limit in medical literature (Ogundimu *et al.,* 2016; Van Smeden *et al.,* 2016). For observational studies with large population size that involve logistic regression in the analysis, the EPV of 50 rule is advised in order to achieve significant sample size and high statistical power (Austin and Steyerberg, 2017).

For this sample size calculation, an EPV of 50 was adopted which yields a larger sample size, thereby minimising the risk of type II error associated with small sample size. Substituting values into the EPV formulae [EPV = 100 + (x) (i)] yields a sample size of 300. Where (x) is an integer chosen by the researcher; (i) is the number of independent variables and 100 is constant;

$$EPV = 100 + (50) \times (4)$$

$$100 + 200 = 300$$

Therefore, the minimum sample size required to achieve significant power for this study was 300.

4.3.10 Statistical method

Descriptive statistics such as absolute number of occurrences (frequency) for categorical variables and the mean for continuous variables were used to summarise the characteristics of the sample. Inferential statistics including the Chi-square (test of independence), bivariate and multivariate logistic regression (test of predictive analysis of relationship) were used to examine the relationships between variables. In determining the appropriateness of these

chosen statistical methods for analysing this data and in order for the results to be valid, considerations were made on whether the data/variables met the assumption for these tests. The Chi-square test was validated on the basis of meeting the minimum cell count of ≥5 and where the minimum cell count was not met, the Fisher's exact test was used as an alternative to Chi square test (Kothari, 2004). For the logistics regression, the Variation Inflation Factor (VIF) was used to check for the presence of multicollinearity among the independent variables as high correlation reduces the power of coefficients and weakens the statistical measure to trust the p-values (Greenland *et al*., 2016). According to Dormann *et al.* (2013) collinearity statistics, there were no multicollinearity between the variables, as shown in appendix A15 and A16, the tolerance and VIF scores of the variables were within limit (Tolerance= <1 and VIF =<5). Lastly the Box-Plot was used to check linearity of the dependent and independent variables, as shown in appendix A21-24, no outliers were detected between the two variables hence no linear relationship.

The survey responses were entered as valid for eligible response, or invalid where ineligible (do not know) or missing answers were entered. A score of one (1) was assigned for every valid response and zero (0) was given to invalid responses in accordance with Kanjee *et al.* (2012) scoring approach. The score for each of the five SQIs (knowledge of AMR surveillance; laboratory capacity for AMR surveillance; readiness to participate in AMR surveillance; status of AMR surveillance participation; and recording/capturing of important AMR surveillance data) for each respondent was presented as percentage of the maximum possible score for each theme using this calculation (score obtained/total possible score × 100%) as earlier documented by Akande (2020). SQI scores were described using mean and standard deviation for continuous variables and frequency for categorical variables. The ranking used for knowledge followed a previously adopted categorisation by Akande (2020) and Talisuna *et al.* (2019) who ranked knowledge theme scores of ≤49% as poor, 50-75% as moderate and ≥80 as excellent.

The ranking for laboratory capacity followed Liu *et al.* (2019) ranking which assigned a score of ≤ 59% as weak capacity, 60-80% as good capacity, and >80% as strong capacity. The rest of the SQI scores were assigned in relative to features of the data and not based on pre-established ranking categorisation. For status of surveillance participation**,** a score of ≤ 59% was regarded as poor participation**,** 60-80% was regarded as fair participation, while >80% was taken as good participation. For readiness to partake in AMR surveillance, a score of ≤59% was regarded as not ready, 60-80% was taken as fairly ready, while >80% was regarded as fully ready. On the AMR surveillance data capturing, a score of ≤59% was regarded as not capturing important AMR surveillance data, ≤90% was taken as partially capturing important AMR surveillance data, while a score of >90% was taken as fully capturing AMR surveillance data. In addition, the scores for each SQIs were further categorised into poor, moderate/fair and good/excellent scores.

Two levels of analysis were done: chi-square test was first used to compare the association between the levels of each SQI score with the categories of laboratories. Those with p value of less than 0.2 were moved into bivariate and multivariate analysis according to Heinze & Dunkler (2016) and Rojanaworarit (2020) recommendations for performing regression test on variables with p-value of ≤0.2 if the sample size is less than 400. Binomial and multinomial logistic regression were then used to determine associations between the laboratory demographic information (an independent variable) and each of the five SQIs (as dependent variables).

Bivariate correlation was used to check for linear relationship (correlation coefficients) and the direction of the relationship between demographic variables and surveillance quality indicators to determine if the impact of a change in one variable will have a significant impact on the other. The correlation coefficients were interpreted in accordance to Schober and Schwarte (2018) guideline. The Statistical Package for Social Sciences (SPSS) version 20.0 software

(IBM Corp, 2011) was used to analyse the data. A p-value cut off of 0.05 was used to determine the level of statistical significance.

4.4 Results

A total of 310 laboratory participants responded to the survey. Of this number, 8 (2.6%) had incomplete information and these were excluded from the analysis. Only 302 (97.4%) completed responses were analysed. Figure 4.3 shows the flow chart of survey responses and characteristics of respondent laboratories.

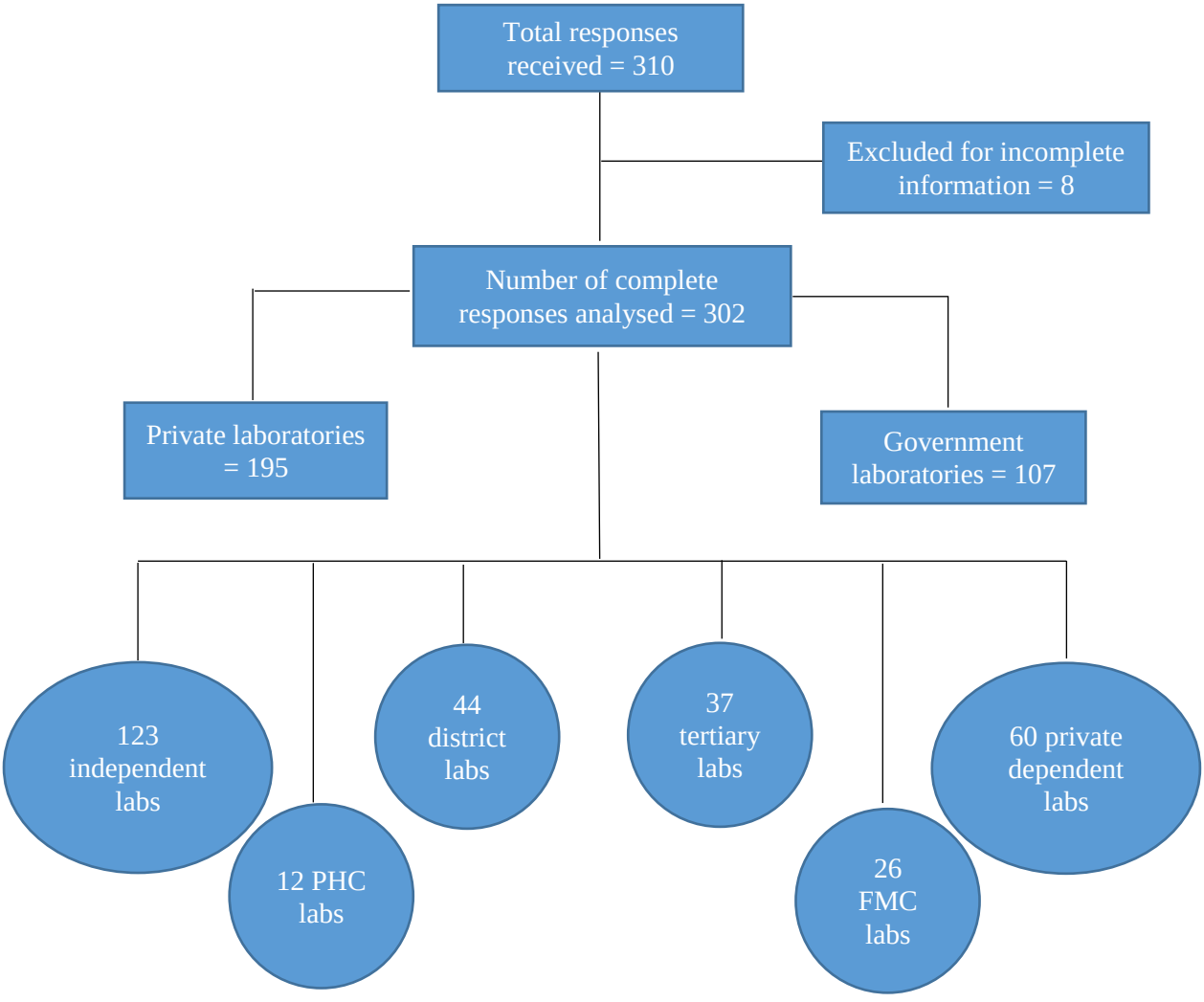


Figure 4.3: Flow-chart of survey responses and characteristics of respondent laboratories

4.4.1 Distribution of demographic characteristics

Of the 302 complete responses, 107 (53.4%) responses were from laboratories with government affiliation, while a higher response of 195 (64.6%) was recorded from laboratories with private affiliation. Based on laboratory connection, independent laboratories accounted for 123 (40.7%) responses, while laboratories connected/linked to teaching hospitals, federal medical centers, general/district hospitals, primary healthcare and private hospitals accounted for 37 (12.3%), 26 (8.6%), 44 (14.6%), 12 (4.0%) and 60 (19.4%) responses respectively. Geopolitically, data showed that highest response was recorded from laboratories located in the South-South zone 72 (23.8%), while South-West, South-East, North-Central, North-West and North-East accounted for 53 (17.5%), 66 (21.9%), 64 (21.2%), 24 (7.9%) and 23 (7.6%) responses respectively. Refer to Table 4.1. Laboratories were also grouped according to their indicated state of operation as shown in figure 4.4.

Table 4.1: Demographic distribution of respondent laboratories

Affiliation of Laboratory	n (%)
Government Owned	107 (35.4)
Private Owned	195 (64.6)
Level of Laboratory connection	n (%)
Teaching Hospital	37 (12.3)
Federal Medical Centre	26 (8.6)
General/District Hospital	44 (14.6)
Primary Health Care	12 (4.0)
Private Hospitals	60 (19.4)
Independent Laboratory	123 (40.7)
Geopolitical Zone of the respondent laboratory	n (%)
South-South	72 (23.8)
South-West	53 (17.5)
South-East	66 (21.9)
North-Central	64 (21.2)
North-West	24 (7.9)
North-East	23 (7.6)
Sources of Samples for the respondent laboratory	n (%)
Human Health Samples	283 (93.7)
Animal Health Samples	7 (2.3)
Environmental Health Samples	5 (1.7)
All Samples Sources	7 (2.3)

Keys: n=number, %=percentage

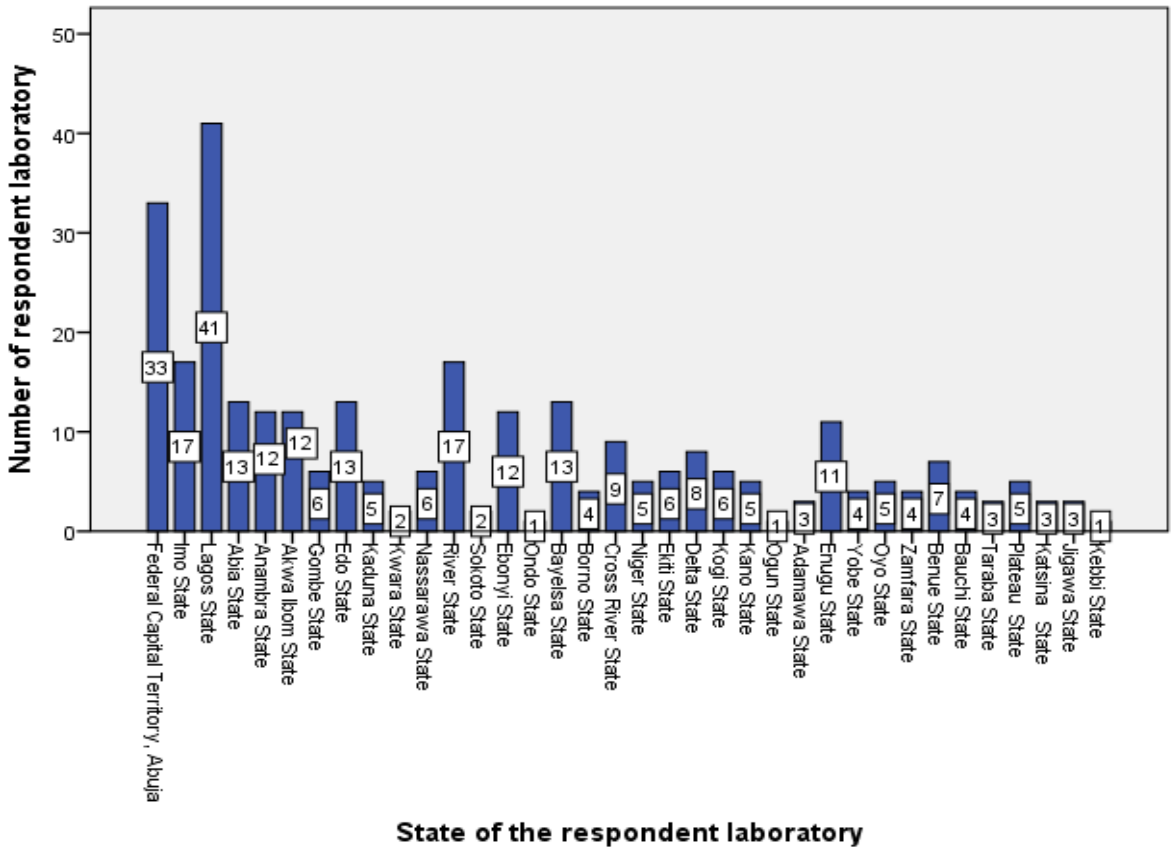


Figure 4.4: Distribution of respondent Laboratory by State

Majority of the laboratories 283 (93.7%) reported their source of sample is from humans, 7 (2.3%) reported sample source from animals, 5 (1.7%) reported sample source from environment, only 7 (2.3%) reported sample source across human, animal and environment. Frequency table for demographic distribution is shown in table 4.1.

4.4.2 Distribution of responses according to surveillance quality indicators

Tables 4.2-4.6 show the distribution of responses according to study theme (i.e. surveillance quality indicators) and their respective mean/average score. The responses and mean scores were reported across SQIs: knowledge, laboratory capacity, readiness to participate, present status of laboratory participation in surveillance and capturing of important AMR surveillance data.

4.4.2.1 Knowledge

The knowledge domain had four questions. Of the items related to knowledge of AMR, 261 (86.4%) of the 302 respondents reported awareness of AMR surveillance in Nigeria, 130 (43.0%) reported knowledge of the national action plan for AMR in Nigeria, 124 (41.1%) respondents were aware of ongoing AMR surveillance in Nigeria, only 100 (33.1%) respondents had knowledge of the Global AMR and Use Surveillance System (GLASS). The mean score for knowledge was 50.99%: 120 (39.7%) respondents had poor knowledge of AMR surveillance, 127 (42.1%) had fair knowledge, only 55 (18.2%) had excellent knowledge of AMR surveillance as shown in Table 4.2.

Table 4.2: Distribution of responses to items related to the knowledge domain (n=302)

Items	Responses n=302	n (%)
Knowledge of AMR Surveillance		
Do you have the Knowledge of AMR in Nigeria?	Yes No	261 (86.4) 41 (13.6)
Are you aware of a national action plan for AMR in Nigeria?	Yes No	130 (43.0) 172 (57.0)
Are you aware of Global AMR Surveillance System (GLASS)?	Yes No	100 (33.1) 202 (66.9)
Are you aware of ongoing AMR surveillance in Nigeria?	Yes No	124 (41.1) 178 (58.9)
Knowledge (%)	M= 50.99 SD=32.78	
Poor knowledge		120 (39.7)
Fair knowledge		127 (42.1)
Excellent knowledge		55 (18.2)

Key: n=number, %=percentage

4.4.2.2 Laboratory capacity

The laboratory capacity domain had five questions. Of the items related to laboratory capacity for AMR surveillance, majority 293 (97.0%) laboratories reported their technical staff were trained to conduct Antimicrobial Susceptibility Testing (AST). Two hundred and seventeen (71.9%) laboratories reported highest level of trained technical staff performing AST as having a degree in microbiology, while 85 (28.1%) reported the highest level of training was at diploma level. From the responses regarding equipment maintenance, 195 (64.6%) laboratories

reported their AST equipment are not maintained and calibrated regularly, only 107 (35.4%) reported regular AST equipment maintenance and calibration. One hundred and fifty-three (50.7%) laboratories generate basic antibiogram table for recording profiles of susceptibility of specific pathogen to antimicrobial agents routinely tested. One hundred and seven (35.4%) laboratories produce their media for culture testing in-house, while 195 (64.6%) laboratories do not produce culture media in their laboratories. The mean score for laboratory capacity for AMR surveillance was 58.1%: 150 (49.7%) laboratories reported poor capacity for surveillance, 75 (24.8%) reported fair capacity and 77 (25.5%) reported good capacity for AMR surveillance. Table 4.3 shows distribution of responses to the capacity domain.

Table 4.3: Distribution of responses to items related to laboratory capacity for AMR Surveillance domain (n=302)

Items	Responses n=302	n (%)
Laboratory Capacity for AMR Surveillance		
Is your technical staff trained to conduct AST?	Yes No	293 (97.0) 9 (3.0)
What is the highest microbiology training of your technical staff?	Degree Diploma	217 (71.9) 85 (28.1)
Are your AST equipment maintained and calibrated regularly?	Yes No	107 (35.4) 195 (64.6)
Does your laboratory generate basic antibiogram?	Yes No	153 (50.7) 149 (49.3)
Does your laboratory produce their own media for culture?	Yes No	107 (35.4) 195 (64.6)
Laboratory Capacity (%)	M=58.08 SD= 29.71	
Poor Capacity		150 (49.7)
Fair Capacity		75 (24.8)
Good Capacity		77 (25.5)

Key: n=number, %=percentage

4.4.2.3 Laboratory readiness

The laboratory readiness domain for AMR surveillance comprised of ten questions. Of the items related to laboratory readiness for AMR surveillance, 253 (83.8%) laboratories perform AST at their laboratory, only 49 (16.2%) do not perform AST at their laboratory. Out of the 49 non AST performing laboratories, 29 (59.2%) forward their culture sample to other laboratories for AST while 20 (40.8%) laboratories do not report AST. On the method used by the

laboratories for AST, 13 (4.3%) use manual method (agar dilution and broth microdilution), 136 (45.0%) use both disk diffusion and broth dilution, 56 (18.5%) use disk diffusion and Etest, 25 (8.3%) use both manual and automated AST identification method, 29 (9.6%) use manual and molecular techniques, 23 (7.6%) use broth dilution only, 20 (6.6%) do not perform AST. On the number of GLASS pathogens identified by the laboratories, majority of the laboratories 224 (74.2%) reported they can identify greater than five GLASS priority organisms, 25 (8.3%) laboratories reported ability to identify four-five, 7 (2.0%) laboratories could identify two-three, 5 (1.7%) laboratories reported they could identify one and 41(13.6%) laboratories could not identify any GLASS priority organism.

In terms of use of standard guidelines, 183 (60.6%) reported awareness of AST guidelines but only 128 (42.4%) laboratories use AST reporting guidelines. Of the laboratories that reported use of AST guidelines, 95 (31.5%) utilised Clinical and Laboratory Standards Institute (CLSI) guidelines, 22 (7.3%), 4 (1.3%) and 7 (2.3%) reported using EUCAST, BSAC and textbook respectively. The laboratories not utilising AST reporting guidelines had varying reasons for not doing so, 67 (22.2%) reported AST guideline are not available, 56 (18.5%) were not aware of AST guideline, 31(10.3%) reported the use of internal Standard Operating Procedure (SOP) and 20 (6.6%) are not performing AST. On the method of reporting AST results, 220 (72.8%) laboratories use qualitative method of reporting (intermediate and sensitive), 29 (9.6%) use both qualitative and quantitative (diameter) methods, 53 (17.6%) reported none. On the method of storing AST results, 169 (56.0%) laboratories store results using logbooks, 99 (32.8%) use computer files, while 34 (11.3%) do not store AST results. The average readiness score for the laboratories was 62.91%: 118 (39.1%) laboratories were not ready for AMR surveillance, 162 (53.6%) were fairly ready, only 22 (7.3%) laboratories were fully ready for AMR surveillance. Table 4.4 shows laboratory response to readiness questions.

Table 4.4: Distribution of responses to items related to laboratory readiness to Participate in AMR Surveillance (n=302)

Items	Responses n=302	n (%)
Laboratory readiness to participate in AMR surveillance		
Does your laboratory perform AST?	Yes No	253 (83.8) 49 (16.2)
Does your laboratory forward samples to other Laboratories for AST?	Yes No	29 (9.6) 20 (6.6)
What Method do you utilise for AST in your laboratory?		
Use Manual Method (Agar dilution and broth microdilution)		13 (4.3)
Use Manual Method (Disk diffusion and broth dilution)		136 (45.0)
Use Manual Method (Disk diffusion and E-test)		56 (18.5)
Use both Manual Method and automated system		25 (8.3)
Use both Manual Method and molecular techniques		29 (9.6)
Use broth dilution		23 (7.6)
We do not perform AST		20 (6.6)
How many GLASS pathogens does your laboratory carry out identification and antimicrobial susceptibility testing for?		
One GLASS priority organism		5 (1.7)
Two-Three GLASS priority organism		7 (2.0)
Four-Five GLASS priority organism		25 (8.3)
> Five GLASS priority organism		224 (74.2)
Other (none)		41 (13.6)
Are you aware of any AST guidelines?	Yes No	183 (60.6) 119 (39.4)
Does your laboratory utilise any AST guidelines?	Yes No	128 (42.4) 174 (57.6)
If Yes, what type?		
CLSI		95 (31.5)
EUCAST		22 (7.3)
BSAC		4 (1.3)
Textbook		7 (2.3)
If No, Why?		
Guideline not Available		67 (22.2)
Not aware of Any Guideline		56 (18.5)
Use internal SOP		31 (10.3)
We do not do AST		20 (6.6)
Method of Reporting AST Results		
Qualitative(R, I, S) and Quantitative(Diameter)		29 (9.6)
Qualitative (R, I, S)		220 (72.8)
None		53 (17.6)
Methods of Storing AST results		
Logbooks		169 (56.0)
Computer files		99 (32.8)
We do not store AST results		34 (11.3)
Laboratory Readiness (%)	M= 62.91 SD=29.02	
Not Ready		118 (39.1)
Fairly Ready		162 (53.6)
Fully Ready		22 (7.3)

Key: n=number, %=percentage

4.4.2.4 Laboratory participation in AMR surveillance

Laboratory participation in surveillance domain comprised of eight questions. Of the items relating to this theme, only 37 (12.3%) laboratories reported participation in AMR surveillance. Of the 37 participating laboratories, 23 (7.6%) started participating in AMR surveillance less than a year, 4 (10.8%) laboratories reported participation for 1-3 years, 3 (8.1%) laboratories reported participation for 4-5 years and 7 (18.9%) laboratories reported participating in surveillance for over 5 years. An additional 3 (0.9%) laboratories report AST data to ministry, organisation or surveillance network. In terms of frequency of reporting, 3 (1.0%) laboratories report their AST data monthly, 19 (6.2%) laboratories report quarterly and 18 (6.0%) report annually. Two hundred and sixty-two (86.8%) laboratories do not submit data to any network. Of laboratories not reporting AST data to any network, 159 (52.9%) reported their facilities have not been listed to participate in AMR surveillance as reason for non-reporting, while 103 (34.1%) reported lack of personnel and infrastructure. 156 (51.7%) respondents indicated use of internal standard operating procedure (SOP) for assuring quality of AST. Ninety-four (31.1%) laboratories indicated their AST results are always reviewed by senior technical staff or medical microbiologist before sending off the result, the rest of the laboratories 208 (68.9%) do not have their results reviewed by senior technical staff. The average score for laboratory participation in AMR surveillance was 18.32%. Thirty-seven (12.3%) laboratories were participating in AMR surveillance, while 265 (87.7%) of laboratories were not participating in AMR surveillance. Table 4.5 shows details of all the indicators measured in this domain.

Table 4.5: Distribution of responses to items related to laboratory participation in AMR Surveillance (n=302)

Items	Responses n=302	n (%)
Laboratory Participation in AMR surveillance		
Is your Laboratory participating in AMR surveillance?	Yes No	37 (12.3) 265 (87.7)
If yes, Length of Participation in AMR surveillance		
< 1 year		23 (62.2)
1-3 years		4 (10.8)
4-5 years		3 (8.1)

>5 years		7 (18.9)
Does your Laboratory report AST data to any Ministry, Organisation or Surveillance network?	Yes No	40 (13.2) 262 (86.8)
If No, what are the significant obstacles faced by your laboratory in getting its data to any ministry or network?		
Our laboratory have not been invited to submit data		159 (52.6)
We need more equipment and personnel		103 (34.1%)
How often do you submit AST data?		
Monthly		3 (1.0)
Quarterly		19 (6.2)
Annually		18 (6.0)
We do not submit any report		262 (86.8)
Does your laboratory have internal SOP for assuring the quality of AST?	Yes No	156 (51.7) 146 (48.3)
Are all your tests reviewed before results are sent?	Yes No	94 (31.1) 208 (68.9)
If Yes, who reviews the result?		
Another member of the technical staff		56 (18.5)
A supervisor/medical microbiology		38 (12.6)
Laboratory Participation (%)	M= 18.32 SD= 19.66	
Not Participating		265 (87.7)
Participating		37 (12.3)

Key: n=number, %=percentage

4.4.2.5 Recording of appropriate data for AMR surveillance

Recording of appropriate data for AMR surveillance comprised of items to help assess patients' data collection, correlation of routine test results at the laboratories and compliance with WHO standards. One hundred and eighteen (39.1%) laboratories link AST result to all patient information (specimen source, patient bio-data, patient population…etc.), 132 (43.7%) laboratories link AST result to specimen source and patient bio-data only, 13 (4.3%) laboratories link AST results with clinical outcome, 39 (12.9%) laboratories do not link AST results to patients data. The criteria for recording all or select patients information vary across laboratories, 5 (1.7%) laboratories record patient population, pathogen type and infection origin only if the pathogen is generally considered clinically significant, 119 (39.4%) laboratories record patient population, pathogen type and infection origin only if the organism is considered clinically significant in the individual patient, 158 (52.3%) laboratories record patient population, pathogen type and infection origin from all isolates regardless of significant level of organism. One hundred and fifty-six (51.7%) laboratories have established guidelines for

the number and type of antibiotic resistance reported from isolates of different infection sites. In terms of compliance with WHO WHONET software for storing laboratory results, only 40 (13.2%) laboratories utilise WHONET for AMR data capturing. Four (1.3%) laboratories are reporting surveillance data to GLASS platform. In terms of staff training for AMR surveillance, only 26 (8.6%) laboratories had received training in the last 3 years, whereas the majority of 276 (91.4%) have not received any form of AMR training in the last three years. The average score for recording of appropriate data for AMR surveillance was 30.35%. Only 3 (1.0%) laboratories record important AMR surveillance data, 107 (35.6%) partially records important AMR surveillance data while 192 (63.6%) laboratories do not record important AMR surveillance data. Table 4.6 shows all the indicators assessed within this domain.

Table 4.6: Distribution of responses to items related to appropriate recording of AMR Surveillance data (n=302)

Items	Responses n=302	n (%)
Are susceptibility results linked to any/all of the following data categories?		
AST results are linked to All Patient Information		118 (39.1)
AST results are linked to only Sample and Patient Bio-data		132 (43.7)
AST results are linked to clinical outcome		13 (4.3)
We do not link results to patient data		39 (12.9)
On what basis are patient population, Pathogen type and infection origin specifically recorded?		
Organisms generally considered clinically significant organisms		5 (1.7)
Organism considered clinically significant in individual patient		119 (39.4)
All organisms		158 (52.3)
We do not perform AST		20 (6.6)
Are guidelines established for the number and type of antibiotics resistance reported for organisms isolated from different sites of infection?	Yes No	156 (51.7) 146 (48.3)
Does your Laboratory use WHONET?	Yes No	40 (13.2) 263 (86.8)
Does your Laboratory report AST data to GLASS?	Yes No	4 (1.3) 298 (98.7)
Has your laboratory received any training on AMR in the last 3 years?	Yes No	26 (8.6) 276 (91.4)
Recording of important AMR surveillance data (%)	M= 30.35 SD= 24.65	
Not capturing AMR surveillance data		192 (63.6)
Partially capturing AMR surveillance data		107 (35.4)
Fully capturing AMR surveillance data		3 (1.0)

Key: n=number, %=percentage

4.4.3 Surveillance quality indicator score in relation to laboratory affiliation (Government and private owned)

Figure 4.5 compared the average surveillance quality indicator scores by laboratory affiliation. The result shows higher mean SQI scores for government laboratories compared to the private laboratories. The average score for knowledge, laboratory capacity, laboratory surveillance participation, laboratory readiness for AMR surveillance and capturing of important AMR surveillance data from government owned laboratories were 67.99%, 84.30%, 35.36%, 74.97% and 46.73% while those of the private owned laboratories were 43.69%, 43.69%, 8.97%, 56.30% and 21.37% respectively**.**

Distribution of average SQI scores by laboratory affiliation.

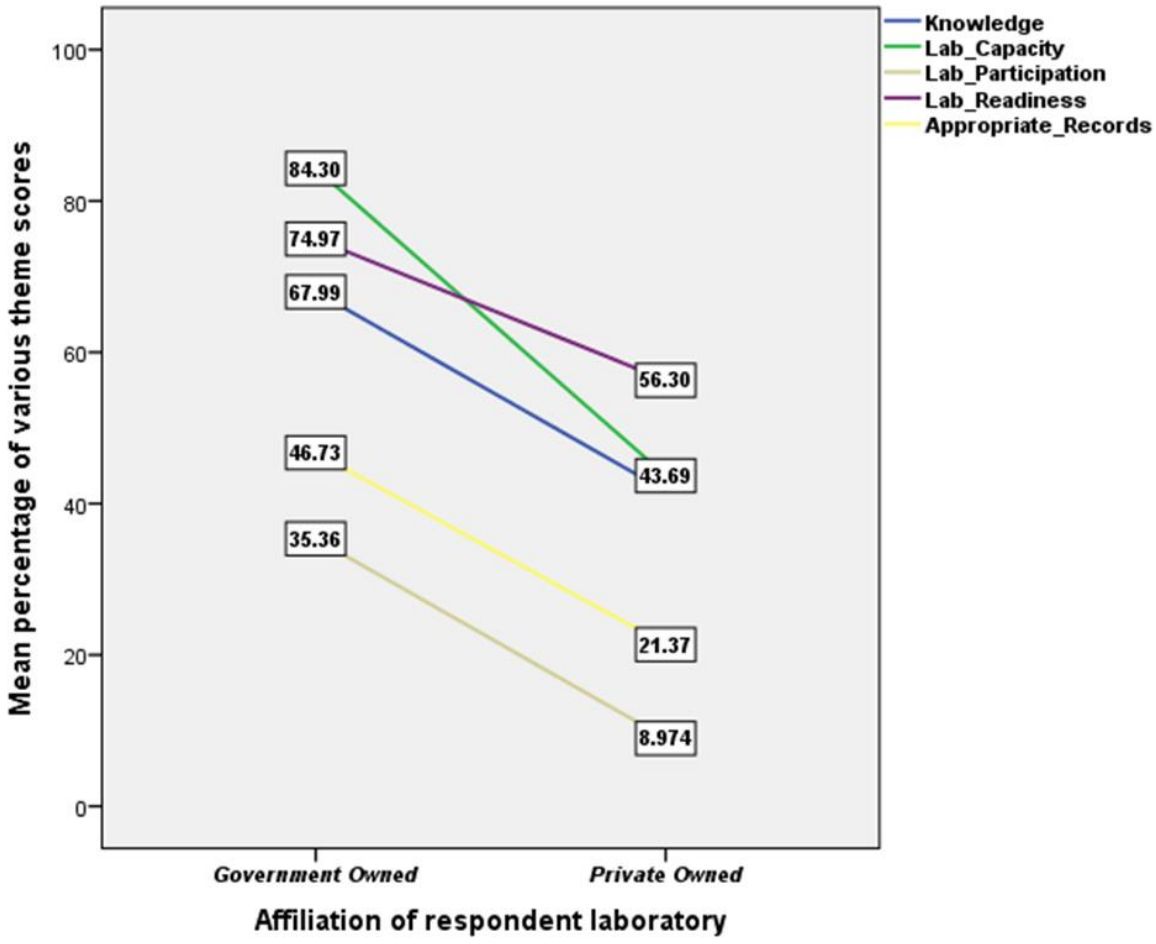


Figure 4.5: Comparing average SQI scores in relation to laboratory affiliation. Response shows that laboratories affiliated to government scored higher across all SQI compared to private laboratories.

4.4.4 Surveillance Quality Indicator scores by laboratory connection

Figure 4.6 shows mean score of the five SQIs in relation to laboratory connection (teaching, general, independent, FMCs, PHC, and private hospital). One-way ANOVA, a test used to compare the means of three or more groups was used to compare the mean difference of each of the SQI (knowledge, capacity, participation, readiness, and appropriate records) between groups of laboratory connection. Results from the test (appendix A17) indicated there are statistically significant differences in mean knowledge score between respondents of the various groups of laboratory connections (F(5,297)=14.29, p<.001). Similarly there was

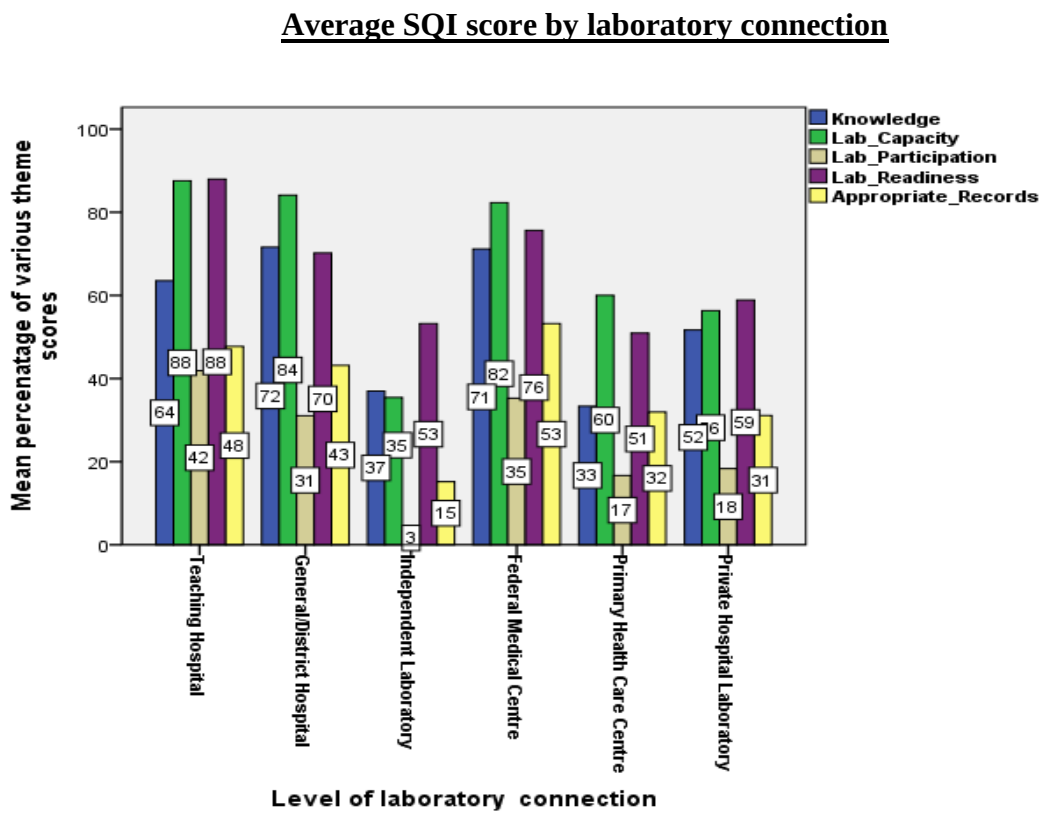


Figure 4.6: Compares average SQI scores with laboratory connection. The graph shows laboratories connected to teaching hospital had better average scores across all five SQI compared to laboratories connected to other level of healthcare providers.

statistically significant differences in the mean score of laboratory capacity to undertake AMR surveillance (F(5, 297)=66,38, p<.001), laboratory participation in AMR surveillance (F(5, 297)=70.14, p<.001), laboratory readiness to undertake AMR surveillance (F(5, 297)=12.47,

p<.001) and recording of appropriate AMR data (F(5, 297)=29.20, p<.001) between the various groups of laboratory connections. A post-hoc Tukey's test shows laboratories connected to teaching hospitals, Federal Medical Centers and State general hospitals had better performance scores on AMR knowledge, laboratory capacity, laboratory surveillance participation, laboratory readiness for AMR surveillance and capturing of important AMR surveillance data compared to those connected to primary healthcare, private hospital and independent laboratories. Overall, laboratories connected to teaching hospitals had better average scores as shown in post-hoc test available in appendix A18.

4.4.5 SQI scores by geopolitical location of laboratory

Figure 4.7 shows mean score of the five SQI in relation to the geopolitical zones of laboratories.

Mean score of the five SQIs in relation to geopolitical zone of laboratory

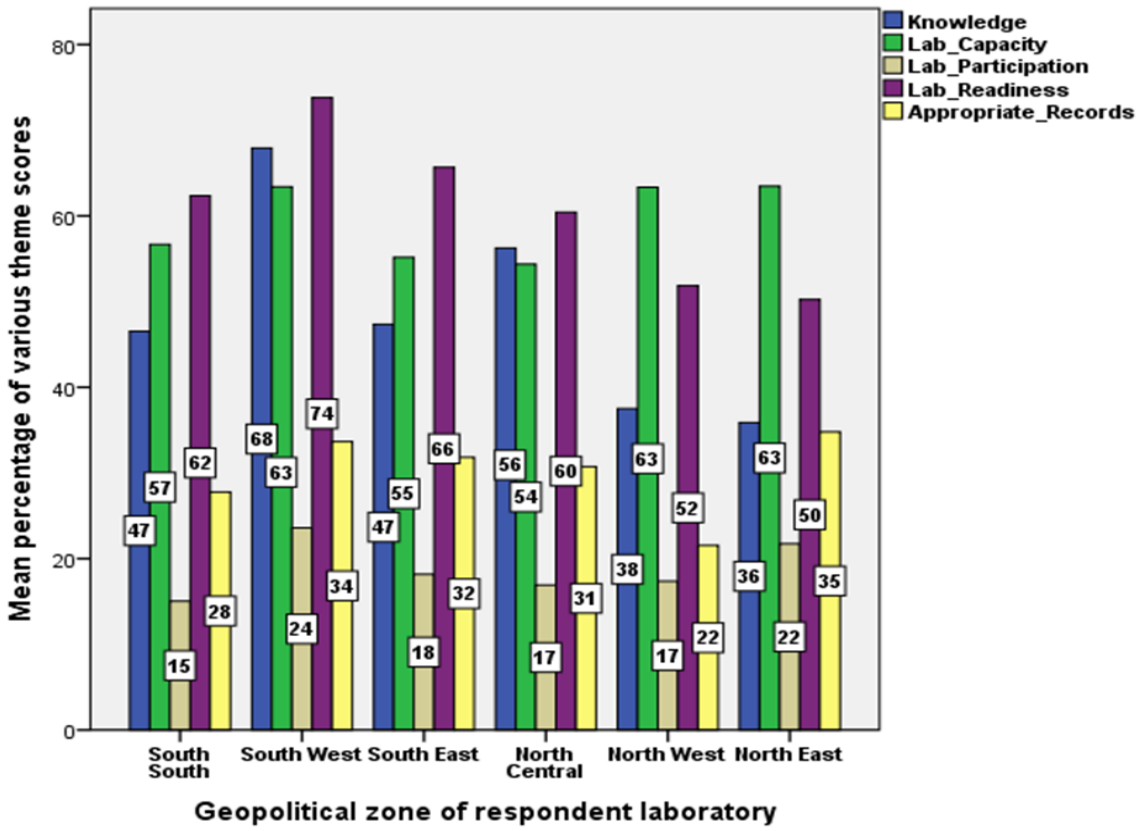


Figure 4.7: Comparing SQI scores of laboratories with geopolitical zones. The graph shows significant difference in the mean score of only two SQIs (knowledge, readiness). No difference was observed in the mean scores of the other three SQIs by geopolitical location.

Results of the One way ANOVA test available in appendix A19 indicated no statistically significant differences in the mean score of laboratory capacity to undertake AMR surveillance ($F(5, 297)=1.00$, $p =0.417$); laboratory participation in AMR surveillance activities ($F(5, 297)=1.38$, $p=0.230$); and recording of appropriate AMR data ($F(5, 297)=1.163$, $p=0.327$) by laboratory zones. However, there were statistically significant differences in the average scores of knowledge ($F(5, 297)=5.81$, $p<0.001$) and laboratory readiness to undertake AMR surveillance ($F(5, 297)=3.414$, $p=0.005$) by laboratory zones as shown in post-hoc turkey test available in appendix A20.

4.5 Association between SQIs and demographic data

4.5.1 Association between knowledge level of AMR surveillance and demographic characteristics of respondent laboratories

Table 4.7 shows outcome of the association between the respondents' knowledge of AMR surveillance and demographic data. In terms of laboratory affiliation, of the 107 respondents from government owned laboratories, 33 (30.8%) had excellent knowledge of AMR surveillance in Nigeria, while 58 (54.2%) and 16 (16.0%) had moderate and poor knowledge respectively. Similarly, amongst 195 respondents from private laboratories, 22 (11.3%) had excellent knowledge while 69 (35.4%) and 104 (53.3%) had moderate and poor knowledge of AMR surveillance respectively. A Chi square test of independence performed to assess the relationship between laboratory affiliation and knowledge shows statistically significant relationship between the two variables $\chi^2(2, N=302) = 45.95$, $p = 0.001$. Knowledge is found to be higher from respondents of government laboratories compared to those from private laboratories.

In terms of laboratory connection, 10 (27.0%) of the laboratories connected to teaching hospitals recorded excellent AMR surveillance knowledge, while respondents connected to federal medical centre, general hospitals, private hospitals and independent laboratory recorded

10 (38.5%), 14 (31.9%), 10 (16.7%) and 11 (8.9%) excellent knowledge respectively. Moderate AMR knowledge was recorded from 20 (54.1%) laboratories connected to teaching hospitals while those connected to federal medical centre, general hospitals, private hospitals and independent laboratories recorded 13 (50.0%), 24 (54.5%), 5 (41.7%), 27 (45.0%) and 38 (30.9%) respectively. Poor AMR surveillance knowledge was recorded from 7 (18.9%) laboratories connected to teaching hospitals, while those connected to federal medical centres, general hospitals, private hospitals laboratories and independent laboratory recorded 3 (11.5%), 6 (13.6%), 7 (58.3%), 23 (38.3%) and 74 (60.2%) respectively. A Chi square test of independence performed to assess the relationship between laboratory connection and knowledge shows statistically significant relationship between the two variables $\chi^2(10, N=302) = 57.80$, $p = 0.001$. Respondents from laboratories connected to teaching hospital are more likely to show higher knowledge of AMR surveillance compared to respondents from laboratories connected to other hospitals.

Geographically, the zones reported staggered levels of knowledge. The South-West zone reported 16 (30.2%) knowledge, South-South 11 (15.3%), South-East 10 (15.2%), North-Central 13 (20.3%), North-West 3 (12.5%) and North-East 2 (8.7%). A Chi square test of independence performed to assess the association between geopolitical location of laboratory and knowledge shows statistically significant relationship $\chi^2(10, N=302) = 20.77$, $p = 0.02$.

Table 4.7: Association between knowledge level of AMR surveillance and demographics characteristics of respondents' laboratory

	Knowledge Level of AMR Surveillance			
	Poor Knowledge n (%)	Moderate Knowledge n (%)	Excellent Knowledge n (%)	χ^2 Cal(p-value)
Affiliation of Laboratory				45.95(0.001)
Government Owned n=107	16(15.0)	58(54.2)	33(30.8)	
Private Owned n=195	104(53.3)	69(35.4)	22(11.3)	
Level of Laboratory				
Teaching Hospital n=37	7(18.9)	20(54.1)	10(27.0)	57.80(0.001)
Federal Medical Centre n=26	3(11.5)	13(50.0)	10(38.5)	
General/District Hospital n=44	6(13.6)	24(54.5)	14(31.9)	

Primary Health Care n=12	7(58.3)	5(41.7)	0(0.0)	
Private Hospital Laboratory n=60	23(38.3)	27(45.0)	10(16.7)	
Independent Laboratory n=123	74(60.2)	38(30.9)	11(8.9)	
Geopolitical zone of respondent laboratories				
South-South n=72	33(45.8)	28(38.9)	11(15.3)	20.77(0.02)
South-West n=58	10(18.9)	27(50.9)	16(30.2)	
South-East n=66	31(47.0)	25(37.9)	10(15.2)	
North-Central n=64	20(31.3)	31(48.4)	13(20.3)	
North-West n=24	13(54.2)	8(33.3)	3(12.5)	
North-East n=23	12(56.5)	8(34.8)	2(8.7)	

Key: n=number, %=percentage, SD=standard deviation, χ^2Cal=Chi-square Calculated, p-value=Significant level, $p<0.05$= statistically significant, $p>0.05$=not statistically significant

4.5.2 Association between capacity for AMR surveillance and demographic characteristics of laboratories

Table 4.8 shows outcome of the association between laboratory capacity for AMR surveillance and demographic data. Of the 107 government affiliated laboratories, 66 (61.7%) reported good capacity for AMR surveillance while 12 (5.7%) reported good capacity from 195 private owned laboratories. A Chi square test of independence performed to assess the association between laboratory capacity and laboratory affiliation shows statistically significant relationship between the two variables $\chi^2(2, N=302) = 140.49$, $p=0.001$. Capacity for AMR surveillance was found to be highest amongst government affiliated laboratories.

In terms of laboratory connection, of the 37 laboratories connected to teaching hospitals, 25 (67.6%) reported capacity for AMR surveillance, 27 (61.4%) general/district level laboratories reported capacity for AMR surveillance from 44 responses received, 15 (57.7%) federal medical centre laboratories recorded capacity for AMR surveillance from 26 responses received, 7 (11.7%) private hospital laboratories reported capacity for AMR surveillance of 60 responses received, 5 (25.0%) primary health care laboratories recorded capacity for AMR surveillance of 12 responses received while independent laboratories recorded 0 (0.0%) of 122 responses received. Test of independence to assess relationship between laboratory capacity for AMR surveillance and laboratory connection equally shows statistically significant relationship between the two variables $\chi^2(10, N=302) = 190.38$, $p = 0.001$. Laboratories

connected to teaching hospitals showed greater capacity for AMR surveillance compared to laboratories connected to other levels of hospital.

Association between laboratory capacity for AMR surveillance and geopolitical zone of laboratory show no statistically significance difference $\chi^2(10, N=302) = 13.72$, $p = 0.11$. Laboratory capacity does not have association with geopolitical zone of the laboratory or the observed difference may have occurred by chance.

Table 4.8: Association between laboratory capacity for AMR surveillance and the demographic characteristics of respondents' laboratories

	Laboratory Capacity to uptake AMR Surveillance			
	Poor Capacity n (%)	Partial Capacity n (%)	Good Capacity n (%)	χ^2Cal(p-value)
Affiliation of Laboratory				140.49(0.001)
Government Owned n=107	10(9.3)	31(29.0)	66(61.7)	
Private Owned n=194	140(72.2)	43(22.2)	12(5.7)	
Level of Laboratory				
Teaching Hospital n=37	3(8.1)	9(24.3)	25(67.6)	190.38(<0.001)
Federal Medical Centre n=26	3(11.5)	8(30.8)	15(57.7)	
General/District Hospital n=44	4(9.1)	13(29.5)	27(61.4)	
Primary Health Care n=12	6(50.0)	3(25.0)	5(25.0)	
Private Hospital Laboratory n=60	25(41.7)	28(46.7)	7(11.7)	
Independent Laboratory n=122	109(89.3)	13(10.7)	0(0.0)	
Geopolitical zone of laboratories				
South-South n=72	33(45.8)	27(37.5)	12(16.7)	13.72(0.11)
South-West n=58	22(41.5)	13(24.5)	18(34.0)	
South-East n=65	36(55.4)	14(21.5)	15(23.1)	
North-Central n=64	38(59.4)	10(15.6)	16(25.0)	
North-West n=24	10(41.7)	5(20.8)	9(37.5)	
North-East n=23	11(47.8)	5(21.7)	7(30.4)	

Key: n=number, %=percentage, SD=standard deviation, χ^2Cal=Chi-square Calculated, p-value=Significant level, $p<0.05$= statistically significant, $p>0.05$=not statistically significant.

4.5.3 Association between readiness for AMR surveillance and demographic characteristics of respondent laboratories

Table 4.9 shows outcome of the association between readiness for AMR surveillance and demographic data. For laboratory readiness and laboratory affiliation, of the 107 response received from government laboratories, 17 (15.9%) reported readiness for surveillance whereas only 5 (2.6%) private laboratories from a total of 195 records received reported readiness. Chi

square test reveals that the association between the two variables is statistically significant $\chi^2(2, N=302) = 36.51$, $p = 0.001$. Government affiliated laboratories are more likely to be ready for AMR surveillance compared to private affiliated laboratories.

In terms of laboratory readiness for AMR surveillance and laboratory connection, more readiness for AMR surveillance was observed from laboratories connected to teaching hospitals compared to those connected to other levels of healthcare services. From data collected, 11 (29.7%) teaching hospital laboratories were found to be ready to participate in AMR surveillance, 4 (9.1%) district/general hospital laboratories were found ready, 4 (3.3%), 2 (7.7%) and 1 (1.7%) readiness for AMR surveillance was found from independent laboratories, federal medical center laboratories and private laboratories. No primary health centre laboratory reported full readiness for AMR surveillance. Chi square test of association to assess the relationship between readiness and laboratory connection shows statistically significant relationship between the two variables $\chi^2(10, N=302) = 64.47$, $p=0.001$. Laboratories connected to teaching hospitals show more readiness compared to laboratories connected to other levels of hospital.

Geopolitically, readiness scores reflected varying magnitude across zones: 7 (13.3%) in South-West whereas 4 (16.7%), 3 (4.7%), 3 (4.5%), 3 (4.2%), 2 (8.7%) readiness was recorded from North-West, North-Central, South-East, South-South and North-East respectively. Chi square test of association to assess the relationship between readiness and geopolitical location also shows statistical significance $\chi^2(10, N=302) = 25.09$, $p = 0.005$.

Table 4.9: Association between Readiness of Laboratory to participate in AMR surveillance and the demographic characteristics of respondent laboratories

	Laboratory Readiness to participate in AMR Surveillance			
	Not Ready n (%)	Fairly Ready n (%)	Fully Ready n (%)	χ^2Cal(p-value)
Affiliation of Laboratory				36.51(<0.001)
Government Owned n=107	21(19.6)	69(64.5)	17(15.9)	

Private Owned n=195	97(49.7)	93(47.7)	5(2.6)	
Level of Laboratory				
Teaching Hospital n=37	2(5.4)	24(64.9)	11(29.7)	64.47(<0.001)
Federal Medical Centre n=26	6(23.1)	18(69.2)	2(7.7)	
General/District Hospital n=44	9(20.5)	31(70.5)	4(9.1)	
Primary Health Care n=12	6(50.0)	5(50.0)	0(0.0)	
Private Hospital Laboratory n=60	28(46.7)	31(51.7)	1(1.7)	
Independent Laboratory n=123	67(54.5	52(42.3)	4(3.3)	
Geopolitical zone of respondent laboratory				
South-South n=72	27(37.5)	42(58.3)	3(4.2)	25.09(0.005)
South-West n=53	12(22.6)	34(64.1)	7(13.3)	
South-East n=66	27(40.9)	36(54.5)	3(4.5)	
North-Central n=64	27(42.2)	34(53.1)	3(4.7)	
North-West n=24	14(58.3)	6(25.0)	4(16.7)	
North-East n=23	11(47.8)	10(43.5)	2(8.7)	

Key: n=number, %=percentage, SD=standard deviation, χ^2Cal=Chi-square Calculated, p-value=Significant level, p<0.05=significant statistically, p>0.05=not significant statistically.

4.5.4 Association between AMR surveillance participation and demographic characteristics of laboratories

Table 4.10 shows outcome of AMR surveillance participation and demographic characteristics. More surveillance participation was observed amongst government affiliated laboratories compared to the private laboratories. Of the 107 responses received from government laboratories, 31 (29.0%) indicated participation in AMR surveillance while only 6 (3.1%) of private affiliated laboratories indicated surveillance participation from a total number of 195 records received. A Chi square test to assess the relationship between AMR surveillance participation and laboratory affiliation shows a statistically significant relationship between the two variables $\chi^2(1, N=302) = 43.09$, $p = 0.001$. Government laboratories are more likely to participate in AMR surveillance compared to private laboratories.

Table 4.10: Association between status of AMR surveillance participation and demographic characteristics of respondents' laboratories.

	Laboratory status of AMR Surveillance participation		
	Not capable participating n (%)	Capable of participating n (%)	χ^2Cal(p-value)
Affiliation of Laboratory			43.09(<0.001)
Government Owned n=107	76(71.0)	31(29.0)	
Private Owned n=195	189(96.9)	6(3.1)	
Level of Laboratory			
Teaching Hospital n=37	23(62.2)	14(37.8)	

Federal Medical Centre n=26	18(69.2)	8(30.8)	52.84(<0.001)
General/District Hospital n=44	34(77.3)	10(22.7)	
Primary Health Care n=12	12(100.0)	0(0.0)	
Private Hospital Laboratory n=60	57(95.0)	3(5.0)	
Independent Laboratory n=123	121(98.4)	2(1.6)	
Geopolitical Zone respondent laboratory			
South-South n=72	67(93.1)	5(6.9)	2.61(0.76)
South-West n=53	45(84.9)	8(15.1)	
South-East n=66	57(86.4)	9(13.6)	
North-Central n=64	55(85.9)	9(14.1)	
North-West n=24	21(87.5)	3(12.5)	
North-East n=23	20(87.0)	3(13.0)	

Key: n=number, %=percentage, SD=standard deviation, χ^2Cal=Chi-square Calculated, p-value=Significant level, $p<0.05$= statistically significant, $p>0.05$=not statistically significant.

When surveillance participation was compared with laboratory connection, participation followed order of hospital hierarchy. Fourteen (37.8%) laboratories connected to teaching hospitals reported surveillance participation while laboratories connected to federal medical centre, district/general hospital, private hospitals, independent and primary healthcare reported surveillance in the following order; 8 (30.8%), 10 (22.7%), 3 (5.0%), 2 (1.6%) and 0 (0.0%). No surveillance participation was reported from laboratories connected to primary healthcare centre. The observed association between laboratory participation and connection shows statistical significance $\chi^2(5, N=302) = 52.84$, $p = 0.001$. Laboratory connection has effect on laboratory participation for AMR surveillance and laboratories connected to teaching hospitals are more likely to participate in AMR surveillance.

In terms of geopolitical zones and laboratory participation, no statistically significant association was found between the two variables. Although data shows varying degree of participation across zones, these do not follow a particular pattern. Test of significance shows p-value of 0.76, which is greater than the threshold of 0.05 and regarded statistically insignificant. This implies that geopolitical location does not have significant effect on surveillance participation and the observed association is not greater than what would have occurred by chance.

4.5.5 Association between knowledge, laboratory capacity, readiness, and surveillance participation of laboratory with demographic characteristics using logistic regression.

Bivariate and multinomial logistic regression analysis were performed to ascertain the effect of demographic characteristics (affiliation, connection, and zone) independent variable on the likelihood of increased knowledge, capacity, readiness and participation (dependent variable). The regression analysis revealed statistically significant association between each of the SQIs assessed and the demographic characteristics of the laboratories.

A lower odd of (OR=0.72, 95%CI [0.52, 0.98]) knowledge of AMR surveillance was found among respondents from private affiliated laboratories compared to their government affiliated counterpart. In terms of laboratory connection, there is a greater odd of better knowledge of AMR surveillance amongst respondents connected to teaching hospitals compared to federal medical centre respondents at an odd ratio of (OR=2.35, 95%CI[1.45, 4.42], p=0.008); similar trends were observed when knowledge of teaching hospital respondents was compared with general/district hospital respondents at an odd ratio of (OR=3.02, 95%CI [1.68, 5.43], p<0.001); likewise a higher odd of (OR=1.15, 95%CI (0.53-2.48), p<0.001) was found when compared to respondents connected to primary healthcare; (OR=1.88, 95%CI [1.07, 3.31], p=0.03) for respondents connected to private hospital and (OR=1.32, 95%CI [072, 2.45], p=0.37) for respondents connected to independent laboratories. A lower odd of (OR=0.41, 95%CI [0.31, 0.56]) laboratory capacity for AMR surveillance was found amongst private affiliated laboratories compared to the government laboratories that was used as reference category. Also in terms of level of laboratory connection, there were lower odd of laboratory capacity in the other level of laboratory connection compared to teaching hospital laboratories as shown in table 4.11.

Table 4.11: Association of demographic characteristics of laboratories with knowledge of AMR surveillance and Laboratory Capacity scores.

	Knowledge			Lab Capacity		
	OR	95%CI	p-value	OR	95%CI	p-value

Affiliation of Laboratory* Government Owned(Reference)						
Private Owned	0.72	0.52-0.98	0.04	0.41	0.31-0.56	0.0001
Level of Laboratory ** Teaching Hospital (Reference)						
Federal Medical Centre	2.35	1.45-4.42	0.008	0.93	0.54-1.58	0.77
General/District Hospital	3.02	1.68-5.43	0.0001	1.15	0.69-1.88	0.35
Primary Health Care	1.15	0.53-2.48	0.73	0.58	0.29-1.13	0.11
Private Hospital Laboratory	1.88	1.07-3.31	0.03	0.49	0.30-0.79	0.004
Independent Laboratory	1.32	072-2.45	0.37	0.26	0.15-0.47	0.0001
Geopolitical Zone of respondent laboratory** South-West (Reference)						
South-South	0.62	0.43-0.88	0.008	1.08	0.77-1.49	0.68
South-East	0.56	0.39-0.81	0.002	0.86	0.62-1.21	0.83
North-Central	0.86	0.60-1.23	0.40	0.32	0.89-0.64	0.39
North-West	0.48	0.28-0.82	0.007	1.49	0.94-2.36	0.09
North-East	0.38	0.22-0.66	0.001	1.13	0.71-1.82	0.60

Key: *=binary logistic regression, **=multinomial logistic regression, OR=odd ratio, 95%CI= 95% Confidence interval, p-value=Significant level, p<0.05=significant statistically, p>0.05=not significant statistically.

Table 4.12 shows association between readiness and participation with laboratory affiliation and connection. The result shows a lower odd of (OR=1.07 95%CI 0.81-1.26) readiness for AMR surveillance amongst laboratories affiliated to private ownership compared to those affiliated to government. Also a lower odd of readiness was found in laboratories connected to teaching hospitals (the reference category) compared to other laboratories.

Laboratory participation was also significantly associated with laboratory affiliation, government owned laboratories are 59% (1-0.41) more likely to participate in AMR surveillance than private owned laboratories. Also, laboratories connected to teaching hospitals are more likely to participate in surveillance than other laboratories.

Table 4.12: Association of demographic characteristics of laboratories with readiness for AMR surveillance and Laboratory participation scores.

n =302	AMR Surveillance Readiness			Lab Participation		
	OR	95%CI	p-value	OR	95%CI	p-value
Affiliation of Laboratory* Government Owned(Reference)						
Private Owned	1.07	0.81-1.26	0.0001	0.41	0.25-0.67	0.0001

Laboratory Connection** Teaching Hospital (Reference)						
Federal Medical Centre	0.50	0.32-0.79	0.003	0.37	0.18-0.78	0.009
General/District Hospital	0.45	0.29-0.69	0.0001	0.35	0.17-0.69	0.002
Primary Health Care	0.46	0.28-0.75	0.002	0.25	0.08-0.80	0.02
Private Hospital Laboratory	0.46	0.29-0.71	0.0001	0.28	0.13-0.58	0.001
Independent Laboratory	0.53	0.34-0.84	0.006	0.05	0.02-0.12	0.0001
Geopolitical Zone of respondent laboratory** South-West (Reference)						
South-South	0.94	0.77-1.13	0.49	0.77	0.47-1.25	0.29
South-East	0.98	0.80-1.19	0.85	1.01	0.63-1.63	0.97
North-Central	0.84	0.69-1.02	0.08	0.88	0.55-1.41	0.59
North-West	0.79	0.62-1.01	0.06	1.38	0.68-2.82	0.37
North-East	0.77	0.61-0.98	0.03	1.49	0.73-3.07	0.27

Key: *=binary logistic regression, **=multinomial logistic regression, OR=odd ratio, 95%CI= 95% Confidence interval, p-value=Significant level, p<0.05= statistically significant, p>0.05=not statistically significant.

Table 4.13 tested the relationship between the five assessed SQIs. The results show moderate positive correlation between laboratory capacity and laboratory participation [r(302)=0.66, p=0.001] as well as capturing of important AMR data and laboratory participation [r(302)=0.67, p=0.001]. The correlation coefficient is rated on the basis of the conventional approach to interpreting correlation according to Schober and Schwarte (2018). There was generally positive correlation from one SQI to another, it therefore shows that the performance of one SQI has a positive impact on the other though at varying degree.

Table 4.13: Correlation between Score of Knowledge, Laboratory Capacity, Laboratory participation, Readiness and capturing important data for AMR surveillance in the study.

n =302	Knowledge of AMR surveillance	Laboratory Capacity	Laboratory Participation in AMR surveillance	Readiness to uptake AMR surveillance	Capturing of important data
Knowledge of AMR surveillance					
Laboratory Capacity	r=0.33, p=0.001				
Laboratory Participation	r=0.47, p=0.001	r=0.66, p=0.001			
Readiness to uptake AMR surveillance	r=0.52, p=0.001	r=0.36, p=0.001	r=0.43, p=0.001		
Capturing of important data	r=0.43, p=0.001	r=0.52, p=0.001	r=0.67, p=0.001	r=0.38, p=0.001	

Key: r=Pearson correlation coefficient, p=Significant level, p<0.05= statistically significant, p>0.05=not statistically significant.

4.6 Discussion

The laboratory is a major component of the global system for AMR surveillance. As highlighted in the global action plan (GAP) for AMR, early detection of resistant pathogens is regarded as a strategic tool for tackling AMR (World Health Organisation, 2015). This recognition further emphasises the importance of the participatory role of the laboratory in this process. Noting that their participatory role is more enhanced when they are organised systematically within the system (Altorf-van der Kuil *et al.*, 2017).

Findings from this study reveals absence of an organisational structure for collecting surveillance data at local, regional and national levels which impacts flow of surveillance data across time and space. The results also highlight the current state of NAP implementation in the scope of laboratory participation. The outcomes show that routine surveillance using routinely generated data from sentinel sites is ongoing for AMR albeit low with disproportionate distribution of laboratory participation which is skewed towards tertiary level care. The tertiary care is the highest referral care unit in the organisational structure of Nigeria healthcare system, and what this means for surveillance focused on this level is that resistance in the population of people with no recourse to attend tertiary hospital will not have any chances of being picked up. This could potentially be overestimating resistance cases and consequently impact the representativeness of data. Another concern that emerges from conducting surveillance at referral centre is the mix up of demographic information. As patients whose infection could not be managed at the lower healthcare centres are transferred to tertiary hospitals for specialist care, the place of specimen collection is usually recorded as part of demographic information for surveillance purpose which may not be an accurate proxy for the actual geographical location of the patient. The implication of this is that any targeted interventions for that particular patient population will be directed at the wrong setting, thus making AMR containment more challenging. Being that the goal of surveillance is to provide

reliable data that will ensure development of policies and strategies that are informed by the population situation, accurate recording of patients' information and equitable laboratory recruitment are important for optimised surveillance.

Of particular concern is complete absence of surveillance at the primary healthcare level as indicated by the outcome of this study. This shows a negative precedence as the population of people within the primary healthcare catchment live in the rural areas where potential for misuse of antimicrobials is high. Studies show high rate of misuse of antimicrobial agents amongst individuals in the rural settings due to over the counters purchase and absence of regulation on non-prescription access to drugs (Badger, Emeka, and Okosi, 2018; Manyi *et al.*, 2018; Ayukekbong, Ntemgwa, and Atabe, 2017). Most importantly, the organisation of healthcare system in Nigeria mirrors the governance structure where policy actions flow from top to bottom with the lower tiers being the least to be considered. It is expected that this should informed the action plan implementation by ensuring strategic approach that will include lowest level of healthcare since AMR affects everyone equally regardless of location (Ceric *et al.*, 2019). It is noteworthy that the burden of AMR is better estimated when surveillance is comprehensive rather than fragmented and until this happens, AMR estimates will remain largely exaggerated (Tacconelli *et al.*, 2018).

In addition to analysing progress of NAP implementation in the context of laboratory surveillance, this study also assessed opportunities for increasing laboratory networks for AMR surveillance as well as improving quality of data. To determine this, laboratories in Nigeria were assessed on five SQIs: knowledge, laboratory capacity to undertake surveillance, readiness of the laboratory to participate in AMR surveillance, status of laboratory participation in AMR surveillance and ability of the laboratory to collect and record important AMR surveillance data. Generally, there are significant differences between the laboratory demographics (laboratory affiliation, laboratory connection and laboratory location) and the

SQIs investigated in the study which has major implications for future laboratory iterations into the surveillance system.

The knowledge indicator shows only 55 laboratories had excellent knowledge of AMR surveillance activities but knowledge score was noted to taper down the laboratory hierarchy ladder. Higher knowledge of AMR, NAP, AMR surveillance and GLASS were found amongst tertiary care level laboratories. The level of the awareness and knowledge of AMR surveillance could be attributed to the media efforts of the Nigeria Centre for Disease Control (NCDC) and the effort of the developmental partners. One of such efforts is the development of a surveillance guideline for AMR by NCDC which was made available to laboratories in the country through the national coordinating centre for AMR (NCDC, 2018). Knowledge of AMR correlates with antimicrobial usage amongst healthcare providers and the consumers and thus considered an essential element in AMR containment. Mccubbin *et al.* (2021) study on knowledge gaps in AMR surveillance concluded that there is also a relationship between level of AMR knowledge and the presence of surveillance in any given country. Surveillance tends to be prioritised in settings where knowledge of AMR is high. An earlier study of the knowledge of antimicrobial use and resistance amongst Nigerian population showed that the number of respondents with knowledge of AMR was below 50% (Akande-Sholabi & Ajamu, 2021; Chukwu *et al.,* 2020). These findings support other reports by the World Health Organisation (2015) and Klein *et al*. (2018) which demonstrated association between low knowledge of AMR and antimicrobial use. There were increases in antimicrobial use and resistance in places were AMR knowledge was low particularly in low and medium countries as exemplified in these studies. This suggest that knowledge plays a crucial role in AMR containment (World Health Organisation, 2015). Therefore, for surveillance to be successful, knowledge and educational activities must be prioritised as strategic action for AMR containment (World Health Organisation, 2016). Government investment in the areas of

advancing knowledge must be all encompassing, involving all healthcare providers irrespective of level, affiliation and location. Evidence from this study has not reflected that much of this is happening, even at the laboratory level, only 26 (8.6%) laboratories reported to have undertaken training/continuing education in relation to AMR in the past three years and that does not reflect sufficient investment in educating the clinicians. Education is imperative to containing AMR at national, regional and global level, and health systems must reflect this awareness and ensure inclusiveness in relation to educational activities across settings.

The capacity assessment provided insight into types of laboratories with good potential as sentinel sites for participating in national or early warning surveillance. These laboratories ranked at the same performance level as those currently participating in surveillance according to the indicators measured in the survey. The most important requirements for participating in surveillance such as EQA enrolment and conducting AST testing utilising the GLASS recommended disc diffusion methods were detected in some private and state level laboratories that are not currently involved in surveillance. The implementers and the AMR-TWG need to be aware of these eligible laboratories which are largely under-utilised and develop pathways to integrate them into the existing surveillance system in order to expand surveillance and increase representativeness. Other indicators of capacity for AMR surveillance such as use of reporting guidelines, accuracy checks, technical level of staff and equipment maintenance were equally assessed. These parameters help to assure the quality of laboratory testing procedure as well as ensure errors are eliminated from results through accuracy checks. Most technical staff were trained to conduct AST, but procurement and maintenance of AST material and equipment were identified as a limitation factor. Only few laboratories participate in external quality assurance, with public sector laboratories' having strong involvement in internal quality assurance programs. This difference in EQA participation between public and private sector laboratories may be impacting recruitment from private sector laboratories. In order to bridge

this gap and successfully deploy robust quality checks for AST, Saeed *et al.* (2017) recommended short courses on how to establish useful models for improving national laboratory testing capacity. In addition, mentoring of laboratories with low baseline through continuous trainings have been advocated to overcome gaps in quality assurance, including formulation and implementation of SOPs, frequent use of standardised quality control strains, and uniform inoculum for AST (Datema *et al.,* 2020). Several studies from resource-limited countries and policies illustrates the efficacy of proficiency testing (PT) training programs to build a sustainable network for knowledge and talent transfer through cooperation with weaker laboratories to address fundamental capacity gaps (Saeed *et al.*, 2017; World Health Organisation, 2013). Such laboratory partnerships may reduce costs and increase diagnostic capabilities thus providing a strong system for AMR surveillance.

The highest score of laboratory readiness for AMR was recorded from government affiliated laboratories. This corroborates with information regarding AMR and other healthcare strengthening programmes and activities which are focused on government facilities. The Fleming fund for instance which was aimed at supporting AMR capacity and laboratory upgrade was limited to government hospitals alone, no private facility benefited from this project (Gordon *et al.,* 2020). This irrational preference for government laboratories justifies the high readiness score recorded from these group of laboratories. AMR surveillance needs to be comprehensive, with a wider reach in order to be effective. There is need for the inclusion of private sector laboratories in strengthening projects, by doing so, the private laboratories will be building the eligibility required to be part of the national surveillance.

Laboratory connection is another strong impacting factor revealed from this study. The study indicate that laboratories connected to teaching hospitals were found to be more relevant to AMR surveillance activities. This is agreeable as the laboratories in teaching hospitals are more prepared and supported by government, multinational organisations and grants from donor

agencies. Another factor that support their preparedness is that most teaching hospitals also serve as centers for surveillance of other diseases and illness. For instance, the Nigeria President's Emergency Plan for AIDS Relief (PEPFAR) which was set up to strengthen surveillance capacity for AIDS in select tertiary laboratories is able to also provide support for other disease surveillance (PEPFAR, 2019). Even though PEPFAR was not originally commissioned for AMR related activities, AMR surveillance could leverage on the existing infrastructure of this project for seamless and integrated operation. Some of these opportunities are often not available to secondary and primary healthcare centers which impacts on their capacity, readiness and meeting the selection criteria for surveillance (Hamel *et al.,* 2015; Abimiku *et al.,* 2010).

Geopolitically, knowledge and readiness were the only indicators that showed statistical significance in relation to zones. The South-West showed more readiness and knowledge scores compared to the rest of the zones which demonstrated staggered pattern. It is not clear from the study why this is so but it could possibly be due to variability in relation to number, categories and affiliations of laboratory sites recruited. Thus, establishing the true impact of geopolitical zones on SQIs based on the recruited sites for this study could lead to incorrect inferences.

4.7 Limitations

Although the overall survey response exceeded the estimated sample size for the study, uneven representation in number and laboratory affiliation across states limit the generalisability of result to all laboratories and states in relation to AMR surveillance and laboratory capacity. Inferences with respect to geopolical zones and SQIs do not provide valid estimates of the causal relationship due to disproportionate sample distribution across zones. Thus, limiting the ability to establish the influence of geographical zones on SQIs.

In addition to the capacity indicators assessed in this study (reporting guidelines, accuracy checks, technical level and equipment maintenance), capacity of laboratories also depend on critical infrastructure (e.g. electricity, water) especially in LMICs. Though these aspects were not assessed in this study, they are import quality indicators which have implication on technical characteristics of laboratories. Their exclusion might have had a negative/positive influence on the capacity findings and results of this study.

The questionnaire was designed for persons with significant role in the organisation (directors, practice managers, senior staff members) to guarantee reliability, accuracy and authenticity of information, chances are that the survey might have been completed by someone other than the designated persons. Even though measures were in place to mitigate this, there are likelihoods this might have occurred and since no personal identifiable information was collected, this could not be verified and such response might misrepresent the laboratory situation.

Lastly, the lack of ranking score for some of the SQIs (readiness, participation and capturing) necessitated assigning arbitrary ranking score. This might have raised the ranking band to unrealistic range which has impact on the overall performance benchmarking score. Regardless of these limitations, this study provides snapshot of SQI scores for various laboratory as well as an overview of AMR surveillance implementation accomplishments and serve as the NAP post implementation report.

4.8 Conclusion

AMR surveillance implementation in Nigeria varies across laboratories, settings and regions. Laboratory capacity improvement programmes are more focused on government laboratories and surveillance participation is skewed towards tertiary laboratories. This widening equity gap between government and private affiliated laboratories as well as rural and urban healthcare services does not serve the purpose of good surveillance. Absence of surveillance at the lower-level laboratory means data on AMR situation from these levels are not picked up

and consequently, soaring AMR rates in the community without data to inform control measures. Interestingly, a number of the lower-level laboratories reported excellent capacity as the laboratories currently participating in AMR surveillance but remain largely under-utilised. This could be attributed to recruitment shortfalls, lack of systematic laboratory assessment metrics and failure of oversight function by responsible bodies. These gaps have implications on representativeness and validity of surveillance data although findings from this study have highlighted ways of mitigating this problem.

4.9 Recommendations

The implementation of AMR surveillance must be prioritised across all levels of healthcare to ensure effective monitoring of resistance trends. Programmes or activities targeted at building both human and laboratory capacity should be inclusive irrespective of laboratory affiliation, connection, level or geographical location. A targeted laboratory capacity assessment study is required, specifically, from underrepresented laboratory levels and geographical locations to give more insights to the challenges and opportunities of actualising comprehensive surveillance, more importantly at the community level. Also, a qualitative study will be required to draw a causal relationship and rationale for the observed pattern of laboratory recruitment as well as explore cost effective ways for proper utilisation of laboratory services with the right capacity to undertake AMR surveillance. This will not only ensure that laboratories at various levels are involved, but it will also provide a more representative snapshot of samples whilst at the same time contributing towards the building blocks for sustainable surveillance operations. Lastly, a unified template indicating all the important patients' data (clinical, epidemiological, population) required for surveillance purpose must be developed and circulated to all laboratories to ensure data completeness as well as effective monitoring.

Chapter 5 Stakeholders' Perspective of Antimicrobial Resistance Surveillance Implementation: a Qualitative Approach to Situational Analysis

5.1 Introduction

Following the findings from the preceding chapter (cross sectional study) which identified weaknesses within the laboratory network system, a qualitative study was conducted to further explore the domains of national action plan (NAP) and to examine the contribution of poor policy implementation to these problems. By exploring stakeholders' opinion, this chapter offered perspective to causal factors within the health system, including political and economic factors and mapped the implementation issues associated to them using the governance framework. The NAP strategic objective was analysed to provide context to the domains of AMR surveillance.

5.2 Background

Stakeholders play integral roles in policy implementation worldwide (Alemanno, 2015). In AMR containment, stakeholder engagement throughout the NAP policy development circle (exploration, programme installation, initial implementation, full operation, and sustainability) is essential for understanding the needs of different groups, sectors, and organisations and for increasing equity in policy framework (Bordier *et al.*, 2021; Gilson *et al.*, 2020). Timely stakeholder engagement helps to give additional legitimacy through contribution to evidence in support of policies. This in effect helps to shape the policy, increases accountability of government to stakeholders thus achieving a robust and more effective policy implementation (Gilson *et al.,* 2020). Moreso, in-depth stakeholders' knowledge of policy framework including the timelines and expected milestones are advantageous for scrutinising and appraisal of the policy implementation and progress over time. (Kakkar, Sharma, and Vong, 2017; World Health Organisation, 2010).

Evidence shows that antimicrobial selection pressure and transmission of resistant pathogens are the main drivers of AMR but drivers at the level of policies also contribute (Chereau *et al.*, 2017; World Health Organisation, 2016). As one of the biggest threats to global health in the twenty first century, systematic approaches to better understand and manage complex problems such as AMR requires the bridging of activities carried out across human, animal, and environmental sectors (World Health Organisation, 2016).Thus, mobilising the different professionals and decision-making bodies across these disciplines through establishing robust interdisciplinary approaches which brings them together will stimulate better multisectoral participation in the surveillance of AMR (Gilson *et al.,* 2020; De Kraker, Stewardson and Harbarth, 2016).

Whilst it is fundamental for every country to implement the surveillance objective of the GAP, countries with operational surveillance are strongly encouraged to carry out systematic analysis of their surveillance system to identify challenges and needs as well as review of deliverables identified at project installation phase. This is essential for generating robust information needed for project sustainability and system renewal. According to Kakkar, Sharma, and Vong (2017), this analysis should focus on areas where active participation, political will and stakeholder engagement are crucial to success which can be used to access achievement.

Situational analysis is more or less regarded as a health check for systems which helps to make features of a situation more visible through mapping (Clarke *et al.*, 2017; Helfrich *et al.,* 2010). Though frequently conducted at the exploration phase which is prior to project installation, it is seldom conducted post-project launch for most systems (Fixsen *et al.,* 2005). Regardless of the implementation phase of a surveillance system, situational analysis serves to provide important information that can aid system restructuring, scaling-up, resource prioritisation, and sustainability as well as a glimpse into the extent of government and political machinery involvement in tackling AMR concerns (Kakkar *et al.,* 2017).

It is noteworthy that sustainability of a project is crucial for achieving overall project goal and this makes situational analysis an important exercise particularly for health intervention programs. This is fundamental in LMICs including Nigeria where projects are more likely to stall after initial implementation phase (*i.e*. third phase in the incremental scale for implementing a programme for AMR prevention and control) (Fixsen *et al.,* 2005). This is in part due to implementers being less cautious of certain external factors that can impair operational efficiency at the project design phase and to a larger part to resource allocation, budget appropriations, structural and framework issues (Monedero-Recuero *et al.,* 2021). Interestingly, through appropriate systematic assessment, these grey areas with potential to impair program success could be identified in a timely manner for actions to be taken towards building projects that are resilient to changes arising from external factors.

Given the limited resources, competing interests and political challenges faced by Nigeria, reaching the surveillance goal of AMR could be derailed if there are changes in funding volume and partner agency support (Angell *et al.,* 2022; Ubi and Ndem, 2019). With the enormous threats associated with AMR, it is important for surveillance systems to have long term survival and to function at the highest level of operational efficiency to be able to monitor trends and prevalence. Preparedness ranging from monitoring and evaluation, capacity building and assessment of the determinants of programme longevity are ways to ensure the surveillance system functions without extensive disruptions. At the same time ensuring that governance framework is followed in the implementation of these objectives is vital to achieving overall NAP goals (Chua *et al.*, 2021).

Despite general agreement that tackling AMR could easily be achieved through utilising the governance framework to guide successful implementation, it is not clear how this framework (which offer guidance for both the development and assessment of national action plans on AMR) has been followed in various projects undertaken to implement NAP in Nigeria. This

study will therefore analyse the implementation of NAP using the AMR governance framework by Chua *et al.* (2021) to provide guidance. This framework will assess five governance areas involved in AMR surveillance implementation which includes: policy design, implementation tools, monitoring and evaluation, sustainability and One Health engagement. Specifically, the framework was used to help the assessment and understanding of several contextual factors which provided insights into: (i) how the surveillance objective of NAP is being implemented; (ii) if the programme is on track and whether it needs to be adjusted and how; (iii) if intervention have had an impact, but also whether intervention is efficient, effective and sustainable; (iv) data and information sharing and (v) need for improvement.

5.2.1 Conceptual framework of analysis

The Chua *et al.* (2021) governance framework was used as the basis to conceptualise this situational analysis of NAP-AMR implementation in Nigeria. The framework offers a systematic approach to governance of NAPs and thus provides guidance for development and assessment of AMR national action plans. This framework was conceptualised as a cyclical process to consider the dynamic nature of AMR and allows for continuous improvement and adaptation. It consists of five governance areas which include: policy design, implementation tools, monitoring and evaluation, sustainability and one health engagement. Policy design is concerned with procedural issues like coordination across sectors and levels, broad participation of relevant persons in the NAP development process, transparency, equity, and accountability. The implementation tools focus on strategic interventions for combating AMR which includes: AMR surveillance, antimicrobial stewardship, medicine regulation, infection prevention and control (IPC) measures, public awareness and education of relevant professionals. Monitoring and evaluation refers to the mechanism for reporting and feed-back which allows for regular review and evaluation of the NAP performance and effectiveness. This domain also assesses whether relevant policies and incentives are on track and when

they need to be adjusted. Sustainability focuses on resource allocation and funding arrangements for NAP policy implementation. The One Health governance area highlights the importance of multisectoral involvement of human, animal and environmental health in the implementation of the NAP (Chua *et al.*, 2021). The complex nature of AMR demands a comprehensive framework for assessing a range of barriers in implementing its policies especially those demanding effective governance (Birgand *et al.*, 2018).

In addition, the WHO South-East Asia Regional Office (SEARO) instrument for situational analysis and monitoring of AMR was utilised to map the current implementation phase of each of the NAP focus areas (Kakkar *et al.*, 2017). This instrument was developed on the supposition that not all countries have the capacity to develop a comprehensive and holistic national action plan. This is in concordance with an earlier review of the NAPs of 133 countries by the WHO which shows that very few countries have a comprehensive multisectoral NAP for containment of AMR (World Health Organisation, 2015). Thus, conducting a situational analysis using the right instrument is essential for identifying NAP issues that are peculiar to a particular setting, which would guide tailoring of subsequent steps of the process. The instrument therefore identifies vulnerabilities in the system, stage of implementation of AMR NAP, and assesses progress made over time. The SEARO instrument shares some similarities with the WHO monitoring tool but there are some differences in the details of the sub-indicators and in the assessment methodology between the two tools. While the methodology for the latter is self-assessment, the former relies on stakeholders responsible for the five specific objectives which mitigates bias associated with the latter.

5.2.2 Theoretical framework

Holloway and Todre (2003), observed that the flexibility of thematic analysis can lead to inconsistency and lack of coherence when developing themes derived from studies. Thus applying and explicitly stating an epistemological position that can coherently underpin the

study's empirical claims can promote consistency and cohesion (Holloway and Todre, 2003). In line with this requirement, this study situates within the phenomenological research tradition which seeks to understand the world through directly experiencing the phenomena within it and is laid on the interpretivist epistemological foundation (Wimpenny and Gass, 2000). This is based on the assumption that reality is subjective, multiple and socially constructed and rely on questioning and observation to develop deep understanding of the phenomenon being examined (Antwi and Kasim, 2015).

The purpose of this approach is to illuminate the specifics, gain insights and identify phenomena through how they are perceived by the actors in a situation. This approach is used to uncover causal relationship, support or challenge policy and action and usually starts from a perspective free from hypothesis or preconceptions thus suspending the researchers' preconceived assumption (Antwi and Kasim, 2015). This is in line with the objective of this study which seeks to understand the perspective of stakeholders' towards the NAP implementation. Phenomenological approach to research is chosen for this study as it does not require to state hypothesis at the start of the study like grounded theory (GT) thus limiting the risk of researchers imposing their opinions on the data rather than those of the persons being researched (Wimpenny and Gass, 2000; Glaser and Strauss, 1967). Unlike grounded theory which aims to generate a theory to describe and explain a phenomena, phenomenology draws on characteristics identified during data analysis.

As phenomenology tries to examine the subjective perceptions of the person being studied, it allow themes to emerge naturally, though recent humanist researchers repudiate the likelihood of starting without preconceptions or bias, and emphasise the importance of making clear how personal perspective and interpretation have been placed on the finding (Wimpenny and Gass, 2000; Bennett and Plummer, 1984). This requires making the researcher visible in the frame of the research as a subjective actor rather than a detached impartial observer from the finding

(Stanley and Wise, 2002; Bennett and Plummer, 1984). The challenge that lies therein is to describe things as they are and accounting for the researcher's reflexivity (concerned with researcher's personal reflections of their values, interests, and insights information about self 'the human instrument') to improve trustworthiness of results and demonstrate attempts at eliminating prejudgement or presupposition (Moustakas, 1994).

5.2.3 Establishing investigator's authority

Patton (1990) recognises the position of the researcher as central to data collection and analysis process in qualitative studies. Likewise, the importance of the researcher's credibility and skill is paramount since they double as research instrument and not just passive within the research frame (Stanley and Wise, 2002; Bennett and Plummer, 1984).

The investigator is a PhD student who has received training in qualitative research methods and approach. Prior to this study, the investigator had trained as an optometrist and has undertaken research as part of a team and thus has acquired interview skills from previous experience. The investigator has no personal relationship with the participants but relationship was established in the course of the preliminary steps prior to commencement of interview to foster knowledge of participant and to help the investigator decipher their suitability for inclusion in the study. A research peer was also involved who is also a PhD researcher within the faculty with qualitative training and skill set in conducting qualitative research.

All interviews were conducted by the investigator (Obiageli) and a reflexive journal was maintained as a means of demonstrating credibility and trustworthiness throughout and to ensure that the researcher's subjectivity or bias is eliminated in the study. All aspects including evolving perceptions, methodological decision points, and personal introspections about the research process, adapting and revising the interview guides were carefully noted during and after each session.

5.3 Materials and methods

5.3.1 Study design and rationale

Situational analysis often used interchangeably with formative or explorative study is a research methodology that uses the situation broadly conceived as the unit of analysis (Tejeda, 2007). It combines several approaches so as to triangulate different sources of information and perspectives to identify, examine and answer the question, where are we now? (Tejeda, 2007). It earned its name as an avenue for critical qualitative research tools used to examine a broad range of complex conditions through creating new imaginaries for future qualitative inquiry (Pérez and Cannella, 2013). Situation analysis can be used as part of continually emergent research designs, implementation, and reconceptualisation of practice which are some of the underpinnings of this research (Martin, Pauly, and MacDonald, 2016).

This study design was considered appropriate for this research which seeks to explore views of stakeholders as it allows collection of data that explains the causal processes and linkages between outcomes and context in the situation under assessment. Due to the complexity of the research objectives and the need to accurately draw tangible interpretations of current state of NAP implementation, a qualitative approach to situational analysis was adopted. This type of study design is particularly advantageous for gathering rich data on the contextual influences of public health interventions which are embedded in systems performance (Howe, 2016). It is also beneficial for the study of public health implementation research where the context of implementation has a strong influence on the outcomes of policies and programs (Helfrich *et al*., 2010).

This study analysed the implementation of AMR surveillance and related activities of the NAP in Nigeria using the governance framework as a guide (Chua *et al.,* 2021). Qualitative in-depth interviews were conducted using a semi-structured interview guide and open-ended questions that enabled depth and flexibility in exploring opinions, experiences, and influences of

respondents on the NAP. The interview guide was specifically developed to capture data from stakeholders on what is working well in the system, where there are gaps and how the system can be improved and efficiency increased.

This study was complimented with literature to illuminate richness of data. King (2004) argued that if researchers merely report the codes and themes that appeared in transcripts, the study findings will only provide a flat descriptive account. Accordingly, Aronson (1994) suggests that when literature interweaves with research findings, the story constructed stands with merit. In order to build a valid argument for choosing the themes and to articulate what each theme means as well as the assumption that underpin it, references were made to literature which also helped to theorise the significance of the themes and their broader meanings and implications (Braun and Clarke, 2006).

Data reporting for this study followed the Consolidated criteria for Reporting Qualitative research (COREQ). The COREQ is a 32-item checklist developed to help researchers to explicitly and comprehensively report important aspects of a qualitative research which is broadly grouped into three domains: research team; study design; and data analysis and reporting (Tong, Sainsbury and Craig, 2007).

5.3.2 Study Settings

This was a nationwide study and as such, participants where purposively sampled to reflect all the regions and represent various level of stakeholders. Abuja was selected as the setting for recruiting national level respondents. This is because of the centrality of Abuja as the Federal Capital Territory of Nigeria and the seat of power which houses the federal ministries and parastatals including government agencies and departments. The Nigeria Centre for Disease Control, and the headquarters of the ministries of health, agriculture and environment are all domiciled in Abuja. The stakeholders working within the AMR space, donor agencies and implementing partners operate from this location. Sub-national-level participants were

recruited from the six geopolitical zones of Nigeria which includes: South-South, South-East, South-West, North-East, North-South, and North-Central. The inclusion of both national and sub-national participants was to get the perspective of implementation from both state and council actors. This is specifically important due to urban and rural diversities, and the tiered system of governance in Nigeria which are determinants in public health, so in order to have a balanced opinion, representatives from the various zones and settings were included.

5.3.3 Selection and Recruitment of Study Participants

The NAP contains a list of contributors including policy makers, implementers and potential consumers that were involved in the NAP development. Interviewees were purposefully selected from this list and were also identified using snowball sampling (*i.e*. participant referrals of other participants).

The national level participants were selected based on their roles in the development and supervision of the implementation of the NAP as well as their knowledge and expertise in AMR and across the One Health spectrum. These included stakeholders from top government levels in the ministries responsible for human health, animals, food and agriculture. Other national key informants were drawn from members of the Antimicrobial Resistance Technical Working Group (AMR-TWG), Nigeria Centre for Disease Control, national laboratory network, donor agencies, regulatory bodies, professional societies and political office holders.

For the sub-national participants, key informants were selected from the following group of actors: Health commissioners, Directors in the state ministries of health, agriculture and environment, primary healthcare, and regulatory bodies. Key informants from these levels were identified through mapping and directory of office holders from the various ministries' websites. Selecting participants who were able to provide rich and in-depth information about the research questions was critical for this study and efforts were made to ensure this through series of review and reassessment of participants' designation, roles, and responsibilities. The

organisations that participated in the interviews and the number of respondent from each organisation is shown in table 5.1. Two pilot interviews were conducted to test the interview guide and unclear questions were modified according to the feedback received.

5.3.4 Sample size statement

According to Seidman (2006) and Errasti-Ibarrondo *et al*. (2018) sufficiency and saturation are the two criteria for deciding the number of participants for qualitative studies involving interviews. While sufficiency refers to the amount and range of participants needed to reflect the population, saturation refers to the point where data collection no longer reveals new information. Boyd (2001) and Draganova (2015) suggest that saturation can often be reached after interviewing two to ten participants. But in terms of sufficiency, this number is often too few to meet sufficiency standard depending on the context of discourse, hence the need to aim for a numerical and contextual balance. Since this study aims to cover issues around the implementation of AMR surveillance, identifying key stakeholders and potential participants from variety of working areas is key to gaining multiple perspectives on the topic as well as achieving sufficiency and saturation. These two elements were considered in the selection of participants for this study in order to strike technical balance for a robust and better information quality.

The initial target was to recruit five or more members from each participants' category and interview a target sample size of 40 or more until saturation is reached. However, saturation was reached at the 34th participant on the overall. At the national level, saturation was reached at the 10th participant but this was staggered at the sub-national level. In South-West, saturation was reached at the 6th participant, whereas in South-East, South-South, North-Central, North-South and North-East, saturation was reached at the 5th, 4th, 4th, 3rd, and 2nd participant respectively.

Table 5.1: Category of key informants involved in the interviews with the number of participants from each organisation

Participants' category	National level participants	Zonal level participants
Ministry of Health, National Primary Healthcare Development Agency	2	4
Ministry of Environment	1	2
Ministry of Agriculture and Rural Development	1	2
Policy and regulatory bodies (Nigerian Centre for Disease Control; National Agency for Food and Drug Administration and Control; National Environmental Standards and Regulatory Enforcement Agency	2	5
Implementing partners (Fleming Fund)	1	-
Professional bodies (Pharmaceutical Council of Nigeria; Laboratory Science Council; Medical and Dental council; Veterinary Council of Nigeria	2	6
Medical directors in-charge of health facilities	-	2
Federal and state legislators in health committee, health commissioners	1	3
Total	10	24

5.3.5 Data Collection and Management

A total of 34 in-depth interviews were conducted involving participants from national, sub-national, zonal, state and council levels. The interviews were conducted by the researcher between September 2021 and February 2022 (two via Skype and thirty-two via Zoom) and each interview lasted up to an average time of 45 minutes. The interviews followed strict compliance to ethical guidelines for the conduct of interviews including obtaining verbal consent before the interview. Prior to the interview schedule, all participants received an information sheet with background information of intended study and data protection statement and they had a chance to ask for clarity on any issues before the interview. To ensure consistency and stability of the research instrument as well as for quality control, the interviewer followed a semi-structured interview guide which covered issues around NAP implementation. Although the topics were common across interviews, the order and emphasis on different themes and sub-themes varied to focus on the issues most relevant for each participant. All interviews were conducted in English and recorded using the recording option available within the Skype and Zoom meeting interphase. Audio recordings were converted to MP4 and stored on the University of the West of England OneDrive secure database with

access restricted to researcher and supervisory team members only. Interviews were transcribed verbatim and the transcripts were stored in a secure password protected document. The findings were anonymised to protect the identity of participants using codes 'Rn' to represent the respondents. Where R stands for respondent and n numbers ranged from 1 to 34.

5.3.6 Data Analysis

The method of analysis chosen for this study was a combined approach of qualitative methods of thematic analysis which incorporated both data-driven inductive and theory-driven deductive codes (Boyatzis, 1988; Crabtree and Miller, 1999). The conceptual framework was initially utilised to deductively develop the main themes, some of which matched an interview question. Subthemes were formed inductively from the experiences and views of respondents without trying to fit them into pre-existing coding frame. This hybrid approach of thematic analysis has been demonstrated by Fereday and Muir-Cochrane (2006) to allow the tenets of social phenomenology to be integral to the process of deductive thematic analysis while allowing themes to emerge directly from data using inductive coding. Through this approach, the researcher was able to leverage on the advantages of deductively derived themes which provides more detailed analysis of some aspects of data, as well as inductive themes which are strongly linked to the data themselves (Boyatzis, 1988; Crabtree and Miller, 1999). Furthermore, two levels of interpretative inquiry was used to describe and interpret observed social action in the course of the interviews (Pontoretto, 2006): level one reported participants views or experience of NAP implementation from a subjective/objective perspective; level two was to understand the meaning of the participants' views/experience based on their involvement in the NAP development. This involves reporting the emotion, social relationship, actions, feelings and context necessary for understanding and interpreting the significance of event and observation (Pontoretto, 2006). To highlight this even better, both shorter quotes and longer block quotes were included in the reports, and all quotes were accompanied by

anonymised respondent number to demonstrate that various participants were represented across the results.

Data management and analysis was completed using the NVivo 12 qualitative data analysis software (QSR International Pty Ltd. Version 12, 2018). A line-by-line analysis was conducted using the software after the transcripts were read and re-read and emerging themes identified and validated to ensure consistency of information. Analysis followed the six phase thematic analysis approach which is a method for identifying, analysing and reporting patterns (themes) within data and is frequently used to summarise key features in people's views, opinions, knowledge, experiences or value (Braun and Clarke, 2006).

Steps of data analysis

Through a six-step process of: Data familiarisation, coding, constructing themes, reviewing themes, defining themes and analysis, data was sorted and emerging themes were categorised (Braun and Clarke, 2006).

- Data familiarisation: After each interview, audio recordings were transcribed into text and potential identifiable participant information replaced with pseudonyms. The transcripts were read and re-read to fully familiarise and embed with the content of the interaction.
- Coding: Having engaged and familiarised with the data in an active way, ideas and possible patterns that may form the basis of themes across the data set were brought into focus. During coding, important sections of the text that appear to correlate with the study objectives and provided indication of the context of the conversation were identified as preliminary codes. Individual extracts of data were coded in as many different themes as they fit and these were constantly reviewed to examine how thoughts and ideas were emerging.

- Constructing themes: In this phase, all initially coded data from the previous phase were collated and sorted. Potentially relevant codes that appear to have significant to the main themes that were deducted from the conceptual framework of the study were extracted. Codes that do not fit into the main themes were represented as subthemes. A miscellaneous theme was created to temporarily house codes that do not seem to belong anywhere. Data within themes were deeply reviewed in relation to the coded extracts for coherence and meaningfulness.
- Reviewing themes: Coded extracts for each theme was reviewed to ensure coherent pattern was apparent. During this process, themes that did not have clear distinctiveness between each other were combined and refined whilst themes that do not reflect meaning in the data set as a whole were discarded. This was done in two phases and the thematic map generated from this step is available in figure 5.1.

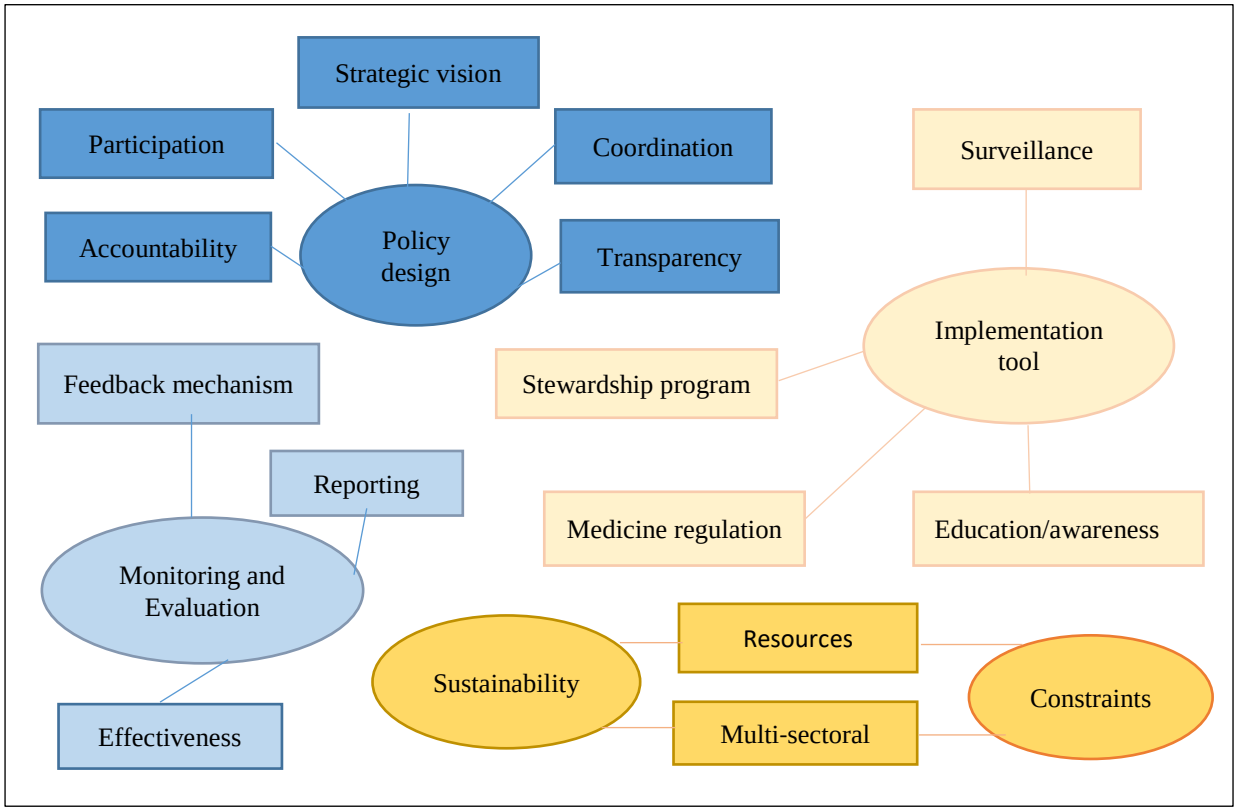


Figure 5.1: Overview of the main themes (ovals) and subthemes (rectangles) that emerged from the study.

- Defining and naming themes: The aspects of data each theme captures is identified with a detailed analysis of the story each theme tells in relation to how they fit into the overall research question. During this phase, the themes were reviewed for succinctness and reorganised in a way that best reflected the data. Main themes were used as headings to organise the study report.
- Report: Summarised thematic information from all participants were included in the report and the most illustrative quotes from the interviews were used to highlight critical points.

5.3.7 Ethical Approval

In order to meet the ethical standard requirements for the conduct of research projects at the University of the West of England, ethical approval was sought for this study from the Faculty Research Ethics Committees (FRECs). The ethics review process involved presentation of all documents prepared for the study including interview guide, participants' information sheet, consent statement, privacy notice, data protection statement and formal letter of invite. Detailed explanation of participant recruitment process to ensure it is transparent and devoid of coercion; thorough description of methodological approach including data analysis plan; clarity on whether personal identifiable information will be collected and how these will be preserved; and how verbal consent will be collected and recorded. Final ethical approval was granted on 2nd October, 2020 with the reference number UWE REC REF No: HAS.20.05.180. A copy of ethical approval obtained for this study is provided in appendix A1.

5.4 Findings

Themes were broadly classified under four governance areas namely: policy design, implementation tools, monitoring and evaluation, and sustainability. In the following sections,

the main themes identified are presented. An overview of the themes and sub-themes that emerged from this study are presented in figure 5.1.

5.4.1 Policy Design

Policy design is generally concerned with procedural issues of NAPs, such as wide participation of key persons in NAP development and coordination across multiple sectors at national and sub-national levels (Chua *et al.,* 2021). Five sub-themes emerged from exploring the policy design theme which focused on: strategic vision, coordination, participation, accountability and transparency.

5.4.1.1 Strategic vision

Strategic vision is the centrality of the goals and ideas of NAPs (Chua *et al.,* 2021). It implies that the objectives outlined in the action plan are informed by country specific situation regarding the extent of AMR and its drivers and contains clearly defined goals and objectives to direct interventions (Anderson *et al.,* 2019). The objectives should be measurable and timed to facilitate the measurement and implementation of quantitative targets (Anderson *et al*., 2019). An assessment of the Nigeria NAP shows it has clearly defined goals which were informed by the situation of AMR in the country (Nigeria Centre for Disease Control, 2017). The strategic plan identified 5 focal areas, 21 objectives and 46 strategic interventions for each objective with quantifiable indicators (NAP, 2017).

- Focus 1: Increasing awareness and knowledge of AMR and related topics has two objectives (Increase awareness of AMR among Nigerians by 2022 and improve knowledge of AMR and related topics) (NAP, 2017).
- Focus 2: Building a One Health AMR surveillance system has five objectives (Set up a national surveillance for AMR, strengthen institutional capacities for early detection and trends monitoring of AMR, build laboratory capacity to produce high-quality

microbiological data, contribute to global surveillance and implement a research agenda for AMR burden assessment) (NAP, 2017).

- Focus 3: Intensifying infection prevention and control (IPC) in the tripartite sectors has seven objectives (Strengthen IPC at all health care facilities, promote IPC in animal health, promote food safety, improve IPC practices at the community level, improve environmental sanitation and hygiene, improve hygienic practices at the community level, increase the use of vaccines to prevent new infections in humans and animals) (NAP, 2017).
- Focus 4: Promoting rational access to antimicrobials and antimicrobial stewardship has three objectives (improve access to quality antimicrobial agents, promote antimicrobial stewardship in human and animals, and strengthen regulatory agencies across all sectors) (NAP, 2017).
- Focus 5: Investing in AMR research and development has four objectives (Map current funding and promote use of innovative investment channels for AMR research, incorporate AMR research at advanced education institutions, encourage research and development of expertise on antibiotic alternatives, and invest in advanced diagnostic and pharmaceutical techniques for AMR research and development) (NAP, 2017).

Finally, an operational plan detailing step by step protocol of activities for actualising the NAP core objectives is also available. For each of the strategic interventions, details of sub-activities, responsible units, quantity, timeline, location, responsible entity, source of funding and indicators were succinctly provided in the NAP (Nigeria Centre for Disease Control, 2017).

This study is centred on surveillance implementation (focus 2) of the NAP. However, due to the overlapping influence of knowledge (focus 1) and antimicrobial stewardship (focus 4) on AMR, they were also covered in the interviews and analysis.

5.4.1.2 Coordination

The Nigeria Centre for Disease Control (NCDC) is the National Coordinating Centre (NCC) for AMR surveillance (Nigeria Centre for Disease Control, 2017). This nomination came into effect after an approval by the Health Minister for establishment of AMR control coordinating body at the NCDC in collaboration with the Federal Ministry of Agriculture and Rural Development (FMARD) and the Federal Ministry of Environment (MoE). The purpose of the tripartite structure is to provide One Health approach for AMR response (Nigeria Centre for Disease Control, 2017). AMR Technical Working Group (TWG) and AMR National Steering Committee (NSC) drawn from the three ministries (FMARD, MoH, MoE) were also instituted to oversee AMR related activities within all sectors to ensure a systematic and comprehensive approach at all levels of surveillance (Nigeria Centre for Disease Control, 2017). These governance structures are responsible for leading and facilitating the coordination, planning, implementation, monitoring progress of AMR activities, and to make recommendations.

5.4.1.3 Participation

This is concerned with the constitution of responsible members towards preparation of the NAP (Chua *et al.,* 2021). A review of the national action plan document indicates that key stakeholders participated in the development of the NAP. The NAP contributors were drawn from different ministries (MoH, MoE, FMARD); agencies (National Environmental Standards and Regulatory Enforcement Agency, National Agency for Food and Drug Administration and Control, National Primary Healthcare Development Agency); international organisations (Global Antibiotics Resistance Partnership, World Health Organisation); professional bodies (Pharmacists Council of Nigeria, laboratory science council, Medical and Dental Council of Nigeria, Association of Community Pharmacists of Nigeria, Pharmaceutical Manufacturers Group, Veterinary Council of Nigeria); universities and research institutes (NAP, 2017).

Although the NAP highlighted multi-sectoral participation, the interviewees had varying opinions on the involvement and roles of different sectors in the development of the AMR NAP. While some respondents agreed that the key sectors concerned with AMR were equally involved in the NAP development and stating that their roles in the action plan could easily be identified, others were of the opinion that although all necessary sectors had influence on the preparation of the action plan, their contributions were at varying levels:

> *"I was aware of the call for cross ministerial participation during the policy design of NAP. I can say this because my association played their part in that process though not as central as the ministries directly involved but each sector played their individual roles according to the task assigned to them."* (R2)

Another respondent expressed concerns that the MoH had more influence on the NAP preparation than the rest of the ministries impacted by AMR. They stressed that the environmental sector which is responsible for managing AMR drivers from the environment was not strategic in the NAP development despite substantial mention within the NAP.

> *"AMR affects every body and I don't think that any sector is more important than the other as all sectors need to be actively involved. It is understandable why the Ministry of health had more influence because human health sector has often been at the forefront of AMR talks but the environment, livestock and fisheries are equally as important. Personally, I don't think other sectors had adequate contribution in the NAP development."* (R4)

A number of interviewees stated that the community members were not involved in NAP development and stressed they should have been involved as consumers of antimicrobials. Majority did not see any need for involving them at the development stage of the NAP. Though community engagement is indicated as one of the strategic interventions of the NAP, the focus is dissemination of information and awareness creation:

> *"I think some members of the society that have huge influence on the people should have been involved in the process. In Nigeria these influencers have a way of*

communicating to their followers in the language they understand, this is one arm that could have played a good role in promoting AMR related activities though not in technical context but promoting knowledge which ultimately builds caution in use of antibiotics." (R5)

5.4.1.4 Accountability

This is concerned with internal organisation of monitoring and feedback mechanisms (Chua *et al.,* 2021). In terms of NAP implementation, it is crucial that whichever entity is responsible for coordination and implementation should also be accountable to a higher government body and there should be responsible persons nominated in each sector to further improve accountability (Anderson *et al.,* 2019). To ensure accountability within the Nigeria NAP implementation, a clear governance structure was established under the supervision of National Coordination Centre (NCC) at NCDC. The structure is responsible for monitoring all AMR activities. It also provides platform for sharing knowledge, information and experience across sectors. Though all respondents were in general agreement to the existence of a governance structure to ensure smooth running of the NAP, some raised concerns about the inactivity of responsible persons and lack of publicly available progress information:

"There is monitoring and evaluation arm but based on where we are with implementation, there isn't much to monitor and feedback". (R19)

"I have said this to many people who are interested in understanding what is going on in Nigeria, a lot of things are happening but they are not published so it is very difficult to see them if you are not already inside the system". (R6)

"One of the things that the national AMR program has not done well is that some of its recent activity is not yet published. It is not published because it is all at initiation stage, no but because we've set up a surveillance system when you hope that surveillance system will have over 400 hospitals and it just has 11, so it is not yet at the stage where you want to tell the story but it is not also at the stage where I will say nothing is happening." (R8)

5.4.1.5 Transparency

This ensures that the plan itself, progress reports, and funding allocations are published with open access to the public. This information must be presented in an understandable format to promote public engagement, which can encourage greater political awareness and civil society involvement in AMR policy implementation. To ensure transparency, the NAP is available online with designated sources of funding to include: Federal Ministry of Health (FMoH), Federal Ministry of Agriculture and Rural Development (FMARD), Federal Ministry of Environment (FMEnv), State Ministry of Health (SMoH), State Ministry of Agriculture and Rural Development (SMARD), State Ministry of Environment (SMoEnv), donor agencies and development partners. There is a plan to create a database for storing and sharing funding information to make the process more transparent but this is yet to be established and some respondents expressed concerns about that:

> *"People can only trust a process when it is transparent and open in all its mission. It is true that direct government budget is not in place yet but current donors and prospective donors want to see clarity of achievements made with some funding that we have received. Doing this will project us as a transparent system and attract more funders."* (R10)

> *"One of the reports that came out around when we were about to set up our surveillance system was that Nigeria is not the best place for AMR surveillance and it was because there wasn't anything documented. So if we want people to be more involved, we have to create a database where information are readily available and this database must be updated regularly. That is one way to show accountability and transparency and attract donors since our surveillance system still has no budget".* (R13)

5.4.2 Implementation tool

The NAP outlines six strategic interventions, which are being referred to as tools for implementing AMR containment activities. Some of these includes: surveillance, antimicrobial

stewardship programs, education/public awareness activities, and medicine regulation. The following section will analyse the situation of each of these interventions;

5.4.2.1 Surveillance

Surveillance is fundamental for the planning, conducting, and evaluation of all other AMR policies (Dar *et al.*, 2016). The Nigeria NAP contains an operational schedule which provides guidelines on how each strategic intervention will be actualised based on national needs and priorities. Included in the action plan is a framework of how AMR surveillance would be conducted across humans, terrestrial and aquatic animals, food and environment using a One-Health approach. A standardised protocol for the surveillance system has been developed with ten sentinels performing surveillance in human and eight sentinel sites for AMR surveillance in animals. When the respondents were asked why AMR surveillance is yet to reach national coverage, their opinions suggest that although the expected long-term goals have not been met, some progress has been recorded. They also stressed some challenges encountered in implementing the action plan so far:

> *"I think we have made good progress, we essentially started the surveillance system from nothing, while we don't yet have representative coverage, we have been able to establish it and we have been able to expand the number of sentinel sites overtime and we are collecting data. Though looking from where we are now with the action plan, the progress we have made so far and the future threat from AMR, I don't think we are well positioned to tackle the tasks ahead".* (R18)

> *"When we wrote our action plan in 2017, we knew that by 2022 we will not have an adequate surveillance system. Our intention which we have largely succeeded was to set up a new surveillance system from scratch and we fully recognised that it will take a long time to grow it. So the surveillance system have been built and grown faster than we anticipated then but if the question is whether it is adequate the answer is NO and we always knew that is the case because it takes a while to build and grow things".* (R14)

When the respondents were asked what is required to enhance, or strengthen the surveillance system and why laboratories with core capabilities for AMR surveillance are not being utilised:

> *"At the time the NAP was written with a plan to set up a surveillance system, there was no budget for implementing or setting up a surveillance system. So what NCDC did as the NCC was to invite tertiary care labs to apply to be potential sentinel labs knowing these labs will have to make investments. When they sent out this invitation, only a very small handful applied and they were assessed by NCDC and a couple of experts including myself and after the assessment, only a fraction of those that volunteered were found to have the resources necessary to be part of a surveillance system. So in my opinion, budget, budget, budget".* (R22)

> *"NCDC started with the core group of labs with potentials for capacity which happens to be the tertiary labs. Now even the tertiary labs were missing one thing which was essential for any lab participating in surveillance which is to be enrolled in regular External Quality Assurance (EQA) and so NCDC got these labs EQA and they were signed up as the initial sentinels. To recruit more labs, these labs must be enrolled on EQA and the constraint here is lack of sufficient resource to extend to other level of labs".* (R20)

> *"The surveillance is not currently representative with only tertiary labs involved. Even with the tertiary labs, the first batch of volunteers were almost entirely from the South-West of the country and NCDC was concerned that it will take us too long to get to national representation if the whole lab is coming from the South. I agree there could be labs with surveillance capacity out there which the NCC could reach out to but resources will be required. Interestingly, Nigeria has become a Fleming fund country and the Fleming fund equipped the National Reference Laboratory (NRL) and sentinel labs to be able to perform surveillance. So essentially, more resource is needed and the NCDC will need to invite more labs, which is one good way to grow the surveillance system". (R19)*

> *"The surveillance system requires strengthening. It is not set now but it continuous to grow. The only thing is it grows largely by volunteers so a lab will have to step forward and say I will like to be part of the surveillance system, and currently that lab has to be a tertiary government lab. NCDC has plans of bringing in general hospitals, and private*

labs but that has not yet been rolled out. I think the NCC need to develop a system to identify and partner with labs with surveillance capabilities rather than wait for labs to step forward to volunteer". (R27)

"One thing worthy of mention is that the NCDC which is the national coordinating centre is a new agency. So if 400 labs apply to be sentinel labs, NCDC does not have the capacity to on-board all of them right now. I think NCDC is being strategic by asking labs to volunteer and starting with tertiary labs as it is essential that these labs are doing surveillance to a certain level of quality and the data are quality assured and vetted by the reference lab. The capacity of the national reference laboratory is quite limited and so that lab will also need not to be overwhelmed. So I completely agree with you that there are many labs that could be surveillance labs, but it will be a bad strategy to say look we need one thousand labs, when actually we do need, spend a lot of resources on that awareness knowing fully well that the national reference laboratory is not yet in a place where it could take up over 1000 labs. Ultimately it will be and the plan is obviously to reach out to labs that are well equipped to do surveillance and make them part of the surveillance system but the capacity to do that does not exist at this time". (R25)

When asked about community surveillance and whether that approach is being contemplated in Nigeria considering that misuse/overuse of antimicrobials is likely to occur more in rural settings, below is the response from some participants:

"I think one of the downsides to surveillance worldwide particularly in LMICs is that most of the surveillance data that we get are from tertiary care centres and these are referral centres, so what this means is that before a patient will end up in that kind of situation/institution chances are they have an infection that cannot be treated. So when we base our surveillance on tertiary care centres, we may actually be over estimating the amount of resistance that we have because somebody at a rural area is most likely to receive antibiotics without testing. If they get better, the surveillance system does not see them, it is only when they do not get better that the surveillance system sees them, so doing surveillance at community level will actually provide a more realistic picture of what resistance actually is. However, one of the constraints we have is the challenge of getting quality assured microbiology done in that kind of setting. So what we have to

do is to develop new methods that will allow us do surveillance at sentinels that are community based, another thing is tertiary care bias which has to be dealt with". (R32)

"Apart from misuse of antimicrobials in rural settings, community-based surveillance will help shift AMR surveillance from isolate based to patient based. To do this we have to develop a framework that will allow us base surveillance on people rather than on bacteria, like what proportion of people are been affected by the bacteria that are being tested in the labs. I think all of those are lovely ideas, I know many people, and ourselves included are piloting different ways of doing these sort of things with the hope that surveillance in the future will be more robust than it is right now". (R29)

When asked what gaps they have observed in the current surveillance arrangements and what in their view needs to be done to fill those gaps going forward to enhance surveillance generally:

"A lot! many, a lot! many, a lot! many, a lot! many. First of all the surveillance system is not representative, while the aim is to be representative it is going to take a long time for that to happen because the surveillance system still has no budget. It is only when you have a national budget for a surveillance system then you simply look at which areas are underrepresented and then you go there and do more work but essentially most of the activity is dependent on volunteer activity so that will make it very difficult for it to be representative". (R21)

"There is one important aspect of AMR surveillance that is not receiving attention and that is early warning system. With such system, routine microbiological results can be better utilised and analysed to give spatial view of local areas with rising concerns of resistant infection. The data from this system may not be of standard quality but they provide important microbiological indicators". (34)

"I observed within our existing surveillance sentinels that what is being surveyed is very very little. If you've read the GLASS guidelines, it recommends that when funds are limited, you start with blood borne bacteria, so we are looking at isolates of blood cultures from just 9 or 11 sentinels meanwhile a lot is going on in urine, stool and others that will be nice to survey but with no budget and very few people involved in coordinating it we have to start small so the current surveillance is giving us very limited information in that regard". (R29)

"The big issue is our surveillance system is entirely focused on tertiary care systems. Whilst this is not unusual, in fact in most countries that is the case but I think particularly in Nigeria, the problem is that the vast majority of people have no access to tertiary care system and the fact that we don't have surveillance in all the tertiary care system is such a huge gap". (R1)

"You need both internal and external quality assurance if you are going to collect high quality surveillance data, a lot of labs in the country are not yet aware of these quality requirements. Currently as far as I know, the only accredited bacteriology labs in Nigeria are private, even the non-accredited ones that we are using for surveillance are yet to start to take a step-wise progress towards accreditation and building those quality metrics and I think that is a big gap" (R28)

5.3.2.2 Antimicrobial Stewardship Programs

This is important as it is concerned with responsible use of antimicrobials across all sectors, and more specifically, selection of the most appropriate antimicrobials, course of treatment, dose and route of administration (Agunos *et al.*, 2021). Most importantly, for the enhancement of AMR surveillance, it is advisable for surveillance systems to integrate antimicrobial use (AMU) surveillance alongside AMR surveillance for a more comprehensive output (World Health Organisation, 2017; Haworth-Brockman *et al,* 2021). When respondents were asked about the status of stewardship programs and AMU/AMR integrated surveillance in the country:

"This is not happening on any huge or sufficient scale, but as I mentioned, the NAP has five pillars, one of these pillars is stewardship and the stewardship pillar in Nigeria is actually quite active". (R33)

"We have a unique problem in Nigeria in connection to antibiotics usage. We are trying to figure out firstly how to implement stewardship at all tertiary care hospitals as well as to address the issues of 'how do you actually do antimicrobial use surveillance in a country where antimicrobials are freely available'. So one of the issues is how to document use in Nigeria were the vast majority of people swallowing antimicrobials do not have a prescription and they are not also buying from official supply chain. Whereas

in countries like the UK you can do use surveillance with documenting prescriptions that are picked, so we need ingenious ways to be able to get a sense of how antimicrobial use should be measured". (R29)

"I know there is a whole group in the stewardship pillar looking at this but I can tell you for sure that we are not measuring antimicrobial use in parallel with AMR. This is because we have two problems that require new surveillance systems to be built from foundation. So to your question on AMR/AMU surveillance yes, that's the gold standard and that's what we are working on". (R30)

"Stewardship is happening at tertiary level. Even-though this might be perceived as minimal progress, considering where we are coming from, I think this is commendable. Much efforts should be put towards controlling the growth of unregistered drug sellers as that will help limit access to antibiotics misuse and self-medication". (R34)

"Stewardship is very important and the Federal Ministry of Health has developed and disseminated antimicrobial stewardship working guidelines for hospitals and discussions are ongoing for animal treatment guidelines which will be available at facility levels". (R2)

5.4.2.3 Education/public awareness

Very critical to AMR containment is slowing down antimicrobial misuse which is a major driver because vast majority of people do not understand the dangers of overuse or unnecessary use of antimicrobial agents. For this reason, education is regarded as a very strong and impactful objective to AMR containment (Ogoina *et al.*, 2021). It is believed that if more people have the right knowledge of AMR and begin to apply rational use of antimicrobial agents, ultimately selective pressure and resistance will be reduced (Harbarth *et al.*, 2015). When the respondents were asked about AMR education and awareness activities in the country, below is what some of them had to say:

"As I mentioned before, awareness is one of the five pillars of the National Action plan and there's a lot going on in reaching out to the populace, the health workers and so on. Just to give you an indication, the WHO tries to keep tab of what happens during AMR awareness week (third week in November or so), if you look at their records you

will find that more events occur in Nigeria than any other African country and a lot of these events are happening at the grass root. Lots of these are organised by students, civil societies, health workers and NCDC does keep a record just to be sure of what is going on". (R26)

"In my own understanding, it is not necessarily the poor that misuse or overuse antibiotics, in LMICs Nigeria included, it is relatively the affluent that misuse antibiotics because they don't want to queue at the hospital and they have a means to afford the drugs. The poor people are relatively too poor to afford drugs in some cases, so awareness activities has to focus on all cadres in society including the healthcare workers. By the way because health workers in their institutions often are not using antibiotics appropriately even though they are supposed to be the gate keepers". (R15)

"In my view, I would say the awareness team is the most active of all other national action plan implementing arms. Awareness is happening at a very massive scale yearly and I believe people are beginning to understand. The public needs to be aware of the harm associated with over-administering antimicrobials so they themselves can query the prescribers who want to sell drugs without proper testing because of out of pocket payment for medicare. The action plan is quite elaborate on educational strategies including adding it as part of curriculum and mandatory for certain license renewal. Some of these will require approval from the government and I believe a lot is going on behind the scenes". (R34)

"Different organisations are promoting awareness at different levels including the society I belong and I am also aware of other bodies organising sessions within their teams to educate healthcare workers. Awareness as part of the strategies should focus on other areas of awareness in AMR including the use of surveillance data. There is lot more to do to give AMR awareness a nationwide recognition including appointing important personalities as AMR champions and ambassadors which has not been implemented yet". (R17)

5.4.2.4 Medicine regulation

Well designed and effective regulations have been utilised in variety of ways to conserve the use of currently available antimicrobials (Anderson *et al.*, 2020). One of the ways is by having an Essential Drug Lists (EDLs) and Standard Treatment Guidelines (STGs) for use at all levels

of healthcare. However, presence of regulation and guidelines alone is not sufficient as with the case in Nigeria. To be more effective, there must be appropriate legislative mandate, a clear legal framework and a regulator in place to monitor and enforce compliance as well as institute strict penalties on defaulters. Nigeria has a health legislation on the use of antibiotics (Food and Drug Act, Cap 150 of 1990) which prohibits dispensing antimicrobials without prescription as well as Essential Drug Lists (EDLs) and Standard Treatment Guidelines (STGs). The interviewed policy makers reported that, although regulations are in place, they may only be partially implemented due to challenges arising from compliance and enforcement and shortage of licensed drug dispensary outlets. These are expressed in the comments below:

> *"Compliance to these regulations across boards may not be realisable in the nearest future due to lack of capacity within primary healthcare centres and a lot of other health service providers. These facilities often do not have adequate financial and human resources and therefore lack diagnostic equipment required to perform culture and antimicrobial susceptibility testing before dispensing drugs as recommended. What has happened recently is the appointment of focal persons to lead advocacy to government for enforcement of these regulations regardless of the hospital level. We believe the result of these efforts will become clearer soon".* (R11)

> *"I can tell you for sure that monitoring and supervision of drug dispensers to enforce restriction of over the counter sale of antimicrobials is seriously happening now than before. The problem is that a lot of areas are not easily assessable especially this our northern zone which makes supervision more difficult. Another problem is unregistered medicine stores that are not part of any regulatory association and so do not comply with the laws".* (R13)

> *"I think the problem with achieving nationwide regulations to prohibit over the counter sale of antibiotics is not with the registered vendors but the unregistered ones. Within our council, and with the support of the NAP regularly team, we have developed strategies to support registration of all antimicrobial sales agents and clamp down on those operating without regulation. We need the government to strengthen the capacity of regulatory agencies across one health sectors for this to be achievable".* (R20)

5.4.3 Monitoring and evaluation

Monitoring and evaluation is an important unit of governance framework in NAP implementation and a useful mechanism that generates evidence used to gauge effectiveness of policies and achievements (Chua *et al.*, 2021). It also generates information that are disseminated across stakeholders which is useful for surveillance system operation. Through a functional mechanism for monitoring and evaluation, capacity of a project is systematically improved to enable it function without extensive need to invest in continued capacity building. The M&E framework of NAP is designed to (1) report progress across the five NAP focal areas, (2) provide feedback mechanism and (3) effectiveness measures. The following section reports the status of each of these sub categories;

5.4.7.1 Reporting

This involves surveillance data generation and dissemination with international surveillance network as well as internally among stakeholders (World Health Organisation, 2015). Review of literature shows that reporting arrangements are in place as part of the Nigeria's surveillance protocol and surveillance data is currently being reported to the GLASS global database. In addition, the respondents reported that there is an established internal mechanism for sharing surveillance and progress reports at national level to inform active decision making. Furthermore, launch of One Health Weekly Epidemiology Report (WER) on AMR and the National AMR Community of Practice (AMR CoP) is also an effort to bring together and share information amongst key partners in AMR (field implementers, researchers and stakeholders) and serves as an essential instrument for the rapid and accurate information dissemination (Achi *et al.,* 2021)

5.4.3.2 Feedback Mechanisms

Like data reporting, routine data feedback at national, zonal and organisational levels is essential if surveillance must be useful for system improvement (Chua *et al.,* 2021). The

interviewees reported that efforts have been made to appoint State Technical Working Group (STWG) and focal persons who will periodically identify and articulate surveillance gaps and AMR burden estimation needs and provide feedback to the national level stakeholders. However, some respondents observed that feedback mechanism at zonal levels are suboptimal and this could be attributable to low surveillance activities at those zones.

5.4.3.3 Effectiveness

In the context of NAP, it requires that measures be put in place to enable measuring effectiveness (e.g. measure of impact on human and animal health) of specific AMR policy or interventions (Fixsen *et al.,* 2005). The effectiveness measure provide feedback on the impact of policies in reducing antimicrobial resistance rates, inappropriate use of antibiotics and antimicrobial consumption (Bennani *et al.,* 2021). The Nigerian NAP policy document recognises the importance of this process and it emphasised strongly on the need for effective M&E structure to evaluate whether activities are executed as planned and outcomes achieved as anticipated (Nigeria Centre for Disease Control, 2017). An M&E framework has been developed which shows a proposed information flow from all AMR related activities to enable systematic impact assessment of interventions. Although the interviewees agreed that M&E of sectoral activities are currently running they observed that no assessment of effectiveness of interventions or cost effectiveness have been carried out. Some respondents are of the opinion that the system needs more time and investment before it can be ready for measure of effectiveness:

> *"I would say it's rather too early for assessment of the effectiveness of the surveillance system, too early not in terms of number of years but in relation to the investment made and achievement. There is not much yet to measure. We need to roll out the interventions to a national level so we can have something to measure and compare".* (R10)

> *"We need to wait a few more years. There is a lot to implement in the action plan. Take stewardship for instance, to measure the effectiveness of stewardship in relation to*

antimicrobial usage, we have to ensure that at least 70% of healthcare and dispensary outlets follow the stewardship guidelines, it is at this point that we can have a significant measure of effectiveness and not when only a handful is implementing a policy you start measuring impact. What is important at this stage is to create an environment that will enable these assessments which are already in place". (R20)

5.4.4 Sustainability

Sustainability in terms of surveillance of AMR is a state of efficient program operation and should be the goal of any NAP for AMR (Kakkar *et al.*, 2017). It is characterised by a myriad of indicators including being resilient to changes, developed indicators for measure of effectiveness, and most importantly sufficient funding and resource allocation. Without a dedicated budget for the NAP and AMR related activities, it is likely that actors will have limited resources to implement AMR polices. The respondents expressed varying degrees of concern over lack of adequate funding for national coverage and sustainability of the surveillance system. Currently, the funding source is largely dependent on donor agencies which cannot suffice without dedicated government budgetary allocation. Despite the mention of certain federal and state ministries in the funding arrangements, the respondents decry that the major setback suffered by the action plan is lack of government funding support:

"Sustainability of the action plan depends much on the allocation of resources and provision of continuous government budget on an annual basis. Majority of the funds received for implementing the AMR surveillance so far is from development partners and there is no way we can make the desired progress if we continue like this. The government must be involved and appropriate funds for the project to survive". (R30)

"Funding is a challenge. The action plan activities are more of donor funded project than the government so what happens when the donors leave, the situation will be difficult because the project will suffer or ultimately end. There is no national budget for the surveillance system so essentially most of the activity is dependent on volunteer and donor". (R29)

"All our surveillance structures are under-resourced, the sentinel labs do not have enough resource, including the national reference laboratory and national coordinating centre. Not having enough resources to on-board hundreds of laboratories that could be part of surveillance is actually a very big gap. Interestingly, when we asked the labs to volunteer, of the labs that volunteered so far, less than a quarter have been able to be on-boarded because many labs that think they have capacity to be part of the surveillance system actually don't. So there are things that must be in place for that lab to be competent in doing surveillance, they include certain equipment and so on but also a lot of quality metrics that many of our labs are not aware of and this is also a barrier to growing the system rapidly because you have to ensure that quality is maintained". (R33)

5.5 Quality and trustworthiness of study

As a traditional research method that rely on researcher interpretations to generate data, there is a need for greater disclosure and more sophisticated approach to facilitate researchers in conducting legitimate qualitative study, and trustworthiness is one way researchers can meet this (Guba and Lincoln, 1982). To ensure high level of rigour, the four criteria (credibility, transferability, dependability, and confirmability) introduced by Guba and Lincoln (1982) were used to demonstrate trustworthiness in this study. These criteria are defined below with description of how each was implemented in the study;

5.5.1 Credibility

Credibility refers to the measure of truth between respondents' views and how the researcher represents them and thus regarded as the most important criterion for establishing confidence in the truth of a study (Guba and Lincoln, 1982). Techniques undertaken to address credibility in this study includes activities such as prolonged engagement, persistent observation, triangulation, peer debriefing and member checking.

a) Prolonged engagement

The researcher had prolonged engagement through repeated reading of the collected data in order to become immersed and familiar with the data. By actively doing so, ideas, patterns,

growing insight and developing theories from all aspects of the data were identified before coding, thus opening the researcher to multiple influences and contextual factors that impinge on the phenomena being studied (Guba and Lincoln, 1982). As data were collected through interactive means (interviews), this provided the researcher with another avenue for engaging with the data and having some prior knowledge of some initial analytic thoughts, interpretations, questions and meaningful patterns. Theoretical and reflexive thoughts that emerge from this process as well as codes/themes were documented as evidence for audit trails.

b) Persistent observation

Persistent observation is a technique that helps researchers to identify characteristics that are most relevant in the situation being pursued in order to provide depth (Guba and Lincoln, 1982). The researcher systematically worked through the entire dataset by reading and re-reading the transcripts and giving full and equal attention to each data item. The codes and emerging themes were constantly reviewed to ensure they were meaningful, had explicit boundaries and not interchangeable. This helped deepen the researchers understanding of the phenomena under study and eased data analysis.

c) Triangulation

Methodological triangulation uses three or more data points to corroborate information that converges on a single point to improve reliability (Santos *et al.,* 2020). Campbell *et al.* (2020) noted that information provided by stakeholders may be biased or inaccurate and therefore, the use of triangulation in research involving stakeholders' interview is crucial. This concept is in agreement with Dervin's theory of circling reality which highlighted the necessity of obtaining a variety of perspectives in order to get a better, more stable view of reality based on a wide spectrum of observation from a wide base of points in time-space (Dervin, 1983). In line with this order, this study demonstrated credibility by triangulating data from different categories of stakeholders distinguished by geographical locations and ministries so as to corroborate

information. Participants included national and state-level stakeholders as well as stakeholders across human health, animal and the environment. Researcher triangulation was also utilised to enhance credibility and interpretive meaning to emerging theories throughout the study. Regular meeting and briefs were held with the supervisory team about developing codes and themes and justifications for the inclusion of each code and how it will be used were clearly defined.

d) Peer debriefing

Peer debriefing provides an external check on the research process, thus increasing credibility. This technique was used to probe the researcher's subjectivity, bias and assumptions throughout the process of analysis by allowing a qualified colleague who has no personal interest in the study to review the anonymised transcripts, methodology and findings. Through debriefs, areas of methodological error, and where participants' perspectives were overlooked as well as aspects that needed more detailed descriptions were highlighted.

e) Member checking

Member checking is one of the most important technique for establishing study credibility in qualitative inquiry (Guba and Lincoln, 1982). In this process, the transcripts of the raw audio recording of the respondents' interview were emailed to them using a password protected file format assessable to the recipient only. This was done to allow the participants review and agree that their perspectives have been adequately interpreted and represented or disagree if there were any misrepresentation.

5.5.2 Transferability

Transferability refers to the extent to which the research method or findings of a particular study can have applicability in another context or setting (Thomas and Magilvy, 2011; Guba and Lincoln, 1982). To meet this criteria, the researcher must provide thick description to

enable other researchers evaluate the transferability of the study results. Steps taken to provide thick description is highlighted below;

a) Thick description

The researcher has provided adequate details of the entire research process from participant sampling, to data collection and analysis technique, the sample size, categories of stakeholders, the ministries included and geographical location of respondents. Furthermore, direct quotes from interviews have been provided to illuminate the contexts that surround these experiences (Pontoretto, 2006).

5.5.3 Dependability

Dependability of a study is enhanced when the researcher can demonstrate that the research process is clearly documented, traceable and logical. To establish dependability, Guba and Lincoln (1982) suggested the entire process to be audited to allow other researcher to follow the decision trail regarding theoretical and methodological issues. An account of the audit trail process includes sampling frame and criteria; interview notes; raw data; transcripts; interpretation of study findings; and a reflexive journal was maintained throughout the study which help the researcher, relate, and cross reference data, as well as ease the reporting of the research process (Halpern, 1983).

5.5.4 Confirmability

Confirmability is established when the results from the study are clearly derived from the data and should demonstrate how conclusions and interpretations have been reached (Tobin and Begley, 2004). As part of meeting this criteria, the researcher maintained an audit trail of detailed step of data analysis to show that the findings are not influenced by the researcher's conscious or unconscious bias. Also, the content of each theme was summarised so that others can understand how and why the conclusions were reached (Koch, 1994).

5.6 Discussion

This is the first study to assess and report the situation of implementation of Nigerian NAP for AMR using a governance framework adapted from Chua *et al.* (2021). The framework allowed a structured format of assessing three governance areas: policy design, implementation tools and monitoring and evaluation which helped to provide context-specific analysis of NAP implementation in Nigeria. This is specifically important to fill any knowledge gaps regarding NAP implementation progress five years after its development and implementation.

This study revealed that the implementation of the Nigeria NAP for AMR has realised several goals some of which are the building blocks for surveillance initiation and sustainability. Some recorded achievements include:

a) The establishment of a functional multi-sectoral coordinating committee for coordinating, facilitating and monitoring the implementation of AMR activities;
b) Establishment of National Reference Laboratory and surveillance sites for humans and animals;
c) GLASS enrolment and surveillance data reporting;
d) Availability of guidelines at the health facility level to ensure AMR stewardship;
e) Establishment of National Steering Committee and National Coordinating Centre;
f) Set up of Technical working Groups (TWG) at national and state levels;
g) Existence of governance structure;
h) Creation of AMR awareness programs; and
i) Establishment of antimicrobial stewardship programs.

Table 5.2 shows mapping of the implementation phases of some of the Nigerian NAP focus area using the SEARO instrument with justification (Kakkar *et al.,* 2017). This mapping follows the indicators and grading highlighted in SEARO tool. This study further revealed that

some domains of governance such as, accountability, transparency, resource allocation for research and sustainability of AMR plans, reporting and feedback mechanisms to monitor the NAP progress, were not effectively implemented. These domains are essential for effective implementation of the NAP, hence resolving them through a systematic governance approach will support the achievements of NAP goals and objectives.

Table 5.2: Mapping of implementation phase of the Nigeria NAP focus area using the SEARO instrument. The justification for the mapped phases where based on stakeholders' responses and reviewed documents.

Focus area	Indicators	Phase	Justification
1. Increasing awareness of AMR and related topics	1.1 Awareness campaigns for the public	2	Some government-led activities in parts of the country to raise awareness about AMR and actions to address it
	1.2 Education and training strategies for professionals	2	Relevant policies developed but ad-hoc training courses in some disciplines
2. Building a 'One Health' AMR surveillance system	2.1 National human AMR surveillance	4	Standardised national AMR surveillance in place and contributing to GLASS but limited number of operating sites and not representative of country
	2.2 National laboratory network strengthening	4	A national network of health laboratories that undergo EQA developed in most/ALL surveillance sites
	2.3 Early warning system	1	No system in place or planned
3. Promoting rational access to antibiotics and antimicrobial stewardship	3.1 A national AMR containment policy for control of human use of antimicrobials (stewardship)	4	AMSP implemented by tertiary institutions and regulation for antimicrobial use and availability implemented in limited capacity
	3.2 National Regulatory Agencies (NRAs) or Drug Regulatory Agencies (DRA)	4	NRA/DRA system in place for registration of antibiotics in place but limited capacity for enforcement of policies and regulations
	3.3 Surveillance of antimicrobial use and sales in humans	3	Monitoring sales of antimicrobials at national level not implemented Monitoring of use irregular and limited to a few facilities that are not representative

Key: Phase 1 exploration and adoption; phase 2, programme installation; phase 3, initial implementation; phase 4, full operation; phase 5, sustainable operation.

The Nigeria's NAP for AMR 2017–2022 is robust and has a strategic vision to provide long-term direction. This implies that the NAP contains clearly defined goals, objectives and operational plan to direct and guide interventions (Nigeria Centre for Disease Control, 2017). The 5 focal areas, 21 objectives and 46 strategic interventions are in line with the WHO global

action plan on AMR and follows the governance framework for implementing a NAP for AMR (Chua *et al.*, 2021; Anderson *et al.*, 2020; World Health Organisation, 2016). However, the NCC which is responsible for coordinating, facilitating and overseeing the implementation of all AMR activities, including surveillance, is under resourced to implement some of these interventions. The NCC is largely dependent on development partners' support, which will certainly limit its ability to fully reach sustainable operations particularly for the surveillance pillar which is central to the NAP objectives and AMR containment (Tabak *et al.*, 2016).

Though funding and sustainability were the two most recurring themes emerging from the in-depth interviews, funding remains a major constraint because activities that are central to reaching the NAP goals are dependent on resource mobilisation. This has impacted the ability to expand the capacity of the NRL to on-board more laboratories for surveillance and consequently limited surveillance to tertiary facilities alone. Tertiary focused surveillance by itself has enormous implications for LMICs Nigeria inclusive (Achi *et al.,* 2021; Raouf *et al.*, 2020). This is so because in Nigeria and other LMICs, there is availability of chains of healthcare providers at various levels who attend to patients' need so tertiary care is not frequently required and accessed by majority of the population (Aloh *et al.*, 2020). Majority of the time, a patient is referred to tertiary care only when the condition is critical, not abating or requires specialist care (Pittalis, Brugha, and Gajewski, 2019). Even at this instance, some will choose private specialist care providers over the government tertiary care due to long waiting times. Consequently, having a surveillance system that is tertiary focused in a country where tertiary care is not accessed by majority of the population is already lacking in representativeness. This is in contrast to developed countries where tertiary care is more accessible to majority of the population. This is so because the healthcare services rendered by the GPs are defined and limited so in majority of times, they will refer cases to tertiary care where most treatments happen (Lenjani *et al.*, 2020). Tertiary focused surveillance must be

reviewed to include secondary and primary level care as well as private healthcare providers. Whilst it is understandable from available evidence that the surveillance system is still evolving, it is strategic to include other levels at this stage to allow holistic and comprehensive progress. Currently, AMR surveillance is ongoing at 11 sentinels and the NRL is ensuring that the results are quality assured and data is being collected and shared with GLASS.

Equally worthy of mention is the need for continuous expansion and sustainability of surveillance activities. It is not a disputable fact that achieving NAP for AMR is capital intensive and for this reason, Anderson *et al.* (2019) advised the need to have a written mandate or voluntary agreement from all relevant funders to guarantee resource availability for implementing the NAP. This is important because in the absence of appropriate structure for sustenance of the system, there are tendencies that the system might collapse, stale, or retrogress (Ivers, Dhalla, and Brown, 2018). It is noted from this study that implementation of the NAP is largely driven by donors and volunteers which further questions the capacity for growth and sustainability in the absence of steady government budgetary appropriation. Surveillance of AMR like other healthcare intervention projects cannot completely thrive on donor funding alone, the host government must be involved by playing a lead role. Without that, it is unlikely that the desired goals of the NAP will be achieved. Some studies have proposed setting-up a counterpart funding arrangement with the federal/state government as one way to compel them to match donor's funds and foster government commitment (Ivers *et al.*, 2018; Deoras *et al.*, 2016). Transparency, public availability of funding information, and assessment of future budgetary requirements are some other strategies that could attract interest from relevant bodies.

This analysis also focused on active participation and political will which are crucial to the success of the NAP (Anderson *et al.*, 2020). The creation of NCC reflects government engagement to strengthen AMR surveillance however, the absence of AMR Surveillance

Coordinating Centre (SCC) at the NCDC is a major constraint. The responsibility of NCDC as the NCC for AMR NAP span across all five pillars of the action plan, whilst this is strategic, a dedicated coordinating centre specifically for surveillance activities will ensure surveillance related challenges are easily identified and addressed. More so, it will serve as a reference point for national level surveillance networks which will improve surveillance integration for better information sharing.

Another important aspect of the NAP that came through in the interviews is participation in the development and implementation of the AMR NAP. Some sectors and professional bodies did not consider their inclusion and contribution sufficient even-though they have strategic responsibilities in the NAP implementation (Nigeria Centre for Disease Control, 2017). Though the NAP reflects a One Health multisectoral stakeholder's participation across health, animal and environment, the respondents revealed that the health ministry dominated the process. Other professional bodies and stakeholders like the doctors, laboratory scientists, and microbiologists equally did not consider their participation as integral to the NAP development despite their roles in implementing some of the NAP interventions. While the NAP has clear objectives, strategic interventions, and measurable indicators for monitoring progress, it requires collective responsibility of all sectors concerned to achieve those goals. This is crucial because feeling of inclusiveness increases ownership and acceptance of the plan, thus facilitating its implementation (Frumence *et al.,* 2021).

The education and awareness pillar is another area of concern highlighted from this study. The nature of AMR demands that every individual be considered important in targeted activities for AMR containment especially for rational use of antimicrobials. The community members who are the consumers of antimicrobial agents are not receiving adequate sensitisation. Majority of awareness creation campaigns and exercise are targeted at healthcare workers. Whilst it is important for the healthcare workers as gatekeepers to have this knowledge,

providing the right knowledge for the populace will influence their antimicrobial seeking behaviour from healthcare practitioners (Ogoina *et al*., 2021). Achi *et al.* (2021) also reiterated the need to design remedial strategies across communities and establish AMR-centric learning and activities to specifically educate the younger generation up to higher education. These measures will ultimately reduce the reliance and demand for antimicrobials which will eventually shift the population mind-set regarding antimicrobial need and consumption (Frumence *et al.*, 2021). These areas have not received much implementation attention despite their centrality to achieving AMU control and AMR containment.

Another critical component of the NAP for AMR is antimicrobial stewardship. This study revealed that most stewardship programs are happening at the tertiary care level, equally revealed is the absence of an integrated AMU/AMR surveillance. The collaborative efforts of the European Antimicrobial Resistance Surveillance System (EARSS) and the European Surveillance of Antimicrobial Consumption program (ESAC) have demonstrated that antimicrobial resistance surveillance is enhanced when linked to monitoring of antimicrobial use practices. The integrated monitoring of resistance and antimicrobial use is crucial for successful resistance tracking and containment (Haworth-Brockman *et al,* 2021; World Health Organisation, 2017). This is a useful strategy for optimising available resources in resource limited settings (Karp *et al.*, 2017). Another useful tool to mitigate against empirical use of antimicrobials at healthcare settings is by implementing the standard treatment guidelines and essential drug lists. While standard treatment guidelines and essential drug lists have been provided as part of systematic approach to ensure prudent antimicrobial usage, there is no evidence to suggest optimal implementation of these guidelines at facility level. This further highlights some gaps in policy enforcement and implementation. These gaps make it impossible to measure effectiveness of these interventions as it is unclear the extent to which these different approaches have been effective since they have been poorly implemented.

5.7 Limitations

The original design of this study included in-person interviews to accommodate a broad range of eligible respondents and in order not to unintentionally screen out candidates who are not technologically savvy but are otherwise very suited as participants. Due to the COVID-19 pandemic and travel restrictions at the time, in-person interviews were not possible so all interviews were conducted remotely. The implication is that respondents without access to video conferencing apps were no longer eligible for inclusion into the study which might have impacted the perspectives of information received. Another limitation was connectivity and technical problems that are inherent in remote interviews. Some interview sessions were severely impacted by poor network connections. A number of respondents allowed an overshoot of the agreed interview timeframe to compensate for the glitches, however, a few others could not afford extra time due to other engagements. Those missed sessions might have yielded more useful information for this study. However, since the participants recruited for this study involved a wide range of professionals and stakeholders with overlapping roles/function, it is believed that key opinions would have been captured and the findings represents the real-life situation. Another limitation of this study is the impact posed by evolving nature of health system, although findings from this study provides an overview of the status of the project at the time of conducting the research, the status of each activity could change or become outdated after a period of time as the activities of AMR containment are dynamic and can change with time. Lastly, the phenomenological approach used in this research is prone to researcher's subjectivity and findings may be influenced by researcher's bias. Bearing this in mind, additional precautionary steps were taken to establish transparency and ensured that weakness inherent in this type of research does not bar achieving the study objectives.

5.8 Conclusion

The Nigeria's NAP is quite robust, has clear strategic interventions and objectives but deficient in government budgetary appropriation which is fundamental for its full implementation, operationalisation and sustainability. The NAP has made observable implementation progress at the national and tertiary level but progress at zones are inconsistent and disparate.

In addition to the established NCC for AMR and related activities, a Surveillance Coordination Centre (SCC) with a focus solely on surveillance activities will help to further ensure goal driven outcomes for the surveillance system. The absence of a SCC creates difficulties in identifying, tracking and managing surveillance specific challenges. There is some evidence that the NAP implementation has realised several goals with the support of implementing partners, but the future of sustainable operations still looks bleak because of the uncertainty of continued resourcing. This in part is to the NAP related activities being volunteer driven. Specifically, the current surveillance is based on volunteer laboratories and resource mobilisation rely on donor and funding partners. The challenge of this sort of arrangement is the unpredictability of the future of the project should the donors and volunteers withdraw their funding support. The project will eventually suffer setbacks without sufficient government intervention.

Despite these challenges, the project has managed to establish operational capacity with the assemblage of rich human resources, a network of surveillance ready laboratories, excellent knowledge base, technical working groups and multisectoral networks. These indicators shows the system has ability to exceed surveillance expectations if given the required financial support at the same time, strengthening of the NRL and One Health approach, advocacy for policy enforcement, careful planning, and transparency will support effective implementation of the NAP across levels.

5.9 Recommendations

The immediate short-term recommendations will be firstly to increase the capacity (human and resources) of the NRL to be able to rapidly scrutinise and on-board surveillance ready laboratories. Then make an open call to all levels of laboratories with the requisite capacity to participate in surveillance to step forward for enrolment. These will ensure that surveillance is decentralised, more comprehensive and representative.

The next steps will consider setting up a surveillance coordinating centre, declare a state of emergency on funding, and lead advocacy to the government for budgetary allocation. These steps are vital for project sustenance.

Accreditation of all medicine stores will help build a database of all medicine handlers and make monitoring and enforcement of policies targeted at drug outlets a lot easier. Government can encourage unregistered drug outlets to enrol with professional bodies by providing incentives for dues and levies and also provide tailored education programs. This will close the gap created by shortage of licensed drug dispensers.

Extend stewardship programme to other healthcare levels; strengthen the regulatory and enforcement agencies; address gaps in the multisectoral ecosystem; encourage inclusiveness, transparency, accountability, and M&E.

Additionally, develop and pilot a framework focused on community-based surveillance approach; instrument for individual-level data generation from household surveys to inform antimicrobial usage in the population; and indicators for measures of effectiveness of interventions.

Lastly, there is a Nigeria primary health care (PHC) project called Rapid Result Initiative (RRI) which has operationalising NCDC as one of its key focus areas. The target is to make 110 PHCs functional, one per senatorial zone with linkages and referral networks that are able to collect,

process and ship surveillance specimen to testing laboratories across Nigeria. Though AMR is not included in the routine surveillance goal of PHC RRI project, it is highly recommended to integrate PHCs AMR surveillance with this project and establish zonal hubs for aggregation of surveillance data.

Chapter 6 Proposed toolkit to facilitate AMR surveillance and implementation in Nigeria

6.1 Introduction

This chapter presents an important component of the overall research project objective which proposes development of solution toolkit in response to the gaps apparent from the research. The major gaps being absence of standardised microbiological data collection proforma, absence of sub-national data collection structure for early warning and policies to optimise existing activities as identified from the preceding chapters. This section describes the proposed toolkit in more detail, the impact and elements of each tool, steps taken towards the development, data flow logic and strategies to optimise its implementation.

6.2 Background

The complex nature of antimicrobial resistance (AMR) and challenges associated with implementing comprehensive surveillance in low-resource settings warrants harnessing alternative sources of AMR data using tools that address various facet of implementation bottlenecks (Ashley *et al.*, 2019). Specifically, tools that take into account the diversities from one system and another, the dichotomies in resource allocation, literacy level, out of pocket spending and existing local policies and barriers. Surveillance in Nigeria is currently concentrated on one hospital type which excludes other health care providers. Surveillance needs to be inclusive and strategic with the aim of a balanced geographical, demographic and socio-economic distribution (Rempel, Pitout, and Laupland, 2011). This inclusiveness is dependent on the number and distribution of health facility types to include community and hospital-based sampling (O'Brien *et al.*, 2019). Adding additional hospital type might be beneficial for the surveillance but that will also increase cost for the system.

Balancing cost and efficiency is often a dilemma for LMICs such as Nigeria with constrained health budget (Jayatilleke, 2020). Therefore a model that delivers cost-effective surveillance is

needed. The proposed toolkit will try to address this problem by proposing a combination of strategies that could be cost effective to implement while optimising efficiency. The denominator of the proposed tool is efficiency which takes into account the effectiveness attributes (bias of resistant proportion, representativeness, sensitivity and coverage) of a system.

A toolkit, or a collection of adaptable documents to inform and facilitate policy implementation can improve the use of evidence based interventions as well as serve as a solution to public health challenges (Margaryan, Littlejohn, and Lukic, 2018; Keddem *et al.*, 2017). Implementation of public health intervention worldwide is associated with improved patient outcomes, reduced healthcare cost, increased quality of care and life expectancy but they are still ineffectively implemented in real world despite the potential benefits (Warren *et al.*, 2016). Oftentimes, health systems desire for adopting an intervention does not consistently translate to actual implementation of same intervention (Melnyk *et al.*, 2012). This is so because the content of most of these interventions often focus on the steps required to complete the clinical intervention with less emphasis on the strategies that will facilitate implementation and transmission in real-world settings (Vargas *et al.*, 2020).This implementation challenge could be attributed to the translational gap between evidence and practice in healthcare intervention (Shelton, Cooper, and Stirman, 2018). In order to bridge this gap, there is a need for tools that supplement translation of evidence into practice and designed to meet the need of specific intervention at different settings and stages (Kraemer and Van Zutphen, 2019). Stakeholders and implementers may find that tools developed prior to implementation may not meet all of their intended needs and over time, new tools may be developed to provide information or guidance that supports existing implementation strategies. In addition to the use of tools to support adoption and implementation of interventions, they can also be used for sustenance of interventions (Keddem *et al.*, 2017).

Surveillance has been identified as a multiple approach intervention with associated improvement in AMR containment, but their implementation remains challenging (Malla *et al.*, 2014). Approaches such as laboratory-based, case-based, and case-finding are evidence based surveillance interventions that have demonstrated effectiveness in identifying, tracking and containment of drug resistant pathogens, yet global adoption by health systems has been limited particularly in LMICs settings (Lim *et al.,* 2021). With the implementation challenges of current approaches to AMR surveillance becoming clearer, resource limited settings must adopt a strategy for monitoring and maintaining the global surveillance momentum. One way is through advancing the development and utilisation of tools that are home grown and addresses core thematic areas of surveillance implementation.

6.3 Purpose of the toolkit

The purpose of this toolkit is to facilitate robust AMR surveillance through ensuring representativeness, improvement in data completeness/quality, and provision of early warning information. The toolkit provides a blueprint to guide both clinical intervention for healthcare providers and implementation activities for policy makers which will all together provide a better indication of population-wide trends in antimicrobial resistance. This should over time build a pool of evidence-based data useful for policy decisions and interventions aimed at controlling antimicrobial resistance.

Findings from Chapter 3 'the systematic review of methodology for AMR surveillance in Africa' Okolie *et al*. (2022), evidence from literature, and expert opinions suggests that data quality, representativeness and timeliness are the important performance attributes for surveillance system (George *et al.,* 2020; Calba *et al.,* 2015). These in addition to having early warning systems in place makes for an ideal surveillance system. These qualities are missing in the current surveillance strategy which creates bias and impacts on validity of data.

Each tool in the surveillance enhancement toolkit is designed to address these missing attributes and to mitigate some observed threats, constraints, limitations, weaknesses, and barriers, while leveraging on strengths, opportunities and success of existing surveillance. The individual tools are tailored to meet the needs of a typical low-medium income setting like Nigeria though it could be adapted to meet local needs of a broad range of income settings. It is developed to allow integration into existing structures which reduces the need for huge financial investment as well as to facilitate quick uptake.

The early warning tool is designed to utilise routine microbiology data to develop heat map of hot spot zones. This will inform the surveillance system of imminent threat and also guide the choice of appropriate strategy such as modification of treatment guidelines. The data completeness tool will utilise a template of mandatory clinical and epidemiological descriptors which will form part of routine patient recording. This will address the concerns on completeness of reported data which have been consistently raised in literature (Acharya *et al.*, 2021; Podewils *et al*., 2015). The policy tool presents a set of policies that will address some factors associated with representativeness of the system and critical areas of system performance and AMR containment. The policy tool will define a model for practice and elements which must be standard in order to achieve the desired goal. While some elements must be standard, some can be adaptable to meet local needs. The tools are designed to complement each order. Figure 6.1 shows the surveillance enhancement toolkit which reflects the cyclical relationship between tools and the connection of all the tools to the central objective.

6.4 Development of the toolkit

This toolkit was developed in response to the challenges of implementing AMR surveillance in Nigeria. It draws from knowledge of experts, lessons learnt from other systems, and

effectiveness of different strategies for implementing AMR surveillance. This evidence was gathered from data generated from various phases of this research project. The first phase included a systematic review which assessed the methodology for AMR surveillance in Africa. The second phase was a cross sectional study involving 302 laboratories using 46 items questionnaire which assessed laboratory quality indicators. The third phase utilised qualitative in-depth interviews of 34 key opinion leaders with roles in AMR who offered expert opinion on implementation challenges and possible solutions. Lastly, in-depth literature search was also conducted to identify studies which reviewed approaches for implementing AMR surveillance in LMICs. In addition, the toolkit considers the three major issues in designing alternative sources of surveillance data (cost, sustainability, and goal) and a thorough review of the state of the current system, the desired characteristics of the "ideal" system, and strategies for attaining a better system (Keddem *et al.*, 2017).

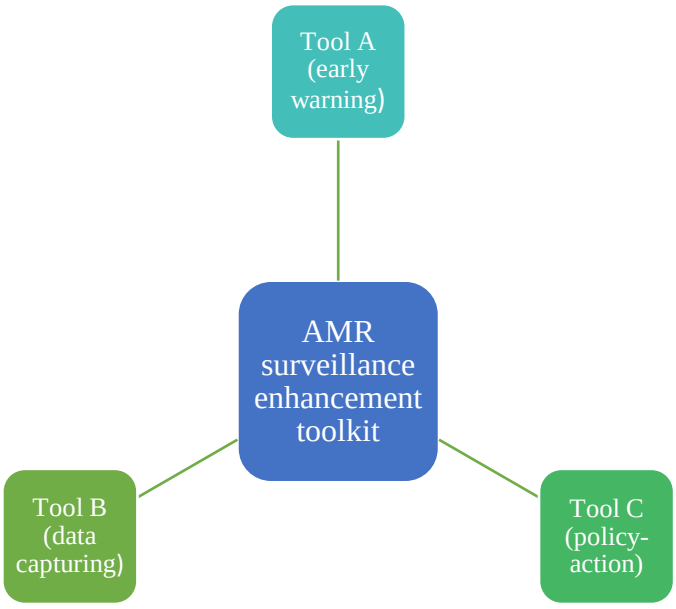


Figure 6.1: Diagrammatic representation of the surveillance enhancement toolkit and its component tools.

The University of California Social Work Education Center (CalSWEC) structure for toolkit development was adopted for developing this toolkit (CalSWEC, 2019). The CalSWEC guide

was followed on the basis of its approach for successful development of implementation tool which considers amongst others the use of multiple strategies and networking; support from multiple stakeholders; integration; and the ability to adapt the intervention. The CalSWEC resource for building an implementation toolkit describes a 9 step process which occurs in sequence prior to toolkit development and includes: definitions, engagement, communication, assessment, planning, training, evaluation, policy and procedure, and finance. Although the CalSWEC structure was followed, the process for developing this toolkit was modified which may not follow the linear structure of CalSWEC protocol. This is due to overlap and some elements meeting the purpose of multiple categories as well as exclusion of categories not intended for the development of this toolkit. Table 6.1 shows the elements that were considered in developing this toolkit. The final toolkit comprised of 3 main tools (early warning, data capturing, and the policy tool which has 3 sub–implementation activities). Figure 6.1 shows the surveillance enhancement toolkit.

6.4.1 Tool A-early warning

There is general agreement that the national reference laboratory lacks the capacity and resources to coordinate and undertake quality assurance of eligible laboratories for the purpose of surveillance which has impact on surveillance expansion (as evidenced from in-depth stakeholders' interview reported in chapter 5). This limitation calls for a strategy that can facilitate microbiological data quality assurance at the laboratory level and a scheme that can collate this data systematically to inform local preparedness action. The qualitative study confirms absence of an early warning plan, a critical but often overlooked component of surveillance system that can provide population level data that could give indication for robust or targeted AMR surveillance (Espona, 2021). Response from the cross sectional study reveals absence of coordinated structure at state and regional levels for reporting resistant pathogens of public health priority apart from the channel available to sentinel laboratories. This gap

creates opportunity for early warning system. Interestingly, findings from the cross-sectional study (surveillance quality indicators) and the SWOT analysis in figure 6.2 highlights opportunities within the system that can support the implementation of early warning system which can be accommodated within the existing chain of laboratory network. Data flow logic showing the pathway for implementing this tool is presented in figure 6.3.

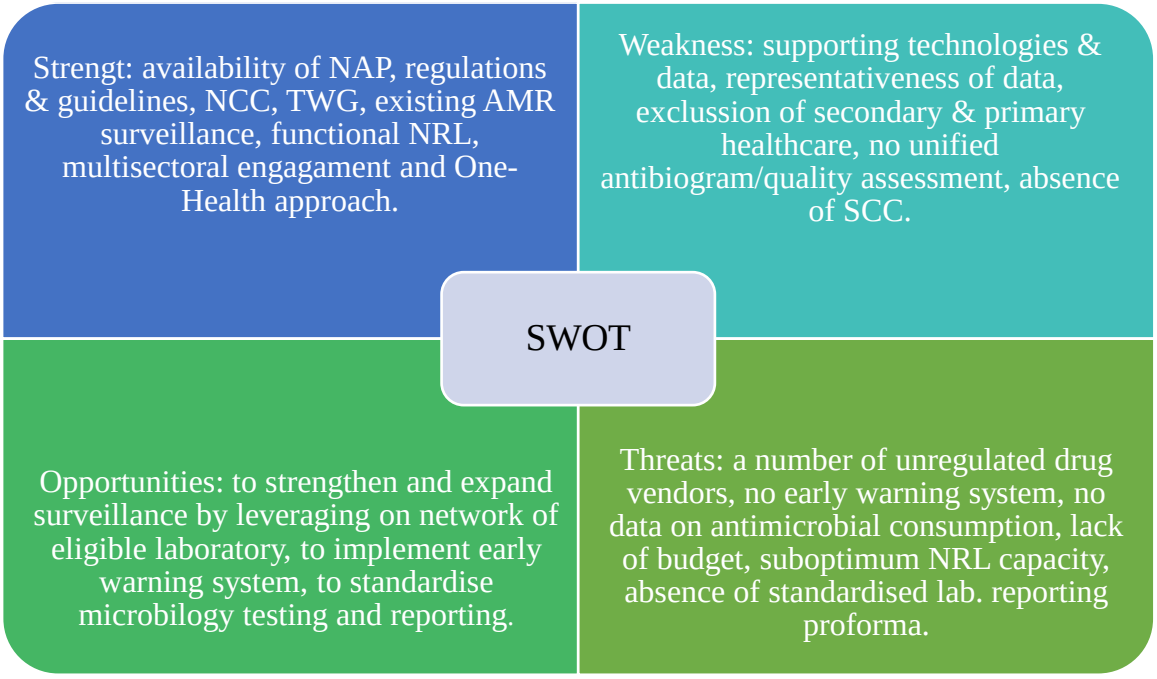


Figure 6.2: SWOT analysis of the current surveillance system highlighting areas of strength, weakness, threats as well as opportunities. These indicators are informed by the results of the cross-sectional and qualitative studies reported in chapter 4 and 5.

An early warning system enables timely detection of the peaking of symptoms levels above-threshold before cases surge, or prompt recognition of small clustering of cases before prevailing illnesses overwhelm health systems (Meckawy *et al.*, 2022; Epsona, 2021). This is particularly important in Nigeria with fragile and fragmented health system. The early warning tool will bridge this data gap and improve population-level surveillance through provision of geographical pattern of high risk area for AMR outbreak using routine laboratory AST results. Routine microbiological tests are performed daily using samples of healthy and sick individuals collected from various compartment for varying medical/non-medical purposes. Oftentimes, the results of these laboratory investigations lay waste in the laboratory/hospital database or

destroyed whereas they could be a source of public health surveillance data if properly collected (Lim *et al*., 2021).

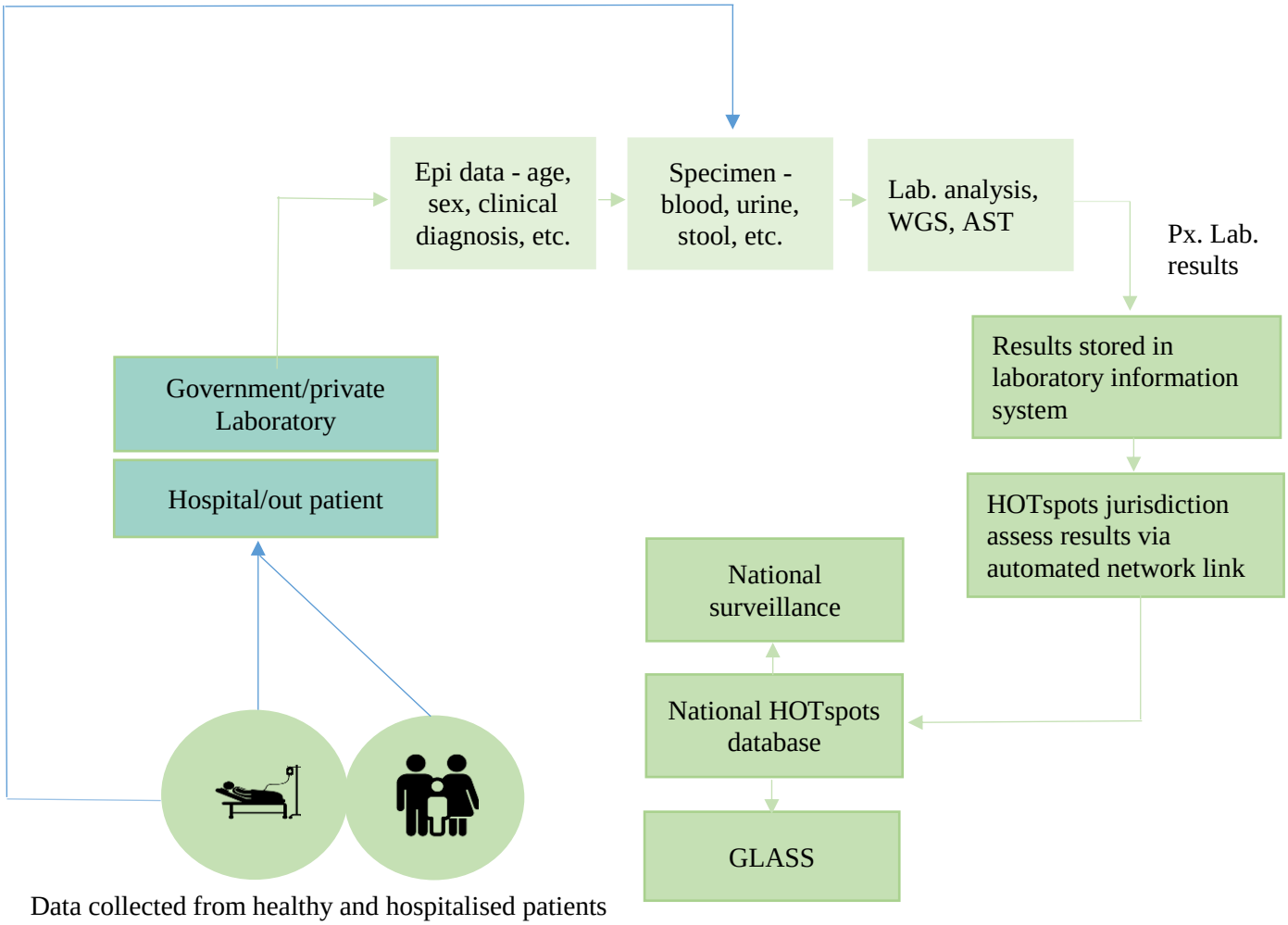


Figure 6.3: Data flow logic for early warning tool

This tool maximises locally existing microbiological data to narrow the data gap in trends of DRI/AMR (Wozniak, Smith-Vaughan, and Andrews, 2021). It utilises existing structure with minimal need for both human and capital investment and as such can be implemented in financial constraints systems. Findings from the laboratory assessment questionnaire shows there is capacity (human, structure) to adopt/integrate this tool into existing network of laboratory systems. It has added benefit of potential to mop up data from previously

underrepresented geographical locations with the capacity to include primary, secondary and private health care (Acharya *et al.,* 2021). In keeping with surveillance goal, early detection, timely and appropriate response are important in achieving surveillance system role in disease prevention. With frequency of pandemics over the past decade revealing the sub-optimum operationalisation of surveillance systems handling human health data, EWSs serves an alternative or complimentary roles which have been found to be effective and more proactive to detect outbreaks (Meckawy *et al.,* 2022). Effective implementation of this tool will provide timely updates of AMR by regions and facilitate communication and data informatics needed for public health response. Table 6.2 shows the implementation protocol for this tool.

6.4.2 Tool B-data capturing

The purpose of this tool is to facilitate completeness of reported data by providing template of important clinical and epidemiological data that must be collected as part of routine laboratory testing. To complement the early warning tool, a standardised and unified proforma to include epidemiological, microbiological and clinical data will need to be designed and adapted to reflect parameters that are most important for the purpose of surveillance. According to WHO (2020), completeness of reported data is the proportion of surveillance reports with no missing required information. To ensure completeness of surveillance data, there is need for a standardised proforma combining patient and microbiological data which should be completed by the attending clinician and must accompany every sample sent for AST or routine laboratory testing (World Health Organisation, 2015). Important surveillance metrics can be calculated from these results if denominators that will allow their estimation is collected (Suleiman and Fola, 2013).

Modern research recognises that poor quality data is not useful. Oftentimes they are a waste of resources and time as they do not inform meaningful action. Current system for data collection does not include relevant clinical information required to distinguish infection origin in terms

of community or hospital acquired infection. Good quality data combining microbiological data and patients' information can serve as a good source of data for AMR surveillance (Alvarez *et al.*, 2020). A number of surveyed laboratories perform AST using one of the GLASS recommended methods (disc diffusion, semi-automated or manual testing using minimum inhibitory concentration and gradient diffusion), but failed to record important patient and clinical parameters.

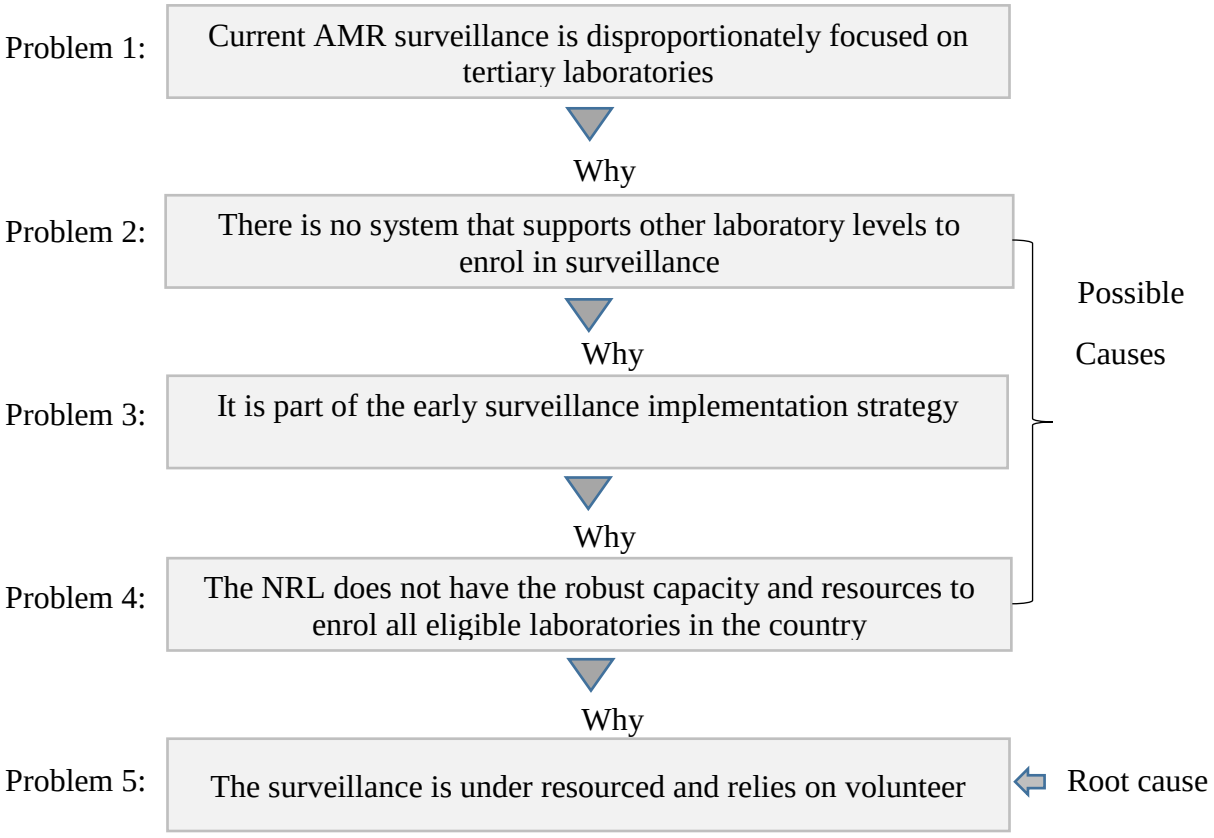


Figure 6.4: Root cause analysis of why surveillance is restricted to tertiary laboratories

A baseline assessments of these laboratories shows capabilities to follow standardised data request proforma if available. Therefore, improvements in data quality including strengthening the capacity to collect and record good-quality data through innovative and collaborative strategies can fill the gap in completeness of surveillance data with minimal financial and human resource investment. This will ensure data quality and validity which are essential in

estimation of burden of AMR in the population. These data can also be analysed for new resistant trends to priority antimicrobials. Table 6.3 shows the implementation protocol of this tool.

6.4.3 Tool C-policy action

The purpose of this tool is to guide stakeholders on implementable strategies to support robust and representative AMR surveillance. The current surveillance is disproportionately focused on one hospital type (as recorded from stakeholders' interview) which raises concerns on external and internal validity of data recorded from such system. Following stakeholders' interview and analysis of expert opinion, the lean six-sigma structured problem-solving methodology using the 5 Why's framework approach was used to identify the possible factors underlying the inclusion of only tertiary laboratories into the national surveillance (Antony *et al.*, 2021; Peimbert-García, 2019).

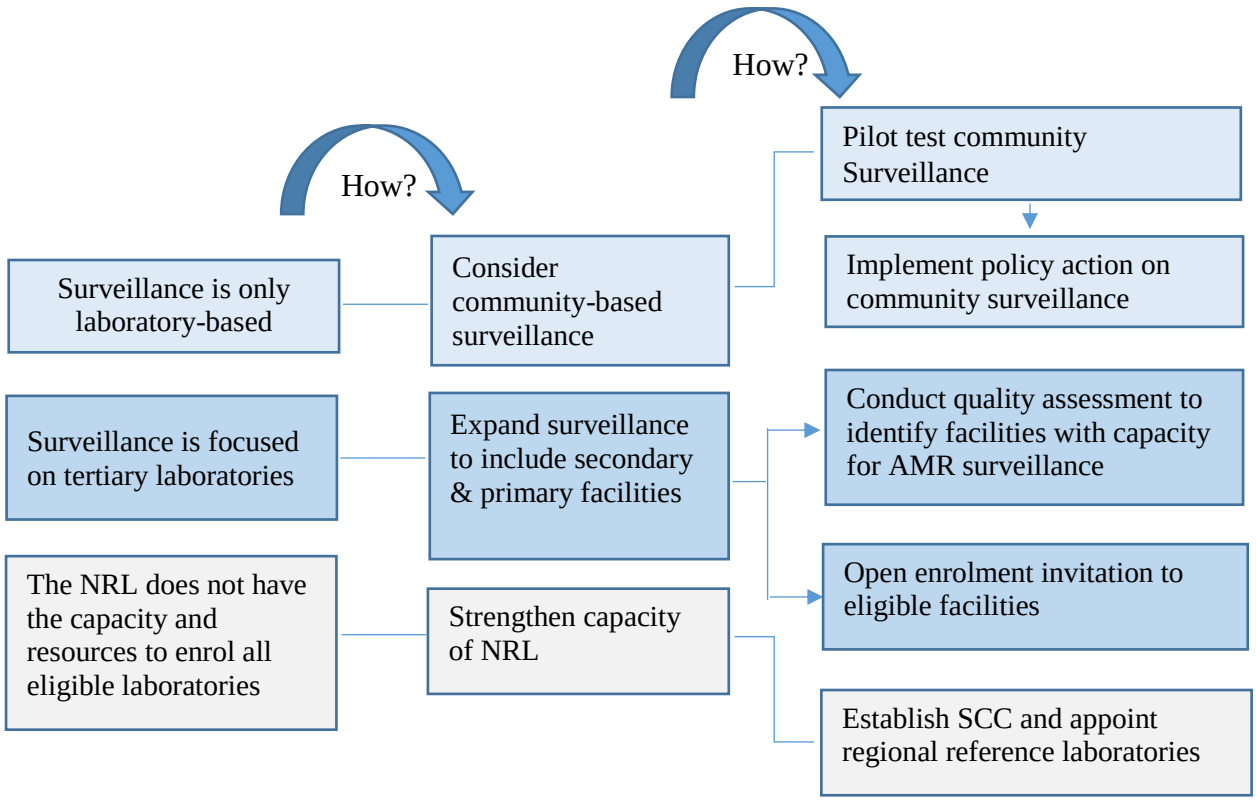


Figure 6.5: How-how analysis showing set of implementable policies identified to the right

The 5 Why's is one of the cause-and-effect analysis tools that helps to identify possible sources of problem in a system. By asking a series of Why's, will help to drill down to the core of the problem thus making the root cause more apparent rather than just focusing on the symptom. Figure 6.4 shows the root cause analysis of the problem. Having identified the root cause and other possible causes, the How's approach was used to generate multiple ideas to solving the problems by repeatedly asking 'how can this be solved'(Kulkarni, 2022). The how-how analysis provides an effective structure for organising possible ideas and solution options all in one place. Figure 6.5 shows the outcome of the how-how analysis. Following the root cause and how-how analysis of expert opinion, 3 policy actions emerged for recommendation. Table 6.4 shows key areas which will have observable impact on the surveillance system if implemented as part of the policy action tool (Tool C).

6.5 Conclusion

Implementing new policies are often hindered by a plethora of complex challenges (Iyamu *et al.,* 2022). Significant among these are those associated with finance and budgetary allocation, legislation, training and deployment, fitting into existing system, stakeholder buy-in, networking and partnership, as well as complexities inherent with integrating digital technologies. Specifically, integrating tools of high-income countries in low medium income countries which presents considerable challenges (Jayatilleke, 2020). To mitigate these challenges, development of public health interventions must leverage high-quality evidence and comprehensive research process, diverse stakeholder in-put and informed by the peculiarities and circumstances of the target system. This will ensure that the true root of policy implementation barriers (individual, institutional, political, structural, sociological or cultural) are identified and considered in developing targeted solution (Iyamu *et al.,* 2022).

In the context of Nigeria, evidence emerging from this study indicated areas of potential challenges of implementing a new system, the major been funding, resources, integration and compliance. In line with this knowledge, and to mitigate other challenges inherent in the system, this research exhausted available evidence sources, data analysis including SWOT analysis and these form the bases for the strength and uniqueness of this evidence-based toolkit been that it is informed by robust data from this specific context. It takes into consideration potential challenges of implementing a new system in the context of Nigeria in designing a robust, convincing, timely and relatively simple to implement toolkit. It goes without saying that implementing the proposed toolkit is not devoid of challenges. Other foreseeable challenges that could potentially impact the implementation of this tool include stakeholder buy-in, multi-sectoral collaboration. These can easily be overcome as the intended benefits of the system becomes apparent. Specifically, as it addresses the core needs of the system and can be easily implemented without extensive need to alter existing structures.

Table 6.1: Elements of the CalSWEC structure that were observed in developing the surveillance enhancement toolkit.

Toolkit elements	Indicators/descriptors
Definition	All tools were defined in accordance with function.
Engagement/ communication	A formal stakeholder's engagement was undertaken as a prerequisite for implementation toolkit development.
Assessment	The current surveillance system was assessed and a clear implementation plan was drawn. The implementation plan for each of the tool defines how the practice, program, intervention or initiative will be implemented as well as the implementation process.
Evaluation	The system was evaluated for strengths, weakness, opportunities, and threats using the checklist of AMR implementation core indicators to identify missing (but priority) indicators as well as possible enablers and barriers to implementing AMR surveillance. Figure 6.2 shows report of the SWOT analysis.
Policy and procedure	The current (NAP) policy was extensively reviewed to ensure the proposed toolkit can be accommodated within the existing surveillance framework.

Table 6.2: Implementation protocol/plan for early warning tool

Tool name	Early warning tool
Key audience	Ministry of Health, NCC, healthcare facility, labs, lab. scientists
Preliminary activities	▪ Call a stakeholders meeting of concerned department, agencies and clinicians across levels and geopolitical zones; ▪ Assess for readiness by conducting local needs assessment and identify facilitator(s) per zone; ▪ Develop a formal implementation blueprint detailing key persons involved and timeframe of action; ▪ Agree on technological appropriate method of data transmittal.
Structure and governance	▪ Appoint team members/persons from existing public health structures or TWG to coordinate HOTspot activities at various level of data aggregation; ▪ Assign tasks and responsibilities to the appointees with clear terms of reference and feedback circle
Core requirements/resources required	▪ A central/regional data aggregation hub; ▪ Build a network system that links the HOTspot jurisdiction database to laboratories within its catchment; ▪ Strong multi-sectoral collaboration and networking between the laboratories, clinicians, and ministries.
Methodology	▪ Identify sources of data (type of hospital, lab); ▪ Collect details of all laboratories and build database of laboratory services directory; ▪ Appoint HOTspot jurisdiction at zones, states, and council level and link the laboratories to their jurisdiction hotspot database; ▪ Collect AST results recorded as part of routine microbiology testing quarterly or pro-rata.
Data collection and validation	▪ Collate, clean, remove duplicate and validate data; ▪ Aggregate/stratify data by susceptibility, intermediate and resistance; infection origin, age, sex, population.
Data analysis	Analyse the data and develop geospatial map that can be used to visualise heat map areas of AMR threat.
Use of data	As this tool supports early identification of AMR, it allows organisation more time to prepare and respond to AMR threats. By highlighting defined geographical areas, it helps to facilitate surveillance study designs appropriate for the location as well as population estimates.

Table 6.3: Implementation protocol/plan for data capturing tool

Tool name	Data completeness/capturing
Key audience	Healthcare facility, labs, clinician
Preliminary activities	▪ Call a stakeholders meeting of concerned department, agencies, clinicians and professional groups across geopolitical zones; ▪ Discuss and itemise checklist of patient metrics/parameters and specimen information to be recorded as part of routine laboratory testing which are crucial for AMR surveillance (figure 6.6 shows an adaptable data request proforma for AST); ▪ Agree on manual format (electronic, paper…etc.), language(s) of instruction, and route of disseminating the document to laboratories, clinicians, and hospitals; ▪ Develop a formal implementation blueprint with indicators for measuring compliance
Structure and governance	▪ Nominate facilitators at zonal and state level from within existing surveillance actors to coordinate the exercise; ▪ Assign tasks and responsibilities to the appointees with proposed milestone deliverables; ▪ Designate point of progress feedback and channel of complaints resolution
Core laboratory requirements	▪ Meet minimum standard operating procedure; ▪ Perform AST, WGS, or send samples to other laboratories for AST assessment; ▪ Have data storage system (computer, logbook…etc.)
Methodology	▪ Develop standardised form to include epidemiological and clinical data [i.e. origin of infection (hospital, community), age, underlying illness; specimen (blood, urine, csf. Stool); ▪ Finalisation and adoption of a standardized patient's reporting template; ▪ Produce and disseminate document in print and online formats to laboratories, hospitals and relevant healthcare facilities; ▪ Training/supervision to ensure adherence
Data collection and validation	Collate data using existing data collection network or via with HOTspots database link.
Data analysis	Analyse data according to predefined priority antimicrobial pathogens and highlight areas with high resistant rate to antimicrobial agents on country's watch list.
Use of data	Data can be used to inform local treatment guidelines, influence prescription pattern and serve as source of early warning information for the surveillance system.

Table 6.4: Proposed policy action highlighting current situation and benefit of implementing the recommended actions.

Current position	Proposed policy action	Benefit(s)
The surveillance system currently includes only tertiary level facilities which excludes secondary and primary healthcare. The exclusion of other healthcare levels limits the ability to use reports from the surveillance to infer the AMR status of the entire population (Pezzani et al., 2021)	To review current surveillance approach to allow more inclusiveness of other levels of healthcare with good capacity for surveillance participation including the private laboratories.	Inclusion of other levels of laboratory in the surveillance system will benefit the system in multiple ways; Firstly, it will help the surveillance to be more representative which minimises bias and thus improves data validity (Yau *et al.*, 2021 Cole *et al.*, 2019) Secondly, there will be reduced chances of over estimation of resistance when surveillance is generated from a larger number of laboratories rather than a sub-set of labs (Schubert *et al*., 2021); Thirdly, robust data means better understanding of the burden of AMR which in-turn will inform meaningful action that addresses the countries challenges in a pragmatic way (Sharma *et al.*, 2022).
The NRL does not have sufficient capacity to carry out some of its responsibilities including laboratory assessment and enrolment. As a result, the surveillance system is constrained and unable to take up more eligible laboratories because of inability to perform supervisory/oversight duties to additional labs.	To prioritize strengthening of the NRL through provision of human and capital resources. To establish regional reference laboratories (RRL)	In addition to expanding surveillance coverage for more data robustness, strengthening the NRL will ensure that data are quality assured using EQA of highest standard. This will also guarantee timeliness of data transmission across space thus making the data available and useful to global AMR surveillance. Establishing regional reference laboratories will break the overwhelming responsibility of the NRL and ease the process of data quality assurance
The NCC currently coordinates and performs oversight function of all AMR related activities across the five GAP pillars including surveillance. This responsibility is quite broad and requires that some strategic objectives of high priority like surveillance should have a dedicated coordinating centre to allow a governance structure that is more surveillance focused rather than generalised (Nabadda et al., 2021). The complexities of surveillance warrants such institutionalisation of tasks in order for the surveillance system to achieve its desired goals. This structure is lacking in the current AMR containment strategy.	Establish AMR Surveillance Coordinating Centre (SCC).	Establishing a SCC explicitly for surveillance related activities will offer coordinated guidance to the surveillance system, foster national surveillance productivity, identify defects in the system, and propose strategies to rapidly address them, promote greater M&E and feedback mechanism. A dedicated centre for surveillance will ensure accelerated turnaround of surveillance data to rapidly inform public health actions which ultimately yields better output for the system.

Chapter 7 General discussion, conclusion and future directions

7.1 Study recap and general discussion

Low data quality of epidemiological surveillance systems has been a matter of concern worldwide (Costa-Santos *et al.,* 2021). Developing and implementing national and international surveillance platforms that consistently gather AMR data in real-time are essential first steps for quantifying the burden of AMR, assessing geographic and temporal trends, benchmarking implementation action and optimising containment strategies (Murray *et al.,* 2022; Frost *et al.,* 2021). The accuracy and reliability of surveillance data is often impacted by quality and representativeness of data which depend on many factors, including laboratory quality, diagnostic capacity, information systems and staff capability (Frost *et al.,* 2021). Despite ongoing national and international efforts aimed at strengthening AMR surveillance for global data aggregation, Frost *et al.* (2021) warned that data needs to be interpreted with caution as majority of surveillance sites are located at hospitals, hence community-acquired drug-resistant infections may be under-represented.

Murray *et al.* (2022) also raised concerns about grossly exaggerated and tentative global estimates of AMR and the impacts of under or over estimation of AMR on control policies and strategies, thus highlighting the need to closely monitor and improve quality of data collected by surveillance systems. As with many LMICs, very few studies have evaluated surveillance methodology for AMR to determine the quality and representativeness of surveillance data (Costa-Santos *et al.,* 2021). Evaluation of surveillance system is crucial for improving performance, effectiveness, sustainability and system strengthening (Walugembe *et al.,* 2019). More so, with the rapid expansion of dimensions of surveillance in recent years, it is important to regularly assess all surveillance activities (from data input to output) using established criteria to ensure they are of high quality and fit for purpose (PHE, 2017). In Nigeria, the national surveillance system for AMR has not been evaluated. With very little currently known

about the surveillance system in Nigeria, this study examined the capacity and sustainability of the AMRSS to identify the components of the system that require modification and build knowledge base for policy and practice recommendation.

Capacity and sustainability of the Antimicrobial Resistance Surveillance System (AMRSS) in Nigeria forms the outcome of focus for this research. These aspects of surveillance systems are crucial as they are concerned with quality and continued delivery which are integral to fulfilling the goals of surveillance (Malik *et al.,* 2020; Van Herwerden, Palermo, and Reidlinger, 2019; Walugembe *et al.,* 2019). They also account for why some systems are able to improve their health gains or *vice versa* highlighting capacities that are needed and of the training, facilities, professional and organisational support that must be mobilised to establish these capacities (Beyene *et al.,* 2023).

The capacity of a surveillance system is assessed by its ability to effectively and efficiently collect data that describe the pattern of resistance as closest as possible to the local situation which tells us how well the system can detect and report cases, monitor trends and facilitate early warning for emergency preparedness (Walugembe *et al.,* 2019; Iera *et al.,* 2023). To determine the capacity of the surveillance system in Nigeria, a thorough assessment involving a systematic review, a cross sectional study and a situation analysis were undertaken. The outcome of the evaluation indicates that the surveillance system for AMR in Nigeria has limited capacity being that it is focused on a few tertiary hospitals in order to correspond with the capacity of the reference laboratory; there is absence of early warning system; there is potential for over-estimating AMR; and resistance in the community is not captured. These factors have implication on data completeness and representativeness which have far-reaching impact on data quality, usefulness, validity and reliability of data (Costa-Santos *et al.,* 2021). The evaluation also identified considerable variation in other aspects of the surveillance systems including capacity of participating laboratories, quality assurance measures, AST testing and

interpretation standards, and correlation of clinical and epidemiological information. These variations impact data aggregation, and lead to considerable difficulties in making comparison across laboratories and in understanding the magnitude of AMR (Beyene *et al*., 2023; Willemsen, Reid, and Assefa, 2022).

The assessment further highlighted the support needed to establish appropriate capacity in line with the core components of a national surveillance system for AMR (World Health Organisation, 2015). Specifically, the cross sectional study (Chapter four) demonstrated the barriers, vulnerabilities and weaknesses within the laboratory system that impacts data quality. Some of these include underutilisation of standard operating procedures and antibiogram; absence of unified data collection proforma; absence of structures for reporting resistance at sub-national level; exclusion of secondary, primary and private laboratories; and poor AMR and surveillance knowledge. In both the surveillance participating and non-participating laboratories, the indicators associated with data recording were identified as the weakest and most vulnerable aspects of surveillance quality indicators (SQIs). This finding is useful for informing modification of internal procedures and guide targeted interventions towards strengthening the capacity for improved data quality. Flaws and frailties along data recording processes have been identified to have significant impact on quality and completeness of surveillance data and as such, surveillance systems need to be designed having data quality as a high priority and thus promoting, rather than relying on, users' efforts to ensure data quality (Costa-Santos *et al.*, 2021).

Sustainability of the surveillance system in Nigeria was also assessed in line with the aim of the research. Sustainability has been identified as an important but often overlooked component of surveillance system which is concerned with the ability to maintain a state of ongoing operational efficiency (Kakkar *et al.,* 2017; Fixsen *et al.,* 2005). Undoubtedly, the long-term effects of intervention can only be achieved where the system is sustainable and resilient to

external/internal influence including termination of major financial and technical assistance from an external donor (Walugembe *et al*., 2019; Van Herwerden, Palermo, and Reidlinger, 2019). According to Otto and Haase (2022) programmes that are able to sustain themselves are more likely to produce lasting results and healthier outcomes. To ascertain the sustainability of the surveillance system in Nigeria, a SWOT analysis and qualitative study (Chapter five) involving stakeholders' interviews were conducted. These were undertaken to explore the domains of NAP for AMR and to examine the dimensions of policy design and implementation in order to identify barriers and enablers of programme sustainability. Implementation challenges associated with political, economic, multi-sectoral collaboration and organisation of the sectors required to implement the policy can constraint expansion of surveillance activities and consequently impact sustainability (Walugembe *et al*., 2019). By exploring stakeholder's opinion, threats to sustainability within the system were mapped and the implementation issues associated with them identified using the governance framework for better visualisation (Chua *et al.,* 2021). Key threats such as absence of early warning systems, absence of structures for reporting resistance at sub-national and community level, poor education and surveillance knowledge, inadequate capacity of the reference laboratory which is a core component of a national surveillance system, and poor overall implementation of the NAP were all associated with insufficient budgetary allocation and poor multisectoral collaboration. As frequently mentioned in the literature, lack of appropriate budgetary allocation is a major constraint to programme sustainability, and where this co-exists with other implementation challenges, reaching programme goal could be severely impacted (Otto and Haase, 2022; Walugembe *et al*., 2019). There is general agreement from the stakeholders' interview that the surveillance system in Nigeria is fragile and lacks the potential to sustain itself due to inadequate and fragmented funding sources majorly from donor agencies and volunteers. This position suggests that funding is a major threat to the sustainability of the

surveillance system in Nigeria. In order to accelerate the strengthening of surveillance systems, there should be a stronger focus on the 'enablers' of the system including governance, financing, public health legislation, organisation of laboratory networks and workforce and multisectoral collaboration (Van Herwerden, Palermo, and Reidlinger, 2019; Kakkar *et al.*, 2017).

Consistent with the overarching goal and core objective of this research, a solution toolkit was developed (Chapter six) in an attempt to fill the gaps identified from the system. Significant amongst these is absence of standardised microbiological data collection proforma, absence of sub-national data collection structure (supplementary system for early warning) and lack of appropriate policies to complement existing local policies. The proposed surveillance enhancement toolkit comprises of three individual tools (early warning, data capturing and policy tool) designed to complement each other. In developing the toolkit, human-centric barriers and other hindrances to introducing new processes in a system that suffers considerable implementation challenges were taken into account. As evidenced from this study, majority of the implementation barriers identified in the system were associated with funding constraint and compliance. Drawing from this knowledge, the proposed toolkit was designed to be implemented with minimal resources and simplified protocol to allow seamless integration into existing laboratory activities which promotes compliance.

The early warning tool is designed to leverage on existing human and capital resources, laboratory infrastructure and technical capacity to generate supplementary data for the national surveillance system. The tool will assemble routine AST laboratory results through regional hot-spots into a single database. This data will then be analysed to build evidence for targeted surveillance, inform treatment guidelines for specific geographical locations and at risk communities and serve as information source for early warning. Early warning system for emerging AMR is fundamental for informing emergency preparedness and response action

(Iera *et al*., 2023; Meckawy *et al.,* 2022). Iera *et al*. (2023) deemed as particularly relevant the implementation of an early warning surveillance at sub-national levels taking into consideration that current AMR surveillance systems mainly focus on tertiary levels. Participants at the first GLASS platform meeting agreed that there was an urgent need to develop a system for early detection and reporting of emerging AMR to help map global spread (Bellino *et al.,* 2020; EC, 2017).

The data capturing tool is designed to optimise the efficiency of the early warning tool by ensuring completeness of data. Boes and colleagues concluded from their assessment of surveillance systems that data quality in terms of completeness of information decreased considerably (Boes *et al.,* 2020). In their report, they stressed that improved data completeness is required to adequately design prevention activities and using datasets without carefully examining the metadata and documentation that describes the overall context of data can be harmful (Boes *et al.,* 2020; Chen *et al.,* 2014). The data capturing tool proposes a unified proforma for reporting antimicrobial susceptibility testing (AST) that includes clinical, epidemiological and microbiological information. A combination of epidemiological and laboratory data allows stratification of populations for ascertaining the type of infection (Tacconelli *et al.,* 2018; World Health Organisation, 2015). The unified proforma can be utilised in any document format including soft version to allow seamless data entry and ease of accessibility to the hot-spot database.

Lastly is the policy tool. This tool proposes three policy recommendation for immediate implementation. The first recommendation is to review the surveillance strategy to allow inclusion of other levels of laboratories with good SQI including private laboratories. This will enhance representativeness as data will be generated from a larger number of laboratories rather than a subset of laboratories. Consequently bias is minimised as data validity is improved (Pezzani *et al*., 2020; Cole *et al.,* 2019). The second policy recommends strengthening capacity

of the national reference laboratory (NRL) and establishment of regional reference laboratories (RLL) to supplement the NRL. Thirdly, is establishing a surveillance coordinating centre (SCC) specifically for surveillance related activities. Presently, the NCDC is the national coordinating centre and performs robust and oversight function of all AMR related activities across the five GAP pillars including surveillance. Constituting all the AMR related activities under a single coordinating body is not very practicable. For a more accelerated productivity, strategic objectives of high priority like surveillance need to have a dedicated coordinating centre to allow a governance structure that is more surveillance focused rather than generalised (Nabadda *et al.*, 2021).

In developing the protocol for this project, four research questions (RQ) emerged to help explore different aspects of the topic and substantiate a need for purposeful investigation (Ratan, Anand, and Ratan, 2019). The RQ reflects the characteristics of a good research question including feasibility, interesting, novel, ethical, relevant, manageable, appropriate, publishable, and systematic (FINERMAPS). The RQ also served as a guide to ensure investigations are consistent with the construct under research. A restatement of how this research addressed the proposed RQ is summarised below.

- *What are the gaps in AMR surveillance designs and reporting methodology in Africa?*

The systematic review of 23 surveillance systems (Chapter three) in Africa highlighted gaps in the systems that have implications on data quality and representativeness which consequently impact the usability, validity, and trustworthiness of data (Boes *et al.*, 2020; Chen *et al.*, 2014). Specifically, EQA were not routinely performed across participating laboratories; important surveillance parameters (infection site, patient population, and specimen type) were not frequently recorded; information on incidence-based-indicators were generally lacking and these are data that are needed for disease burden estimates to ensure data-driven action.

- *To what extent is Nigeria implementing the surveillance component of its National Action Plan on AMR?*

From the stakeholders' interview (Chapter five) and the cross-sectional studies (Chapter four), there were evidence that the NAP is being implemented and the strategic steps taken towards its implementation are in-line with the NAP governance framework NAP (Chua *et al.*, 2021). However, some short-medium-long term goals of the NAP have not been met. Some of these goals include standardisation of laboratory capacity for monitoring AMR across human, aquatic, terrestrial and environment; unified system for total quality management of laboratories; adoption of a system for certification and standardisation of laboratories; strengthening capacity of the NRL, and support of eligible sites with technical assistance to meet the minimum requirement for surveillance (NAP, 2017). Consequently, the surveillance has not expanded as anticipated due to these shortcomings despite reaching the 5 year initial implementation timeline of the NAP version one (NAP, 2017). Nevertheless, the NAP has achieved several goals and implemented policies to support surveillance activities including establishment of the three core components of national AMR surveillance indicators (NCC, NRL and surveillance sites); a dedicated technical working group for AMR; ongoing surveillance; mechanism for information sharing; GLASS enrolment and contribution of surveillance data to GLASS.

- *What strategies are currently being used for AMR surveillance in Nigeria?*

The current surveillance strategy for AMR is based on case-finding approach. This approach aims to combine epidemiological, clinical and microbiological data from routine laboratory investigations, although there are concerns around case-finding surveillance system built on tertiary care (Lim *et al.*, 2021; Ryu *et al.*, 2019). Tertiary care is the highest referral centre and oftentimes, health conditions that are referred to this setting are mostly chronic or complex medical conditions and infections that might have failed to respond to treatment (Pezzani *et*

al., 2020). Basing surveillance data on tertiary care level alone has potential for over representing resistant in the population. This is because the denominator (i.e. number of sampled population) for defining the actual case number comprises predominantly of sick people who are more likely to have drug resistant infections compared to the actual ratio in the population (Schnall *et al.*, 2019).

- *How efficient and effective are these strategies in tackling AMR?*

Recall that the efficiency and effectiveness of a surveillance system is associated with its capacity to collect accurate data (Walugembe *et al.*, 2019; Iera *et al.*, 2023). This capacity takes into account the extent to which the surveillance method secures valued outcomes (Reygaert, 2018; Yigit *et al.*, 2011). In determining the efficiency and effectiveness of the surveillance strategy in Nigeria, the organisation of the laboratory network, surveillance approach, data reporting protocol including important metadata, and the quality of data were assessed through a combination of studies. A review of these determinants alongside the health system organisational structure (hierarchical) shows that the current strategy (tertiary-based sentinel) bears a number of limitation which has significant impact on representativeness of data. Although sentinel surveillance is an efficient surveillance method that allows intensive investigation of cases in order to collect necessary information, its efficiency is optimised where there are more sites undertaking surveillance for a system that is based on case-finding approach (Kaur *et al.*, 2021; Bennani *et al.*, 2021). GLASS requires AMR data to be collected through comprehensive surveillance if the system is based on case-finding approach otherwise, case-based surveillance is more appropriate (Ryu *et al.*, 2019; World Health Organisation, 2016). The efficiency and effectiveness attribute also examines the utility and impact of data collected through the system (Walugembe *et al.*, 2019). The current strategy has minimal impacts in terms of its contribution to planning, monitoring and outbreak detection as the surveyed population represent only a fragment of the entire population. Not only does this

exclude patients with mild or asymptomatic cases, it underrepresent community cases, thus making data skewed towards severe cases which can distort the overall AMR spectrum. Tackling AMR requires realistic surveillance data and integrating hospital-based surveillance with other approaches like community-based surveillance which can provide a more accurate understanding of the pattern of AMR in the country (Cornejo *et al.*, 2022).

7.2 Final conclusions

We know that the surveillance system in Nigeria is tertiary-based, but we do not fully understand the surveillance approach, the implications of tertiary-based AMR surveillance on the reliability of data, and the appropriateness of the surveillance approach in the context of Nigeria. As with surveillance systems worldwide, the surveillance system in Nigeria requires strengthening to reach and maintain operational efficiency, although current evidence needed to inform modification and direction of intervention is lacking.

Through a systematic evaluation involving data triangulation from a combination of studies, this research establishes a convergence of evidence that highlight limitations of current approaches and its implications on quality and representativeness of data. This research stands as the first study to evaluate the current surveillance system for AMR following the NAP implementation. From this evaluation, we now know the weaknesses, vulnerabilities and opportunities within the surveillance system and focus for targeted interventions towards improving capacity, and sustainability for future laboratory iteration into the surveillance.

7.3 Recommendations

Based on the results of this research, the following recommendation are put forward as steps towards improving the operationalisation of AMR surveillance in Nigeria and in other LMIC settings:

- The current structure comprising 11 tertiary hospitals is not optimal. Increasing the number of the tertiary hospitals and including secondary and primary care hospitals is

necessary to improve representativeness. However, this will require a cost modelling study to understand the most cost effective combination of hospitals for optimised data output.

- Integrate a feasible evaluation plan to the current national AMR surveillance network that will regularly monitor and improve technical capacity, performance and efficiency of the system. This will ensure continuous observation and improvement of developing frailties to enable the system consistently provide accurate information needed to drive meaningful action.
- Consider additional, alternative or combination of AMR surveillance strategy such as alert organism tracking, enhanced routine, and AMU/AMR integrated surveillance to meet local needs. A comprehensive impact and feasibility assessment as well as economic evaluation of these components will be needed to identify the most effective combination.
- Surveillance is an important NAP strategy for AMR control as they inform design and evaluation of local and international actions as well as treatment guidelines for therapeutic purposes. To meet this target, surveillance protocol should be extended to include key clinical patient information, specifically information on the origin of infection (community or hospital). This is a useful indicator for improving utility of surveillance data.

7.4 Future research

This study highlighted a number of gaps that requires further research:

- Future research will need to pilot test the proposed surveillance enhancement toolkit using a sub-set of laboratories to evaluate its practicability, ease of integration and compliance.

- The SQIs items developed for this research will benefit from further evaluation and testing to qualify as a standardised set of items for assessing the five aspects of laboratory capacity for AMR surveillance. This will allow national surveillance systems to quickly assess and identify laboratories that meet the requirements for surveillance.
- The statistical analysis in chapter 4 shows correlation amongst the SQIs, where performance of one indicator has positive influence on another and vice versa. A further study involving a mix of laboratories is required to test the impact of this correlation in real life. By improving one indicator for each group of laboratory, its impact on the rest of the quality indicators will be measured. The outcome will provide evidence-based information on the most influential quality indicator for overall improvement.

References

Abdu, A., Aboderin, A.O., Elusiyan, J.B., Kolawole, D.O., Lamikanra, A. (2013) Serogroup distribution of Shigella in Ile-Ife, southwest Nigeria. *Tropical gastroenterology : official journal of the Digestive Diseases Foundation*. 34 (3), pp. 164–169. doi:10.7869/tg.121.

Abdullahi, M., Olonitola, S., Inabo, I. (2010) Isolation of bacteria associated with diarrhoea among children attending some hospitals in Kano metropolis, Kano state, Nigeria. *Bayero Journal of Pure and Applied Sciences*. 3 (1), . doi:10.4314/bajopas.v3i1.58549.

Abimiku, A. G., Croxton, T., Akintunde, E., Okelade, B., Jugu, J., Peters, S., Constantine, N. (2010). Experiences in establishing a PEPFAR-supported laboratory quality system in Nigeria. *American Journal of Clinical Pathology*, *134*(4), 541–549. https://doi.org/10.1309/AJCP5RP4QWEQLUZR

Abraham, E.P., Chain E. (1988) An enzyme from bacteria able to destroy penicillin. 1940. Rev.Infect. Dis,10(4):677–8

ACDC (2017) *The impetus to Africa CDC's mandate in curbing the rising trend of Antimicrobial Resistance (AMR) in Africa: the launch of the Africa CDC AMR surveillance network during the 8th advanced course in diagnostics (ACDx)*. 8688 pp. 8–11. doi:10.11604/pamj.2017.28.271.14388.

Acharya, J., Zolfo, M., Enbiale, W., Kyaw, K. W. Y., Bhattachan, M., Rijal, N., Jha, R. (2021). Quality assessment of an antimicrobial resistance surveillance system in a province of Nepal. *Tropical Medicine and Infectious Disease*. https://doi.org/10.3390/tropicalmed6020060

Achi, C. R., Ayobami, O., Mark, G., Egwuenu, A., Ogbolu, D., Kabir, J. (2021). Operationalising One Health in Nigeria: Reflections From a High-Level Expert Panel Discussion Commemorating the 2020 World Antibiotics Awareness Week. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2021.673504

Acuña L, G. (2003). Evolución de la terapia antimicrobiana: Lo que era, lo que es y lo que será. *Revista Chilena de Infectologia*. https://doi.org/10.4067/s0716-10182003020100001

Adams, J., Hillier-Brown, F. C., Moore, H. J., Lake, A. A., Araujo-Soares, V., White, M., Summerbell, C. (2016). Searching and synthesising "grey literature" and "grey information" in public health: Critical reflections on three case studies. *Systematic Reviews*, *5*(1), 1–11. https://doi.org/10.1186/s13643-016-0337-y

Adamu, A. A., Gadanya, M. A., Jalo, R. I., Uthman, O. A., Wiysonge, C. S. (2020). Factors influencing non-prescription sales of antibiotics among patent and proprietary medicine vendors in Kano, Nigeria: A cross-sectional study. *Health Policy and Planning*. https://doi.org/10.1093/heapol/czaa052

Adebowale, O. O., Jimoh, A. B., Adebayo, O. O., Alamu, A. A., Adeleye, A. I., Fasanmi, O. G., Fasina, F. O. (2023). Evaluation of antimicrobial usage in companion animals at a Veterinary Teaching Hospital in Nigeria. *Scientific Reports*. https://doi.org/10.1038/s41598-023-44485-w

Adeniji, F. (2018). Global analysis of strategies to tackle antimicrobial resistance. *International Journal of Pharmacy Practice*, *26*(1), 85–89. https://doi.org/10.1111/ijpp.12365

Adesokan, H. K., Akanbi, I. O., Akanbi, I. M., Obaweda, R. A. (2015). Pattern of antimicrobial usage in livestock animals in South-Western Nigeria: The need for alternative plans. *Onderstepoort Journal of Veterinary Research*. https://doi.org/10.4102/ojvr.v82i1.816

Adeyemi, A.I., Sulaiman, A.A., Solomon, B.B., Chinedu, O.A., Victor, I.A. (2010) Bacterial bloodstream infections in HIV-infected adults attending a lagos teaching hospital. *Journal of Health, Population and Nutrition*. 28 (4), pp. 318–326. doi:10.3329/jhpn.v28i4.6037.

Aenishaenslin, C., Häsler, B., Ravel, A., Parmley, J., Stärk, K., Buckeridge, D. (2019).

Evidence needed for antimicrobial resistance surveillance systems. *Bulletin of the World Health Organisation*, *97*(4), 283. https://doi.org/10.2471/BLT.18.218917

Afolabi, O., Onipede, A., Omotayo, S., Oluyede, C., Olajide, F., Oyelese, A., Olawande, O. (2011) Hospital Acquired Infection in Obafemi Awolowo University Teaching Hospital, Ile-Ife, Southwest, Nigeria: A Ten Year Review (2000-2009). *Sierra Leone Journal of Biomedical Research*. 3 (2), . doi:10.4314/sljbr.v3i2.71812.

Agunos, A., Gow, S. P., Deckert, A. E., Léger, D. F. (2021). Informing stewardship measures in canadian food animal species through integrated reporting of antimicrobial use and antimicrobial resistance surveillance data—part ii, application. *Pathogens*. https://doi.org/10.3390/pathogens10111491

Aibinu, I.E., Ohaegbulam, V.C., Adenipekun, E.A., Ogunsola, F.T., Odugbemi, T.O., Mee, B.J. (2003) Extended-spectrum β-lactamase enzymes in clinical isolates of *Enterobacter* species from Lagos, Nigeria. *Journal of Clinical Microbiology*. 41 (5), pp. 2197–2200. doi:10.1128/JCM.41.5.2197-2200.2003.

Ait Ouakrim, D., Cassini, A., Cecchini, M., Plauchoras, D. (2020). The health and economic burden of antimicrobial resistance. *European Journal of Public Health*. https://doi.org/10.1093/eurpub/ckaa165.1201

Akande-Sholabi, W., Ajamu, A. T. (2021). Antimicrobial stewardship: Assessment of knowledge, awareness of antimicrobial resistance and appropriate antibiotic use among healthcare students in a Nigerian University. *BMC Medical Education*, *21*(1), 1–8. https://doi.org/10.1186/s12909-021-02912-4

Akande, P. A. (2020). Knowledge and practices regarding tuberculosis infection control among nurses in Ibadan , south-west Nigeria : a cross-sectional study. *BMC Health Services Research*, 1–10.

Akindolire, A.E., Tongo, O., Dada-Adegbola, H., Akinyinka, O. (2016) Etiology of early

onset septicemia among neonates at the university college hospital, Ibadan, Nigeria. *Journal of Infection in Developing Countries*. 10 (12), pp. 1338–1344. doi:10.3855/jidc.7830.

Akinjogunla, O.J., Eghafona, N.O., Ekoi, O.H. (2009) Diarrheagenic *Escherichia coli (DEC):* prevalence among ambulatory patients and susceptibility to antimicrobial chemotherapeutic agents. *Journal of Hospital Infection* 1 (3), pp. 34–38.

Akinyemi, K.O., Fakorede, C.O. (2018) Antimicrobial resistance and resistance genes in *salmonella* enterica serovars from Nigeria. *Journal of Antimicrobial Chemotherapy*. 51 (2), pp. 427–429. doi:10.1093/jac/dkg080.

Akinyemi, K.O., Oyefolu, A.O.B., Mutiu, W.B., Iwalokun, B.A., Ayeni, E.S., Ajose, S.O., Obaro, S.K. (2018) Typhoid fever: Tracking the trend in Nigeria. *American Journal of Tropical Medicine and Hygiene*. doi:10.4269/ajtmh.18-0045.

Akortha, E., Egbule, O. (2008) Transfer of tetracycline resistance gene (tetr) between replicons in some enteric bacteria of diarrhoeal origin from some hospitals in South-South, Nigeria. *African Journal of Biotechnology*. 7 (18), . doi:10.4314/AJB.V7I18.59255.

Alemanno A. (2015) Stakeholder engagement in regulatory policy. Brussels: OECD Publishing.

Alexander, F. (1945). Nobel price lecture: https://www.nobelprize.org/uploads/2018/06/fleming-lecture.pdf

Allegranzi, B., Pittet, D. (2009) Role of hand hygiene in healthcare-associated infection prevention *Journal of Hospital Infection*. doi:10.1016/j.jhin.2009.04.019.

Aloh, H. E., Onwujekwe, O. E., Aloh, O. G., Okoronkwo, I. L., Nweke, C. J. (2020). Impact of socioeconomic status on patient experience on quality of care for ambulatory healthcare services in tertiary hospitals in Southeast Nigeria. *BMC Health Services Research*. https://doi.org/10.1186/s12913-020-05332-0

Altorf-van der Kuil, W., Schoffelen, A. F., de Greeff, S. C., Thijsen, S. F. T., Alblas, H. J., Notermans, D. W., Wolfhagen, M. J. H. M. (2017). National laboratory-based surveillance system for antimicrobial resistance: a successful tool to support the control of antimicrobial resistance in the Netherlands. *Eurosurveillance*. https://doi.org/10.2807/1560 7917.ES.2017.22.46.17-00062

Alvarez, J., Lopez, G., Muellner, P., de Frutos, C., Ahlstrom, C., Serrano, T., Ugarte-Ruiz, M. (2020). Identifying emerging trends in antimicrobial resistance using Salmonella surveillance data in poultry in Spain. *Transboundary and Emerging Diseases*. https://doi.org/10.1111/tbed.13346

Amann, S., Neef, K., Kohl, S. (2019) Antimicrobial resistance (AMR). *European Journal of Hospital Pharmacy* . 26 (3), pp. 175–177. doi:10.1136/ejhpharm-2018-001820.

Amin, M. Al, Pasha, M. H., Hoque, M. N., Siddiki, A. Z., Saha, S., Kamal, M. M. (2022). Methodology for laboratory-based antimicrobial resistance surveillance in animals. *Veterinary World*. https://doi.org/10.14202/vetworld.2022.1066-1079

Aminov, R.I. (2010) A brief history of the antibiotic era: Lessons learned and challenges for the future. *Frontiers in Microbiology*. doi:10.3389/fmicb.2010.00134.

Amukele, T. (2017) Africa CDC: Establishing Integrated surveillance and laboratory networks for rapid disease detection and response, control, prevention, and clinical care in africa. *African Journal of Laboratory Medicine*. 6 (1), pp. 2002–2004. doi:10.4102/ajlm.v6i1.638.

Anagaw, B., Gezachew, M., Biadgelgene, F., Anagaw, B., Geleshe, T., Taddese, B., Getie, B., Endris, M., Mulu, A., Unakal, C. (2013) Antimicrobial susceptibility patterns of Streptococcus pneumoniae over 6 years at Gondar University Hospital, Northwest Ethiopia. *Asian Pacific Journal of Tropical Biomedicine*. 3 (7), pp. 536–541. doi:10.1016/S2221-1691(13)60109-4.

Anderson, M, Schulze, K., Cassini, A., Plauchoras, D., Mossialos, E. (2020). Strengthening implementation of antimicrobial resistance national action plans. *European Journal of Public Health*. https://doi.org/10.1093/eurpub/ckaa165.1200

Anderson, Michael, Schulze, K., Cassini, A., Plachouras, D., Mossialos, E. (2019). A governance framework for development and assessment of national action plans on antimicrobial resistance. *The Lancet Infectious Diseases*. https://doi.org/10.1016/S1473-3099(19)30415-3

Angell, B., Sanuade, O., Adetifa, I. M. O., Okeke, I. N., Adamu, A. L., Aliyu, M. H., Abubakar, I. (2022). Population health outcomes in Nigeria compared with other west African countries, 1998–2019: a systematic analysis for the Global Burden of Disease Study. *The Lancet*. https://doi.org/10.1016/S0140-6736(21)02722-7

Anon (2019) The European union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2017. *EFSA Journal*. doi:10.2903/j.efsa.2019.5598.

Antony, J., Lancastle, J., McDermott, O., Bhat, S., Parida, R., Cudney, E. A. (2021). An evaluation of Lean and Six Sigma methodologies in the national health service. *International Journal of Quality and Reliability Management*. https://doi.org/10.1108/IJQRM-05-2021-0140

Antwi, S. K., Kasim, H. (2015). Qualitative and Quantitative Research Paradigms in Business Research: A Philosophical Reflection Performance Management Practices in the Ghanaian local government system View project. *European Journal of Business and Management*.

Anzaku, A.A., Alagi, M., Upla, P., Godwin, O., Owoseni, M., Dauda, O., Juliet, A., Oa, O.T., Uchenna, O. (2018) Surveillance of Antimicrobial Resistance in Emerging and Reemerging Infectious Diseases in Nigeria. *EC Microbiology*. 14 (2015), pp. 567–577.

Arenas, N.E., Abril, D.A., Valencia, P., Khandige, S., Soto, C.Y., Moreno-Melo, V.

(2017) Screening food-borne and zoonotic pathogens associated with livestock practices in the Sumapaz region, Cundinamarca, Colombia. *Tropical Animal Health and Production*. doi:10.1007/s11250-017-1251-6.

Arnold, J.W., Simpson, J.B., Roach, J., Kwintkiewicz, J., Azcarate-Peril, M.A. (2018) Intra-species genomic and physiological variability impact stress resistance in strains of probiotic potential. *Frontiers in Microbiology*. 9 (FEB), . doi:10.3389/fmicb.2018.00242.

Aromataris, E., Fernandez, R., Godfrey, C. M., Holly, C., Khalil, H., Tungpunkom, P. (2015). Summarizing systematic reviews: Methodological development, conduct and reporting of an umbrella review approach. *International Journal of Evidence-Based Healthcare*. https://doi.org/10.1097/XEB.0000000000000055

Aronson J. (1994). A pragmatic view of thematic analysis. *The Qualitative Report*, 2, 1–3. Retrieved from http://www.nova.edu/ssss/QR/BackIssues/QR2-1/aronson.html
Ashkenazi, S., Levy, I., Kazaronovski, V., Samra, Z. (2003) Growing antimicrobial resistance of Shigella isolates. *Journal of Antimicrobial Chemotherapy*. 51 (2), pp. 427–429. doi:10.1093/jac/dkg080.

Ashley, E. A., Shetty, N., Patel, J., Van Doorn, R., Limmathurotsakul, D., Feasey, N. A., Peacock, S. J. (2019). Harnessing alternative sources of antimicrobial resistance data to support surveillance in low-resource settings. *Journal of Antimicrobial Chemotherapy*, *74*(3), 541–546. https://doi.org/10.1093/jac/dky487

Ashraf, M., -Mustafa, B.-E., -Rehman, S.-U., Khalid Bashir, M., Adnan Ashraf, M. (2019). Emergence of Antimicrobial Resistance, Causes, Molecular Mechanisms, and Prevention Strategies: A Bovine Perspective. In *Bovine Science - A Key to Sustainable Development*. https://doi.org/10.5772/intechopen.79757

Aslam, S., Emmanuel, P. (2010). Formulating a researchable question: A critical step for facilitating good clinical research. *Indian Journal of Sexually Transmitted Diseases*. https://doi.org/10.4103/0253-7184.69003

ASLM-MAAP (2018) *Public health laboratory capacity to control infectious diseases threats*. 5 (347), pp. 196–197. doi:10.1787/health_glance_eur-2018-58-en.

ASOA (2020) Alliance to save our antibiotics. https://www.saveourantibiotics.org/media/1791/comparison-of-us-and-uk-farm-antibiotic-use.pdf

Austin, P. C., Steyerberg, E. W. (2017). Events per variable (EPV) and the relative performance of different strategies for estimating the out-of-sample validity of logistic regression models. *Statistical Methods in Medical Research*. https://doi.org/10.1177/0962280214558972

Ayukekbong, J. A., Ntemgwa, M., Atabe, A. N. (2017). The threat of antimicrobial resistance in developing countries: Causes and control strategies. *Antimicrobial Resistance and Infection Control*, *6*(1), 1–8. https://doi.org/10.1186/s13756-017-0208-x

Ball, T.A., Fedorka-Cray, P.J., Horovitz, J. and Thakur, S. (2018) Molecular Characterization of Salmonella spp. from Cattle and Chicken Farms in Uganda. *Online Journal of Public Health Informatics*. doi:10.5210/ojphi.v10i1.8934.

Bancroft, E.A. (2019) *CDC Approach to Controlling AMR : Domestic and International Projects*.

Badger-Emeka, L. I., Emeka, P. M., Okosi, M. (2018). Evaluation of the extent and reasons for increased non-prescription antibiotics use in a University town, Nsukka Nigeria. *International Journal of Health Sciences*, *12*(4), 11.

Becker, L., Kaase, M., Pfeifer, Y., Fuchs, S., Reuss, A., von Laer, A., Sin, M.A., Korte-Berwanger, M., Gatermann, S., Werner, G. (2018) Genome-based analysis of Carbapenemase-producing Klebsiella pneumoniae isolates from German hospital patients, 2008-2014. *Antimicrobial Resistance and Infection Control*. doi:10.1186/s13756-018-0352-y.

Bellino, S.; Iacchini, S.; Monaco, M.; Del Grosso, M.; Camilli, R.; Errico, G.; Giufrè, M.; Sisi, S.; D'ancona, F.; Pantosti, A. (2021) *AR-ISS: Sorveglianza Nazionale Dell'Antibiotico-Resistenza. Dati 2020*; Rapporti ISS Sorveglianza RIS-1/2021; Istituto Superiore di Sanità: Rome, Italy.

Bengtsson-Palme, J., Kristiansson, E., Larsson, D.G.J. (2018) Environmental factors influencing the development and spread of antibiotic resistance *FEMS Microbiology Reviews*. doi:10.1093/femsre/fux053.

Bennani, H., Cornelsen, L., Stärk, K. D. C., Häsler, B. (2021). Evaluating Integrated Surveillance for Antimicrobial Use and Resistance in England: A Qualitative Study. *Frontiers in Veterinary Science*. https://doi.org/10.3389/fvets.2021.743857

Bennett, J., Plummer, K. (1984). Documents of Life: An Introduction to the Problems and Literature of a Humanistic Method. *Contemporary Sociology*. https://doi.org/10.2307/2068320

Benzies, K. M., Premji, S., Hayden, K. A., Serrett, K. (2006). State-of-the-evidence reviews: Advantages and challenges of including grey literature. *Worldviews on Evidence-Based Nursing*. https://doi.org/10.1111/j.1741-6787.2006.00051.x

Bernabé, K.J., Langendorf, C., Ford, N., Ronat, J.B., Murphy, R.A. (2017) Antimicrobial resistance in West Africa: a systematic review and meta-analysis *International Journal of Antimicrobial Agents*. doi:10.1016/j.ijantimicag.2017.07.002.

Beyene, A. M., Andualem, T., Dagnaw, G. G., Getahun, M., LeJeune, J., Ferreira, J. P. (2023). Situational analysis of antimicrobial resistance, laboratory capacities, surveillance systems and containment activities in Ethiopia: A new and one health approach. *One Health*. https://doi.org/10.1016/j.onehlt.2023.100527

Birgand, G., Castro-Sánchez, E., Hansen, S., Gastmeier, P., Lucet, J. C., Ferlie, E., Ahmad,

R. (2018). Comparison of governance approaches for the control of antimicrobial resistance: Analysis of three European countries. *Antimicrobial Resistance and Infection Control*. https://doi.org/10.1186/s13756-018-0321-5

Boeras, D. I., Peeling, R. W., Onyebujoh, P., Yahaya, A. A., Gumede-Moeletsi, H. N., Ndihokubwayo, J. B. (2016). The WHO AFRO external quality assessment programme (EQAP): Linking laboratory networks through EQA programmes. *African Journal of Laboratory Medicine*. https://doi.org/10.4102/ajlm.v5i2.560

Boes L, Houareau C, Altmann D. (2020) Evaluation of the German surveillance system for hepatitis B regarding timeliness, data quality, and simplicity, from 2005 to 2014. *Public Health 2020;180:141–*
8.doi:10.1016/j.puhe.2019.11.012pmid:http://www.ncbi.nlm.nih.gov/pubmed/31918048

Bolarinwa, O. A. (2020). Sample size estimation for health and social science researchers: The principles and considerations for different study designs. *The Nigerian Postgraduate Medical Journal*. https://doi.org/10.4103/npmj.npmj_19_20

Bordier, M., Goutard, F. L., Antoine-Moussiaux, N., Pham-Duc, P., Lailler, R., Binot, A. (2021). Engaging Stakeholders in the Design of One Health Surveillance Systems: A Participatory Approach. *Frontiers in Veterinary Science*. https://doi.org/10.3389/fvets.2021.646458

Bortolaia, V., Espinosa-Gongora, C. and Guardabassi, L. (2016) Human health risks associated with antimicrobial-resistant enterococci and Staphylococcus aureus on poultry meat *Clinical Microbiology and Infection*. doi:10.1016/j.cmi.2015.12.003.

Boyatzis Richard. (1998). Transforming qualitative information : thematic analysis and code development - Plymouth University (Alma). In *Qualitative Health Research*.

Boyd, N. K., Teng, C., Frei, C. R. (2021). Brief Overview of Approaches and Challenges in New Antibiotic Development: A Focus On Drug Repurposing. *Frontiers in Cellular and*

Infection Microbiology. https://doi.org/10.3389/fcimb.2021.684515

Boyd, C. (2001). Phenomenology the method. In *Nursing research: A qualitative perspective*.

Braun, V., Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*. https://doi.org/10.1191/1478088706qp063oa

Browne, A. J., Chipeta, M. G., Haines-Woodhouse, G., Kumaran, E. P. A., Hamadani, B. H. K., Zaraa, S., Dolecek, C. (2021). Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study. *The Lancet Planetary Health*. https://doi.org/10.1016/S2542-5196(21)00280-1

Brown, K., Uwiera, R.R.E., Kalmokoff, M.L., Brooks, S.P.J., Inglis, G.D. (2017) Antimicrobial growth promoter use in livestock: a requirement to understand their modes of action to develop effective alternatives *International Journal of Antimicrobial Agents*. doi:10.1016/j.ijantimicag.2016.08.006.

Browne, A. J., Chipeta, M. G., Haines-Woodhouse, G., Kumaran, E. P. A., Hamadani, B. H. K., Zaraa, S., Dolecek, C. (2021). Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study. *The Lancet Planetary Health*. https://doi.org/10.1016/S2542-5196(21)00280-1

Bryskier, A. (2005) Antimicrobial agents: Antibacterials and antifungals. *ASM Press*. doi:10.1093/jac/dkl218.

Bujang, M. A, Omar, E.D, Baharum, N. A.(2018) A Review on Sample Size Determination for Cronbach's Alpha Test: A Simple Guide for Researchers. *Malays J Med Sci*. Nov;25(6):85-99. doi: 10.21315/mjms2018.25.6.9. Epub 2018 Dec 28. PMID: 30914882; PMCID: PMC6422571.

Burls, A. (2009) What is a critical appraisal:

https://www.academia.edu/92786872/What_Is_Critical_Appraisal

Calba, C., Goutard, F. L., Hoinville, L., Hendrikx, P., Lindberg, A., Saegerman, C., Peyre, M. (2015). Surveillance systems evaluation: A systematic review of the existing approaches. *BMC Public Health*, *15*(1). https://doi.org/10.1186/s12889-015-1791-5

CalSWEC., University of California Berkeley (2019). How to build an implementation toolkit from start to finish. https://calswec.berkeley.edu/toolkits/implementation-toolkits/how-build-implementation-toolkit-start-finish

Campbell, M., McKenzie, J. E., Sowden, A., Katikireddi, S. V., Brennan, S. E., Ellis, S., Thomson, H. (2020). Synthesis without meta-analysis (SWiM) in systematic reviews: Reporting guideline. *The BMJ*, *368*, 1–6. https://doi.org/10.1136/bmj.l6890

Campbell, R., Goodman-Williams, R., Feeney, H., Fehler-Cabral, G. (2020). Assessing Triangulation Across Methodologies, Methods, and Stakeholder Groups: The Joys, Woes, and Politics of Interpreting Convergent and Divergent Data. *American Journal of Evaluation*. https://doi.org/10.1177/1098214018804195

Cani, E., Park, T.E., Kavanagh, R. (2019) Antiviral drugs. In: *Side Effects of Drugs Annual*. doi:10.1016/bs.seda.2019.10.005.

Caniça, M., Manageiro, V., Abriouel, H., Moran-Gilad, J., Franz, C.M.A.P. (2019) Antibiotic resistance in foodborne bacteria *Trends in Food Science and Technology*. doi:10.1016/j.tifs.2018.08.001.

Centers for Disease Control (CDC). (1988). Guidelines for evaluating surveillance systems. *MMWR Supplements*.

Ceric, O., Tyson, G. H., Goodman, L. B., Mitchell, P. K., Zhang, Y., Prarat, M., Reimschuessel, R. (2019). Enhancing the one health initiative by using whole genome sequencing to monitor antimicrobial resistance of animal pathogens: Vet-LIRN collaborative

project with veterinary diagnostic laboratories in United States and Canada. *BMC Veterinary Research*. https://doi.org/10.1186/s12917-019-1864-2

Chalmers, J.D., Rother, C., Salih, W., Ewig, S. (2014) Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: A systematic review and meta-analysis *Clinical Infectious Diseases*. doi:10.1093/cid/cit734.

Chang, Q., Wang, W., Regev-Yochay, G., Lipsitch, M., Hanage, W.P. (2015) Antibiotics in agriculture and the risk to human health: How worried should we be? *Evolutionary Applications*. doi:10.1111/eva.12185.

Chastre, J. (2008) Evolving problems with resistant pathogens *Clinical Microbiology and Infection*. doi:10.1111/j.1469-0691.2008.01958.x.

Chatterjee, A., Modarai, M., Naylor, N. R., Boyd, S. E., Atun, R., Barlow, J., Robotham, J. V. (2018). Review Quantifying drivers of antibiotic resistance in humans: a systematic review. *www.Thelancet.Com/Infection*. https://doi.org/10.1016/S1473-3099(18)30296-2

Chee-Sanford, J.C., Mackie, R.I., Koike, S., Krapac, I.G., Lin, Y.-F., Yannarell, A.C., Maxwell, S., Aminov, R.I. (2009) Fate and Transport of Antibiotic Residues and Antibiotic Resistance Genes following Land Application of Manure Waste. *Journal of Environmental Quality*. 38 (3), pp. 1086–1108. doi:10.2134/jeq2008.0128.

Chen H., Hailey D., Wang N., Yu P. (2014). A review of data quality assessment methods for public health information systems. *International Journal of Environmental Research and Public Health*, 11(5), 5170–5207. https://doi.org/10.3390/ijerph110505170

Chereau, F., Opatowski, L., Tourdjman, M., Vong, S. (2017). Risk assessment for antibiotic resistance in South East Asia. *BMJ (Online)*. https://doi.org/10.1136/bmj.j3393

Chokshi, A., Sifri, Z., Cennimo, D., Horng, H. (2019). Global contributors to antibiotic resistance. *Journal of Global Infectious Diseases*. https://doi.org/10.4103/jgid.jgid_110_18

Chua, A. Q., Verma, M., Hsu, L. Y., Legido-Quigley, H. (2021). An analysis of national action plans on antimicrobial resistance in Southeast Asia using a governance framework approach. *The Lancet Regional Health - Western Pacific*. https://doi.org/10.1016/j.lanwpc.2020.100084

Chukwu, E. E., Oladele, D. A., Awoderu, O. B., Afocha, E. E., Lawal, R. G., Abdus-Salam, I., Audu, R. A. (2020). A national survey of public awareness of antimicrobial resistance in Nigeria. *Antimicrobial Resistance and Infection Control*. https://doi.org/10.1186/s13756-020-00739-0

Chung, D.R., Song, J.H., Kim, S.H., Thamlikitkul, V., Huang, S.G., Wang, H., So, T.M.K., Yasin, R.M.D., Hsueh, P.R., Carlos, C.C., Hsu, L.Y., Buntaran, L., Lalitha, M.K., Kim, M.J. (2011) High prevalence of multidrug-resistant nonfermenters in hospital-acquired pneumonia in Asia. *American Journal of Respiratory and Critical Care Medicine* [online]. 184 (12), pp. 1409–1417. Available from: http://www.atsjournals.org/doi/abs/10.1164/rccm.201102-0349OCdoi:10.1164/rccm.201102-0349OC

Clark, N.M., Zhanel, G.G., Lynch, J.P. (2016) Emergence of antimicrobial resistance among Acinetobacter species: A global threat *Current Opinion in Critical Care* 22 (5) p.pp. 491–499. doi:10.1097/MCC.0000000000000337.

Clarke, A. E., Friese, C., Washburn, R. S. (2017). Situational analysis grounded theory after the interpretive turn. *Situational Analysis Grounded Theory after the Interpretive Turn*.

Clift, C. (2019) Review of Progress on Antimicrobial Resistance: Background and Analysis. *Centre on Global Health Security*. (October), pp. 54. doi:10.13140/RG.2.2.22042.80323.

Cokol, M., Chua, H.N., Tasan, M., Mutlu, B., Weinstein, Z.B., Suzuki, Y., Nergiz, M.E., Costanzo, M., Baryshnikova, A., Giaever, G., Nislow, C., Myers, C.L., Andrews, B.J., Boone, C. (2011) Systematic exploration of synergistic drug pairs. *Molecular Systems*

Biology. doi:10.1038/msb.2011.71.

Cole, M. J., Quaye, N., Jacobsson, S., Day, M., Fagan, E., Ison, C., Unemo, M. (2019). Ten years of external quality assessment (EQA) of Neisseria gonorrhoeae antimicrobial susceptibility testing in Europe elucidate high reliability of data. *BMC Infectious Diseases*, *19*(1), 1–11. https://doi.org/10.1186/s12879-019-3900-z

Corburn, J. (2017). Concepts for Studying Urban Environmental Justice. *Current Environmental Health Reports*. https://doi.org/10.1007/s40572-017-0123-6

Cornejo, J., Asenjo, G., Zavala, S., Venegas, L., Galarce, N., Hormazábal, J. C., Lapierre, L. (2022). Advances in Integrated Antimicrobial Resistance Surveillance and Control Strategies in Asia-Pacific Economic Cooperation Economies: Assessment of a Multiyear Building Capacity Project. *Antibiotics*. https://doi.org/10.3390/antibiotics11081022

Costa-Santos, C., Neves, A. L., Correia, R., Santos, P., Monteiro-Soares, M., Freitas, A., Fonseca, J. A. (2021). COVID-19 surveillance data quality issues: A national consecutive case series. *BMJ Open*. https://doi.org/10.1136/bmjopen-2020-047623

Cox, J.A., Vlieghe, E., Mendelson, M., Wertheim, H., Ndegwa, L., Villegas, M. V., Gould, I., Levy Hara, G. (2017) Antibiotic stewardship in low- and middle-income countries: the same but different? *Clinical Microbiology and Infection* [online]. 23 (11), pp. 812–818. Available from: https://doi.org/10.1016/j.cmi.2017.07.010doi:10.1016/j.cmi.2017.07.010.

Crabtree B., Miller W. (1999). Using codes and code manuals: A template for organizing style of interpretation. *Doing qualitative research* (2nd ed., pp. 163–178). Newbury Park, CA: Sage.

Crotty, M. (1998). Foundations of Social Research: Meaning and perspective in the research process (1st ed.). Routledge. https://doi.org/10.4324/9781003115700

Dacombe, R., Bates, I., Bhardwaj, M., Wallis, S., Pulford, J. (2016) *Fleming Fund:*

supporting surveillance capacity for antimicrobial resistance An analysis of approaches to laboratory capacity strengthening for drug resistant infections in low and middle income countries. (June), .

Dar, O. A., Hasan, R., Schlundt, J., Harbarth, S., Caleo, G., Dar, F. K., Heymann, D. L. (2016). Exploring the evidence base for national and regional policy interventions to combat resistance. *The Lancet*. https://doi.org/10.1016/S0140-6736(15)00520-6

Datema, T. A. M., Oskam, L., Broerse, J. E. W., Klatser, P. R. (2020). Review of the Stepwise Laboratory Quality Improvement Process towards Accreditation (SLIPTA) version 2:2015. *African Journal of Laboratory Medicine*, *9*(1), 1–7. https://doi.org/10.4102/AJLM.V9I1.1068

De Clercq, E., Li, G. (2016) Approved antiviral drugs over the past 50 years *Clinical Microbiology Reviews*. doi:10.1128/CMR.00102-15.

De Kraker, M. E. A., Stewardson, A. J., Harbarth, S. (2016). Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? *PLoS Medicine*, *13*(11), 1–6. https://doi.org/10.1371/journal.pmed.1002184

Deoras, G., Mantel-Teeuwisse, A. K., Iessa, N., Pal, S. (2016). Economic costs of adverse reactions to drugs (ADRs) in low and middle-income countries (LMICs). *Drug Safety*.

Dervin, B. (1983). An overview of sense-making research: Concepts, methods and results. Paper presented at the annual meeting of the International Communication Association, Dallas, TX, May. [On-line]. Available: http://communication.sbs.ohio-state.edu/sense-making/art/artdervin83.html

Dheda, K., Gumbo, T., Maartens, G., Dooley, K.E., McNerney, R., Murray, M., Furin, J., Nardell, E.A., London, L., Lessem, E., Theron, G., van Helden, P., Niemann, S., Merker, M. (2017) The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis *The Lancet*

Respiratory Medicine. doi:10.1016/S2213-2600(17)30079-6.

Diene, S.M., Rolain, J.-M. (2013) Investigation of antibiotic resistance in the genomic era of multidrug-resistant Gram-negative bacilli, especially Enterobacteriaceae, Pseudomonas and Acinetobacter. *Expert review of anti-infective therapy* [online]. 11 (3), pp. 277–296. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23458768doi:10.1586/eri.13.1.

Dismukes, W.E. (2000) Introduction to Antifungal Drugs. *Clinical Infectious Diseases*. doi:10.1086/313748.

Dormann, C. F., Elith, J., Bacher, S., Buchmann, C., Carl, G., Carré, G., Lautenbach, S. (2013). Collinearity: A review of methods to deal with it and a simulation study evaluating their performance. *Ecography*, *36*(1), 27–46. https://doi.org/10.1111/j.1600 0587.2012.07348.x

Draganova, A. (2015). Book Review: Irving Seidman, Interviewing as Qualitative Research: A Guide for Researchers in Education & the Social Sciences . *Qualitative Research*. https://doi.org/10.1177/1468794114535050

Dramowski, A., Bekker, A., Anugulruengkitt, S., Bayani, O., Martins Gonçalves, F., Naizgi, M., Coffin, S. (2022). Keeping It Real: Infection Prevention and Control Problems and Solutions in Low- and Middle-income Countries. *Pediatric Infectious Disease Journal*. https://doi.org/10.1097/INF.0000000000003319

Driscoll, J.A., Brody, S.L., Kollef, M.H. (2007) The epidemiology, pathogenesis and treatment of Pseudomonas aeruginosa infections *Drugs*. doi:10.2165/00003495-200767030-00003.

Dunachie, S. J., Day, N. P., Dolecek, C. (2020). The challenges of estimating the human global burden of disease of antimicrobial resistant bacteria. *Current Opinion in Microbiology*. https://doi.org/10.1016/j.mib.2020.09.013

Dung, N.T.T., Truong, B.D., Cuong, N. V., Van, N.T.B., Phu, D.H., Kiet, B.T., Rueanghiran, C., Hien, V.B., Thwaites, G., Rushton, J. and Carrique-Mas, J. (2020) A survey of retail prices of antimicrobial products used in small-scale chicken farms in the Mekong Delta of Vietnam. *Globalization and health*. 16 (1), pp. 8. doi:10.1186/s12992-019-0539-x.

Duru, E.E., Umoren, F.E. (2014) *Bacterial Agents Associated With Infantile Diarrhea and Their Antibiotics Susceptibility Pattern in Port Harcourt, South- South, Nigeria*.

EARS-NET (2022) Antimicrobial resistance in the EU/EEA - Annual epidemiological report https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2022

EARS-NET (2018) Surveillance of antimicrobial resistance in Europe 2018 https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2018

EC. (2017) European Commission: Regulation (EU) 2017/2101 https://www.emcdda.europa.eu/drugs-library/regulation-eu-20172101-european-parliament-and-council-15-november-2017-amending-regulation-ec-no-19202006-regards-information-exchange-and-early-warning-system-and-risk-assessment-procedure-new-psychoactive-substance_hu

Economou, V., Gousia, P. (2015) Agriculture and food animals as a source of antimicrobial-resistant bacteria *Infection and Drug Resistance*. doi:10.2147/IDR.S55778.

Egbule, O. (2014) Antimicirobial Susceptibility Patterns of *Escherichia coli* and *Shigella* sp Isolated from Diarrhoea Stool of Children. *Bayero Journal of Pure and Applied Sciences*. 6 (1), pp. 62. doi:10.4314/bajopas.v6i1.13.

Ellington, M. J., Ekelund, O., Aarestrup, F. M., Canton, R., Doumith, M., Giske, C., Woodford, N. (2017). The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST Subcommittee. *Clinical Microbiology and*

Infection. https://doi.org/10.1016/j.cmi.2016.11.012

Enzenbach, C., Wicklein, B., Wirkner, K., Loeffler, M. (2019). Evaluating selection bias in a population-based cohort study with low baseline participation: The LIFE-Adult-Study. *BMC Medical Research Methodology*. https://doi.org/10.1186/s12874-019-0779-8

Errasti-Ibarrondo, B., Jordán, J. A., Díez-Del-Corral, M. P., Arantzamendi, M. (2018). Conducting phenomenological research: Rationalizing the methods and rigour of the phenomenology of practice. *Journal of Advanced Nursing*. https://doi.org/10.1111/jan.13569

ESPAUR-UK (2019) *Public Health England: English Surveillance Programme for Animicrobial Utilisation and Resistance (ESPAUR) - Report 2018-2019*. pp. 150. Available from:https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment data/file/843129/English_Surveillance_Programme_for_Antimicrobial_Utilisation_and_Resistance_2019.pdf.

Espinel-Ingroff, A. (2019) Antifungal agents. In: *Encyclopedia of Microbiology*. doi:10.1016/B978-0-12-801238-3.02386-2.

Espona, M. J. (2021). Early warning and disease surveillance: Anew model research-in-progress. *Proceedings of the Information Systems Education Conference, ISECON*.

Essack, S.Y., Desta, A.T., Abotsi, R.E., Agoba, E.E. (2017) Antimicrobial resistance in the WHO African region: Current status and roadmap for action *Journal of Public Health (United Kingdom)*. doi:10.1093/pubmed/fdw015.

European Centre for Disease Prevention and Control (2014). *Data quality monitoring and surveillance system evaluation.* Retrieved from https://www.ecdc.europa.eu/en/publications-data/data-quality-monitoring-and- surveillance-system-evaluation-handbook-methods-and

European Centre for Disease Prevention and Control (2018) *Surveillance of antimicrobial resistance in Europe Annual report of the European Antimicrobial Resistance Surveillance*

Network (EARS-Net) 2017.

FAO/OIE/WHO (2016) *WHO | FAO/OIE/WHO Collaboration (Tripartite)*. Available from: https://www.who.int/foodsafety/areas_work/zoonose/concept-note/en/

FAO (2017) *Kenya launches 'One Health' national plan and policy to tackle antimicrobial resistance |Antimicrobial Resistance|FAO*. Available from: http://www.fao.org/antimicrobial-resistance/news-and-events/news/news-details/en/c/1069750/

Fashae, K., Ogunsola, F., Aarestrup, F.M., Hendriksen, R.S. (2010a) Antimicrobial susceptibility and serovars of Salmonella from chickens and humans in Ibadan, Nigeria. *Journal of Infection in Developing Countries*. doi:10.3855/jidc.909.

Fashae, K., Ogunsola, F., Aarestrup, F.M., Hendriksen, R.S. (2010b) Antimicrobial susceptibility and serovars of Salmonella from chickens and humans in Ibadan, Nigeria. *Journal of Infection in Developing Countries*. 4 (8), pp. 484–494. doi:10.3855/jidc.909.

Fereday J., Muir-Cochrane E. (2006). Demonstrating rigor using thematic analysis: A hybrid approach of inductive and deductive coding and theme development. *International Journal of Qualitative Research*, 5, 80–92. Retrieved from http://ejournals.library.ualberta.ca/index.php/IJQM/article/view/4411/3530

Ferguson, N.M., Cummings, D.A.T., Cauchemez, S., Fraser, C., Riley, S., Meeyai, A., Iamsirithaworn, S., Burke, D.S. (2005) Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature*. doi:10.1038/nature04017.

Ferri, M., Ranucci, E., Romagnoli, P., Giaccone, V. (2017) Antimicrobial resistance: A global emerging threat to public health systems. *Critical Reviews in Food Science and Nutrition*. doi:10.1080/10408398.2015.1077192.

Figueiredo, R., Henriques, A., Sereno, R., Mendonça, N., Da Silva, G.J. (2015) Antimicrobial resistance and extended-spectrum β-lactamases of Salmonella enterica

serotypes isolated from livestock and processed food in Portugal: An Update. *Foodborne Pathogens and Disease*. doi:10.1089/fpd.2014.1836.

Fixsen, D. L., Naoom, S. F., Blase, K. a, Friedman, R. M., Wallace, F. (2005). Implementation Research: A Synthesis of the Literature. *Tampa, FL: University of South Florida, Louis de La Parte Florida Mental Health Institute, The National Implementation Research Network*. https://doi.org/10.1017/CBO9781107415324.004

Flannelly, L. T., Flannelly, K. J., Jankowski, K. R. B. (2014). Independent, Dependent, and Other Variables in Healthcare and Chaplaincy Research. *Journal of Health Care Chaplaincy*. https://doi.org/10.1080/08854726.2014.959374

Fleming Fund-Nigeria (2019) *Nigeria: Country Grant | Fleming Fund*. Available from: https://www.flemingfund.org/grants/nigeria-country-grant/

Fleming Fund. (2019) *Nigeria: Professional Fellowship | Fleming Fund*. Available from: https://www.flemingfund.org/grants/nigeria-professional-fellowship/

Fonjungo, P.N., Kebede, Y., Messele, T., Ayana, G., Tibesso, G., Abebe, A., Nkengasong, J.N., Kenyon, T. (2018) Laboratory equipment maintenance: A critical bottleneck for strengthening health systems in sub-Saharan Africa. *Journal of Public Health Policy*. 33 (1), pp. 34–45. doi:10.1057/jphp.2011.57.

Fortini, D., Fashae, K., Villa, L., Feudi, C., García-Fernández, A., Carattoli, A. (2015) A novel plasmid carrying blaCTX-M-15 identified in commensal Escherichia coli from healthy pregnant women in Ibadan, Nigeria. *Journal of Global Antimicrobial Resistance*. 3 (1), pp. 9–12. doi:10.1016/j.jgar.2014.12.002.

Fouz, N., Pangesti, K.N.A., Yasir, M., Al-Malki, A.L., Azhar, E.I., Hill-Cawthorne, G.A., El Ghany, M.A. (2020) The contribution of wastewater to the transmission of antimicrobial resistance in the environment: Implications of mass gathering settings *Tropical Medicine and Infectious Disease* 5 (1). doi:10.3390/tropicalmed5010033.

Freire-Moran, L., Aronsson, B., Manz, C., Gyssens, I.C., So, A.D., Monnet, D.L., Cars, O. (2011) Critical shortage of new antibiotics in development against multidrug-resistant bacteria - Time to react is now. In: *Drug Resistance Updates*. 2011 doi:10.1016/j.drup.2011.02.003.

Frost, I., Kapoor, G., Craig, J., Liu, D., Laxminarayan, R. (2021). Status, challenges and gaps in antimicrobial resistance surveillance around the world. *Journal of Global Antimicrobial Resistance*. https://doi.org/10.1016/j.jgar.2021.03.016

Fruci, M., Poole, K. (2016) Bacterial Stress Responses as Determinants of Antimicrobial Resistance. In: *Stress and Environmental Regulation of Gene Expression and Adaptation in Bacteria*. doi:10.1002/9781119004813.ch10.

Frumence, G., Mboera, L. E. G., Katale, B. Z., Sindato, C., Kimera, S., Durrance-Bagale, A., Matee, M. (2021). Policy actors and human and animal health practitioners' perceptions of antimicrobial use and resistance in Tanzania: A qualitative study. *Journal of Global Antimicrobial Resistance*. https://doi.org/10.1016/j.jgar.2021.02.027

Gail, M. H., Altman, D. G., Cadarette, S. M., Collins, G., Evans, S. J. W., Sekula, P., Woodward, M. (2019). Design choices for observational studies of the effect of exposure on disease incidence. *BMJ Open*. https://doi.org/10.1136/bmjopen-2019-031031

Galimand, M., Courvalin, P., Lambert, T. (2003) Plasmid-mediated high-level resistance to aminoglycosides in Enterobacteriaceae due to 16S rRNA methylation. *Antimicrobial Agents and Chemotherapy*. doi:10.1128/AAC.47.8.2565-2571.2003.

GASP (2021) Gonococcal Antimicrobial Surveillance Programme: https://www.who.int/initiatives/gonococcal-antimicrobial-surveillance-programme

Gelband, H., Delahoy, M. (2014) Policies to Address Antibiotic Resistance in Low- and Middle-Income Countries. *The Lancet Global Health* [online]. 6 (7), pp. e732. Available

from: http://dx.doi.org/10.1016/S2214-109X(18)30270-5%0Ahttp://dx.doi.org/10.1111/j.1469-0691.2009.02725.x%0Ahttps://www.cddep.org/sites/default/files/abrinlmics_cddep_gelband and_delahoy_9-14.pdfdoi:10.1111/1469-0691.2009.02725.

George, J., Häsler, B., Mremi, I., Sindato, C., Mboera, L., Rweyemamu, M., Mlangwa, J. (2020). A systematic review on integration mechanisms in human and animal health surveillance systems with a view to addressing global health security threats. *One Health Outlook*. https://doi.org/10.1186/s42522-020-00017-4

Gerrard, E. (2016) *Infection control and hygiene: ensuring high standards in practice*. *Infection Control & Hospital Epidemiology*. doi:10.1086/591861.

Ghannoum, M.A., Rice, L.B. (1999) Antifungal agents: Mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance *Clinical Microbiology Reviews*. doi:10.1128/cmr.12.4.501.

Ghose, C. (2013) Clostridium difficile infection in the twenty-first century *Emerging Microbes and Infections*. doi:10.1038/emi.2013.62.

Ghoshal, U., Vasanth, S.,Tejan, N. (2020). A guide to laboratory diagnosis of Corona Virus Disease-19 for the gastroenterologists. *Indian Journal of Gastroenterology*. https://doi.org/10.1007/s12664-020-01082-3

Giedraitiene, A., Vitkauskiene, A., Naginiene, R., Pavilonis, A. (2011) Antibiotic resistance mechanisms of clinically important bacteria *Medicina*. doi:10.3390/medicina47030019.

Gilson L, Erasmus E, Borghi J, Macha J, Kamuzora P, Mtei G. (2020) Using stakeholder analysis to support moves towards universal coverage: lessons from the SHIELD project. Health Policy Plan. 27:64–76.

GLASS-Report (2019) *Global antimicrobial resistance surveillance system (GLASS) report - Early implementation 2016-2017 - World | ReliefWeb*. Available from: https://reliefweb.int/report/world/global-antimicrobial-resistance-surveillance-system-glass-report-early-implementation.

Gootz, T.D. (1990) Discovery and development of new antimicrobial agents. *Clinical Microbiology Reviews*. 3 (1), pp. 13–31. doi:10.1128/CMR.3.1.13.

Gordon, N., Aggarwal, V., Amos, B., Buhler, C., Huszar, A., McKenzie, J., Leslie, T. (2020). The UK Fleming Fund: Developing AMR surveillance capacity in low- and middle-income countries. *International Journal of Infectious Diseases*. https://doi.org/10.1016/j.ijid.2020.09.137

GRAM, IHME (2020) https://www.healthdata.org/sites/default/files/files/Projects/GRAM/Nigeria_0.pdf

Gray, D. A., Wenzel, M. (2020). Multitarget Approaches against Multiresistant Superbugs. *ACS Infectious Diseases*. https://doi.org/10.1021/acsinfecdis.0c00001

Greenland, S., Senn, S. J., Rothman, K. J., Carlin, J. B., Poole, C., Goodman, S. N., Altman, D. G. (2016). Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *European Journal of Epidemiology*. https://doi.org/10.1007/s10654-016-0149-3

Grünewald, T., Ruf, B.R. (2016) Clostridium difficile infections. *Gynakologische Praxis*. doi:10.7748/nop.22.4.13.s19.

Guba, E. (1990) The Alternative Paradigm Dialogue. In Guba, E. (Ed.) *The Paradigm Dialogue.* London, Sage.

Guba, E. G., Lincoln, Y. S. (1982). Epistemological and methodological bases of naturalistic inquiry. *Educational Communication & Technology*. https://doi.org/10.1007/BF02765185

Gutiérrez, O., Juan, C., Cercenado, E., Navarro, F., Bouza, E., Coll, P., Pérez, J.L., Oliver, A. (2007) Molecular epidemiology and mechanisms of carbapenem resistance in Pseudomonas aeruginosa isolates from Spanish hospitals. *Antimicrobial Agents and Chemotherapy*. doi:10.1128/AAC.00810-07.

Halpern E. S. (1983). *Auditing naturalistic inquiries: The development and application of a model*. PhD thesis, Indiana University, Bloomington.

Hamblion, E. L., Raftery, P., Wendland, A., Dweh, E., Williams, G. S., George, R. N. C., Nagbe, T. K. (2018). The challenges of detecting and responding to a Lassa fever outbreak in an Ebola-affected setting. *International Journal of Infectious Diseases*. https://doi.org/10.1016/j.ijid.2017.11.007

Hamel, D. J., Sankalé, J.-L., Samuels, J. O., Sarr, A. D., Chaplin, B., Ofuche, E., Kanki, P. J. (2015). Building laboratory capacity to support HIV care in Nigeria: Harvard/APIN PEPFAR, 2004–2012. *African Journal of Laboratory Medicine*, *4*(1), 2004–2012. https://doi.org/10.4102/ajlm.v4i1.190

Haque, S.F., Ali, S.Z., TP, M., Khan, A.U. (2012) Prevalence of plasmid mediated bla TEM-1 and bla CTX-M-15 type extended spectrum beta-lactamases in patients with sepsis. *Asian Pacific Journal of Tropical Medicine*. doi:10.1016/S1995-7645(12)60003-0.

Harbarth, S., Balkhy, H. H., Goossens, H., Jarlier, V., Kluytmans, J., Laxminarayan, R., Pittet, D. (2015). Antimicrobial resistance: One world, one fight! *Antimicrobial Resistance and Infection Control*. https://doi.org/10.1186/s13756-015-0091-2

Hawkey, P.M., Jones, A.M. (2009) The changing epidemiology of resistance. *Journal of Antimicrobial Chemotherapy*. doi:10.1093/jac/dkp256.

Haworth-Brockman, M., Saxinger, L. M., Miazga-Rodriguez, M., Wierzbowski, A., Otto, S. J. G. (2021). One Health Evaluation of Antimicrobial Use and Resistance Surveillance: A

Novel Tool for Evaluating Integrated, One Health Antimicrobial Resistance and Antimicrobial Use Surveillance Programs. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2021.693703

Heinze, G., Dunkler, D. (2016). *Five myths about variable selection*. https://doi.org/10.1111/tri.12895

Helfrich, C. D., Damschroder, L. J., Hagedorn, H. J., Daggett, G. S., Sahay, A., Ritchie, M., Stetler, C. B. (2010). A critical synthesis of literature on the promoting action on research implementation in health services (PARIHS) framework. *Implementation Science*. https://doi.org/10.1186/1748-5908-5-82

Hidron, A.I., Edwards, J.R., Patel, J., Horan, T.C., Sievert, D.M., Pollock, D.A., Fridkin, S.K. (2008) Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Annual Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infection Control & Hospital Epidemiology*. doi:10.1086/591861.

Hindler, J.F., Stelling, J. (2007) Analysis and Presentation of Cumulative Antibiograms: A New Consensus Guideline from the Clinical and Laboratory Standards Institute. *Clinical Infectious Diseases*. 44 (6), pp. 867–873. doi:10.1086/511864.

Høiby, N., Bjarnsholt, T., Givskov, M., Molin, S., Ciofu, O. (2010) Antibiotic resistance of bacterial biofilms *International Journal of Antimicrobial Agents*. doi:10.1016/j.ijantimicag.2009.12.011.

Holloway, I., Todres, L. (2003). The Status of Method: Flexibility, Consistency and Coherence. *Qualitative Research*. https://doi.org/10.1177/1468794103033004

Holmes, A.H., Moore, L.S.P., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P.J., Piddock, L.J.V. (2016) Understanding the mechanisms and drivers of antimicrobial resistance *The Lancet*. doi:10.1016/S0140-6736(15)00473-0.

Holt, K.E., Wertheim, H., Zadoks, R.N., Baker, S., Whitehouse, C.A., Dance, D., Jenney, A., Connor, T.R., Hsu, L.Y., Severin, J., Brisse, S., Cao, H., Wilksch, J., Gorrie, C. (2015) Genomic analysis of diversity, population structure, virulence, and antimicrobial resistance in Klebsiella pneumoniae, an urgent threat to public health. *Proceedings of the National Academy of Sciences of the United States of America*. doi:10.1073/pnas.1501049112.

Hong, P.Y., Al-Jassim, N., Ansari, M.I., Mackie, R.I. (2013) Environmental and public health implications of water reuse: Antibiotics, antibiotic resistant bacteria, and antibiotic resistance genes *Antibiotics*. doi:10.3390/antibiotics2030367.

Hopewell, S., McDonald, S., Clarke, M. J., Egger, M. (2007). Grey literature in meta-analyses of randomized trials of health care interventions. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.MR000010.pub3

Howe, K. R. (2016). Mixed methods, mixed causes? In *Qualitative Inquiry and Global Crises*. https://doi.org/10.4324/9781315421612-6

Hudzicki, J. (2009) Kirby-Bauer disk diffusion susceptibility test protocol. *... -Kirby-Bauer-Disk-Diffusion-Susceptibility-Test-Protocol.*

IBM Corp. (2011). *IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.*

Iera, J., Seghieri, C., Tavoschi, L., Isonne, C., Baccolini, V., Petrone, D., D'Ancona, F. (2023). Early Warning Systems for Emerging Profiles of Antimicrobial Resistance in Italy: A National Survey. *International Journal of Environmental Research and Public Health*. https://doi.org/10.3390/ijerph20095623

Imade, P.E., Eghafona, N.O. (2015) Microbial Agents and Associated Factors of Persistent Diarrhoea in Children Less Than 5 Years of Age in Edo State, Nigeria. *British Journal of Medicine and Medical Research*. pp. 1–6.

Inglis, T. J. J., Paton, T. F., Kopczyk, M. K., Mulroney, K. T., Carson, C. F. (2020). Same-day antimicrobial susceptibility test using acoustic-enhanced flow cytometry visualized with supervised machine learning. *Journal of Medical Microbiology*. https://doi.org/10.1099/jmm.0.001092

Isabel, N. A., Efe, A. E., Joshua, O. I. (2021). ACCESSIBILITY AND USE OF ANTIBIOTICS AMONG PATIENTS VISITING COMMUNITY PHARMACIES IN BENIN CITY, NIGERIA. *African Journal of Health, Safety and Environment*. https://doi.org/10.52417/ajhse.v2i2.170

Iskandar, K., Murugaiyan, J., Halat, D. H., Hage, S. El, Chibabhai, V., Adukkadukkam, S., Van Dongen, M. (2022). Antibiotic Discovery and Resistance: The Chase and the Race. *Antibiotics*. https://doi.org/10.3390/antibiotics11020182

Iskandar, K., Molinier, L., Hallit, S., Sartelli, M., Hardcastle, T. C., Haque, M., Roques, C. (2021). Surveillance of antimicrobial resistance in low- and middle-income countries: a scattered picture. *Antimicrobial Resistance and Infection Control*, Vol. 10, p. 63. https://doi.org/10.1186/s13756-021-00931-w

Ivers, N. M., Dhalla, I., Brown, A. (2018). Aligning innovations in health funding with innovations in care. *CMAJ*. https://doi.org/10.1503/cmaj.171312

Iwuafor, A.A., Ogunsola, F.T., Oladele, R.O., Oduyebo, O.O., Desalu, I., Egwuatu, C.C., Nnachi, A.U., Akujobi, C.N., Ita, I.O., Ogban, G.I. (2016) Incidence, clinical outcome and risk factors of intensive care unit infections in the lagos university teaching hospital (LUTH), Lagos, Nigeria. *PLoS ONE*. 11 (10), pp. 1–15. doi:10.1371/journal.pone.0165242.

Iyamu, I., Gómez-Ramírez, O., Xu, A. X. T., Chang, H. J., Watt, S., Mckee, G., Gilbert, M. (2022). Challenges in the development of digital public health interventions and mapped solutions: Findings from a scoping review. *Digital Health*. https://doi.org/10.1177/20552076221102255

Jackson, N., Czaplewski, L., Piddock, L. J. V. (2018). Discovery and development of new antibacterial drugs: Learning from experience? *Journal of Antimicrobial Chemotherapy*. https://doi.org/10.1093/jac/dky019

Jayatilleke, K. (2020). Challenges in Implementing Surveillance Tools of High-Income Countries (HICs) in Low Middle Income Countries (LMICs). *Current Treatment Options in Infectious Diseases*, *12*(3), 191–201. https://doi.org/10.1007/s40506-020-00229-2

JBI. (2020). Critical Appraisal Tools | Joanna Briggs Institute. *Joanna Briggs Institute (JBI)*.

Jean, S.S., Hsueh, P.R., Lee, W.S., Chang, H.T., Chou, M.Y., Chen, I.S., Wang, J.H., Lin, C.F., Shyr, J.M., Ko, W.C., Wu, J.J., Liu, Y.C., Huang, W.K., Teng, L.J. (2009) Nationwide surveillance of antimicrobial resistance among Enterobacteriaceae in intensive care units in Taiwan. *European Journal of Clinical Microbiology and Infectious Diseases*. 28 (2), pp. 215–220. doi:10.1007/s10096-008-0610-7.

Jee, Y., Carlson, J., Rafai, E., Musonda, K., Huong, T.T.G., Daza, P., Sattayawuthipong, W., Yoon, T. (2018) Antimicrobial resistance: a threat to global health *The Lancet Infectious Diseases*. doi:10.1016/S1473-3099(18)30471-7.

Jido, T., Garba, I. (2012) Surgical-site infection following cesarean section in Kano, Nigeria. *Annals of Medical and Health Sciences Research*. 2 (1), pp. 33. doi:10.4103/2141-9248.96934.

Johnson R. B., Anthony J. O., Susan a. T., Marjorie L. I. (2014) 'Conducting Mixed Methods Research: Using Dialectical Pluralism and Social Psychological Strategies', in Patricia Leavy (ed.), *The Oxford Handbook of Qualitative Research*, Oxford Library of Psychology online https://doi.org/10.1093/oxfordhb/9780199811755.013.022

Joshua, A., Moses, A., Akinkunmi, E. O. (2018) A Survey of Antimicrobial Agents Usage in Poultry Farms and Antibiotic Resistance in Escherichia Coli and Staphylococci Isolates from

the Poultry in Ile-Ife, Nigeria. *Journal of Infectious Diseases and Epidemiology* doi.org/10.23937/2474-3658/1510047

Kakkar, M., Sharma, A., Vong, S. (2017). Developing a situation analysis tool to assess containment of antimicrobial resistance in South East Asia. *BMJ (Online).* https://doi.org/10.1136/bmj.j3760

Kan, B. (2022). Performing Laboratory Network Surveillance to Monitor the Emergence and Spread of Infectious Diseases. *China CDC Weekly*. https://doi.org/10.46234/ccdcw2022.057

Kang, C.I., Song, J.H. (2013) Antimicrobial resistance in Asia: Current epidemiology and clinical implications *Infection and Chemotherapy* 45 (1) p.pp. 22–31. doi:10.3947/ic.2013.45.1.22.

Kanjee, Z., Amico, K. R., Li, F., Mbolekwa, K., Moll, A. P., Friedland, G. H., Africa, S. (2012). Tuberculosis infection control in a high drug-resistance setting in rural South Africa : Information , motivation , and behavioral skills. *Journal of Infection and Public Health*, *5*, 67–81. https://doi.org/10.1016/j.jiph.2011.10.008

Karp, B. E., Tate, H., Plumblee, J. R., Dessai, U., Whichard, J. M., Thacker, E. L., … McDermott, P. F. (2017). National antimicrobial resistance monitoring system: Two decades of advancing public health through integrated surveillance of antimicrobial resistance. *Foodborne Pathogens and Disease*. https://doi.org/10.1089/fpd.2017.2283

Kathiravan, M.K., Salake, A.B., Chothe, A.S., Dudhe, P.B., Watode, R.P., Mukta, M.S., Gadhwe, S. (2012) The biology and chemistry of antifungal agents: A review *Bioorganic and Medicinal Chemistry*. doi:10.1016/j.bmc.2012.04.045.

Kapoor, G., Saigal, S., Elongavan, A. (2017) Action and resistance mechanisms of antibiotics: A guide for clinicians *Journal of Anaesthesiology Clinical Pharmacology*. doi:10.4103/joacp.JOACP_349_15.

Kappagoda, S., Singh, U., Blackburn, B.G. (2011) Antiparasitic therapy *Mayo Clinic Proceedings*. doi:10.4065/mcp.2011.0203.

Kariuki, S., Keddy, K.H., Antonio, M., Okeke, I.N. (2018) Antimicrobial resistance surveillance in Africa: Successes, gaps and a roadmap for the future. *African Journal of Laboratory Medicine*. 7 (2), pp. 1–2. doi:10.4102/ajlm.v7i2.924.

Kaur, J., Dhama, A. S., Buttolia, H., Kaur, J., Walia, K., Ohri, V., Singh, H. (2021). ICMR's Antimicrobial Resistance Surveillance system (i-AMRSS): A promising tool for global antimicrobial resistance surveillance. *JAC-Antimicrobial Resistance*. https://doi.org/10.1093/jacamr/dlab023

Kay A., B. (2021). The role of the laboratory in disease surveillance. *Eastern Mediterranean Health Journal*. https://doi.org/10.26719/1996.2.1.68

Keddem, S., Agha, A. Z., Long, J. A., Werner, R. M., Shea, J. A. (2017). Creating a Toolkit to Reduce Disparities in Patient Engagement. *Medical Care*. https://doi.org/10.1097/MLR.0000000000000748

Keith, J.W., Pamer, E.G. (2019) Enlisting commensal microbes to resist antibiotic-resistant pathogens *Journal of Experimental Medicine*. doi:10.1084/jem.20180399.

Kim, S.H., Chung, D.R., Baek, J.Y., Thamlikitkul, V., Wang, H., Carlos, C., Ahmad, N., Arushothy, R., Tan, S.H., Lye, D., Kang, C.I., Ks, K., Peck, K.R., Song, J.H. (2017) Antimicrobial resistance of Streptococcus pneumoniae isolates from adult patients with invasive pneumococcal disease or pneumonia in Asia. *International Journal of Antimicrobial Agents*.

Kim, S.H., Song, J.H., Chung, D.R., Thamlikitkul, V., Yang, Y., Wang, H., Lu, M., So, T.M.K., Hsueh, P.R., Yasin, R.M., Carlos, C.C., Van Pham, H., Lalitha, M.K., Shimono, N. (2012) Changing trends in antimicrobial resistance and serotypes of Streptococcus pneumoniae isolates in Asian countries: An Asian Network for Surveillance of Resistant

Pathogens (ANSORP) study. *Antimicrobial Agents and Chemotherapy*. doi:10.1128/AAC.05658-11.

King, N. (2004). Essential Guide to Qualitative Methods in Organisational Research. Using templates in the Thematic Analysis of Text. *Essential Guide to Qualitative Methods in Organisational Research*.

Kırmusaoğlu, S., Gareayaghi, N., S. Kocazeybek, B. (2019) Introductory Chapter: The Action Mechanisms of Antibiotics and Antibiotic Resistance. In: *Antimicrobials, Antibiotic Resistance, Antibiofilm Strategies and Activity Methods*. (no place) IntechOpen. doi:10.5772/intechopen.85211.

Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(15), E3463–E3470. https://doi.org/10.1073/pnas.1717295115

Ko, K.S. (2019) Antibiotic-resistant clones in Gram-negative pathogens: presence of global clones in Korea *Journal of Microbiology* 57 (3) p.pp. 195–202. doi:10.1007/s12275-019-8491-2.

Koch T. (1994). Establishing rigour in qualitative research: The decision trail. *Journal of Advanced Nursing*, 19, 976–986. doi:10.1111/j.1365-2648.1994.tb01177.x

Kontopoulou, K., Protonotariou, E., Vasilakos, K., Kriti, M., Koteli, A., Antoniadou, E., Sofianou, D. (2010) Hospital outbreak caused by Klebsiella pneumoniae producing KPC-2 β-lactamase resistant to colistin. *Journal of Hospital Infection*. doi:10.1016/j.jhin.2010.03.021.

Kothari, J. (2004). *Research methodology (Methods and Techniques)* (2nd ed.). New Age International Limited Publisherss: New Delhi.

Kraemer, K., Van Zutphen, K. G. (2019). Translational and Implementation Research to Bridge Evidence and Implementation. *Annals of Nutrition and Metabolism*. https://doi.org/10.1159/000503675

Kristinsson, K.G., Georgsson, F. (2015) [Infection risks associated with importation of fresh food in Iceland]. *Laeknabladid*.

Kuhn, T. S. (1996). *The structure of scientific revolutions* (3rd ed.). University of Chicago Press. https://doi.org/10.7208/chicago/9780226458106.001.0001

Kulkarni, S. (2022). *APPLICATION OF LEAN-SIX SIGMA TO IMPROVE QUALITY IN HEALTH CARE INDUSTRY*. https://doi.org/10.18260/1-2-620-39080

Kulshreshtha, N.M., Jadhav, I., Dixit, M., Sinha, N., Shrivastava, D., Bisen, P.S. (2017) Nanostructures as Antimicrobial Therapeutics. In: *Antimicrobial Nanoarchitectonics: From Synthesis to Applications*. doi:10.1016/B978-0-323-52733-0.00002-1.

Kunißen, K. (2019). From Dependent to Independent Variable: A Critical Assessment of Operationalisations of 'Welfare Stateness' as Macro-Level Indicators in Multilevel Analyses. *Social Indicators Research*. https://doi.org/10.1007/s11205-018-1930-3

Lai, C.C., Lee, K., Xiao, Y., Ahmad, N., Veeraraghavan, B., Thamlikitkul, V., Tambyah, P.A., Nelwan, R.H.H., Shibl, A.M., Wu, J.J., Seto, W.H., Hsueh, P.R. (2014) High burden of antimicrobial drug resistance in Asia *Journal of Global Antimicrobial Resistance*. doi:10.1016/j.jgar.2014.02.007.

Langmuir, A. D. (1980). The Epidemic Intelligence Service of the Center for Disease Control. *Public Health Reports*. https://pubmed.ncbi.nlm.nih.gov/6106957/

Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen J, Klugman K, D.S. (2015) *Antimicrobials: access and sustainable effectiveness*. LK - http://ze6dt7rj9y.search.serialssolutions.com?sid=EMBASE&issn=1474547X&id=doi:10.10

16%2FS0140-6736%2815%2900474-

Laxminarayan, R., Matsoso, P., Pant, S., Brower, C., Rottingen, J.-A., Klugman, K., Davies, S. (2016) Access to effective antimicrobials: A worldwide challenge. *The Lancet*. doi:10.1016/S0140-6736(15)00474-2

Lee, K. J., Tilling, K. M., Cornish, R. P., Little, R. J. A., Bell, M. L., Goetghebeur, E., Carpenter, J. R. (2021). Framework for the treatment and reporting of missing data in observational studies: The Treatment And Reporting of Missing data in Observational Studies framework. *Journal of Clinical Epidemiology*. https://doi.org/10.1016/j.jclinepi.2021.01.008

Lee, L. M. L. M., Women with Disabilities Development Foundation, Health Service Executive, Agency, C., Brandon, R. M., German, R. R., Herrera, G. (2014). Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. *MMWR. Recommendations and Reports : Morbidity and Mortality Weekly Report. Recommendations and Reports / Centers for Disease Control*.

Lee, K., Kim, M.N., Kim, J.S., Hong, H.L., Kang, J.O., Shin, J.H., Park, Y.J., Yong, D., Jeong, S.H., Chong, Y. (2011) Further increases in carbapenem-, amikacin-, and fluoroquinolone-resistant isolates of Acinetobacter spp. and P. aeruginosa in Korea: KONSAR study 2009. *Yonsei Medical Journal*. 52 (5), pp. 793–802. doi:10.3349/ymj.2011.52.5.793.

Lee, K., Lee, M.A., Lee, C.H., Lee, J., Roh, K.H., Kim, S., Kim, J.J., Koh, E., Yong, D., Chong, Y. (2010) Increase of ceftazidime- and fluoroquinolone-resistant Klebsiella pneumoniae and imipenem-resistant Acinetobacter spp. In Korea: Analysis of KONSAR study data from 2005 and 2007. *Yonsei Medical Journal*. 51 (6), pp. 901–911. doi:10.3349/ymj.2010.51.6.901.

LENJANI, B., BAFTIU, N., RASHITI, P., BUNJAKU, I., ARSLLANI, N., KRASNIQI, B., DEMI, A. (2020). Reference System from Health Levels to Emergency Clinic Center in

Kosovo. *Albanian Journal of Trauma and Emergency Surgery*. https://doi.org/10.32391/ajtes.v4i2.121

Liakopoulos, A., Mavroidi, A., Katsifas, E.A., Theodosiou, A., Karagouni, A.D., Miriagou, V., Petinaki, E. (2013) Carbapenemase-producing Pseudomonas aeruginosa from central Greece: Molecular epidemiology and genetic analysis of class I integrons. *BMC Infectious Diseases*. doi:10.1186/1471-2334-13-505.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Moher, D. (2009). *Guidelines and Guidance The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration*. https://doi.org/10.1371/journal.pmed.1000100

Lim, C., Ashley, E. A., Hamers, R. L., Turner, P., Kesteman, T., Akech, S., van Doorn, H. R. (2021). Surveillance strategies using routine microbiology for antimicrobial resistance in low- and middle-income countries. *Clinical Microbiology and Infection*. https://doi.org/10.1016/j.cmi.2021.05.037

Lin, K.Y., Lauderdale, T.L., Wang, J.T. and Chang, S.C. (2016) Carbapenem-resistant Pseudomonas aeruginosa in Taiwan: Prevalence, risk factors, and impact on outcome of infections. *Journal of Microbiology, Immunology and Infection*. doi:10.1016/j.jmii.2014.01.005.

Ling, L.L., Schneider, T., Peoples, A.J., Spoering, A.L., Engels, I., Conlon, B.P., Mueller, A., Schäberle, T.F., Hughes, D.E., Epstein, S., Jones, M., Lazarides, L., Steadman, V.A., Cohen, D.R. (2015) A new antibiotic kills pathogens without detectable resistance. *Nature*. doi:10.1038/nature14098.

Liu B., Ma F., Rainey J.J., Liu X., Klena J., Liu X., Kan B., Yan M., Wang D., Zhou Y., Tang G., Wang, M., Zhao C (2019) Capacity assessment of the health laboratory system in two resource-limited provinces in China. *BMC Public Health*.10;19(Suppl 3):467. doi: 10.1186/s12889-019-6777-2. PMID: 32326939; PMCID: PMC6696693

Lockwood, C., Munn, Z., Porritt, K. (2015). Qualitative research synthesis: Methodological guidance for systematic reviewers utilizing meta-aggregation. *International Journal of Evidence-Based Healthcare*. https://doi.org/10.1097/XEB.0000000000000062

LSHTM (2016) *Supporting surveillance capacity for antimicrobial resistance LABORATORY CAPACITY STRENGTHENING FOR DRUG RESISTANT*. pp. 1–16.

Lu, P.L., Liu, Y.C., Toh, H.S., Lee, Y.L., Liu, Y.M., Ho, C.M., Huang, C.C., Liu, C.E., Ko, W.C., Wang, J.H., Tang, H.J., Yu, K.W., Chen, Y.S., Chuang, Y.C. (2012) Epidemiology and antimicrobial susceptibility profiles of Gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009-2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). *International Journal of Antimicrobial Agents*. 40 (SUPPL. 1), . doi:10.1016/S0924-8579(12)70008-0.

Ludden, C., Raven, K.E., Jamrozy, D., Gouliouris, T., Blane, B., Coll, F., de Goffau, M., Naydenova, P., Horner, C., Hernandez-Garcia, J., Wood, P., Hadjirin, N., Radakovic, M., Brown, N.M. (2019) One health genomic surveillance of escherichia coli demonstrates distinct lineages and mobile genetic elements in isolates from humans versus livestock. *mBio*. doi:10.1128/mBio.02693-18.

Lupindu, A.M., Dalsgaard, A., Msoffe, P.L.M., Ngowi, H.A., Mtambo, M.M., Olsen, J.E. (2015) Transmission of antibiotic-resistant Escherichia coli between cattle, humans and the environment in peri-urban livestock keeping communities in Morogoro, Tanzania. *Preventive Veterinary Medicine*. doi:10.1016/j.prevetmed.2014.12.005.

Lynn, M. R. (1986). Determination and quantification of content validity. *Nursing Research, 35*(6), 382–385. https://doi.org/10.1097/00006199-198611000-00017

Ma, L., Wang, J.T., Wu, T.L., Siu, L.K., Chuang, Y.C., Lin, J.C., Lu, M.C., Lu, P.L. (2015) Emergence of OXA-48-producing Klebsiella pneumoniae in Taiwan. *PLoS ONE*. doi:10.1371/journal.pone.0139152.

Malania, L., Wagenaar, I., Karatuna, O., Tambic Andrasevic, A., Tsereteli, D., Baidauri, M., Ruesen, C. (2021). Setting up laboratory-based antimicrobial resistance surveillance in low and middle-income countries: lessons learned from Georgia. *Clinical Microbiology and Infection*. https://doi.org/10.1016/j.cmi.2021.05.027

Malik, M. R., Abubakar, A., Kholy, A. E., Buliva, E., Khan, W. M., Lamichhane, J., Obtel, M. (2020). Improved capacity for influenza surveillance in the WHO Eastern Mediterranean Region: Progress in a challenging setting. *Journal of Infection and Public Health*. https://doi.org/10.1016/j.jiph.2019.07.018

Malla, S., Dumre, S. P., Shakya, G., Kansakar, P., Rai, B., Hossain, A., Rahman, M. (2014). The challenges and successes of implementing a sustainable antimicrobial resistance surveillance programme in Nepal. *BMC Public Health*. https://doi.org/10.1186/1471-2458-14-269

Mann, J. (2005) Antibiotics: Actions, Origins, Resistance. *Natural Product Reports*. doi:10.1039/b417591n.

Manyi-Loh, C., Mamphweli, S., Meyer, E., Okoh, A. (2018). Antibiotic Use in Agriculture and Its Consequential Resistance in Environmental Sources: Potential Public Health Implications. *Molecules : A Journal of Synthetic Chemistry and Natural Product Chemistry*, *23*(4). https://doi.org/10.3390/MOLECULES23040795

Margaryan, A, Littlejohn, A Lukic, D (2018) 'The development and evaluation of a Learning from Incidents toolkit', Policy and Practice in Health and Safety , vol. 16, no. 1, pp. 57-70. https://doi.org/10.1080/14773996.2018.1465263

Martin, W., Pauly, B., MacDonald, M. (2016). Situational Analysis for Complex Systems: Methodological Development in Public Health Research. *AIMS Public Health*. https://doi.org/10.3934/publichealth.2016.1.94

Mathew, A.G., Cissell, R., Liamthong, S. (2007) Antibiotic resistance in bacteria associated with food animals: A United States perspective of livestock production *Foodborne Pathogens and Disease*. doi:10.1089/fpd.2006.0066.

Marston, H.D., Dixon, D.M., Knisely, J.M., Palmore, T.N., Fauci, A.S. (2016) Antimicrobial resistance. *JAMA - Journal of the American Medical Association*. doi:10.1001/jama.2016.11764.

Marvasi, M., Casillas, L., Vassallo, A., Purchase, D. (2021). Educational activities for students and citizens supporting the one-health approach on antimicrobial resistance. *Antibiotics*. https://doi.org/10.3390/antibiotics10121519

Mccubbin, K. D., Anholt, R. M., Jong, E. De, Ida, J. A., Nóbrega, D. B., Kastelic, J. P., Götte, M. (2021). Knowledge Gaps in the Understanding of Antimicrobial Resistance in Canada. *Frontier in Public Health*, *9*(October), 1–14. https://doi.org/10.3389/fpubh.2021.726484

McManus, D.S., Shah, S. (2019) Antifungal drugs. In: *Side Effects of Drugs Annual*. doi:10.1016/bs.seda.2019.09.002.

Meckawy, R., Stuckler, D., Mehta, A., Al-Ahdal, T., Doebbeling, B. N. (2022). Effectiveness of early warning systems in the detection of infectious diseases outbreaks: a systematic review. *BMC Public Health*. https://doi.org/10.1186/s12889-022-14625-4

Melnyk, B. M., Fineout-Overholt, E., Gallagher-Ford, L., Kaplan, L. (2012). The state of evidence-based practice in US nurses: Critical implications for nurse leaders and educators. *Journal of Nursing Administration*. https://doi.org/10.1097/NNA.0b013e3182664e0a

Mendelson, M., Røttingen, J.A., Gopinathan, U., Hamer, D.H., Wertheim, H., Basnyat, B., Butler, C., Tomson, G., Balasegaram, M. (2016) Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries *The Lancet* 387 (10014) p.pp. 188–198. doi:10.1016/S0140-6736(15)00547-4.

Meremikwu, M.M., Nwachukwu, C.E., Asuquo, A.E., Okebe, J.U., Utsalo, S.J. (2005) Bacterial isolates from blood cultures of children with suspected septicaemia in Calabar, Nigeria. *BMC Infectious Diseases*. 5 pp. 1–4. doi:10.1186/1471-2334-5-110.

Ministry of Health (2017) *NATIONAL POLICY ON PREVENTION AND CONTAINMENT OF ANTIMICROBIAL RESISTANCE, Kenya*. (April), pp. 7,13

Mishra, M., Panda, S., Barik, S., Sarkar, A., Singh, D.V., Mohapatra, H. (2020) Antibiotic Resistance Profile, Outer Membrane Proteins, Virulence Factors and Genome Sequence Analysis Reveal Clinical Isolates of Enterobacter Are Potential Pathogens Compared to Environmental Isolates. *Frontiers in Cellular and Infection Microbiology*. 10 . doi:10.3389/fcimb.2020.00054.

Moe, M. M., Okio, K. K. (2020). Comparative results of dependent and independent variables focused on regression analysis using test-driven development. *WCSE 2020: 2020 10th International Workshop on Computer Science and Engineering*. https://doi.org/10.18178/wcse.2020.02.006

Mohammed, Y., Ibrahim, B., Galalain, S., Dalhat, M., Nguku, P. (2018) Antimicrobial resistance surveillance system in Nigeria: Suggested models. *Sahel Medical Journal*. doi:10.4103/smj.smj_17_17.

Mokuolu, O.A., Jiya, N.M., Adesiyun, O.O. (2002) *Neonatal septicaemia in Ilorin : bacterial pathogens and antibiotic sensitivity pattern*. (July), .

Monedero-Recuero, I., Gegia, M., Wares, D. F., Chadha, S. S., Mirzayev, F. (2021). Situational analysis of 10 countries with a high burden of drug-resistant tuberculosis 2 years post-UNHLM declaration: progress and setbacks in a changing landscape. *International Journal of Infectious Diseases*. https://doi.org/10.1016/j.ijid.2021.06.022

Monnet, D.L. (2016) Trends in antimicrobial resistance in Europe. *International Journal of*

Infectious Diseases. doi:10.1016/j.ijid.2016.11.060.

Moustakas, C. E. (1994). Phenomenological research methods. *Phenomenological Research Methods*. https://psycnet.apa.org/record/1996-97117-000

Muloi, D., Ward, M.J., Pedersen, A.B., Fèvre, E.M., Woolhouse, M.E.J., Van Bunnik, B.A.D. (2018) Are Food Animals Responsible for Transfer of Antimicrobial-Resistant Escherichia coli or Their Resistance Determinants to Human Populations? A Systematic Review. *Foodborne Pathogens and Disease*. doi:10.1089/fpd.2017.2411.

Munn, Z., Peters, M. D. J., Stern, C., Tufanaru, C., McArthur, A., Aromataris, E. (2018). Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Medical Research Methodology*. https://doi.org/10.1186/s12874-018-0611-x

Murray, C. J., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*. https://doi.org/10.1016/S0140-6736(21)02724-0

Mustafa, M.H., Chalhoub, H., Denis, O., Deplano, A., Vergison, A., Rodriguez-Villalobos, H., Tunney, M.M., Stuart Elborn, J., Kahl, B.C., Traore, H., Vanderbist, F., Tulkens, P.M., Van Bambeke, F. (2016) Antimicrobial susceptibility of pseudomonas aeruginosa isolated from cystic fibrosis patients in northern Europe. *Antimicrobial Agents and Chemotherapy*. doi:10.1128/AAC.01046-16.

Nabadda, S., Kakooza, F., Kiggundu, R., Walwema, R., Bazira, J., Mayito, J., Mwebasa, H. (2021). Implementation of the World Health Organisation Global Antimicrobial Resistance Surveillance System in Uganda, 2015-2020: Mixed-Methods Study Using National Surveillance Data. *JMIR Public Health and Surveillance*. https://doi.org/10.2196/29954

Nadimpalli, M. L., Marks, S. J., Montealegre, M. C., Gilman, R. H., Pajuelo, M. J., Saito, M., Pickering, A. J. (2020). Environmental Transmission. *Nature Microbiology*.

NAP, (2017) Nigeria: National action pla for antimicrobial resistance https://www.who.int/publications/m/item/nigeria-national-action-plan-for-antimicrobial-resistance

Nasir, I.A., Babyo, A., Emeribe, A.U., Sani, N.O. (2015) Surveillance for antibiotic resistance in Nigeria: Challenges and possible solutions. *Trends in Medical Research* [online]. 10 (4), pp. 106–113. Available from: http://dx.doi.org/10.3923/tmr.2015.106.113doi:10.3923/tmr.2015.106.113.

Naylor, N. R., Atun, R., Zhu, N., Kulasabanathan, K., Silva, S., Chatterjee, A., Robotham, J. V. (2018). Estimating the burden of antimicrobial resistance: a systematic literature review. *Antimicrobial Resistance and Infection Control*. https://doi.org/10.1186/s13756-018-0336-y

NCDC. (2018). *Guideline for Laboratory Base Antimicrobial Resistance Surveillance* https://www.afro.who.int/publications/guide-establishing-laboratory-based-surveillance-antimicrobial-resistance

NCDCAMRS (2017) *Nigeria Center for Disease Control Antimicrobial Resistance (AMR) Symposium | DokiLink*. Available from: https://dokilink.com/events/nigeria-center-disease-control-antimicrobial-resistance-amr-symposium.

Ndihokubwayo, J. B., Yahaya, A. A., Desta, A. T., Ki-Zerbo, G., Odei, E. A., Keita, B., … Nkhoma, W. (2013). Antimicrobial resistance in the African Region: issues, challenges and actions proposed. Key Determinants for the African Region. *The African Health Monitor*.

Ndjomou, J., Shearrer, S., Karlstrand, B., Asbun, C., Coble, J., Alam, J. S., Altmann, S. (2021). Sustainable Laboratory Capacity Building After the 2014 Ebola Outbreak in the Republic of Guinea. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2021.659504

Ng'etichi, A. K. S., Voyi, K., Kirinyet, R. C., Mutero, C. M. (2021). A systematic review

on improving implementation of the revitalised integrated disease surveillance and response system in the African region: A health workers' perspective. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0248998

Nguyen, M., Long, S. W., McDermott, P. F., Olsen, R. J., Olson, R., Stevens, R. L., Davis, J. J. (2018). Using machine learning to predict antimicrobial minimum inhibitory concentrations and associated genomic features for nontyphoidal Salmonella. *BioRxiv*, *57*(2), 1–15. https://doi.org/10.1101/380782

Nigeria Centre for Disease Control. (2017). *Antimicrobial use and resistance in Nigeria*. 1–158.

Nicolau, C.J., Oliver, A. (2010) Carbapenemasas en especies del género Pseudomonas. *Enfermedades Infecciosas y Microbiologia Clinica*. doi:10.1016/S0213-005X(10)70004-5.

Nigeria Centre for Disease Control (NCDC). (2017). National Action Plan for Antimicrobial Resistance 2017-2022. *Federal Ministries of Agriculture, Environment and Health*.

Njoga, E. O., Ogugua, A. J., Nwankwo, I. O., Awoyomi, O. J., Okoli, C. E., Buba, D. M., Ogunniran, T. M. (2021). Antimicrobial drug usage pattern in poultry farms in nigeria: Implications for food safety, public health and poultry disease management. *Veterinaria Italiana*. https://doi.org/10.12834/VetIt.2117.11956.1

Nkengasong, J. (2017) *Establishing the Africa Centres for Disease Control and Prevention: the upside of a crisis*. (May), pp. 16–18. Available from: https://africa-health.com/wp-content/uploads/2017/05/8.-CDC-feature.pdf.

Norad-Malawi (2016) *Malawi development*. Available from: https://norad.no/en/front/countries/africa/malawi/.

Noreen, N., Khan, A. W., Badar, N., Khan, F. K., Khudaidad, F., Khan, N. U., … Malik, T. (2019). Evaluation of Lab-based Influenza Surveillance System in Pakistan, 2017. *Global*

Biosecurity. https://doi.org/10.31646/gbio.26

Nsofor, A. (2013) Antibiotic resistance profile of Escherichia coli isolated from five major geopolitical zones of Nigeria. *Journal of Bacteriology Research*. 5(3), pp. 29–34. doi:10.5897/jbr2012.035.

Nsubuga, P., White, M., Thacker, S., Anderson, M., Blount, S., Broome, C., Sosin, D. (2006). Public health surveillance: A tool for targeting and monitoring interventions. In disease control priorities project. *Disease Control Priorities in Developing Countries.*

Núñez-Núñez, M., Navarro, M. D., Palomo, V., Rajendran, N. B., Toro, M. D., Voss, A., Zingg, W. (2018). The methodology of surveillance for antimicrobial resistance and healthcare-associated infections in Europe (SUSPIRE): a systematic review of publicly available information. *Clinical Microbiology and Infection*, *24*(2), 105–109. https://doi.org/10.1016/j.cmi.2017.07.014

Nwadike, V.U., Ojide, C.K., Kalu, E.I. (2014) Multidrug resistant acinetobacter infection and their antimicrobial susceptibility pattern in a Nigerian tertiary hospital ICU. *African Journal of Infectious Diseases*. 8 (1), pp. 14–18. doi:10.4314/ajid.v8i1.4.

Nwankwo, E., Shehu, A., Farouk, Z. (2011) Risk Factors and Bacterial Profile of Suspected Neonatal Septicaemia at a Teaching Hospital in Kano, Northwestern, Nigeria. *Sierra Leone Journal of Biomedical Research*. 3 (2), pp. 104–109. doi:10.4314/sljbr.v3i2.71811.

Obaro, S.K., Hassan-Hanga, F., Olateju, E.K., Umoru, D., Lawson, L., Olanipekun, G., Ibrahim, S., Munir, H., Ihesiolor, G., Maduekwe, A., Ohiaeri, C., Adetola, A., Shetima, D., Jibir, B.W. (2015) Salmonella bacteremia among children in central and Northwest Nigeria, 2008-2015. *Clinical Infectious Diseases*. 61 pp. S325–S331. doi:10.1093/cid/civ745.

O'Brien, D. T., Farrell, C., Welsh, B. C. (2019). Looking Through Broken Windows: The Impact of Neighborhood Disorder on Aggression and Fear of Crime Is an Artifact of

Research Design. *Annual Review of Criminology*. https://doi.org/10.1146/annurev-criminol-011518-024638

Odetoyin, B.W., Hofmann, J., Aboderin, A.O., Okeke, I.N. (2016) Diarrhoeagenic Escherichia coli in mother-child Pairs in Ile-Ife, South Western Nigeria. *BMC Infectious Diseases* [online]. 16 (1), pp. 1–9. Available from: http://dx.doi.org/10.1186/s12879-016-1365-xdoi:10.1186/s12879-016-1365-x.

Ogoina, D., Iliyasu, G., Kwaghe, V., Otu, A., Akase, I. E., Adekanmbi, O., Habib, A. G. (2021). Predictors of antibiotic prescriptions: a knowledge, attitude and practice survey among physicians in tertiary hospitals in Nigeria. *Antimicrobial Resistance and Infection Control*. https://doi.org/10.1186/s13756-021-00940-9

Ogundare, E. O., Taiwo, A. B., Olatunya, O. S., Afolabi, M. O. (2022). Incidence of Catastrophic Health Expenditures Amongst Hospitalized Neonates in Ekiti, Southwest Nigeria. *ClinicoEconomics and Outcomes Research*. https://doi.org/10.2147/CEOR.S360650

Ogundeji, Y. K., Akomolafe, B., Ohiri, K., Butawa, N. N. (2019). Factors influencing willingness and ability to pay for social health insurance in Nigeria. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0220558

Ogundimu, E. O., Altman, D. G., Collins, G. S. (2016). Adequate sample size for developing prediction models is not simply related to events per variable. *Journal of Clinical Epidemiology*. https://doi.org/10.1016/j.jclinepi.2016.02.031

OIE (2018) *conference on antimicrobial resistance and prudent use Under the high patronage of His Majesty, King Mohammed VI*. (October)

Okeke, I.N., Fayinka, S.T., Lamikanra, A. (2000) Antibiotic resistance in escherichia coli from nigerian students, 1986-1998. *Emerging Infectious Diseases*. 6 (4), pp. 393–396. doi:10.3201/eid0604.009913.

Okolie, O.J., Igwe, U., Ismail SU, Ighodalo, U.L., Adukwu, E.C. (2022) Systematic review of surveillance systems for AMR in Africa. *J Antimicrob Chemother*. dkac342. doi: 10.1093/jac/dkac342. Epub ahead of print. PMID: 36227707.

Okoro, C.K., Kingsley, R.A., Connor, T.R., Harris, S.R., Parry, C.M., Al-Mashhadani, M.N., Kariuki, S., Msefula, C.L., Gordon, M.A., De Pinna, E., Wain, J., Heyderman, R.S., Obaro, S., Alonso, P.L. (2012) Intracontinental spread of human invasive Salmonella Typhimurium pathovariants in sub-Saharan Africa. *Nature Genetics*. 44 (11), pp. 1215–1221. doi:10.1038/ng.2423.

Olonitola, O.S., Fahrenfeld, N., Pruden, A. (2015b) Antibiotic resistance profiles among mesophilic aerobic bacteria in Nigerian chicken litter and associated antibiotic resistance genes. *Poultry Science*. doi:10.3382/ps/pev069.

Oloso, N.O., Fagbo, S., Garbati, M., Olonitola, S.O., Awosanya, E.J., Aworh, M.K., Adamu, H., Odetokun, I.A. and Fasina, F.O. (2018) Antimicrobial resistance in food animals and the environment in Nigeria: A review. *International Journal of Environmental Research and Public Health*. 15 (6), . doi:10.3390/ijerph15061284.

Olowe, O.A., Aboderin, B.W., Idris, O.O., Mabayoje, V.O., Opaleye, O.O., Catherine Adekunle, O., Olowe, R.A., Akinduti, P.A., Ojurongbe, O. (2014) Genotypes and phenotypes of Shiga toxin-producing Escherichia coli (STEC) in Abeokuta, Southwestern Nigeria. *Infection and Drug Resistance*. 7 pp. 253–259. doi:10.2147/IDR.S66268.

Oluduro, A., Famurewa, O. (2007) Antibiotic resistant bacteria in faecal samples of apparently healthy individuals in Ado-Ekiti, Nigeria. *Journal of Science and Technology (Ghana)*. 27 (1), pp. 51–60. doi:10.4314/just.v27i1.33024.

O'Neill, J. (2014) Antimicrobial Resistance : Tackling a crisis for the health and wealth of nations. *The Review on Antimicrobial Resistance* https://wellcomecollection.org/works/rdpck35v

O'Neill, J. (2016) The Review on Antimicrobial Resistance. *Wellcome Trust & UK Government*. doi:10.1016/j.jpha.2015.11.005.

Oni, A.A., Ewete, A.F., Gbaja, A.T., Kolade, A.F., Mutiu, W.B., Adeyemo, D.A., Bakare, R.A. (2006) Nosocomial infections: Surgical site infection in UCH Ibadan, Nigeria. *Nigerian Journal of Surgical Research*. 8 (1–2), pp. 19–23. doi:10.4314/njsr.v8i1.54850.

Opintan, J.A., Newman, M.J., Arhin, R.E., Donkor, E.S., Gyansa-Lutterodt, M., Mills-Pappoe, W. (2015) Laboratory-based nationwide surveillance of antimicrobial resistance in Ghana. *Infection and Drug Resistance*. 8 pp. 379–389. doi:10.2147/IDR.S88725.

O'Rourke, A., Beyhan, S., Choi, Y., Morales, P., Chan, A.P., Espinoza, J.L., Dupont, C.L., Meyer, K.J., Spoering, A., Lewis, K., Nierman, W.C., Nelson, K.E. (2020) Mechanism-of-action classification of antibiotics by global transcriptome profiling. *Antimicrobial Agents and Chemotherapy*. 64 (3), . doi:10.1128/AAC.01207-19.

Orubu, E.S.F., Zaman, M.H., Rahman, M.T., Wirtz, V.J. (2020) Veterinary antimicrobial resistance containment in Bangladesh: Evaluating the national action plan and scoping the evidence on implementation. *Journal of Global Antimicrobial Resistance* [online]. 21 pp. 105–115. Available from: https://doi.org/10.1016/j.jgar.2019.09.020doi:10.1016/j.jgar.2019.09.020.

Osinupebi, O., Ogunlesi, T., Fetuga, M. (2013) Pattern of nosocomial infections in the special care baby unit of the Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria. *Nigerian Journal of Paediatrics*. 41 (1), pp. 54. doi:10.4314/njp.v41i1.10.

Otter, J.A., Yezli, S., French, G.L. (2011) The Role Played by Contaminated Surfaces in the Transmission of Nosocomial Pathogens. *Infection Control & Hospital Epidemiology*. doi:10.1086/660363.

Otto, D., Haase, A. (2022). How the COVID-19 pandemic impacts social scientific research on sustainability: questions of methodology, ethics and justice: comment on

Santana 2021. *Sustainability Science*. https://doi.org/10.1007/s11625-021-01066-y

Owens, R.C. (2008) Antimicrobial stewardship: concepts and strategies in the 21st century. *Diagnostic Microbiology and Infectious Disease*. doi:10.1016/j.diagmicrobio.2008.02.012.

Page, M., McKenzie, J., Bossuyt, P., Boutron, I., Hoffmann, T., Mulrow, C. (2021). PRISMA 2020 Checklist Section and Topic Item # Checklist item Location where item is reported TITLE Title 1 Identify the report as a systematic review. *BMJ*.

Pal, C., Bengtsson-Palme, J., Kristiansson, E., Larsson, D.G.J. (2015) Co-occurrence of resistance genes to antibiotics, biocides and metals reveals novel insights into their co-selection potential. *BMC Genomics*. doi:10.1186/s12864-015-2153-5.

Pappas, C., Williams, I. (2011). Grey literature: Its emerging importance. *Journal of Hospital Librarianship*. https://doi.org/10.1080/15323269.2011.587100

Patel, R. (2005) Biofilms and antimicrobial resistance. In: *Clinical Orthopaedics and Related Research*. 2005 doi:10.1097/01.blo.0000175714.68624.74.

Peimbert-García, R. E. (2019). Analysis and Evaluation of Reviews on Lean and Six Sigma in Health Care. *Quality Management in Health Care*. https://doi.org/10.1097/QMH.0000000000000226

Pendleton, J.N., Gorman, S.P., Gilmore, B.F. (2013) Clinical relevance of the ESKAPE pathogens *Expert Review of Anti-Infective Therapy*. doi:10.1586/eri.13.12.

PEPFAR. (2019). Large National Survey Shows Smaller HIV Epidemic in Nigeria Than Once Thought and Highlights Key Gaps Toward Reaching HIV Epidemic Control.

Perdigão-Neto, L. V., Oliveira, M.S., Rizek, C.F., Carrilho, C.M.D.M., Costa, S.F., Levin, A.S. (2014) Susceptibility of multiresistant gram-negative bacteria to fosfomycin and performance of different susceptibility testing methods. *Antimicrobial Agents and*

Chemotherapy. 58 (3), pp. 1763–1767. doi:10.1128/AAC.02048-13.

Pérez, M. S., Cannella, G. S. (2013). Situational Analysis as an Avenue for Critical Qualitative Research: Mapping Post-Katrina New Orleans. *Qualitative Inquiry*. https://doi.org/10.1177/1077800413489514

Perovic, O., Yahaya, A. A., Viljoen, C., Ndihokubwayo, J. B., Smith, M., Coulibaly, S. O., Frean, J. (2019). External quality assessment of bacterial identification and antimicrobial susceptibility testing in African national public health laboratories, 2011-2016. *Tropical Medicine and Infectious Disease*, *4*(4). https://doi.org/10.3390/tropicalmed4040144

Perovic, O., Schultsz, C. (2018) Stepwise approach for implementation of antimicrobial resistance surveillance in Africa. *African Journal of Laboratory Medicine*. 5 (3), pp. 1–7. doi:10.4102/ajlm.v5i3.482.

Pessoa-Silva, C. (2018) Fighting AMR-Partnership in Action: Update on Early GLASS Implementation and Summary Findings. *Regional Symposium on AMR Surveillance* https://www.chp.gov.hk/files/pdf/amrhk_2_1_dr_carmem_l_pessoa_silva_session2_glass_update_descriptive_stats.pdf

Pezzani, M. D., Mazzaferri, F., Compri, M., Galia, L., Mutters, N. T., Kahlmeter, G., Tacconelli, E. (2020). Linking antimicrobial resistance surveillance to antibiotic policy in healthcare settings: The COMBACTE-Magnet EPI-Net COACH project. *Journal of Antimicrobial Chemotherapy*. https://doi.org/10.1093/jac/dkaa425

PHE. (2017) Public Health England annual report and accounts: 2016 to 2017. https://www.gov.uk/government/publications/phe-annual-report-and-accounts-2016-to-2017

Picot, V.S., Bénet, T., Messaoudi, M., Telles, J.N., Chou, M., Eap, T., Wang, J., Shen, K., Pape, J.W., Rouzier, V., Awasthi, S., Pandey, N., Bavdekar, A., Sanghvi. (2014) Multicenter case-control study protocol of pneumonia etiology in children: Global Approach to Biological Research, Infectious diseases and Epidemics in Low-income countries

(GABRIEL network). *BMC Infectious Diseases*. 14 (1), pp. 635. doi:10.1186/s12879-014-0635-8.

Pisoschi, A.M., Pop, A., Georgescu, C., Turcuş, V., Olah, N.K., Mathe, E. (2018) An overview of natural antimicrobials role in food *European Journal of Medicinal Chemistry*. doi:10.1016/j.ejmech.2017.11.095.

Pittalis, C., Brugha, R., Gajewski, J. (2019). Surgical referral systems in low- And middle-income countries: A review of the evidence. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0223328

Pius, S., Bello, M., Galadima, G.B., Ibrahim, H.A., Yerima, S.T., Ambe, J.P. (2016) Neonatal septicaemia, bacterial isolates and antibiogram sensitivity in Maiduguri North-Eastern Nigeria. *The Nigerian postgraduate medical journal*. 23 (3), pp. 146–151. doi:10.4103/1117-1936.190340.

Plüddemann, A., Onakpoya, I., Harrison, S., Shinkins, B., Tompson, A., Davis, R., Price, C.P., Heneghan, C. (2015) Position Paper on Anti-Microbial Resistance Diagnostics Position Paper on Anti-Microbial Resistance Diagnostics. *Centre for Evidence Based Medicine*. (June), pp. 0–142. doi:10.13140/RG.2.1.1135.9846.

Pluye, P., Hong, Q. N. (2014). Combining the power of stories and the power of numbers: Mixed methods research and mixed studies reviews. *Annual Review of Public Health*. https://doi.org/10.1146/annurev-publhealth-032013-182440

Podewils, L. J., Bantubani, N., Bristow, C., Bronner, L. E., Peters, A., Pym, A., Mametja, L. D. (2015). Completeness and Reliability of the Republic of South Africa National Tuberculosis (TB) Surveillance System. *BMC Public Health*. https://doi.org/10.1186/s12889-015-2117-3

Pontoretto, J. G. (2006). Brief Note on the Origins, Evolution, and Meaning of the Qualitative Research Concept “Thick Description.” *The Qualitative Report*.

Poole, K. (2014) Efflux-mediated antimicrobial resistance. In: *Antibiotic Discovery and Development*. doi:10.1007/978-1-4614-1400-1_10.

Powers, J.H. (2004) Antimicrobial drug development - The past, the present, and the future. *Clinical Microbiology and Infection, Supplement*. doi:10.1111/j.1465-0691.2004.1007.x.

Price, L., Gozdzielewska, L., Young, M., Smith, F., Macdonald, J., Mcparland, J., Flowers, P. (n.d.). *Effectiveness of interventions to improve the public's antimicrobial resistance awareness and behaviours associated with prudent use of antimicrobials: a systematic review*. https://doi.org/10.1093/jac/dky076

Qualtrics, Provo, UT, USA (2020). The data analysis for this paper was generated using Qualtrics software, Copyright © [2020]. Qualtrics and all other Qualtrics product or service names are registered trademarks or trademarks of. https://www.qualtrics.com

Ragheb, M.N., Thomason, M.K., Hsu, C., Nugent, P., Gage, J., Samadpour, A.N., Kariisa, A., Merrikh, C.N., Miller, S.I., Sherman, D.R., Merrikh, H. (2019) Inhibiting the Evolution of Antibiotic Resistance. *Molecular Cell* [online]. 73 (1), pp. 157-165.e5. Available from: https://doi.org/10.1016/j.molcel.2018.10.015doi:10.1016/j.molcel.2018.10.015.

Raouf, M., Ghazal, T., Kassem, M., Agamya, A., Amer, A. (2020). Surveillance of surgical-site infections and antimicrobial resistance patterns in a tertiary hospital in Alexandria, Egypt. *Journal of Infection in Developing Countries*. https://doi.org/10.3855/jidc.12124

Ratan, S. K., Anand, T., Ratan, J. (2019). Formulation of research question-Stepwise approach. *Journal of Indian Association of Pediatric Surgeons*. https://doi.org/10.4103/jiaps.JIAPS_76_18

Rawat, D., Nair, D. (2010) Extended-spectrum ß-lactamases in gram negative bacteria.

Journal of Global Infectious Diseases. doi:10.4103/0974-777x.68531.

Razonable, R.R. (2011) Antiviral drugs for viruses other than human immunodeficiency virus. In: *Mayo Clinic Proceedings*. 2011 doi:10.4065/mcp.2011.0309.

Rempel, O., Pitout, J. D. D., Laupland, K. B. (2011). Antimicrobial resistance surveillance systems: Are potential biases taken into account? *Canadian Journal of Infectious Diseases and Medical Microbiology*. https://doi.org/10.1155/2011/276017

Report, G. (2014). World Health Organisation. Antimicrobial Resistance: Global Report on Surveillance. (WHO Press, 2014). *Bulletin of the World Health Organisation*.

Reygaert, W.C. (2018) *An overview of the antimicrobial resistance mechanisms of bacteria*. 4 (April), pp. 482–501. doi:10.3934/microbiol.2018.3.482.

Rezigalla, A. A. (2020). Observational Study Designs: Synopsis for Selecting an Appropriate Study Design. *Cureus*. https://doi.org/10.7759/cureus.6692

Richardson, W. S., Wilson, M. C., Nishikawa, J., Hayward, R. S. (1995). The well-built clinical question: a key to evidence-based decisions. *ACP Journal Club*. https://doi.org/10.7326/acpjc-1995-123-3-a12

Rinsky, J.L., Nadimpalli, M., Wing, S., Hall, D., Baron, D., Price, L.B., Larsen, J., Stegger, M., Stewart, J., Heaney, C.D. (2013) Livestock-Associated Methicillin and Multidrug Resistant Staphylococcus aureus Is Present among Industrial, Not Antibiotic-Free Livestock Operation Workers in North Carolina. *PLoS ONE*. doi:10.1371/journal.pone.0067641.

Roberts, M.C., Schwarz, S. (2017) Tetracycline and Chloramphenicol Resistance Mechanisms. In: *Antimicrobial Drug Resistance*. doi:10.1007/978-3-319-46718-4_15.

Rogers Van Katwyk, S., Jones, S. L., Hoffman, S. J. (2018). Mapping educational opportunities for healthcare workers on antimicrobial resistance and stewardship around the

world. *Human Resources for Health*. https://doi.org/10.1186/s12960-018-0270-3

Rojanaworarit, C. (2020). *Misleading Epidemiological and Statistical Evidence in the Presence of Simpson ' s Paradox : An Illustrative Study Using Simulated Scenarios of Observational Study Designs Scenario 2 : A cohort study with a dichotomous outcome Scenario 3 : A case-control* . *13*(1), 37–44. https://doi.org/10.25122/jml-2019-0120

Rousham, E.K., Unicomb, L., Islam, M.A. (2018) Human, animal and environmental contributors to antibiotic resistance in low-resource settings: Integrating behavioural, epidemiological and one health approaches. *Proceedings of the Royal Society B: Biological Sciences*. 285 (1876), . doi:10.1098/rspb.2018.0332.

Ryu, S., Cowling, B. J., Wu, P., Olesen, S., Fraser, C., Sun, D. S., Grad, Y. H. (2019). Case-based surveillance of antimicrobial resistance with full susceptibility profiles. *JAC-Antimicrobial Resistance*. https://doi.org/10.1093/jacamr/dlz070

Saeed, D. K., Hasan, R., Naim, M., Zafar, A., Khan, E., Jabeen, K., Rao, J. (2017). Readiness for antimicrobial resistance (AMR) surveillance in Pakistan; a model for laboratory strengthening. *Antimicrobial Resistance and Infection Control*, *6*(1), 1–7. https://doi.org/10.1186/s13756-017-0260-6

Sangeda, R. Z., Kibona, J., Munishi, C., Arabi, F., Manyanga, V. P., Mwambete, K. D., Horumpende, P. G. (2020). Assessment of Implementation of Antimicrobial Resistance Surveillance and Antimicrobial Stewardship Programs in Tanzanian Health Facilities a Year After Launch of the National Action Plan. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2020.00454

Santos, K. da S., Ribeiro, M. C., de Queiroga, D. E. U., da Silva, I. A. P., Ferreira, S. M. S. (2020). The use of multiple triangulations as a validation strategy in a qualitative study. *Ciencia e Saude Coletiva*. https://doi.org/10.1590/1413-81232020252.12302018

Sauvage, E., Terrak, M. (2016) Glycosyltransferases and transpeptidases/penicillin-

binding proteins: Valuable targets for new antibacterials *Antibiotics*. doi:10.3390/antibiotics5010012.

Schnall, J., Rajkhowa, A., Ikuta, K., Rao, P., Moore, C. E. (2019). Surveillance and monitoring of antimicrobial resistance: Limitations and lessons from the GRAM project. *BMC Medicine, 17*(1), 10–12. https://doi.org/10.1186/s12916-019-1412-8

Schober, P., Schwarte, L. A. (2018). Correlation coefficients: Appropriate use and interpretation. *Anesthesia and Analgesia*. https://doi.org/10.1213/ANE.0000000000002864

Schrag, S. J., Zell, E. R., Schuchat, A., Whitney, C. G. (2002). Sentinel surveillance: A reliable way to track antibiotic resistance in communities? *Emerging Infectious Diseases*, *8*(5), 496–502. https://doi.org/10.3201/eid0805.010268

Scotland, J. (2012) Exploring the Philosophical Underpinnings of Research: Relating Ontology and Epistemology to the Methodology and Methods of the Scientific, Interpretive, and Critical Research Paradigms. English Language Teaching, 5, 9-16. https://doi.org/10.5539/elt.v5n9p9

Seale, A. C., Hutchison, C., Fernandes, S., Stoesser, N., Kelly, H., Lowe, B., Scott, J. A. G. (2017). Supporting surveillance capacity for antimicrobial resistance: Laboratory capacity strengthening for drug resistant infections in low and middle income countries. *Wellcome Open Research*, *2*(0), 1–18. https://doi.org/10.12688/wellcomeopenres.12523.1

Seale, A. C., Gordon, N. C., Islam, J., Peacock, S. J., Scott, J. A. G. (2017). AMR surveillance in low and middle-income settings - A roadmap for participation in the Global Antimicrobial Surveillance System (GLASS). *Wellcome Open Research*, *2*(0), 1–17. https://doi.org/10.12688/wellcomeopenres.12527.1

Seidman, I. (2006). Interviewing as Qualitative Research : A Guide for Researchers in Education and The Social Sciences. In *Teachers College Press*.

Shaikh, S., Fatima, J., Shakil, S., Rizvi, S.M.D., Kamal, M.A. (2015) Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. *Saudi Journal of Biological Sciences*. doi:10.1016/j.sjbs.2014.08.002.

Shallcross, L.J., Howard, S.J., Fowler, T., Davies, S.C. (2015) Tackling the threat of antimicrobial resistance: From policy to sustainable action. *Philosophical Transactions of the Royal Society B: Biological Sciences*. doi:10.1098/rstb.2014.0082.

Shankar, Pr. (2016) Book review: Tackling drug-resistant infections globally. *Archives of Pharmacy Practice*. 7 (3), pp. 110. doi:10.4103/2045-080x.186181.

Shelton, R. C., Cooper, B. R., Stirman, S. W. (2018). The Sustainability of Evidence-Based Interventions and Practices in Public Health and Health Care. *Annual Review of Public Health*. https://doi.org/10.1146/annurev-publhealth-040617-014731

Silva, V., Capelo, J.L., Igrejas, G., Poeta, P. (2020) Molecular Epidemiology of Staphylococcus aureus Lineages in Wild Animals in Europe: A Review. *Antibiotics (Basel, Switzerland)* [online]. 9 (3), . Available from: http://www.ncbi.nlm.nih.gov/pubmed/32183272doi:10.3390/antibiotics9030122

Singer, R. S., Schrag, N. F. D., Ricke, I., Apley, M. D. (2023). Antimicrobial usage in broiler chicken production in the United States, 2013–2021. *Frontiers in Veterinary Science*. https://doi.org/10.3389/fvets.2023.1139908

Smith J. A., Flowers P., Larkin M. (2012). *Interpretative phenomenological analysis theory, method and research*. Sage Publications.

Smith J. A. (2004). Reflecting on the development of interpretative phenomenological analysis and its contribution to qualitative research in psychology. *Qualitative Research in Psychology*, 1, 39–54.

Sobieraj, D. M., Baker, W. L. (2021). Research and scholarly methods: Systematic

reviews. *JACCP Journal of the American College of Clinical Pharmacy*. https://doi.org/10.1002/jac5.1440

Spoor, L.E., McAdam, P.R., Weinert, L.A., Rambaut, A., Hasman, H., Aarestrup, F.M., Kearns, A.M., Larsen, A.R., Skov, R.L., Ross Fitzgerald, J. (2013) Livestock origin for a human pandemic clone of community-associated methicillin-resistant Staphylococcus aureus. *mBio*. doi:10.1128/mBio.00356-13.

Stanley, L., Wise, S. (2002). Breaking Out Again: Feminist Ontology and Epistemology New Edition. In *Taylor & Francis e-Library*.

Suleiman, I. A., Fola, T. (2013). Usefulness of routine antibacterial susceptibility testing results for resistance surveillance in lagos metropolis. *African Journal of Biomedical Research*, *16*(1), 11–17.

Sulis, G., Adam, P., Nafade, V., Gore, G., Daniels, B., Daftary, A., Pai, M. (2020). Antibiotic prescription practices in primary care in low- And middle-income countries: A systematic review and meta-analysis. *PLoS Medicine*. https://doi.org/10.1371/journal.pmed.1003139

Sun, S. Y., Wang, M. M., Li, L., Ren, R., Li, H. L., Ren, M., Liu, C. X. (2022). Research progress on antibiotic resistance and new antibiotics development. *Drugs and Clinic*. https://doi.org/10.7501/j.issn.1674-5515.2022.02.001

Tabak, R. G., Research Assistant Professor, R., Warren, G., Duggan, K., Manager, R., Smith, C., Becker Professor, B. (2016). Assessing capacity for sustainability of effective programs and policies in local health departments HHS Public Access. *J Public Health Manag Pract*, *22*(2), 129–137. https://doi.org/10.1097/PHH.0000000000000254

Tacconelli, E., Sifakis, F., Harbarth, S., Schrijver, R., van Mourik, M., Voss, A.Wolkewitz, M. (2018). Surveillance for control of antimicrobial resistance. *The Lancet Infectious Diseases*. https://doi.org/10.1016/S1473-3099(17)30485-1

Tacconelli, E., Sifakis, F., Harbarth, S., Schrijver, R., van Mourik, M., Voss, A., Wolkewitz, M. (2018). Surveillance for control of antimicrobial resistance. *The Lancet Infectious Diseases*. https://doi.org/10.1016/S1473-3099(17)30485-1

Tacconelli, E., Carrara, E., Savoldi, A., Harbarth, S., Mendelson, M., Monnet, D.L., Pulcini, C., Kahlmeter, G., Kluytmans, J., Carmeli, Y., Ouellette, M., Outterson, K., Patel, J., Cavaleri, M. (2018) Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *The Lancet Infectious Diseases*. doi:10.1016/S1473-3099(17)30753-3.

Tadesse, B. T., Ashley, E. A., Ongarello, S., Havumaki, J., Wijegoonewardena, M., González, I. J., Dittrich, S. (2017). Antimicrobial resistance in Africa: A systematic review. *BMC Infectious Diseases*. https://doi.org/10.1186/s12879-017-2713-1

Taiwo, S., Aderounmu, A. (2009) Catheter associated urinary tract infection: Aetiologic agents and antimicrobial susceptibility pattern in Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria. *African Journal of Biomedical Research*. 9 (3), pp. 141–148. doi:10.4314/ajbr.v9i3.48897.

Taiwo, S.S., Fadiora, S.O., Fayemiwo, S.A. (2008) High antimicrobial resistance among bacterial isolates of blood stream infections (BSI) in a Nigerian University Teaching Hospital. *World Journal of Microbiology and Biotechnology*. 24 (2), pp. 231–236. doi:10.1007/s11274-007-9461-0.

Taiwo 1, M Bamidele, E A Omonigbehin, K A Akinsinde, S I Smith, B A Onile, A.O.O. (2005) *Molecular Epidemiology of Methicillin-Resistant Staphylococcus Aureus in Ilorin, Nigeria - PubMed*. Available from: https://pubmed.ncbi.nlm.nih.gov/16092307/ [Accessed 19 May 2020].

Talisuna, A., Yahaya, A. A., Rajatonirina, S. C., Stephen, M., Oke, A., Mpairwe, A., Fall, I. S. (2019). Joint external evaluation of the International Health Regulation (2005) capacities :

current status and lessons learnt in the WHO African region. *BMJ Global Health*, (2005), 1–8. https://doi.org/10.1136/bmjgh-2018-001312

Taur, S. R. (2022). Observational designs for real-world evidence studies. *Perspectives in Clinical Research*. https://doi.org/10.4103/picr.picr_217_21

Tejeda, M. J. (2007). Book Review: Clarke, A. E. (2005). Situational analysis: Grounded theory after the postmodern turn. Thousand Oaks, CA: Sage. *Organisational Research Methods*. https://doi.org/10.1177/1094428106290198

Tenover, F.C. (2006) Mechanisms of antimicrobial resistance in bacteria. *American Journal of Infection Control*. doi:10.1016/j.ajic.2006.05.219.

Thandar, M. M., Baba, T., Matsuoka, S., Ota, E. (2020). Interventions to reduce non-prescription antimicrobial sales in community pharmacies. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD013722

Thomas, E., Magilvy, J.K. (2011) Qualitative rigor or research validity in qualitative research. *J Spec Pediatr Nurs*. Apr;16(2):151-5. doi: 10.1111/j.1744-6155.2011.00283.x. PMID: 21439005.

Thu Trang, N.H., Thieu Nga, T.V., Campbell, J.I., Hiep, N.T., Farrar, J., Baker, S., Duy, P.T. (2013) The characterization of ESBL genes in Escherichia coli and Klebsiella pneumoniae causing nosocomial infections in Vietnam. *Journal of Infection in Developing Countries*. doi:10.3855/jidc.2938.

Tiseo, K., Huber, L., Gilbert, M., Robinson, T. P., Van Boeckel, T. P. (2020). Global trends in antimicrobial use in food animals from 2017 to 2030. *Antibiotics*. https://doi.org/10.3390/antibiotics9120918

Tobin, G. A., Begley, C. M. (2004). Methodological rigour within a qualitative framework. *Journal of Advanced Nursing*. https://doi.org/10.1111/j.1365-2648.2004.03207.x

Tong, A., Sainsbury, P., Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. https://doi.org/10.1093/intqhc/mzm042

Toro, M., Sáenz, Y., Cercenado, E., Rojo-Bezares, B., García-Campello, M., Undabeitia, E., Torres, C. (2011) Genetic characterization of the mechanisms of resistance to amoxicillin/clavulanate and third-generation cephalosporins in Salmonella enterica from three Spanish hospitals. *International Microbiology*. 14 (3), pp. 173–181. doi:10.2436/20.1501.01.146.

Tran-Dien, A., Le Hello, S., Bouchier, C., Weill, F.X. (2018) Early transmissible ampicillin resistance in zoonotic Salmonella enterica serotype Typhimurium in the late 1950s: a retrospective, whole-genome sequencing study. *The Lancet Infectious Diseases*. doi:10.1016/S1473-3099(17)30705-3.

Tucker, S. A., Johnson, R. B., Onwuegbuzie, T., Icenogle, M. L. (2020). Conducting mixed methods research: Using dialectical pluralism and social psychological strategies. In *The Oxford Handbook of Qualitative Research*. https://doi.org/10.1093/oxfordhb/9780190847388.013.32

Tyndall J 2010. *AACODS checklist for appraising grey literature*. Retrieved from https://dspace.flinders.edu.au/xmlui/bitstream/handle/2328/3326/AACODS_Checklist.pdf

Ubi, P., Ndem, B. (2019). POVERTY AND HEALTH OUTCOMES IN NIGERIA. *International Journal of Economics and Financial Issues*. https://doi.org/10.32479/ijefi.8704

Uchil, R.R., Kohli, G.S., Katekhaye, V.M., Swami, O.C. (2014) Strategies to combat antimicrobial resistance. *Journal of Clinical and Diagnostic Research*. doi:10.7860/JCDR/2014/8925.4529.

UNAS (2015) *Antibiotic Resistance in Uganda : Situation Anaysis*.

15%5Cnhttp://www.anmjournal.com/text.asp?2013/7/1/1/119978%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3075864&tool=pmcentrez&rendertype=abstract%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/211195doi:10.1186/s12866-015-0510-9.

UN-IACG (2016) *WHO | UN Interagency Coordination Group (IACG) on Antimicrobial Resistance*. Available from: https://www.who.int/antimicrobial-resistance/interagency-coordination-group/en/.

US-CDC (2017) *Senegal - CDC - Center for Global Health*. Available from: https://www.cdc.gov/globalhealth/countries/senegal/default.htm

US-CDC (2018) *Tracking Antibiotic Resistance in Kenya and Senegal | Antibiotic/Antimicrobial Resistance | CDC*. Available from: https://www.cdc.gov/drugresistance/solutions-initiative/stories/surveillance-in-Kenya-Senegal.html.

US-CDC (2019) Antibiotic resistance threats in the United States. *Centers for Disease Control and Prevention*. pp. 1–150.

Uzochukwu, B.S.C., Ughasoro, M.D., Etiaba, E., Okwuosa, C., Envuladu, E., Onwujekwe, O.E. (2015) Health care financing in Nigeria: Implications for achieving universal health coverage. *Nigerian Journal of Clinical Practice*. 18 (4), pp. 437–444. doi:10.4103/1119-3077.154196.

Valavanidis, A. (2017) A new discovery of antibiotic Teixobactin: Treating infections without detectable bacterial resistance *Pharmakeftiki*. 2017; 29 (I): 1-11

Van Boeckel, T. P., Gandra, S., Ashok, A., Caudron, Q., Grenfell, B. T., Levin, S. A., Laxminarayan, R. (2014). Global antibiotic consumption 2000 to 2010: An analysis of national pharmaceutical sales data. *The Lancet Infectious Diseases*. https://doi.org/10.1016/S1473-3099(14)70780-7

Van Duin, D., Lok, J.J., Earley, M., Cober, E., Richter, S.S., Perez, F., Salata, R.A., Kalayjian, R.C., Watkins, R.R., Doi, Y., Kaye, K.S., Fowler, V.G., Paterson, D.L., Bonomo, R.A. (2018) Colistin Versus Ceftazidime-Avibactam in the Treatment of Infections Due to Carbapenem-Resistant Enterobacteriaceae. *Clinical Infectious Diseases*. doi:10.1093/cid/cix783.

Van Herwerden, L. A., Palermo, C., Reidlinger, D. P. (2019). Capacity assessment in public health community interventions: A systematic review. *Health Promotion International*. https://doi.org/10.1093/heapro/day071

Van Hoek, A.H.A.M., Mevius, D., Guerra, B., Mullany, P., Roberts, A.P., Aarts, H.J.M. (2011) Acquired antibiotic resistance genes: An overview *Frontiers in Microbiology*. doi:10.3389/fmicb.2011.00203.

Van Smeden, M., De Groot, J. A. H., Moons, K. G. M., Collins, G. S., Altman, D. G., Eijkemans, M. J. C., Reitsma, J. B. (2016). No rationale for 1 variable per 10 events criterion for binary logistic regression analysis. *BMC Medical Research Methodology*. https://doi.org/10.1186/s12874-016-0267-3

Vargas, I., Eguiguren, P., Mogollón-Pérez, A. S., Bertolotto, F., Samico, I., López, J., Vázquez, M. L. (2020). Understanding the factors influencing the implementation of participatory interventions to improve care coordination. An analytical framework based on an evaluation in Latin America. *Health Policy and Planning*. https://doi.org/10.1093/heapol/czaa066

Varma, J. K., Oppong-Otoo, J., Ondoa, P., Perovic, O., Park, B. J., Laxminarayan, R., Nkengasong, J. N. (2018). Africa Centres for Disease Control and Prevention's framework for antimicrobial resistance control in Africa. *African Journal of Laboratory Medicine*. https://doi.org/10.4102/ajlm.v7i2.830

Vegyari, C., Underwood, A., Kekre, M., Argimon, S., Muddyman, D., Abrudan, M., Aanensen, D. (2020). Whole-genome sequencing as part of national and international

surveillance programmes for antimicrobial resistance: A roadmap. *BMJ Global Health*, *5*(11), 1–13. https://doi.org/10.1136/bmjgh-2019-002244

Von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P. (2014). The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *International Journal of Surgery*. https://doi.org/10.1016/j.ijsu.2014.07.013

Vuitton, D.A., Demonmerot, F., Knapp, J., Richou, C., Grenouillet, F., Chauchet, A., Vuitton, L., Bresson-Hadni, S., Millon, L. (2015) Clinical epidemiology of human AE in Europe. *Veterinary Parasitology*. doi:10.1016/j.vetpar.2015.07.036.

Vuotto, C., Longo, F., Balice, M.P., Donelli, G. and Varaldo, P.E. (2014) Antibiotic resistance related to biofilm formation in Klebsiella pneumoniae *Pathogens*. doi:10.3390/pathogens3030743.

Waele, J.J., Akova, M., Antonelli, M., Canton, R., Carlet, J., De Backer, D., Dimopoulos, G., Garnacho-Montero, J., Kesecioglu, J., Lipman, J., Mer, M., Paiva, J.A., Poljak, M., Roberts, J.A. (2018) Antimicrobial resistance and antibiotic stewardship programs in the ICU: insistence and persistence in the fight against resistance. A position statement from ESICM/ESCMID/WAAAR round table on multi-drug resistance. In: *Intensive Care Medicine*. 2018 doi:10.1007/s00134-017-5036-1.

Walsh, C. (2003). Opinion – anti-infectives: Where will new antibiotics come from? *Nature Reviews Microbiology*. https://doi.org/10.1038/nrmicro727

Walugembe, D. R., Sibbald, S., Le Ber, M. J., Kothari, A. (2019). Sustainability of public health interventions: Where are the gaps? *Health Research Policy and Systems*. https://doi.org/10.1186/s12961-018-0405-y

Wang, X., Ji, X. (2020). Sample Size Estimation in Clinical Research: From Randomized Controlled Trials to Observational Studies. *Chest*. https://doi.org/10.1016/j.chest.2020.03.010

Warren, J. I., Mclaughlin, M., Bardsley, J., Eich, J., Esche, C. A., Kropkowski, L., Risch, S. (2016). The Strengths and Challenges of Implementing EBP in Healthcare Systems. *Worldviews on Evidence-Based Nursing*. https://doi.org/10.1111/wvn.12149

Weese, J.S., van Duijkeren, E. (2010) Methicillin-resistant Staphylococcus aureus and Staphylococcus pseudintermedius in veterinary medicine *Veterinary Microbiology*. doi:10.1016/j.vetmic.2009.01.039.

Weiner, L.M., Webb, A.K., Limbago, B., Dudeck, M.A., Patel, J., Kallen, A.J., Edwards, J.R., Sievert, D.M. (2016) Antimicrobial-Resistant Pathogens Associated with Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. *Infection Control and Hospital Epidemiology*. doi:10.1017/ice.2016.174.

Wellington, E.M.H., Boxall, A.B.A., Cross, P., Feil, E.J., Gaze, W.H., Hawkey, P.M., Johnson-Rollings, A.S., Jones, D.L., Lee, N.M., Otten, W., Thomas, C.M., Williams, A.P. (2013) The role of the natural environment in the emergence of antibiotic resistance in Gram-negative bacteria *The Lancet Infectious Diseases* 13 (2) p.pp. 155–165. doi:10.1016/S1473-3099(12)70317-1.

(WHO), W. H. O., (FAO), F. A. O. of the U. N., (OIE), W. O. A. H. (2016). Antimicrobial Resistance: A Manual for Developing National Action Plans. In *Jama*. https://doi.org/10.1001/jama.2016.11764

WHO-AMR (2017) *WHO AMR Surveillance and Quality Assessment Collaborating Centre Network webinar series : Diagnostic Stewardship*. Retrieved from https://www.who.int/publications/m/item/who-amr-surveillance-and-quality-assessment-collaborating-centres-network---second-meeting

Willemsen, A., Reid, S., Assefa, Y. (2022). A review of national action plans on antimicrobial resistance: strengths and weaknesses. *Antimicrobial Resistance and Infection*

Control. https://doi.org/10.1186/s13756-022-01130-x

Wilson, V. (2016). Research methods: Systematic reviews. *Evidence Based Library and Information Practice*. https://doi.org/10.18438/B8M324

Wimpenny, P., Gass, J. (2000). Interviewing in phenomenology and grounded theory: Is there a difference? *Journal of Advanced Nursing*. https://doi.org/10.1046/j.1365-2648.2000.01431.x

Wintersdorff, C.J.H., Penders, J., van Niekerk, J.M., Mills, N.D., Majumder, S., van Alphen, L.B., Savelkoul, P.H.M., Wolffs, P.F.G. (2016) Dissemination of Antimicrobial Resistance in Microbial Ecosystems through Horizontal Gene Transfer. *Frontiers in microbiology*. doi:10.3389/fmicb.2016.00173.

Woodward, K.N. (2013) *CHAPTER 12. Antiparasitic Drugs*. In: doi:10.1039/9781849736862-00095.

World Bank (2022) April 2022 global poverty update from the World Bank https://blogs.worldbank.org/en/opendata/april-2022-global-poverty-update-world-bankS

World Bank (2016) Drug-Resistant Infections: A Threat to Our Economic Future. *World Bank Report*[online]. 2 (September), pp. 1–132. Available from: www.worldbank.orgdoi:10.1007/s11947-009-0181-3

World Health Organisation. (2020). Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report: Early Implementation 2020. *Global Antimicrobial Resistance and Use Surveillance System*:

World Health Organisation. (2018). *Global antimicrobial resistance surveillance system (GLASS) report: early implementation 2016-2017*. Retrieved from https://apps.who.int/iris/bitstream/handle/10665/259744/9789241513449-eng.pdf

World Health Organisation. (2017). Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria: Application of a One Health Approach. Retrieved from https://www.who.int/publications/i/item/9789241512411

World Health Organisation. (2016) *WHO/Europe | Antimicrobial resistance - Global trends – bacteria*. Available from:http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/about-amr/global-trends-bacteria.

World Health Organisation. (2015). Global action plan on antimicrobial resistance. *WHO Press*. https://doi.org/ISBN 978 92 4 150976 3

World Health Organisation. (2014) Antimicrobial resistance: global report on surveillance 2014. *World Health Organisation*. doi:9789241564748.

World Health Organisation. (2013). *Guide for establishing laboratory-based surveillance for antimicrobial resistance. Disease Surveillance and Response Programme. Area Disease Prevention and Control Cluster.*

World Health Organisation. (1998) Resolution WHA51.17 Emerging and other communicable
diseases: antimicrobial resistance. *World Health Assembly fifty-first session, agenda item 21.3* [online]. (May), pp. 16–17. Available from: http://apps.who.int//iris/handle/10665/79863.

World Health Organisation. (2010)bA framework for national health policies, strategies and plans. Geneva: World Health Organisation.

Wozniak, T. M., Smith-Vaughan, H., Andrews, R. (2021). Convergence of surveillance blind spots with antimicrobial resistance hotspots. *Australian and New Zealand Journal of Public Health*. https://doi.org/10.1111/1753-6405.13165

Xu, Y., Gu, B., Huang, M., Liu, H., Xu, T., Xia, W., Wang, T. (2015). Epidemiology of carbapenem resistant Enterobacteriaceae (CRE) during 2000-2012 in Asia. *Journal of Thoracic Disease*. https://doi.org/10.3978/j.issn.2072-1439.2014.12.33

Yah., No, Eghafona., Io, Enabulele., Hsa, A. (2006) Ampicillin Usage and Ampicillin Resistant (Ampr) Plasmids Mediated Escherichia Coli Isolated from Diarrheagenic Patients Attending Some Teaching Hospital in Nigeria . Abstract : Introduction : *Shiraz E-Medical Journal*. 7 (4), pp. 1–12.

Yam, E.L.Y., Hsu, L.Y., Yap, E.P.-H., Yeo, T.W., Lee, V., Schlundt, J., Lwin, M.O., Limmathurotsakul, D., Jit, M., Dedon, P., Turner, P., Wilder-Smith, A. (2019) Antimicrobial Resistance in the Asia Pacific region: a meeting report. *Antimicrobial resistance and infection control* [online]. 8 (1), pp. 202. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31890158doi:10.1186/s13756-019-0654-8

Yigit, H., Queenan, A.M., Anderson, G.J., Domenech-Sanchez, A., Biddle, J.W., Steward, C.D., Alberti, S., Bush, K., Tenover, F.C., Papp-Wallace, K.M., Endimiani, A., Taracila, M.A., Bonomo, R.A., Nordmann, P. (2011) Carbapenem-resistant and carbapenem-susceptible isogenic isolates of Klebsiella pneumoniae ST101 causing infection in a tertiary hospital. *BMC Microbiology* [online]. 46 (1), pp. 177. Available from: http://jcm.asm.org/lookup/doi/10.1128/JCM.01915.

Yong, D., Shin, H.B., Kim, Y.K., Cho, J., Lee, W.G., Ha, G.Y., Choi, T.Y., Jeong, S.H., Lee, K., Chong, Y. (2014) Increase in the prevalence of carbapenem-resistant acinetobacter isolates and ampicillin-resistant non-typhoidal Salmonella species in Korea: A KONSAR Study Conducted in 2011. *Infection and Chemotherapy*. 46 (2), pp. 84–93. doi:10.3947/ic.2014.46.2.84.

Yusuf, E.O., Airauhi, L.U. (2015) Prevalence and Pattern of Methicillin Resistant Staphylococcus Aureus in a Tertiary Healthcare Facility in Nigeria. *Medical Journal of Zambia*. 42 (1), pp. 7–11.

Xiong, W., Sun, Y., Zeng, Z. (2018) Antimicrobial use and antimicrobial resistance in food animals *Environmental Science and Pollution Research*. doi:10.1007/s11356-018-1852-2.

Zervosen, A., Sauvage, E., Frère, J.M., Charlier, P., Luxen, A. (2012) Development of new drugs for an old target - The penicillin binding proteins *Molecules*. doi:10.3390/molecules171112478.

Zhao, C., Zhang, F., Chu, Y., Cao, B., Sun, H., Yu, Y., Liao, K., Zhang, L., Sun, Z., Hu, B., Lei, J., Hu, Z., Zhang, X., Wang, H. (2017) Changing trends in antimicrobial resistance and serotype distribution of streptococcus pneumoniae isolates in china from 2005 to 2014. *American Journal of Respiratory and Critical Care Medicine*. doi:http://dx.doi.org/10.1164/ajrccm-conference.2017.B61.

Appendices

A1: Full ethics approval

Faculty of Health & Applied Sciences
Glenside Campus
Blackberry Hill
Stapleton
Bristol BS16 1DD

Tel: 0117 328 1170

UWE REC REF No: HAS.20.05.180

2nd October 2020

Obiageli Jovita Okolie

Dear Obiageli

Application title: Assessment of Antimicrobial resistance (AMR) surveillance System in Nigeria

Thank you for responding to the conditions raised in my letter to you of 26th August 2020.

I can now confirm full ethics approval for your project, but please note the proviso below.

Please note: In light of the current situation regarding COVID-19, we can only authorise an immediate start for activities that do not breach either national laws or University policies (for further information please click on the following link https://intranet.uwe.ac.uk/tasks-guides/Guide/research-and-enterprise-covid-19-information#part1). In these uncertain times, law and policy may change swiftly and frequently.

We are, however, continuing to scrutinise and grant ethical approval for activities that cannot take place at present, to ensure that once the situation changes and activities can go ahead, the research is not unnecessarily delayed.

What this means for your application:

1. If your application DOES NOT involve activities affected by the current crisis (e.g. online surveys or telephone interviews etc.) then you may start your research as soon as you receive this formal notification of your ethical approval;
2. If your application DOES involve activities affected by the current crisis then you must not start your research until you are lawfully and safely able to do so, and when it does not breach the University's policies. This will affect the dates you have supplied on your application form in relation to start and finish. When you have new dates, please can you write to us in order that we can add this information to your file?

If you are a doctoral student and this will affect your research timetable, please speak to your Director of Studies and the Graduate School for advice on how time delays will be supported by the University.

A2: Checklist of countries and surveillance systems

Countries	Nap Dev.	Nap Doc	Surveillance	Surv. Info
Algeria			X	X
Angola				
Benin				
Botswana				
Burkina Faso			X	X
Burundi				
Cameroon			X	X
Cabo Verde				
Central African Republic				
Chad			X	X
Comoros				
Congo				
Côte d'Ivoire			X	X
Democratic Republic of the Congo				
Equatorial Guinea				
Eritrea	X	X		
Eswatini	X	X		
Ethiopia	X	X	X	X
Gabon			X	X
Gambia			X	X
Ghana	X	X		X
Guinea				
Guinea-Bissau				
Kenya	X	X	X	X
Lesotho				
Liberia	X	X	X	X
Madagascar			X	X
Malawi	X	X	X	X
Mali			X	X
Mauritania			X	X
Mauritius	X	X	X	X
Mozambique			X	X
Namibia	X	X		
Niger				
Nigeria	X	X	X	X
Rwanda	X	X		
Sao Tome and Principe				
Senegal				
Seychelles				
Sierra Leone	X	X		
South Africa	X	X	X	X
South Sudan				
Togo				
Uganda	X	X	X	X
United Republic of Tanzania	X	X	X	X
Zambia	X	X	X	X
Zimbabwe	X	X	X	X

A3: PICO framework

P = Problem or Patient or Population	Antimicrobial resistance
I = Intervention	Surveillance
C = Comparators	Not applicable
O = Outcome	Surveillance designs, scope, methodology and attributes (data quality, timeliness, representativeness).

A4: Search strategy for database search

Concept 1 AND	Concept 2 AND	Concept 3 AND	Concept 4
((TITLE-ABS-KEY (africa OR "sub saharan Africa" OR "east Africa" OR "eastern africa" OR "north Africa" OR "northern Africa" OR "west Africa" OR "western Africa" OR "south Africa" OR "southern Africa" OR "central Africa" OR comoros OR djibouti OR madagascar) OR TITLE-ABS-KEY (malawi OR seychelles OR cameroon OR "Central African Republic" OR chad OR congo OR "Equatorial Guinea" OR "Atlantic Islands" OR gabon* OR morocco OR "South Sudan" OR sudan OR botswana OR lesotho OR swaziland OR benin) OR TITLE-ABS-KEY ("Burkina Faso" OR "Cape Verde" OR ghana OR guinea OR "Guinea Bissau" OR mauritania OR niger OR senegal OR "Sierra Leone" OR togo OR burundi OR eritrea* OR ethiopia* OR kenya*) OR TITLE-ABS-KEY (mozambique* OR rwanda* OR somalia* OR tanzania* OR uganda* OR zambia* OR zimbabwe* OR angola* OR algeria* OR egypt* OR tunisia* OR namibia* OR "South africa*" OR gambia* OR liberia* OR mali* OR nigeria*)))	((TITLE-ABS-KEY ("antimicrobial resistant" OR amr OR "microbial drug resistant" OR "multidrug resistant" OR mdr OR "multiple drug resistant" OR "antibiotic resistant" OR abr OR "antibiotics resistant" OR "antibacterial resistant" OR "bacteria drug resistan*") OR TITLE-ABS-KEY ("antiviral resistant" OR "drug resistant virus" OR "antifungal resistant" OR "drug resistant fungi" OR "antiparasitic resistan*" OR "drug resistant parasites" OR "drug resistant Enterococcus" OR "drug resistant Staphylococcus") OR TITLE-ABS-KEY ("drug resistant Klebsiella" OR "drug resistant Acinetobacter" OR "drug resistant Pseudomonas" OR "drug resistant Enterobacter" OR	((TITLE-ABS-KEY (surveillance OR tracking OR monitoring OR observation OR containment OR control OR "active surveillance" OR "Passive surveillance" OR "laboratory based surveillance" OR "sentinel surveillance") OR TITLE-ABS-KEY ("targeted surveillance" OR "population based surveillance" OR "integrated surveillance" OR "community-based surveillance")))	(TITLE-ABS-KEY (system OR structure OR approach OR program OR scheme OR plan OR tools OR framework OR method OR "action plan")) AND Humans (Mesh)

	"ESKAPE pathogen")))		

A5: Title and Abstract Screening form

Screening form is designed to reflect the inclusion/exclusion criteria with consideration to problem (including disease condition e.g. antimicrobial resistance and patient characteristic such as age or sex, human), intervention (surveillance), study designs and limits such as language, location and date of publication.

Paper title:

1. Does study report the desired problem? (antimicrobial resistance)
    - Yes (include)
    - No (exclude)
    - Can't tell (include)

2. Does this report include the target demographic? (human, Africa)
    - Yes
    - No

3. Does this report involve intervention? (surveillance)
    - Yes
    - No

4. Is one or more eligible outcome reported? (surveillance method, scope, reporting, representativeness)
    - Yes
    - No

5. Is the report unusable for any of the reasons below?
    - The intervention is not the main focus of the study (e.g. only mentioned in the discussion or references)
    - Report contains insufficient information to assess methodological quality.
    - Report involves animals and environment

- None of the above

6. Would you like this record included in a bibliography for your personal reading/referencing?
    - Yes
    - No

A6: Data extraction form for country

Country name:

1. Status of National action plan development
    - Developed and endorsed
    - Awaiting endorsement/approval
    - Under development
    - Not developed

2. Action plan timeline
    - Indicated
    - Not indicated

3. Indicated surveillance approach
    - One health
    - Integrated
    - Multi-sectoral

4. National reference laboratory
    - Established
    - Not established

5. Surveillance activities for AMR
    - Some surveillance
    - No surveillance
    - No capacity

6. GLASS enrolment/reporting
    - Yes

- No

7. Naps document
    - Assessable
    - Not assessable

A7: Data extraction form for surveillance system
Country name:

1. System focus
    - *Acinetobacter spp.*
    - *E. coli*
    - *K. pneumoniae*
    - *Salmonella spp.*
    - *S. aureus*
    - *S. pneumoniae*

2. representativeness
    - National
    - Sub-national

3. Targeted population
    - Hospital
    - Out patient
    - Laboratory

4. Frequency of reporting
    - Yearly
    - Pooled

5. Technical level of data management

    ……
    ……..

6. Data source

    ……
    ……..

7. Number of surveillance

   ……
   ……..

8. Testing method (s)

   ……
   …….....

9. Resistant criteria
   - CLSI
   - EUCAST

10. Provision of EQA
    - Provided NRL only
    - Provided to laboratory

11. Level of standardization across labs

    ……
    ……..

12. Data on number of tested patients
    - Reported
    - Not reported

A8: Study characteristics/identifier
Study design and characteristics helps to determine which Assessment tool or quality check to use and this was based on the items below;

Paper title:

1. Study design
    - Cross sectional study
    - Systematic review
    - Desktop analysis
    - Manuscript
    - Policy paper

2. Study setting
    - Laboratory
    - Hospital
    - Out patient
    - Report

3. Geographical location
    - Africa
    - Specific country

A9: AACODS Checklist

The AACODS checklist is designed to enable evaluation and critical appraisal of grey literature. The Fourth International Conference on Grey Literature held in Washington, DC, in October 1999 defined grey literature as: "that which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers." Grey literature includes theses or dissertations (reviewed by examiners who are subject specialists); conference papers (often peer-reviewed or presented by those with specialist knowledge) and various types of reports from those working in the field. All of these fall into the "expert opinion"

AACODS		YES	NO	?
Authority	Identifying who is responsible for the intellectual content. **Individual author:** • Associated with a reputable organisation? • Professional qualifications or considerable experience? • Produced/published other work (grey/black) in the field? • Recognised expert, identified in other sources? • Cited by others? (use Google Scholar as a quick check) • Higher degree student under "expert" supervision? **Organisation or group**: • Is the organisation reputable? (e.g. W.H.O) • Is the organisation an authority in the field? **In all cases:** • Does the item have a detailed reference list or bibliography?			
Accuracy	• Does the item have a clearly stated aim or brief? • Is so, is this met?			

	• Does it have a stated methodology? • If so, is it adhered to? • Has it been peer-reviewed? • Has it been edited by a reputable authority? • Supported by authoritative, documented references or credible sources? • Is it representative of work in the field? • If No, is it a valid counterbalance? • Is any data collection explicit and appropriate for the research? • If item is secondary material (e.g. a policy brief of a technical report) refer to • The original. Is it an accurate, unbiased interpretation or analysis?			
Coverage	All items have parameters which define their content coverage. These limits might mean that a work refers to a particular population group, or that it excluded certain types of publication. A report could be designed to answer a particular question, or be based on statistics from a particular survey. • Are any limits clearly stated?			
Objectivity	It is important to identify bias, particularly if it is unstated or unacknowledged. • Opinion, expert or otherwise, is still opinion: is the author's standpoint clear? • Does the work seem to be balanced in presentation?			
Date	For the item to inform your research, it needs to have a date that confirms relevance • Does the item have a clearly stated date related to content? No easily discernible date is a strong concern. • If no date is given, but can be closely ascertained, is there a valid reason for its absence? • Check the bibliography: have key contemporary material been included?			
significance	This is a value judgment of the item, in the context of the relevant research area			

	• Is the item meaningful? (this incorporates feasibility, utility and relevance) • Does it add context? • Does it enrich or add something unique to the research? • Does it strengthen or refute a current position? • Would the research area be lesser without it? • Is it integral, representative, typical? • Does it have impact? (in the sense of influencing the work or behavior of others)			

A10: JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

Reviewer_____
Date_____

Author_____Year_____ Record Number_____

		Yes	No	Unclear	Not applicable
1.	Is the review question clearly and explicitly stated?	□	□	□	□
2.	Were the inclusion criteria appropriate for the review question?	□	□	□	□
3.	Was the search strategy appropriate?	□	□	□	□
4.	Were the sources and resources used to search for studies adequate?	□	□	□	□
5.	Were the criteria for appraising studies appropriate?	□	□	□	□
6.	Was critical appraisal conducted by two or more reviewers independently?	□	□	□	□
7.	Were there methods to minimize errors in data extraction?	□	□	□	□
8.	Were the methods used to combine studies appropriate?	□	□	□	□
9.	Was the likelihood of publication bias assessed?	□	□	□	□

10. Were recommendations for policy and/or practice supported by the reported data?	□	□	□	□
11. Were the specific directives for new research appropriate?	□	□	□	□

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

_____
_____
_____
_____

A11: JBI Critical Appraisal Checklist for Qualitative Research

Reviewer_____
Date_____

Author_____Year_____Record Number_____

	Yes	No	Unclear	Not applicable
12. Is there congruity between the stated philosophical perspective and the research methodology?	□	□	□	□
13. Is there congruity between the research methodology and the research question or objectives?	□	□	□	□
14. Is there congruity between the research methodology and the methods used to collect data?	□	□	□	□
15. Is there congruity between the research methodology and the representation and analysis of data?	□	□	□	□
16. Is there congruity between the research methodology and the interpretation of results?	□	□	□	□
17. Is there a statement locating the researcher culturally or theoretically?	□	□	□	□
18. Is the influence of the researcher on the research, and vice- versa, addressed?	□	□	□	□
19. Are participants, and their voices, adequately represented?	□	□	□	□
20. Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	□	□	□	□

21. Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data? □ □ □ □

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

_____

_____

_____

_____

A12: Reference lists/links of included studies in table 3.1

Authors	Title	Link
Eritrea	National action plan antimicrobial resistance	https://www.who.int/publications/m/item/eritrea-national-action-plan-on-antimicrobial-resistance
Eswatini	Implementation plan: National antimicrobial resistance containment strategy	https://www.who.int/publications/m/item/eswatini-national-antimicrobial-resistance-containment-strategic-plan-2018-2022
Ethiopia	Strategy for the prevention and containment of antimicrobial resistance	https://www.who.int/publications/m/item/ethiopia
Ghana	National action plan for antimicrobial use and resistance	https://www.who.int/publications/m/item/ghana-national-action-plan-for-antimicrobial-use-and-resistance
Kenya	National action plan on prevention and containment of antimicrobial resistance	https://www.who.int/publications/m/item/kenya-national-action-plan-on-prevention-and-containment-of-antimicrobial-resistance
Liberia	National action plan on prevention and containment of antimicrobial resistance	https://www.who.int/publications/m/item/liberia-national-action-plan-on-prevention-and-containment-of-antimicrobial-resistance
Mauritius	National action plan for antimicrobial resistance	https://www.who.int/publications/m/item/mauritius-national-action-plan-on-antimicrobial-resistance
Malawi	Antimicrobial resistance strategy	https://www.who.int/publications/m/item/malawi-antimicrobial-resistance-strategy-2017-2022
Namibia	Antimicrobial resistance national action plan	https://www.who.int/publications/m/item/namibia-antimicrobial-resistance-national-action-plan
Nigeria	National action plan for antimicrobial resistance	https://www.who.int/publications/m/item/nigeria-national-action-plan-for-antimicrobial-resistance
Rwanda	National action plan on antimicrobial resistance	https://www.who.int/publications/m/item/rwanda-national-action-plan-on-antimicrobial-resistance-2020-2024
Sierra Leone	National strategic plan for combating antimicrobial resistance	https://www.who.int/publications/m/item/sierra-leone-national-strategic-plan-for-combating-antimicrobial-resistance

South Africa	Antimicrobial resistance national framework: a one health approach	https://www.who.int/publications/m/item/south-africa-south-african-antimicrobial-resistance-national-strategy-framework-a-one-health-approach
Uganda	Antimicrobial resistance national action plan	https://www.who.int/publications/m/item/uganda-antimicrobial-resistance-national-action-plan-2018-2023
United Republic of Tanzania	The national action plan on antimicrobial resistance	https://www.who.int/publications/m/item/united-republic-of-tanzania-the-national-action-plan-on-antimicrobial-resistance
Zambia	Multi-sectoral national action plan on antimicrobial resistance	https://www.who.int/publications/m/item/zambia-multi-sectoral-national-action-plan-on-antimicrobial-resistance
Zimbabwe	Strategic framework, operational plan, and monitoring and evaluation plan	https://www.who.int/publications/m/item/zimbabwe-one-health-antimicrobial-resistance-national-action-plan-2017-2021
WHO (GLASS) 2021	Implementation status of national AMR surveillance systems	https://www.who.int/publications/i/item/9789240027336
WHO (GLASS) 2020	Early implementation summary report	https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-sel-glass/glassreport2020-launchwebinarpresentation-25may2020-final.pdf?sfvrsn=454123ab_2
WHO (GLASS) 2019	Early implementation summary report	https://www.who.int/publications-detail-redirect/9789241515061
WHO (GLASS) 2018	Early implementation summary report	https://www.who.int/publications-detail-redirect/9789241513449
FAO, OiE and WHO 2017	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	https://amrcountryprogress.org/download/AMR-self-assessment-survey-country-responses-2016-17.xlsx
FAO, OiE and WHO 2018	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	https://amrcountryprogress.org/download/AMR-self-assessment-survey-country-responses-2018-19.xls
FAO, OiE and WHO 2019	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	https://amrcountryprogress.org/download/AMR%20self%20assessment%20survey%20responses%202019-2020%20(Excel%20format).xls

FAO, OiE and WHO 2020	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	https://amrcountryprogress.org/download/Year%20five%20TrACSS%20complete%20data%20for%20publication.xlsx
FAO, OiE and WHO 2021	The Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) report	https://www.who.int/publications/m/item/tripartite-amr-country-self-assessment-survey-(tracss)-2020-2021
WHO 2017-2020	Joint external evaluation (JEE) of International health regulations (IHR) core capabilities	https://extranet.who.int/e-spar#capacity-score
WHO 2015	Global action plan on antimicrobial resistance	https://www.who.int/publications/i/item/9789241509763
Ogyu et al. 2020	National action plan to combat AMR: a One-Health approach to assess policy priorities in action plans	Ogyu, A., Chan, O., Littmann, J., Pang, H. H., Lining, X., Liu, P., … Wernli, Di. (2020). National action to combat AMR: A One-Health approach to assess policy priorities in action plans. *BMJ Global Health*, *5*(7). https://doi.org/10.1136/bmjgh-2020-002427
Seale et al. 2017	Supporting surveillance capacity for antimicrobial resistance: Laboratory capacity strengthening for drug resistance infection in low and middle income countries	Seale, A. C., Hutchison, C., Fernandes, S., Stoesser, N., Kelly, H., Lowe, B., … Scott, J. A. G. (2017). Supporting surveillance capacity for antimicrobial resistance: Laboratory capacity strengthening for drug resistant infections in low and middle income countries. *Wellcome Open Research*, *2*(0), 1–18. https://doi.org/10.12688/wellcomeopenres.12523.1
Jimah & Ogunseitan 2020	National action plan on antimicrobial resistance: stakeholders analysis on implementation in Ghana	Jimah, T., & Ogunseitan, O. (2020). National Action Plan on Antimicrobial Resistance: stakeholder analysis of implementation in Ghana. *Journal of Global Health Reports*. https://doi.org/10.29392/001c.13695
Hazim et al. 2018	Establishment of a sentinel laboratory based AMR surveillance network in Ethiopia.	HazimCarmen, IbrahimRajiha, A., WestercampMatthew, Alebachew, B., KibretBerhanu, A., KanterTheresa, … M., G. (2018). Establishment of a Sentinel Laboratory-Based Antimicrobial Resistance Surveillance Network in Ethiopia. *Https://Home.Liebertpub.Com/Hs*, *16*(S1), S-30-S-36. https://doi.org/10.1089/hs.2018.0052

A15: Tolerance and VIF score of the dependent variable

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	Knowledge	.646	1.549
	Lab Capacity	.553	1.807
	Lab Participation	.387	2.581
	Lab Readiness	.681	1.469
	Appropriate Records	.522	1.915

Dependent Variable: Is your laboratory connected to a hospital service (s)

A16: Collinearity diagnostics score of the dependent variable

Collinearity Diagnostics

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions					
				(Constant)	Knowledge	Lab Capacity	Lab Participation	Lab Readiness	Appropriate Records
1	1	5.106	1.000	.00	.01	.00	.01	.00	.01
	2	.395	3.593	.07	.02	.00	.25	.03	.08
	3	.183	5.285	.07	.66	.14	.00	.00	.02
	4	.157	5.709	.00	.00	.07	.30	.00	.89
	5	.095	7.343	.01	.32	.23	.08	.76	.00
	6	.064	8.918	.84	.00	.55	.37	.20	.01

Dependent Variable: Is your laboratory connected to a hospital service(s)?

A17: SQI mean scores difference in relation to respondent's laboratory connection

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Knowledge	Between Groups	62917.731	5	12583.546	14.297	.000
	Within Groups	260534.256	296	880.183		
	Total	323451.987	301			
Lab_Capacity	Between Groups	140436.097	5	28087.219	66.378	.000
	Within Groups	125249.996	296	423.142		
	Total	265686.093	301			
Lab_Participation	Between Groups	63117.746	5	12623.549	70.135	.000
	Within Groups	53276.661	296	179.989		
	Total	116394.408	301			
Lab_Readiness	Between Groups	44097.302	5	8819.460	12.465	.000
	Within Groups	209427.462	296	707.525		
	Total	253524.764	301			
Appropriate_Records	Between Groups	60410.823	5	12082.165	29.203	.000
	Within Groups	122462.614	296	413.725		
	Total	182873.436	301			

A18: Post Hoc Test of the SQI scores according to laboratory connection

Multiple Comparisons							
Tamhane							
Dependent Variable	(I) Which level of hospital is your laboratory connected to? - Selected Choice	(J) Which level of hospital is your laboratory connected to? - Selected Choice	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Knowledge	Teaching Hospital	State Government	-8.077	5.932	.947	-26.02	9.86
		Independent Laboratory	26.522*	5.272	.000	10.50	42.54
		Federal Medical Centre	-7.640	7.236	.995	-29.84	14.56
		Primary Health Care Centre	30.180	10.868	.185	-7.20	67.56
		Private Hospital Laboratory	11.847	6.067	.566	-6.43	30.13
	State Government	Teaching Hospital	8.077	5.932	.947	-9.86	26.02
		Independent Laboratory	34.599*	4.738	.000	20.35	48.85
		Federal Medical Centre	.437	6.858	1.000	-20.70	21.57
		Primary Health Care Centre	38.258*	10.620	.040	1.17	75.35
		Private Hospital Laboratory	19.924*	5.610	.009	3.10	36.75
	Independent Laboratory	Teaching Hospital	-26.522*	5.272	.000	-42.54	-10.50
		State Government	-34.599*	4.738	.000	-48.85	-20.35
		Federal Medical Centre	-34.162*	6.295	.000	-53.83	-14.49
		Primary Health Care Centre	3.659	10.265	1.000	-33.16	40.47
		Private Hospital Laboratory	-14.675*	4.907	.050	-29.35	.00
	Federal Medical Centre	Teaching Hospital	7.640	7.236	.995	-14.56	29.84
		State Government	-.437	6.858	1.000	-21.57	20.70
		Independent Laboratory	34.162*	6.295	.000	14.49	53.83
		Primary Health Care Centre	37.821	11.400	.054	-.43	76.07
		Private Hospital Laboratory	19.487	6.975	.104	-1.92	40.90
	Primary Health Care Centre	Teaching Hospital	-30.180	10.868	.185	-67.56	7.20

		State Government	-38.258*	10.620	.040	-75.35	-1.17
		Independent Laboratory	-3.659	10.265	1.000	-40.47	33.16
		Federal Medical Centre	-37.821	11.400	.054	-76.07	.43
		Private Hospital Laboratory	-18.333	10.696	.817	-55.49	18.82
	Private Hospital Laboratory	Teaching Hospital	-11.847	6.067	.566	-30.13	6.43
		State Government	-19.924*	5.610	.009	-36.75	-3.10
		Independent Laboratory	14.675*	4.907	.050	.00	29.35
		Federal Medical Centre	-19.487	6.975	.104	-40.90	1.92
		Primary Health Care Centre	18.333	10.696	.817	-18.82	55.49
Lab_Capacity	Teaching Hospital	State Government	3.47666	4.67308	1.000	-10.6357	17.5890
		Independent Laboratory	52.12041*	3.69831	.000	40.7972	63.4436
		Federal Medical Centre	5.25988	5.79466	.999	-12.6012	23.1209
		Primary Health Care Centre	27.56757	8.09736	.054	-.3213	55.4564
		Private Hospital Laboratory	31.23423*	4.36378	.000	18.0711	44.3974
	State Government	Teaching Hospital	-3.47666	4.67308	1.000	-17.5890	10.6357
		Independent Laboratory	48.64375*	3.67036	.000	37.4903	59.7972
		Federal Medical Centre	1.78322	5.77686	1.000	-16.0085	19.5749
		Primary Health Care Centre	24.09091	8.08464	.127	-3.7729	51.9547
		Private Hospital Laboratory	27.75758*	4.34011	.000	14.7161	40.7990
	Independent Laboratory	Teaching Hospital	-52.12041*	3.69831	.000	-63.4436	-40.7972
		State Government	-48.64375*	3.67036	.000	-59.7972	-37.4903
		Federal Medical Centre	-46.86054*	5.02114	.000	-62.7756	-30.9455
		Primary Health Care Centre	-24.55285	7.56314	.099	-52.0013	2.8956
		Private Hospital Laboratory	-20.88618*	3.26747	.000	-30.6885	-11.0839
	Federal Medical Centre	Teaching Hospital	-5.25988	5.79466	.999	-23.1209	12.6012
		State Government	-1.78322	5.77686	1.000	-19.5749	16.0085
		Independent Laboratory	46.86054*	5.02114	.000	30.9455	62.7756

		Primary Health Care Centre	22.30769	8.78076	.253	-6.7640	51.3794
		Private Hospital Laboratory	25.97436*	5.52964	.000	8.8494	43.0993
	Primary Health Care Centre	Teaching Hospital	-27.56757	8.09736	.054	-55.4564	.3213
		State Government	-24.09091	8.08464	.127	-51.9547	3.7729
		Independent Laboratory	24.55285	7.56314	.099	-2.8956	52.0013
		Federal Medical Centre	-22.30769	8.78076	.253	-51.3794	6.7640
		Private Hospital Laboratory	3.66667	7.90988	1.000	-24.0007	31.3340
	Private Hospital Laboratory	Teaching Hospital	-31.23423*	4.36378	.000	-44.3974	-18.0711
		State Government	-27.75758*	4.34011	.000	-40.7990	-14.7161
		Independent Laboratory	20.88618*	3.26747	.000	11.0839	30.6885
		Federal Medical Centre	-25.97436*	5.52964	.000	-43.0993	-8.8494
		Primary Health Care Centre	-3.66667	7.90988	1.000	-31.3340	24.0007
Lab_Participation	Teaching Hospital	State Government	10.83129	3.81100	.083	-.6909	22.3535
		Independent Laboratory	38.63986*	2.96658	.000	29.4265	47.8532
		Federal Medical Centre	6.63548	4.79512	.942	-8.1104	21.3814
		Primary Health Care Centre	25.22523*	3.52031	.000	14.3321	36.1183
		Private Hospital Laboratory	23.55856*	3.35790	.000	13.3395	33.7776
	State Government	Teaching Hospital	-10.83129	3.81100	.083	-22.3535	.6909
		Independent Laboratory	27.80857*	2.63753	.000	19.7125	35.9047
		Federal Medical Centre	-4.19580	4.59882	.999	-18.3943	10.0027
		Primary Health Care Centre	14.39394*	3.24786	.001	4.3371	24.4508
		Private Hospital Laboratory	12.72727*	3.07107	.001	3.4631	21.9914
	Independent Laboratory	Teaching Hospital	-38.63986*	2.96658	.000	-47.8532	-29.4265
		State Government	-27.80857*	2.63753	.000	-35.9047	-19.7125
		Federal Medical Centre	-32.00438*	3.92760	.000	-44.6065	-19.4023
		Primary Health Care Centre	-13.41463*	2.19670	.000	-21.0966	-5.7327
		Private Hospital Laboratory	-15.08130*	1.92572	.000	-20.8858	-9.2768

	Federal Medical Centre	Teaching Hospital	-6.63548	4.79512	.942	-21.3814	8.1104
		State Government	4.19580	4.59882	.999	-10.0027	18.3943
		Independent Laboratory	32.00438*	3.92760	.000	19.4023	44.6065
		Primary Health Care Centre	18.58974*	4.36097	.002	4.8862	32.2933
		Private Hospital Laboratory	16.92308*	4.23096	.005	3.6558	30.1904
	Primary Health Care Centre	Teaching Hospital	-25.22523*	3.52031	.000	-36.1183	-14.3321
		State Government	-14.39394*	3.24786	.001	-24.4508	-4.3371
		Independent Laboratory	13.41463*	2.19670	.000	5.7327	21.0966
		Federal Medical Centre	-18.58974*	4.36097	.002	-32.2933	-4.8862
		Private Hospital Laboratory	-1.66667	2.70193	1.000	-10.2558	6.9225
	Private Hospital Laboratory	Teaching Hospital	-23.55856*	3.35790	.000	-33.7776	-13.3395
		State Government	-12.72727*	3.07107	.001	-21.9914	-3.4631
		Independent Laboratory	15.08130*	1.92572	.000	9.2768	20.8858
		Federal Medical Centre	-16.92308*	4.23096	.005	-30.1904	-3.6558
		Primary Health Care Centre	1.66667	2.70193	1.000	-6.9225	10.2558
Lab_Readiness	Teaching Hospital	State Government	17.78596*	4.60143	.004	3.8058	31.7662
		Independent Laboratory	34.78111*	3.43820	.000	24.5293	45.0329
		Federal Medical Centre	12.34695	5.54329	.391	-5.0842	29.7781
		Primary Health Care Centre	37.06205*	9.86937	.039	1.3040	72.8201
		Private Hospital Laboratory	29.09909*	3.99138	.000	17.1050	41.0932
	State Government	Teaching Hospital	-17.78596*	4.60143	.004	-31.7662	-3.8058
		Independent Laboratory	16.99516*	4.81817	.010	2.4663	31.5240
		Federal Medical Centre	-5.43901	6.49012	1.000	-25.3188	14.4408
		Primary Health Care Centre	19.27609	10.43063	.733	-16.8991	55.4513
		Private Hospital Laboratory	11.31314	5.22730	.396	-4.4052	27.0315
	Independent Laboratory	Teaching Hospital	-34.78111*	3.43820	.000	-45.0329	-24.5293
		State Government	-16.99516*	4.81817	.010	-31.5240	-2.4663

		Federal Medical Centre	-22.43416*	5.72448	.005	-40.2653	-4.6030
		Primary Health Care Centre	2.28094	9.97227	1.000	-33.5121	38.0739
		Private Hospital Laboratory	-5.68202	4.23943	.951	-18.3243	6.9603
	Federal Medical Centre	Teaching Hospital	-12.34695	5.54329	.391	-29.7781	5.0842
		State Government	5.43901	6.49012	1.000	-14.4408	25.3188
		Independent Laboratory	22.43416*	5.72448	.005	4.6030	40.2653
		Primary Health Care Centre	24.71510	10.87902	.423	-12.1293	61.5595
		Private Hospital Laboratory	16.75214	6.07286	.117	-1.9716	35.4759
	Primary Health Care Centre	Teaching Hospital	-37.06205*	9.86937	.039	-72.8201	-1.3040
		State Government	-19.27609	10.43063	.733	-55.4513	16.8991
		Independent Laboratory	-2.28094	9.97227	1.000	-38.0739	33.5121
		Federal Medical Centre	-24.71510	10.87902	.423	-61.5595	12.1293
		Private Hospital Laboratory	-7.96296	10.17625	1.000	-43.8893	27.9633
	Private Hospital Laboratory	Teaching Hospital	-29.09909*	3.99138	.000	-41.0932	-17.1050
		State Government	-11.31314	5.22730	.396	-27.0315	4.4052
		Independent Laboratory	5.68202	4.23943	.951	-6.9603	18.3243
		Federal Medical Centre	-16.75214	6.07286	.117	-35.4759	1.9716
		Primary Health Care Centre	7.96296	10.17625	1.000	-27.9633	43.8893
Appropriate_Records	Teaching Hospital	State Government	4.56593	5.14207	.999	-11.0717	20.2036
		Independent Laboratory	32.57160*	4.59589	.000	18.3979	46.7453
		Federal Medical Centre	-5.45738	6.76655	1.000	-26.1972	15.2825
		Primary Health Care Centre	15.80330	7.05759	.407	-7.0193	38.6259
		Private Hospital Laboratory	16.63664*	4.91348	.019	1.6386	31.6347
	State Government	Teaching Hospital	-4.56593	5.14207	.999	-20.2036	11.0717
		Independent Laboratory	28.00567*	3.27482	.000	18.0977	37.9136
		Federal Medical Centre	-10.02331	5.94882	.794	-28.5477	8.5011
		Primary Health Care Centre	11.23737	6.27788	.762	-10.0915	32.5662

		Private Hospital Laboratory	12.07071*	3.70736	.023	.9273	23.2141
	Independent Laboratory	Teaching Hospital	-32.57160*	4.59589	.000	-46.7453	-18.3979
		State Government	-28.00567*	3.27482	.000	-37.9136	-18.0977
		Federal Medical Centre	-38.02898*	5.48359	.000	-55.4583	-20.5997
		Primary Health Care Centre	-16.76829	5.83894	.180	-37.6327	4.0961
		Private Hospital Laboratory	-15.93496*	2.90274	.000	-24.6132	-7.2567
	Federal Medical Centre	Teaching Hospital	5.45738	6.76655	1.000	-15.2825	26.1972
		State Government	10.02331	5.94882	.794	-8.5011	28.5477
		Independent Laboratory	38.02898*	5.48359	.000	20.5997	55.4583
		Primary Health Care Centre	21.26068	7.66532	.135	-3.1922	45.7136
		Private Hospital Laboratory	22.09402*	5.75238	.007	4.0566	40.1314
	Primary Health Care Centre	Teaching Hospital	-15.80330	7.05759	.407	-38.6259	7.0193
		State Government	-11.23737	6.27788	.762	-32.5662	10.0915
		Independent Laboratory	16.76829	5.83894	.180	-4.0961	37.6327
		Federal Medical Centre	-21.26068	7.66532	.135	-45.7136	3.1922
		Private Hospital Laboratory	.83333	6.09206	1.000	-20.2481	21.9147
	Private Hospital Laboratory	Teaching Hospital	-16.63664*	4.91348	.019	-31.6347	-1.6386
		State Government	-12.07071*	3.70736	.023	-23.2141	-.9273
		Independent Laboratory	15.93496*	2.90274	.000	7.2567	24.6132
		Federal Medical Centre	-22.09402*	5.75238	.007	-40.1314	-4.0566
		Primary Health Care Centre	-.83333	6.09206	1.000	-21.9147	20.2481

*. The mean difference is significant at the 0.05 level.

A19: SQI mean scores difference according to the geopolitical zones of laboratory

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Knowledge	Between Groups	28904.751	5	5780.950	5.809	.000
	Within Groups	294547.236	296	995.092		
	Total	323451.987	301			
Lab_Capacity	Between Groups	4418.856	5	883.771	1.001	.417
	Within Groups	261267.237	296	882.660		
	Total	265686.093	301			
Lab_Participation	Between Groups	2657.133	5	531.427	1.383	.230
	Within Groups	113737.274	296	384.248		
	Total	116394.408	301			
Lab_Readiness	Between Groups	13823.818	5	2764.764	3.414	.005
	Within Groups	239700.946	296	809.800		
	Total	253524.764	301			
Appropriate_Records	Between Groups	3524.104	5	704.821	1.163	.327
	Within Groups	179349.333	296	605.910		
	Total	182873.436	301			

A20: Post Hoc Test of the SQI scores according to the geopolitical zone of the laboratory

Multiple Comparisons

Tamhane

Dependent Variable	(I) Geopolitical Zone	(J) Geopolitical Zone	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Knowledge	South South	South West	-21.397*	5.549	.003	-37.98	-4.82

		South East	-.821	5.337	1.000	-16.72	15.08
		North Central	-9.722	5.528	.718	-26.20	6.76
		North West	9.028	8.447	.994	-17.47	35.52
		North East	10.658	7.504	.931	-12.75	34.06
	South West	South South	21.397*	5.549	.003	4.82	37.98
		South East	20.576*	5.457	.004	4.25	36.90
		North Central	11.675	5.644	.465	-5.20	28.55
		North West	30.425*	8.524	.015	3.73	57.12
		North East	32.055*	7.590	.002	8.42	55.69
	South East	South South	.821	5.337	1.000	-15.08	16.72
		South West	-20.576*	5.457	.004	-36.90	-4.25
		North Central	-8.902	5.435	.807	-25.12	7.32
		North West	9.848	8.387	.986	-16.51	36.21
		North East	11.479	7.436	.878	-11.77	34.72
	North Central	South South	9.722	5.528	.718	-6.76	26.20
		South West	-11.675	5.644	.465	-28.55	5.20
		South East	8.902	5.435	.807	-7.32	25.12
		North West	18.750	8.510	.404	-7.90	45.40
		North East	20.380	7.575	.145	-3.20	43.96
	North West	South South	-9.028	8.447	.994	-35.52	17.47
		South West	-30.425*	8.524	.015	-57.12	-3.73
		South East	-9.848	8.387	.986	-36.21	16.51
		North Central	-18.750	8.510	.404	-45.40	7.90
		North East	1.630	9.909	1.000	-29.03	32.29
	North East	South South	-10.658	7.504	.931	-34.06	12.75
		South West	-32.055*	7.590	.002	-55.69	-8.42
		South East	-11.479	7.436	.878	-34.72	11.77

		North Central	-20.380	7.575	.145	-43.96	3.20
		North West	-1.630	9.909	1.000	-32.29	29.03
Lab Capacity	South South	South West	-6.72956	5.22397	.965	-22.3639	8.9048
		South East	1.51515	4.93584	1.000	-13.1990	16.2293
		North Central	2.29167	5.12674	1.000	-13.0037	17.5870
		North West	-6.66667	7.64553	.999	-30.7110	17.3777
		North East	-6.81159	6.49475	.995	-27.0626	13.4394
	South West	South South	6.72956	5.22397	.965	-8.9048	22.3639
		South East	8.24471	5.42496	.879	-7.9847	24.4741
		North Central	9.02123	5.59921	.826	-7.7257	25.7682
		North West	.06289	7.97005	1.000	-24.7732	24.8990
		North East	-.08203	6.87382	1.000	-21.3154	21.1513
	South East	South South	-1.51515	4.93584	1.000	-16.2293	13.1990
		South West	-8.24471	5.42496	.879	-24.4741	7.9847
		North Central	.77652	5.33139	1.000	-15.1317	16.6848
		North West	-8.18182	7.78424	.995	-32.5540	16.1904
		North East	-8.32675	6.65748	.975	-28.9849	12.3314
	North Central	South South	-2.29167	5.12674	1.000	-17.5870	13.0037
		South West	-9.02123	5.59921	.826	-25.7682	7.7257
		South East	-.77652	5.33139	1.000	-16.6848	15.1317
		North West	-8.95833	7.90667	.990	-33.6261	15.7095
		North East	-9.10326	6.80022	.956	-30.1260	11.9195
	North West	South South	6.66667	7.64553	.999	-17.3777	30.7110
		South West	-.06289	7.97005	1.000	-24.8990	24.7732
		South East	8.18182	7.78424	.995	-16.1904	32.5540
		North Central	8.95833	7.90667	.990	-15.7095	33.6261
		North East	-.14493	8.85515	1.000	-27.5724	27.2825

	North East	South South	6.81159	6.49475	.995	-13.4394	27.0626
		South West	.08203	6.87382	1.000	-21.1513	21.3154
		South East	8.32675	6.65748	.975	-12.3314	28.9849
		North Central	9.10326	6.80022	.956	-11.9195	30.1260
		North West	.14493	8.85515	1.000	-27.2825	27.5724
Lab Participation	South South	South West	-8.53861	3.43536	.197	-18.8350	1.7578
		South East	-3.13552	3.32926	.998	-13.0708	6.7998
		North Central	-1.88079	3.30716	1.000	-11.7535	7.9920
		North West	-2.31481	4.22158	1.000	-15.4898	10.8602
		North East	-6.69283	4.35962	.884	-20.3706	6.9849
	South West	South South	8.53861	3.43536	.197	-1.7578	18.8350
		South East	5.40309	3.79132	.923	-5.9347	16.7409
		North Central	6.65782	3.77194	.715	-4.6258	17.9415
		North West	6.22379	4.59477	.951	-7.9165	20.3640
		North East	1.84578	4.72192	1.000	-12.7471	16.4387
	South East	South South	3.13552	3.32926	.998	-6.7998	13.0708
		South West	-5.40309	3.79132	.923	-16.7409	5.9347
		North Central	1.25473	3.67556	1.000	-9.7113	12.2208
		North West	.82071	4.51599	1.000	-13.0963	14.7377
		North East	-3.55731	4.64529	1.000	-17.9380	10.8233
	North Central	South South	1.88079	3.30716	1.000	-7.9920	11.7535
		South West	-6.65782	3.77194	.715	-17.9415	4.6258
		South East	-1.25473	3.67556	1.000	-12.2208	9.7113
		North West	-.43403	4.49973	1.000	-14.3107	13.4427
		North East	-4.81205	4.62948	.996	-19.1543	9.5302
	North West	South South	2.31481	4.22158	1.000	-10.8602	15.4898
		South West	-6.22379	4.59477	.951	-20.3640	7.9165

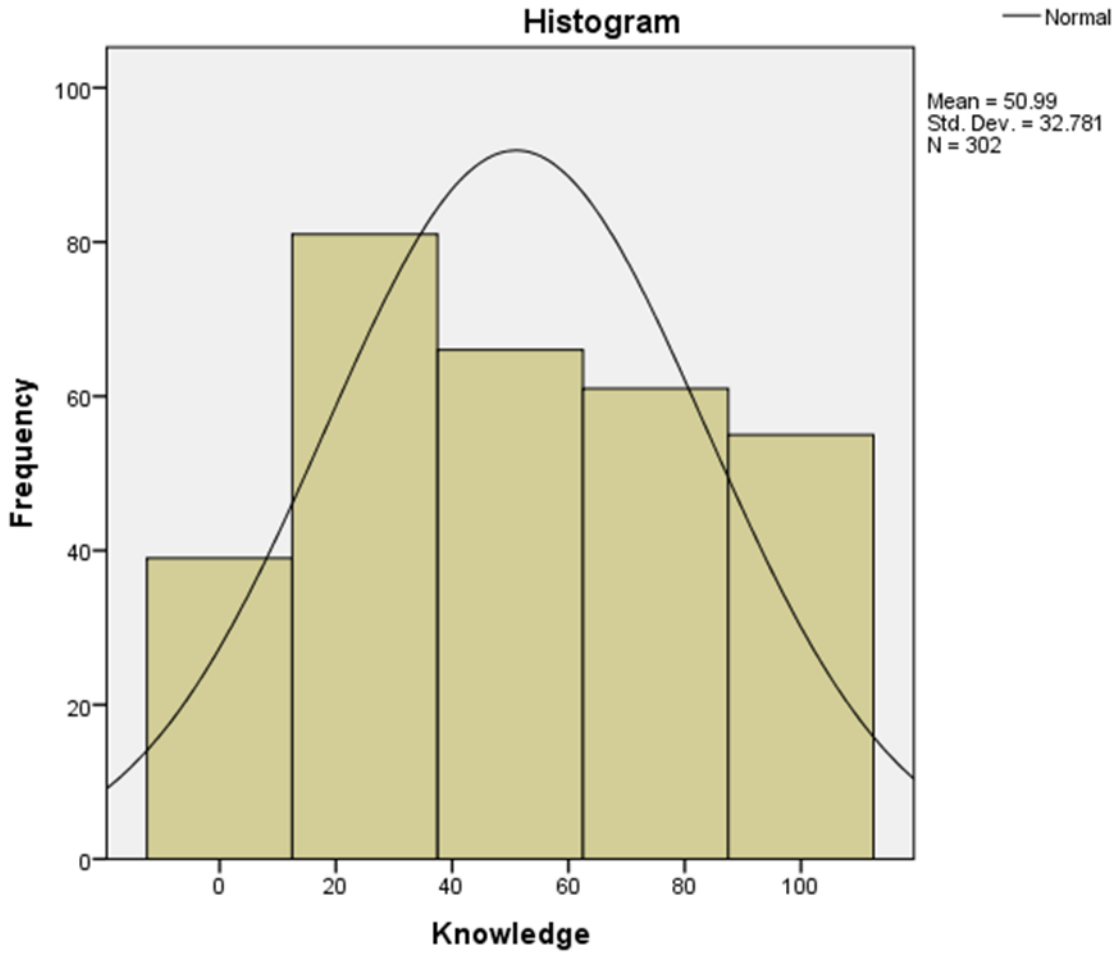
		South East	-.82071	4.51599	1.000	-14.7377	13.0963
		North Central	.43403	4.49973	1.000	-13.4427	14.3107
		North East	-4.37802	5.32133	1.000	-20.8323	12.0762
	North East	South South	6.69283	4.35962	.884	-6.9849	20.3706
		South West	-1.84578	4.72192	1.000	-16.4387	12.7471
		South East	3.55731	4.64529	1.000	-10.8233	17.9380
		North Central	4.81205	4.62948	.996	-9.5302	19.1543
		North West	4.37802	5.32133	1.000	-12.0762	20.8323
Lab Readiness	South South	South West	-11.44887	4.98658	.300	-26.3556	3.4579
		South East	-3.31089	4.38163	1.000	-16.3732	9.7514
		North Central	1.92901	4.96088	1.000	-12.8644	16.7224
		North West	10.49384	8.21832	.971	-15.4494	36.4370
		North East	12.10414	7.93666	.890	-12.9830	37.1912
	South West	South South	11.44887	4.98658	.300	-3.4579	26.3556
		South East	8.13798	4.62668	.721	-5.7316	22.0076
		North Central	13.37788	5.17859	.154	-2.1093	28.8651
		North West	21.94270	8.35155	.175	-4.3176	48.2030
		North East	23.55301	8.07453	.089	-1.8623	48.9684
	South East	South South	3.31089	4.38163	1.000	-9.7514	16.3732
		South West	-8.13798	4.62668	.721	-22.0076	5.7316
		North Central	5.23990	4.59897	.988	-8.5003	18.9801
		North West	13.80472	8.00506	.776	-11.6708	39.2802
		North East	15.41503	7.71562	.573	-9.1905	40.0206
	North Central	South South	-1.92901	4.96088	1.000	-16.7224	12.8644
		South West	-13.37788	5.17859	.154	-28.8651	2.1093
		South East	-5.23990	4.59897	.988	-18.9801	8.5003
		North West	8.56482	8.33623	.996	-17.6516	34.7812

		North East	10.17513	8.05869	.974	-15.1942	35.5445
	North West	South South	-10.49384	8.21832	.971	-36.4370	15.4494
		South West	-21.94270	8.35155	.175	-48.2030	4.3176
		South East	-13.80472	8.00506	.776	-39.2802	11.6708
		North Central	-8.56482	8.33623	.996	-34.7812	17.6516
		North East	1.61031	10.38619	1.000	-30.4986	33.7192
	North East	South South	-12.10414	7.93666	.890	-37.1912	12.9830
		South West	-23.55301	8.07453	.089	-48.9684	1.8623
		South East	-15.41503	7.71562	.573	-40.0206	9.1905
		North Central	-10.17513	8.05869	.974	-35.5445	15.1942
		North West	-1.61031	10.38619	1.000	-33.7192	30.4986
Appropriate Records	South South	South West	-5.87002	4.17654	.930	-18.3704	6.6303
		South East	-4.04040	4.01169	.997	-16.0018	7.9210
		North Central	-2.95139	4.43088	1.000	-16.1875	10.2847
		North West	6.25000	5.35551	.987	-10.4452	22.9452
		North East	-7.00483	5.77226	.981	-25.1500	11.1404
	South West	South South	5.87002	4.17654	.930	-6.6303	18.3704
		South East	1.82962	4.40559	1.000	-11.3470	15.0062
		North Central	2.91863	4.79043	1.000	-11.4043	17.2416
		North West	12.12002	5.65659	.436	-5.3515	29.5915
		North East	-1.13481	6.05264	1.000	-19.9718	17.7022
	South East	South South	4.04040	4.01169	.997	-7.9210	16.0018
		South West	-1.82962	4.40559	1.000	-15.0062	11.3470
		North Central	1.08902	4.64741	1.000	-12.7850	14.9630
		North West	10.29040	5.53599	.662	-6.8557	27.4365
		North East	-2.96443	5.94009	1.000	-21.5110	15.5821
	North Central	South South	2.95139	4.43088	1.000	-10.2847	16.1875

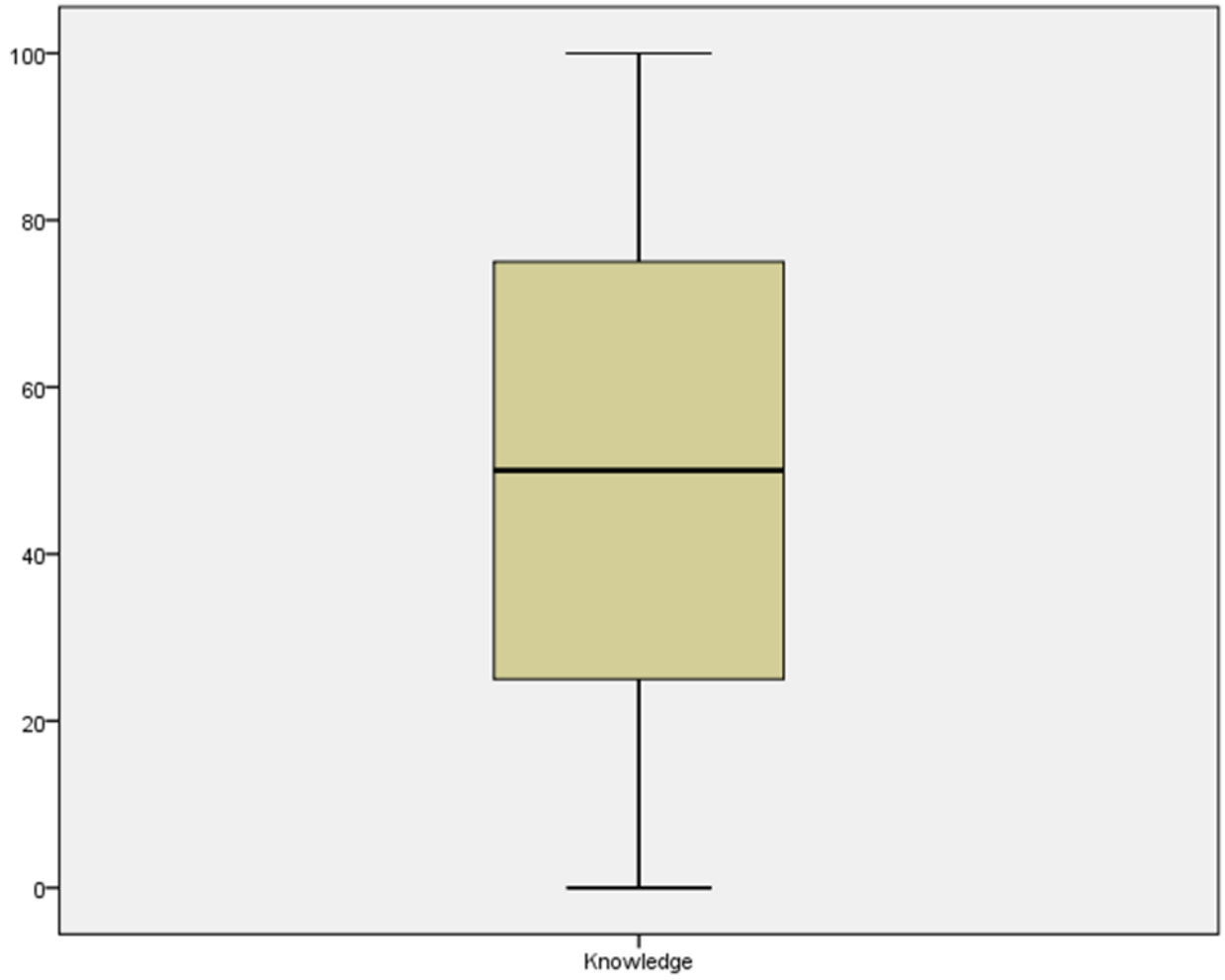
		South West	-2.91863	4.79043	1.000	-17.2416	11.4043
		South East	-1.08902	4.64741	1.000	-14.9630	12.7850
		North West	9.20139	5.84690	.857	-8.7529	27.1557
		North East	-4.05344	6.23087	1.000	-23.3268	15.2199
	North West	South South	-6.25000	5.35551	.987	-22.9452	10.4452
		South West	-12.12002	5.65659	.436	-29.5915	5.3515
		South East	-10.29040	5.53599	.662	-27.4365	6.8557
		North Central	-9.20139	5.84690	.857	-27.1557	8.7529
		North East	-13.25483	6.91900	.616	-34.6613	8.1516
	North East	South South	7.00483	5.77226	.981	-11.1404	25.1500
		South West	1.13481	6.05264	1.000	-17.7022	19.9718
		South East	2.96443	5.94009	1.000	-15.5821	21.5110
		North Central	4.05344	6.23087	1.000	-15.2199	23.3268
		North West	13.25483	6.91900	.616	-8.1516	34.6613

*. The mean difference is significant at the 0.05 level.

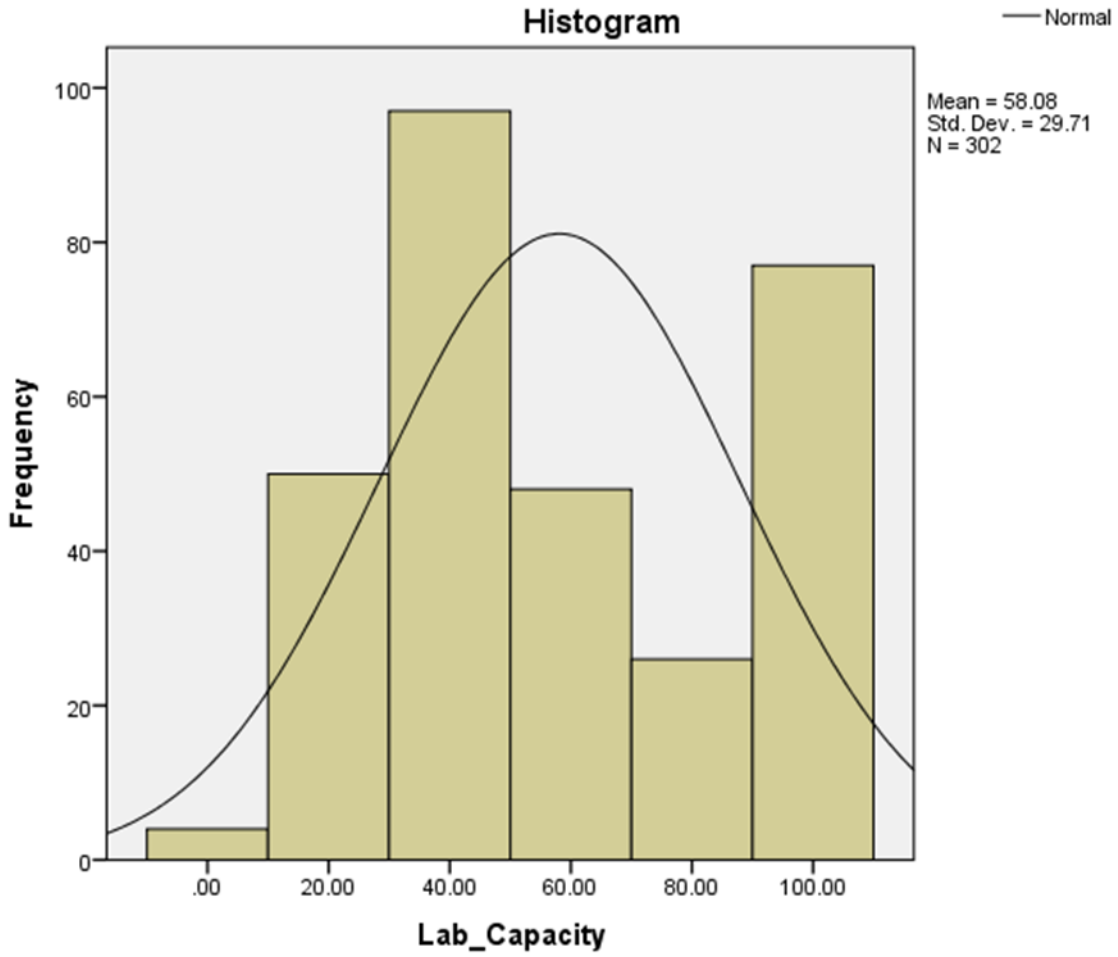
A21: Histogram of the Knowledge score



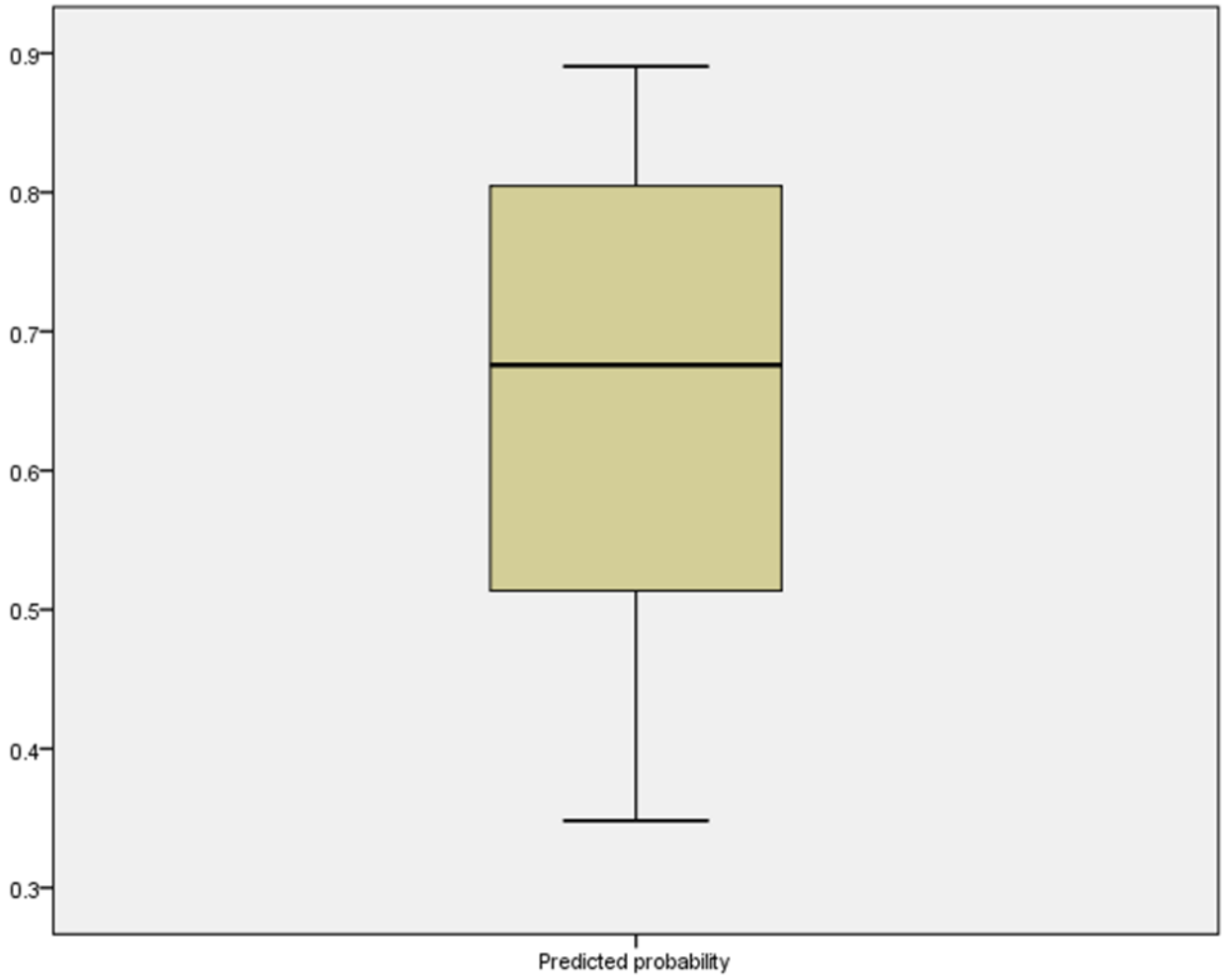
A22: Boxplot of Knowledge score



A23: Histogram of laboratory capacity score



A24: Boxplot of laboratory capacity score



Reflections

The journey to public health has been nothing short of fulfilling. I began my career as a clinician and have dedicated reasonable period of my postgraduate years delivering clinical duties and impacting lives one patient at a time. But then I thought to myself, being part of decision making career that shapes public health research agenda and inform practices has capacity of impacting million lives through one policy action and thus, a more rewarding means of engagement and impact than my clinical roles. Driven by this objective, and the massive gap in evidence and knowledge particularly from low-medium-income countries, I was convinced about the appropriateness of transitioning to a career in research. There has never been a time in our existence that the responsibilities of being a public health researcher is ever so needed than now. With our world been plagued with all manner of communicable and non-communicable diseases, antimicrobial resistance, epidemics and pandemics, climate change, environmental degradation, hunger, poverty and war, public health is at its critical times.

Resolute to pursue my career transition, I set out on a three year doctorate journey which ended on a five year life experience that saw me travel through the good, the bad, and the ugly.

The beginning was good. It gives me a great sense of joy to share that my family witnessed a numeric addition within the first academic year with the blessing of a second child. This was nothing short of icing on the cake of my research voyage. The experience of doing research and nursing a baby fills me with so much sense of accomplishment. It was a tough job which brought to bear my multitasking capabilities as I joggled motherhood, self-care, family and balancing my mental health and wellbeing. Going back in time, I still have chills trying to unravel how I managed to navigate my way through it all. From failing my first progress review and haven to re-submit, writing a portfolio of evidence for the research in contemporary context module, sitting for examinations for the taught elements of the degree and writing up a whopping sensible 80k words. PhD is not for the faint hearted, yes it is tough but it's doable.

If I could do it with two children, I believe anyone can as long as you are determined and resilient.

Then came the bad, accompanied with a wind of sorrow and despair. The unexpected and tragic passing of my beloved father in the second year of my research training. His death still remains the worst event of my life yet and happening at a time when I was on a career journey that he overwhelmingly supported almost extinguished my appetite to press on. He had a huge influence on my academic life, so much so that it seemed like I was euphemistically getting the academic trophy for him. My pain was deep, the grief was inconsolable. I tried to muster all the fortitude I could but the reality of being a fatherless child still stares me in the face. Of course years have gone by, but every single event of this research fills me with the reminiscent of what it could have been if Dad was still here. I cried uncontrollably the day I defended my thesis. I reached out to my phone the moment following the announcement of the outcome of my viva examination, I wanted to share the news with Dad. He could have been on the other side checking his clock and waiting for a phone call from me. I couldn't hold back my tears as I lowered my head on the desk. My PhD story cannot be told without mentioning this sad event and the impact it had on me. I still miss him dearly.

Lastly, the ugly which has become the new norm. I set out on this solitary journey in a world where face masks were reserved for theatre use/clinical settings; where social distancing was not in the conversation; a world that knew no Covid-19 and ended in a world that witnessed a horrible pandemic that swept across the world, infecting a multitude of individuals at a time, and recorded millions deaths in two years. Not to mention its impact on learning mode, research and data collection procedures. From transitioning to hybrid and remote learning, to conducting interviews virtually, the pandemic birthed new ways of doing things which was previously alien to us. Of course I had my own share of the pandemic impact. Interviews and surveys that were designed to be conducted in person had to be completed remotely. Nothing prepared me

for this unexpected change as I had to learn new ways of doing these things digitally. Supervisory meetings could only be possible via Zoom due to complete lockdown. All of these constituted to some form of disruption and unexpected delays as processes were slowed and completely halted in some cases. Thank heavens I managed to finish in five years.

In all, I appreciate the experience this journey has brought and the opportunity of meeting very wonderful people that will be part of my life forever. The wonderful humans that constitute my supervisory team, the professional I have become and skills acquired will remain evergreen.