

**DEVELOPMENT OF AN UNDERGRADUATE
ANTIBIOTIC STEWARDSHIP TRAINING PROGRAMME
FOR MEDICAL STUDENTS**

Muhammad Augie Bashar



UNIVERSITY OF THE
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JOHANNESBURG

A thesis submitted to the Faculty of Health Sciences,

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in fulfilment of the requirements for the degree

of

Doctor of Philosophy

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DECLARATION

I, Muhammad Augie Bashar, declare that this thesis is my own work. It is being submitted for the degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

..... (Signature of Candidate)

Signed on the 23rd day of March 2022

DEDICATION

I dedicate this study to all medical students and medical teachers who participated in the study
- I hope that upon graduation, medical students will use the knowledge and skills they acquired on prudent antibiotic prescribing to improve responsible antibiotic use.

PUBLICATIONS AND PRESENTATIONS

PUBLICATIONS

Published articles

1. Augie, B. M., McInerney, P. A., van Zyl R. L., and Miot, J. Educational antimicrobial stewardship programs in medical schools: a scoping review protocol
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Student's contribution to the paper

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ABSTRACT

Antibiotic resistance is a growing concern because antibiotics are inappropriately over-consumed with few in the development pipeline, leaving prescribers with minimal treatment options. If not addressed, antibiotic resistance could result in prolonged hospital stay, increased mortality and higher healthcare costs. Antibiotic stewardship programmes have been shown to improve prudent antibiotic use. However, most of the antibiotic stewardship programmes are implemented at a postgraduate level with little emphasis given to medical undergraduate students. The World Health Organization highlighted the importance of teaching prudent antibiotic prescribing to undergraduate medical students. This study aimed to develop an educational antibiotic stewardship programme that will assist in teaching medical students in Nigeria and South Africa rational antibiotic prescribing. This study is underpinned by a six-step approach to curriculum development developed by Kern and colleagues. For the purpose of this study, the six-step approach to curriculum development in medical education was modified into two phases.

The study was divided into two phases. The emphasis in Phase One was on problem analysis and information gathering, and in Phase Two, an antibiotic stewardship curriculum was developed. In Phase One, three studies were conducted – a scoping review, a survey, and a summative content analysis of the curricula content of Nigerian and South African medical schools. In Phase Two, one study was conducted – a modified Delphi study. The findings from the three stages of Phase One were triangulated and informed the second phase of the study. Two rounds of the modified Delphi study were conducted in Phase Two, where experts drawn from different disciplines participated in the development of antibiotic stewardship competencies for teaching responsible antibiotic prescribing and therapeutic use to medical students in South African and Nigerian medical schools. The consensus was determined using the median and interquartile range. At the end of the two rounds, 88 of the 105 competencies reviewed by the panellists reached consensus and were categorized into knowledge, attitudes and skills domains. An antibiotic stewardship curriculum is designed to be taught in a spiral curriculum over three years using the principle of constructive alignment.

Keywords: antimicrobial resistance; education; medical students; antimicrobial stewardship

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LIST OF ABBREVIATIONS

AIDS	: Acquired immunodeficiency syndrome
AWaRe	: Access, Watch, and Reserve
AMR	: Antimicrobial Resistance
AMS	: Antimicrobial Stewardship
ASPs	: Antimicrobial Stewardship Programmes
BRICS	: Brazil, Russia, India, China, and South Africa
CDC	: Centres for Disease Control and Prevention
<i>C. difficile</i>	: <i>Clostridioides difficile</i>
CINAHL	: Cumulative Index to Nursing and Allied Health Literature
COVID-19	: Coronavirus disease 2019
DDDs	: Defined Daily Doses
DNA	: Deoxyribonucleic Acid
DOPS	: Observed Procedural Skills
ECDC	: European Centre for Disease Prevention and Control
Embase	: Excerpta Medica Database
EMA	: European Medicines Agency
ERIC	: Education Resources Information Center
FDA	: Food and Drug Administration
GEMP	: Graduate Entry Medical Programme
GMC	: General Medical Council
HIV	: Human Immunodeficiency Virus
JI	: Joanna Briggs Institute
IDSA	: Infectious Diseases Society of America
IPC	: Infection Prevention and Control
IQRs	: Interquartile Ranges
LMICs	: Low and Middle-Income Countries
MEDLINE	: Medical Literature Analysis and Retrieval System Online
MBBS	: Bachelor of Medicine, Bachelor of Surgery
MBChB	: Bachelor of Medicine, Bachelor of Surgery
MBBCh	: Bachelor of Medicine, Bachelor of Surgery
MeSH	: Medical Subject Headings
MCQs	: Multiple Choice Questions

MIC	: Minimum Inhibitory Concentration
mini-CEX	: Mini Clinical Evaluation Exercise
MRSA	: Methicillin-Resistant <i>Staphylococcus aureus</i>
OECD	: Organisation for Economic Co-operation and Development
OSCE	: Objective Structured Clinical Examination
PK-PD	: Pharmacokinetic-Pharmacodynamic
PRISMA	: Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROSPERO	: International Prospective Register of Systematic Reviews
PubMed	: Public/Publisher MEDLINE
RCT	: Randomized controlled trial
RNA	: Ribonucleic acid
REDCap	: Research Electronic Data Capture
SD	: Standard Deviation
SHEA	: Society for Healthcare Epidemiology of America
SUMARI	: System for the Unified Management, Assessment, and Review of Information
Tetfund	: Tertiary Education Trust Fund
UK	: United Kingdom
USA/US	: United States of America
US\$	: United States Dollar
MDR	: Multidrug-resistant
<i>mcr-1</i>	: Mobilized Colistin Resistance
WITS	: University of the Witwatersrand
WHO	: World Health Organization

CHAPTER ONE

Introduction and literature review

“Every antibiotic expected by a patient, every unnecessary prescription written by a doctor, every uncompleted course of antibiotics, and every inappropriate or unnecessary use in animals or agriculture is potentially signing a death warrant for a future patient.”

(Department of Health, 2008, p. 46).

Sir Liam Donaldson,
Former UK Chief Medical Officer.

1.1 Introduction

This chapter provides an overview of the literature that highlights the impact of antimicrobial resistance, as well as the drivers and mechanisms of antibiotic resistance. In addition, the interaction between humans, animals and the environment in the development of resistance and strategies to encourage appropriate antibiotic use are discussed. The theoretical framework underpinning this project is also discussed.

1.2 Antibiotics

Antibiotics are arguably the greatest form of chemotherapy discovered in the 20th century and probably over the entire history of medicine (Wright, 2007; Hsieh, 2016). Infections were the nightmares the world had lived with for centuries before the discovery of antibiotics (Erdem et al., 2011). Thousands of years before the discovery of antibiotics, millions of helpless people died from different types of bacterial infections (Mohr, 2016).

Penicillin was the first antibiotic to be discovered in 1928 by Sir Alexander Fleming (Bendiner, 1989). Fleming noticed an unusual growth of a colony of mould in many petri dishes containing *Staphylococcus* bacteria. It was observed that there was no visible growth of *Staphylococci* around the mould (Bendiner, 1989). The unexpected mould colony had somehow diffused the bacteria around it. A few small semi-transparent groups, defined by his assistant as “ghosts,” were identified as penicillin (Bendiner, 1989). Penicillin was first purified in large quantity by Howard Florey and Ernst Chain in the early 1940s (Ligon, 2004). It became widely available

in 1945 and was used during the Second World War which marked the beginning of the antibiotic era (Adedeji, 2016; Aminov, 2010). Albert Alexander, an Oxford police officer was the first person to ever receive penicillin.

The world witnessed a huge success in the discovery of new classes of antibiotics between 1945 and 1960, a period often called the ‘golden era’ of discovery of novel antibiotics, during which most of the antibiotics currently in clinical use were characterised (Broughton et al., 2016; Wright, 2007). From 1970 to 1980 there was a paradigm shift towards the chemical modification of the antibiotic compounds already in clinical use to improve their pharmacological properties and evade the effect of resistant pathogens, a period often called the ‘golden age of antibiotic medicinal chemistry’ (Wright, 2007). The antibiotics oxazolidinone ‘linezolid’ and the lipopeptide ‘daptomycin’ were approved for clinical use by the Food and Drug Administration (FDA) of the United States of America (USA) in 2000 and 2003, respectively, but it should be noted that daptomycin and the oxazolidinone class were first discovered in the mid-1980s (Wright, 2007), highlighting the length of time it takes from discovery to market regulatory approval. Likewise, a topical antibiotic agent, retapamulin was introduced in 2007 (Silver, 2011) and is the first member of the class pleuromutilins to be approved for human use since the class was discovered and characterised in 1950 (Novak and Shlaes, 2010). These examples highlight the length of time required from discovery to approval into the market; as such there is an urgent need to use available antibiotics judiciously.

One of the greatest challenges with antibiotics is a marked reduction in the discovery of new classes of antibiotics from the 1960s to date. Since 1987 there has been no successful discovery of a new class of antibiotics (Silver, 2011). Additionally, there has not been a novel class in the development pipeline for more than three decades, a situation referred to as a Discovery Void (Silver, 2011). Although some antibiotics find their way into clinical practice as a result of chemical modification of drugs from the existing classes of antibiotics. The lack of new classes of antibiotics with novel mechanisms of action to deal with ever-increasing resistant pathogens is a source of concern as bacteria have developed resistance to antibiotics used in clinical settings (Silver, 2011). Widespread resistance to a class of antibiotics suggests that the class cannot be used to effectively treat resistant pathogens. It should be noted that the antibiotic development pipeline has not been empty over the past years, but it is mostly filled with improved versions of already registered classes (Silver, 2011). Some of the agents in the pipeline if successfully approved may improve the bacterial spectrum, safety, convenient

dosing regimens, and may probably address the concern of resistance that has already developed on the parent compound (Silver, 2011). Lack of effective antibiotics to treat infections necessitates the need to come up with strategies like antimicrobial stewardship (AMS) and infection and prevention control to encourage the responsible use of this scarce resource. Currently, there is a dearth of new antibiotics and it is unlikely that any new class of antibiotics will be developed anytime soon (Hopkins, 2016). This is why it is important to understand the consequences of AMR and bring healthcare institutions, policymakers, researchers, educators, curriculum developers and the general public together to develop strategies that can slow the development of MDR pathogens.

Antibiotic discovery and its subsequent use in clinical practice to treat infectious pathogens have revolutionised modern medicine and transformed the treatment paradigm (Hsieh, 2016; Munita and Arias, 2016). Antibiotics are a prerequisite for conducting cutting-edge surgical procedures, organ transplantation, and cancer chemotherapy (Munita and Arias, 2016) and have improved patients' clinical outcomes from infectious agents, resulting in a decrease in morbidity and mortality in all patients infected with antibiotic-sensitive infections (Hsieh, 2016). Sadly, increased resistant pathogens are affecting these initial successes and jeopardising treatment outcomes of critically ill patients. Antibiotics are a unique class of pharmaceuticals whose inappropriate use will not only negatively affect the index patient using them, but also the general population and exert ecological pressure leading to the development and spread of resistant bacteria (Hopkins, 2016). Antibiotics are different from other classes of drugs in that they have no direct effects on human cells, but act by either inhibiting or killing microorganisms (Gyssens, 2017).

Healthcare providers across different specialities prescribe antibiotics daily in both inpatient and outpatient settings (Dyar and Beović, 2017). Traditionally antibiotics have been prescribed by physicians, but currently a wide range of professionals such as pharmacists, nurses and midwives are also involved in prescribing practices of this scarce resource (Dyar and Beović, 2017). Hence, the need to educate all these professionals on appropriate antibiotic prescribing to address misuse and over use.

Inappropriate use of broad-spectrum antibiotics results in selective pressures leading to antimicrobial resistance (AMR) which is of global concern. Infections as a result of multidrug-resistant (MDR) bacteria are associated with high morbidity and mortality compared to those

as a result of susceptible bacteria (Cosgrove, 2006). MDR bacteria also carry a more important health and economic burden. MDR organisms have increased the frequency of hospital-acquired infections with limited treatment options. “It is unfortunate that no antibiotic has escaped resistance, even last-line agents, such as colistin and daptomycin that act on the cell’s exterior membrane.” (Bonomo and Rossolini, 2008, p. 549).

The use of antibiotics in animal production either to treat infections or as growth promoters have significantly increased the rate of antibiotic-resistant pathogens (Van Boeckel et al., 2015). A couple of years ago the world witnessed the emergence of resistant pathogens that are resistant to last resort antibiotics. For instance, the global emergence of resistance to carbapenem-resistant *Klebsiella pneumoniae* in the USA, plasmid-mediated *bla*_{NDM-1} gene in bacteria that confers resistance to carbapenems in India (Yong et al., 2009) and *Escherichia coli* with the plasmid-mediated *mcr-1* gene that confers resistance to colistin identified in China (Liu et al., 2016). This demonstrates the gravity of the problem and the need for global surveillance of resistant pathogens.

There is a lack of accurate and reliable data on the extent of antibiotic resistance in Africa as only a few countries have an established surveillance programme. An external quality assessment across public health laboratories in Africa conducted between 2002 and 2009 identified poor antimicrobial susceptibility testing in many countries requiring strengthening (Frean et al., 2012). South Africa is one of the leading countries on the continent in terms of surveillance of resistant pathogens. As of 2009, there were only 340 accredited diagnostic laboratories in Africa of which 312 (92%) are all in South Africa, and of the 312 accredited laboratories in South Africa, 90.4% are in the private sector (Gersh-Damet et al., 2010).

1.3 Antimicrobial resistance

The use of antibiotics in clinical, veterinary and agricultural activities has created an avenue for selective pressure for the emergence and spread of bacteria resistant genes since the 1950s (Bonomo and Rossolini, 2008). AMR is defined as the resistance of microorganisms to an antimicrobial agent to which they are sensitive (Jindal et al., 2015). There are different ways by which bacteria can develop resistance, including enzymatic inhibition, penicillin-binding protein modifications, porin mutations, efflux pumps, and target modification.

Sir Alexander Fleming the discoverer of the first antibiotic ‘penicillin’ foresaw the coming of AMR and in an interview with the New York Times magazine on June 26, 1945, he made the following warning statement “The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out. In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted.” (Fleming, 1945a). In addition, during a Nobel Prize lecture in 1945, Fleming also warned that a time may come when penicillin could be sold freely at pharmaceutical outlets without prescriptions. “The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant” (Fleming, 1945b, p. 93). In many developing countries, such as Nigeria and Indonesia, antibiotics have been reported to be dispensed without prescriptions (Akinyandenu and Akinyandenu, 2014; Hadi et al., 2010). In 2015, the World Health Organization (WHO) reported that people are buying antibiotics without prescription – “In most countries, antibiotics can be purchased in markets, shops, pharmacies or over the Internet without prescription or involvement of a health professional or veterinarian. Poor quality medical and veterinary products are widespread, and often contain low concentrations of active ingredients, encouraging emergence of resistant microbes” (WHO, 2015a, p. 4).

1.4 Evolution and spread of antibiotic resistance

It is important to understand that AMR is an ancient phenomenon, which occurs as a result of interaction between organisms and their environment. Many antimicrobial agents occur as natural molecules co-existing with bacteria which stimulates them to develop mechanisms to resist the effects of antibiotics as a survival strategy (Munita and Arias, 2016). However, in clinical settings, the concern is the acquisition of resistant traits by bacteria that were previously susceptible to the antibiotic compound (Munita and Arias, 2016). According to Prof Livermore, a director at the reference laboratory of the Health Protection Agency, "The emergence of antibiotic resistance is the most eloquent example of Darwin's principle of evolution that there ever was, ...It is a war of attrition. It is naive to think we can win." (Boseley, 2010). From an evolutionary viewpoint, bacteria avoid the effects of antibiotics via two main genetic approaches; mutations in the gene(s) and acquisition of foreign DNA coding by way of horizontal gene transfer (Munita and Arias, 2016).

A study conducted at the Galápagos Islands, a remote place in Ecuador where there is limited human activity with little anthropogenic antibiotic exposure, found that antibiotic-resistant genes were absent in bacteria isolated from the land animals (Thaller et al., 2010). Likewise, plasmids obtained from bacterial collections that predate the antibiotic era are found not to contain resistant elements (Davis and Anandan, 1970). This indicates that the presence of antibiotics is a very crucial factor in the evolution and spread of antimicrobial-resistant genes and it also plays a role in changing the natural microbiota (Bhullar et al., 2012).

An examination of soil specimens in The Netherlands involving pre-and antibiotic eras found an increase in antibiotic-resistant genes of classes of antibiotics such as beta-lactams, tetracyclines and macrolides in the contemporary soil specimens compared to specimens from the pre-antibiotic era (Knapp et al., 2010). This evidence suggests that widespread antibiotic resistance is strongly associated with the human use of antibiotics. However, it is reported that antibiotics and antibiotic biosynthetic pathways evolved millions of years ago which implied that antibiotic resistance is an ancient event (Barlow and Hall, 2002; Hall and Barlow, 2004; Baltz, 2008). Hall and Barlow (2004) estimated that the Class A beta-lactamases emerged about 2.4 billion years ago because of the presence of Class A beta-lactamases in the chromosomes of *Cytophaga–Flexibacter–Bacteroides* in both Gram-positive and Gram-negative bacteria.

Additionally, features of antibiotic resistance were highly present in ancient DNA dating from a 30,000-year-old Pleistocene (D'Costa et al., 2011). The idea of the antibiotic resistome forecast that antibiotic resistance occurs because of dynamic and competitive microbial interactions that precede human use of antibiotics (Wright, 2007; 2010). A soil survey found MDR organisms despite the absence of antibiotic sources from human activities (D'Costa et al., 2006). Antibiotic-resistant pathogens were isolated from extreme conditions such as the deep terrestrial subsurface (Brown and Balkwill, 2009), as well as in the deep ocean (Toth et al., 2010); and other environments where there is no influence of human activities. The findings of these studies suggest that antibiotic resistance is an ancient phenomenon and is genetically linked to a natural phenomenon, deeply embedded in the microbial pangenome.

1.5 Drivers of antimicrobial resistance

The major driver of AMR is the inappropriate use of antibiotics and their overconsumption (Sriram et al., 2021). Some of the factors that contribute to inappropriate antibiotic use include overreliance on empirical prescriptions due to inaccurate and expensive diagnostics, the

availability of antibiotics over-the-counter, industry promotion, and a lack of understanding of the consequences of antibiotic overuse (Belachew et al., 2021; Do et al., 2021). AMR is also encouraged by the sale of counterfeit and substandard antibiotics and irrational fixed-dose combinations (Ozawa et al., 2018). Non-prescribed antibiotic dispensing in community drug retail outlets has been identified as one of the contributing factors to widespread antibiotic abuse in sub-Saharan African countries (Belachew et al., 2021).

Globally antibiotics are perhaps the most commonly prescribed class of drugs in a healthcare setting. The use of these precious agents in many countries has increased in recent decades, especially in low and middle-income countries (LMICs) (Sriram et al., 2021). A study that analysed the pattern of antibiotic consumption over 15 years from 2000 to 2015 in 76 countries found an increase in the volume of antibiotic consumption expressed in defined daily doses (DDDs) of 65% (21.1 to 34.8 billion DDDs), and antibiotic consumption rate increased by 39% (11.3 to 15.7 defined daily doses per 1,000 inhabitants per day) (Klein et al., 2018). Data has shown that antimicrobial consumption in Brazil has increased from 2,535 DDDs per 1,000 inhabitants per year in 2000 to 6,763 DDDs per 1,000 inhabitants per year in 2015 (Center for Disease Dynamics Economics and Policy. ResistanceMap, Year not stated). Similarly, over the same time frame, there was a remarkable increase in antimicrobial consumption seen in other countries. For instance, in China, antimicrobial consumption increased from 1,910 to 3,060 DDDs per 1,000 inhabitants per year, in Francophone West African countries from 557 to 2,112 DDDs per 1,000 inhabitants per year and 5,647 to 10,934 DDDs per 1,000 inhabitants per year in Saudi Arabia (Center for Disease Dynamics Economics and Policy. ResistanceMap, Year not stated).

Between 2000 and 2015 an increase in total antimicrobial consumption was also seen in high-income countries, but DDDs per 1,000 inhabitants per year increased slowly or even reduced (Sriram et al., 2021). For instance, in Switzerland, antimicrobial consumption only increased by 716 DDDs per 1,000 inhabitants over 15 years from 2000 to 2015 (Sriram et al., 2021). In the USA, antimicrobial consumption remains high, but the rate reduced from 12,030 to 10,298 DDDs per 1,000 inhabitants between 2000 and 2015 (Sriram et al., 2021). Conversely, it was found that between 2000 and 2015 the per capita antibiotic consumption was low in LMICs compared to high-income countries and increased accessibility to antibiotics is behind the converging consumption rates (Klein et al., 2018). There is an increased use of last-resort antibiotics such as carbapenems, polymyxins, oxazolidinones and glycyclcyclines worldwide,

which advocates the need for stringent regulations to address antibiotic consumption (Klein et al., 2018). The study also predicted that without policy to checkmate the current global trend of antibiotic consumption it could double by 2030 (Klein et al., 2018).

Globally there is limited data on the surveillance of resistant pathogens, however, emerging evidence shows that inappropriate use and overconsumption has increased in some clinical settings particularly in LMICs especially in Africa (Sriram et al., 2021). A Global Point Prevalence Survey was conducted in 2015 to examine the antibiotic prescribing pattern for patients admitted to over 303 hospitals across 53 countries of which 17 were in upper-middle-income countries (Versporten et al., 2018). The survey found a difference in the pattern of antibiotic prescribing practices based on geographic regions and the nature of the clinical setting. Africa has the highest prescription rate of 50% in inpatient settings compared to 27.4% in Eastern Europe (Versporten et al., 2018). The high rate of antimicrobial use seen in Africa could be due to the higher burden of infectious diseases in the region (Morgan et al., 2011). In many countries in Africa and Asia, antibiotics can be accessed from pharmaceutical outlets without prescription, and even where prescriptions are required to dispense antibiotics, the enforcement of law tends to be lax (Morgan et al., 2011). As such those in need of antibiotics can bypass clinicians to purchase them.

The use of antimicrobial agents, both appropriately and inappropriately, is higher in both primary and critical care settings and for neonatal and paediatric patients where specific infection syndromes are treated. Previous studies have shown that inappropriate antibiotic use is high in primary healthcare settings, with reports of 83.6% in Pakistan (Sarwar et al., 2018), 60.6% in China (Wang et al., 2014), 55% in South Africa (Gasson et al., 2018), and 15.4% in Canada (Schwartz et al., 2020).

As AMR rises, people and governments in many LMICs grapple to finance and procure effective antibiotics, especially those in the reserve category of the WHO Access, Watch, and Reserve (AWaRe) list (WHO, 2019a). In its effort to address AMR, the WHO developed the AWaRe framework classification to balance responsible access to antibiotics and antibiotic stewardship (WHO, 2019a). Access antibiotics are antibiotics that can be used to manage conditions caused by a wide range of common bacteria with a low tendency of developing resistance and are regarded as the first-line options over other agents in other groups. Watch antibiotics are those agents with a higher tendency of developing resistance and are considered

critically important antimicrobials for human medicine. While Reserve antibiotics are kept for infections caused by MDR infections that cannot be managed by any other antibiotic (Klein et al., 2021). The burden of AMR is increasing globally because many bacterial species are resistant to most of the first-line antibiotics, necessitating prescribers to resort to the use of more expensive, second-line antibiotics (Klein et al., 2021). There was an increase in the global per capita consumption of Watch antibiotics between 2000 and 2015 by 90.9%, driven mostly by LMICs which witnessed a 165% increase (from 2.0 to 5.3 DDDs per 1,000 inhabitants) compared to 27.9% in high-income countries (from 6.1 to 7.8 DDDs). Across the globe, the use of Access antibiotics has increased by 26.2% between the years 2000 to 2015 (Klein et al., 2021).

One important driver of AMR that is often overlooked is the extensive use of antibiotics in agriculture and aquaculture (Van Boeckel et al., 2014). The high demand for animal protein and dairy products has increased the use of antibiotics in agriculture, where antibiotics are used as growth promoters in addition to treating and preventing infections. There is an urgent need for all countries to develop stringent policies to regulate the use of antimicrobial agents in animals (Sriram et al., 2021). Antimicrobial consumption in animals is almost three times that in humans and is mainly for animal protein production (Princeton University, 2019). Meat production has increased by more than 60% in Africa and Asia, and 40% in South America, since 2000, as countries on those continents transitioned from low-protein to high-protein diets (Princeton University, 2019). Of note, more than 50% of global chickens and pigs grown for production are in Asia (Princeton University, 2019). Research data has shown that the global consumption of all antimicrobials in food animals was 131,109 tons in 2013 and it is predicted to reach 200,235 tons by 2030 (Van Boeckel et al., 2017). The volume of antimicrobial consumption differs considerably from one country to another and it ranges from 8 mg/population correction unit (a kilogram of animal product) in Norway to 318 mg/population correction unit in China (Van Boeckel et al., 2017). China is the biggest consumer of antimicrobials in farm animals globally in both relative and absolute terms (Van Boeckel et al., 2017).

The rate of antimicrobial consumption is rapidly increasing in aquaculture compared to meat and dairy products (Schar et al., 2020). Aquaculture generally contributes 8% of animal protein to the human diet worldwide. Global antimicrobial consumption in aquaculture is estimated at 10,259 tons in 2017 and it is forecast to rise by a third to 13,600 tons in 2030 (UI 4193–59,295)

(Schar et al., 2020). Global antimicrobial use in aquaculture is highest in the Asia-Pacific region accounting for nearly 93.8% where China alone accounted for 57.9% of global antimicrobial consumption in aquaculture in 2017 (Schar et al., 2020).

1.6 States of the antibiotic development pipeline

The world is in urgent need of new antibiotics to manage the burden of resistant bacteria. The antibiotic development pipeline remains insufficient to tackle the challenges of the increasing emergence and spread of AMR (WHO, 2019b). A report issued by the European Centre for Disease Prevention and Control and European Medicines Agency in 2009 indicated that the antibiotic production pipeline is almost empty (ECDC/EMA, 2009). Further, only a few antibiotic agents are under development in the pipeline with a high failure rate. As WHO put it “The clinical pipeline remains insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance.” (WHO, 2019b, p. vii).

For many years pharmaceutical industries were reluctant to invest resources in research and the development of new antibiotics. As of 2004, only about 1.6% of drugs in the development pipeline in the world’s 15 biggest pharmaceutical companies were antibiotics (Spellberg et al., 2004). It should be noted that these 15 pharmaceutical companies developed 93% of the 57 new antibiotics approved by the FDA from January 1980 to December 2003 (Spellberg et al., 2004). Recently an analysis of the antibiotic pipeline by the WHO shows that only 50 antibiotics and combinations, and 10 biologicals are in clinical trial phases 1 to 3 (WHO, 2019a). Of these, 2019b). Only 32 antibiotics target the WHO priority pathogens, with 12 targeting tuberculosis, six targeting *Clostridioides difficile*, while only two are active against the critical MDR Gram-negative bacteria (WHO, 2019b). The 10 biological treatments currently in clinical development target *Staphylococcus aureus* (six treatments), *Pseudomonas aeruginosa* (two treatments) and *C. difficile* (two treatments) (WHO, 2019b). A recent WHO report on the preclinical antibacterial pipeline shows that 252 antibacterial agents are being developed by 145 institutions targeting the WHO priority pathogens, *Mycobacterium tuberculosis* and *C. difficile* (WHO, 2019c). Generally, the preclinical drug pipeline tends to be unstable and involves scientifically diverse pathways where more than one-third of such projects utilise non-traditional approaches, such as immune evasion, anti-virulence, and microbiome-modifying therapies to developing new agents (Theuretzbacher and Piddock, 2019; WHO, 2019c). It should be noted that a greater number of these projects may fail as only a few get to the market

due to many scientific bottlenecks associated with some non-traditional approaches (Theuretzbacher and Piddock, 2019) that are yet to be scientifically proven to work in a clinical setting.

If not addressed, the spread of AMR could make many bacteria much more dangerous than they are now. In 2017, the WHO published 12 families of bacteria for which new antibiotics are urgently needed (WHO, 2017a). The bacteria are subdivided into three critical priority pathogens, six high and three medium priority pathogens (WHO, 2017a). The critical priority pathogens include (i) carbapenem-resistant *Acinetobacter baumannii*, (ii) carbapenem-resistant *Pseudomonas aeruginosa*, and (iii) Extended-spectrum beta-lactamases-producing and carbapenem-resistant *Enterobacteriaceae*. The high priority pathogens are (i) vancomycin-resistant *Enterococcus faecium*, (ii) methicillin-resistant, vancomycin-intermediate and -resistant *Staphylococcus aureus*, (iii) clarithromycin-resistant *Helicobacter pylori*, (iv) fluoroquinolone-resistant *Campylobacter* spp., and (v) fluoroquinolone-resistant *Salmonellae*, (vi) fluoroquinolone-resistant and cephalosporin-resistant *Neisseria gonorrhoeae*. While medium priority are (i) penicillin-non-susceptible *Streptococcus pneumoniae*, (ii) ampicillin-resistant *Haemophilus influenzae*, and (iii) fluoroquinolone-resistant *Shigella* spp. (WHO, 2017a). The six leading bacteria that cause deaths as a result of AMR in 2019 were *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. These six bacteria were responsible for 929,000 deaths attributable to AMR and 3.57 million deaths associated with AMR (Murray et al., 2022). All six of these bacteria are among the group of bacteria considered by the WHO as priority pathogens, where new antibiotics are urgently needed (WHO, 2017a).

There are several factors responsible for the poor investment into the research and development of new antibiotics. Firstly, the rapid development of resistance to antibiotics is a factor discouraging pharmaceutical industries because of fear of non-return of financial investments (Morel and Mossialos, 2010). The second reason is the availability of relatively effective generic antibacterial agents on the market that are used as the first line of treatment for infectious agents (Morel and Mossialos, 2010) with greater competition for the same market share. The third reason is that the new broad-spectrum antibiotics are usually reserved as a last-line drug for treating MDR organisms, which sends a signal to pharmaceutical companies that new antibiotics will be reserved for severe infections (Morel and Mossialos, 2010) with a smaller market share. Fourthly, antibiotics are usually used for a short duration compared to

drugs used to treat chronic conditions making them less profitable compared to agents used for treating chronic conditions (Morel and Mossialos, 2010).

Many pharmaceutical companies have already abandoned the research and development of antibiotics. For instance, in 2018, Novartis and Sanofi shifted their antibiotics searchlight to focus on other areas, such as cancer therapy, while AstraZeneca took a similar position in 2016 (Plackett, 2020). According to a 2017 estimate, the cost of developing an antibiotic is roughly US\$1.58 billion (Towse et al., 2017). Meanwhile, analysts in the pharmaceutical industry believe that the average revenue earned from the sale of an antibiotic is around US\$46 million per year (Plackett, 2020). In the United States, the data from the sales of five of the most recent antibiotics are believed to be US\$ 1 million or less per month, which probably does not cover operational costs (Carr and Springer, 2019). Kasim Kutay, the chief executive officer of Novo Holdings, a Danish investment firm, argues that "That's tiny and nowhere near the amount needed to justify the investment." (Plackett, 2020, p. 850).

1.7 Consequences of antimicrobial resistance

It is difficult to comprehensively quantify the total global effects of AMR because epidemiological and surveillance data are scarce in many countries across the globe, however, the available data is alarming (Marston et al., 2016). Furthermore, AMR disproportionately affects the poor due to limited access to more expensive second-line antibiotics that are used when first-line antibiotics fail (Murray et al., 2022). In the USA, the number of people affected by antibiotic resistance is still far too high. Each year, more than 2.8 million antibiotic-resistant infections occur in the USA, with over 35,000 people dying as a result (CDC, 2019). In addition, over 223,900 people in the USA required hospitalization for *C. difficile*, and at least 12,800 died as a result of the resistant infections in 2017 (CDC, 2019). Despite the fact that the Centres for Disease Control and Prevention's (CDC's) 2019 report on the burden of AMR does not provide a specific estimate for the financial cost of antibiotic-resistant infections on a national scale, the 2013 CDC report estimated that in the USA the direct healthcare cost of AMR is over 20 billion US dollars, with additional costs to society for lost productivity as high as \$35 billion every year (CDC, 2013). Conversely, AMR causes approximately 33,000 deaths each year and costs the European Union/European Economic Area countries' health-care systems approximately 1.1 billion Euros (OECD/ECDC, 2019). If no meaningful action is taken, AMR to second-line antibiotics in the European Union/European Economic Area will be 72% greater

in 2030 compared to 2005. AMR to second-line treatments will more than double throughout the same time span (OECD/ECDC, 2019).

A United Kingdom (UK) commissioned report predicted that unless the current trajectory is checked, antibiotic resistance will cause 10 million people to die prematurely annually by 2050. The report also estimated a reduction of 2.0-3.5% of the global gross domestic product and will cause the global economy to lose up to 100 trillion US dollars (O'Neill, 2014; 2016). Although some experts have criticised these predictions (de Kraker et al., 2016; NOAH, 2016). However, WHO, as well as numerous other similar organisations and researchers, agree that the development and spread of AMR is an important issue that necessitates a globally coordinated action plan to address (CDC, 2019; Prestinaci et al., 2015; WHO, 2015b; WHO, 2021).

More recently, Christopher Murray and colleagues provided a very comprehensive insight on the burden of AMR across the globe in a study that assessed the number of mortalities and disability-adjusted life-years attributed to and associated with bacterial resistance for 23 pathogens and 88 pathogen–drug combinations across 204 countries and territories (Murray et al., 2022). Their findings estimated that 4.95 million people died as a result of bacterial antibiotic resistance across the globe in 2019, including 1.27 million deaths attributable to bacterial resistance (Murray et al., 2022). This is higher than the number of people who died as a result of AMR in 2016 as reported by O'Neill (O'Neill, 2016) or those who died from either malaria or human immunodeficiency virus/acquired immunodeficiency syndromes (HIV/AIDs) in 2019 (Murray et al., 2022). Further, the study found that regionally, West Africa has the highest all-age death rate attributable to AMR, which was estimated at 27.3 deaths per 100,000 compared to Australasia which has the lowest at 6.5 deaths per 100,000 (Murray et al., 2022). The findings of the study show that AMR is not only a serious global health issue but is also a particularly important problem in some of the world's poorest countries in sub-Saharan Africa. In addition, lower respiratory tract infections were the leading causes of death due to AMR in 2019 (Murray et al., 2022). They were responsible for more than 1.5 million deaths, making it the most severe infectious condition (Murray et al., 2022).

Antibiotic resistance is worsened by the lack of a robust antibiotic pipeline, leading to the emergence of MDR organisms that are almost untreatable, leaving prescribers handicapped with no effective agents to treat patients (Munita and Arias, 2016). “It is unfortunate that no

antibiotic has escaped resistance, even last-line agents, such as colistin and daptomycin that act on the cell's exterior membrane.” (Bonomo and Rossolini, 2008, p. 549).

1.8 The relationship between antibiotic use and development of resistance

Antibiotic selective pressure leads to the development of drug-resistant microbes. Both clinical and *in vitro* studies show a direct association between antibiotic use and antibiotic resistance in Gram-positive bacteria (Li and Cosgrove, 2017). A meta-analysis involving 76 clinical studies showed a relative risk of 1.8 for methicillin-resistant *Staphylococcus aureus* (MRSA) among patients with previous antibiotic exposure compared to those not exposed to antibiotics (Tacconelli et al., 2008). A non-linear time series analysis of the population of northeast Scotland observed a high threshold for the development of community-acquired MRSA when some antibiotics such as fluoroquinolones, macrolides, and clindamycin are used (Lawes et al., 2015). A matched case-control study showed an association between extended use of third-generation cephalosporins, metronidazole or fluoroquinolones, with the emergence of vancomycin-resistant *Enterococcus* infection or colonization (Carmeli et al., 2002). Additionally, two randomized trials where antibiotics were used for a short duration to treat ventilator-associated pneumonia demonstrated a low threshold for subsequently developing antibiotic resistance with no effect on patient outcomes (Chastre et al., 2003; Singh et al., 2000).

In 2010, data from the CDC indicated that 55.7% of the discharged patients from 323 hospitals had antibiotics during their inpatient stay, while 29.8% of them received at least one dose of broad-spectrum antibiotics and 37.2% of those prescribed could be improved (Fridkin et al., 2014). Irrational antibiotic therapy can result in the selection of resistant bacteria such as *C. difficile*, antibiotic-related toxicities, and adverse drug reactions, with consequent morbidity, mortality, and increased healthcare costs (Hsieh, 2016). Reduced antibiotic use has been linked to a reduction in antibiotic resistance and *C. difficile* infections (Hsieh, 2016). In an effort to encourage responsible antibiotic use the CDC has inaugurated many campaigns targeted at reducing AMR. The campaigns highlight the need for prudent antimicrobial use in acute care hospitals (Hsieh, 2016).

In 2007, the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) jointly published guidelines for developing institutional antibiotic stewardship programmes (Dellit et al., 2007). According to IDSA and SHEA, the

main goal of antibiotic stewardship programmes (ASPs) is to improve patients' clinical outcomes while minimising the unintended consequences of antibiotic use, such as AMR, organ toxicity, and selection of pathogenic pathogens like *C. difficile* (Dellit et al., 2007).

1.9 Mechanisms of antibiotic resistance

Bacteria have developed sophisticated mechanisms to avoid being killed by antimicrobials, a process that is believed to have occurred millions of years ago because of evolution (Munita and Arias, 2016). AMR is a natural process whereby a microorganism evolves and develops traits that allow it to survive the effects of antimicrobials (Hopkins, 2016). Many years ago, AMR was addressed by developing new effective antibiotics that work against resistant microbes for a while before resistance is developed (Hopkins, 2016).

Antibiotic resistance occurs because of mutations resulting in errors as DNA is replicated or through the transfer of DNA materials among bacteria, usually of an independent loop of DNA called plasmids (Davies, 2013). The use of antibiotics follows the principle of natural selection that favours resistant microbes, allowing them to thrive while sensitive ones are killed (Davies, 2013). As time goes on the resistant pathogens dominate the sensitive bacteria and consequently the effectiveness of antibiotics is lost. There are different ways by which bacteria can exhibit resistance to antibiotics. Bacteria can intrinsically develop resistance to antibiotics or they can become resistant by spontaneous mutations when they horizontally acquire new genetic materials from other bacteria.

1.9.1 Intrinsic resistance

Intrinsic resistance is present in the genome of the microbe and enables bacteria with an ability to develop resistance against the activity of an antibiotic (Kostyaney and Can, 2017). In intrinsic resistance, AMR occurs independently of antibiotic selective pressure and horizontal gene transfer. Intrinsic resistance may occur as a result of the following factors:

- a lack of affinity of the antibiotic for bacterial target
- the inability of the antibiotic to access the bacterial cell
- expulsion of the antibiotic by chromosomally encoded efflux pumps
- presence of enzymes that will degrade antibiotics (Kostyaney and Can, 2017).

A study that used high-throughput screens of genome mutant libraries indicated that many genes cause intrinsic resistance to many antibiotics, such as beta-lactams, aminoglycosides and fluoroquinolones (Kostyanov and Can, 2017). The study also found that synergistic use of antibiotics could help in the treatment of clinically important bacteria such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (Kostyanov and Can, 2017).

1.9.2 Acquired resistance

Acquired resistance occurs among some bacterial strains, where there is an exchange of genes by mutation or horizontal gene transfer through conjugation, transformation or transduction. Three different ways through which acquired resistance occurs are:

- Increased efflux pump activity in the microbe resulting in decreased antibiotic accumulation in the microbe. This mode of antibiotic resistance affects many classes of antibiotics such as protein synthesis inhibitors, β -lactams, polymyxins, fluoroquinolones, and carbapenems (Munita and Arias, 2016). Bacteria are able to confer resistance to antibiotics by developing complicated machinery capable of extruding antibiotics from the cell (Munita and Arias, 2016). The first description of an efflux mechanism capable of pumping tetracycline out of the cytoplasm of *E. coli* was reported in the early 1980s (McMurry et al., 1980).
- Target modification of the antibiotic molecule by a microbial genetic mutation. One of the most common ways that bacteria use to cause resistance is alterations to the target site, which affects practically all classes of antibiotics (Munita and Arias, 2016). For instance, point mutations in the genes encoding the target site, enzymatic modification of the binding site such as the addition of methyl groups, and/or replacement or bypass of the original target site (Munita and Arias, 2016).
- Antibiotic inactivation via hydrolysis in the microbe or modification of the microbial binding site preventing the antibiotic from killing the microbe (Kostyanov and Can, 2017). For instance, β -lactamases use this mechanism to destroy β -lactam antibiotics (Munita and Arias, 2016). The amide bond of the β -lactam ring is destroyed by β -lactamases, rendering the antibiotic ineffective (Munita and Arias, 2016). β -lactamases were discovered in the early 1940s, a year before penicillin was released to the market. However, evidence shows that they have been around for millions of years (Abraham and Chain, 1940; D'Costa et al., 2011).

1.10 An effort to address the burden of antimicrobial resistance

Many countries have developed strategies to address AMR. For instance, in the UK, the magnitude of the risk of AMR and the possible line of actions were outlined in the ‘Annual report of the Chief Medical Officer 2011’ (Davies and Gibbens, 2013). In response to this, the UK government published the ‘UK five-year antimicrobial resistance strategy 2013 to 2018’ where it outlined seven key strategies to address AMR (Davies and Gibbens, 2013). The Global Health Security Agenda, launched by the US government in 2014 has acknowledged AMR as one of major risks to global health (Katz et al., 2014). In its effort to encourage member States to identify strategies to address AMR, the WHO developed a global action plan on AMR, which was approved by the World Health Assembly in 2015 (Hopkins, 2016).

In response to the WHO’s call, both South Africa and Nigeria have developed National Action Plans for AMR. The South African AMR National Strategy Framework 2014 – 2024 provides a structure for managing AMR to reduce the spread of resistant pathogens and improve patient outcomes through four strategic objectives viz, (i) strengthen, coordinate and institutionalize interdisciplinary efforts, (ii) optimise surveillance and early detection of AMR, (iii) enhance infection prevention and control and (iv) promote appropriate use of antimicrobials in human and animal health through the implementation of AMS (South African antimicrobial resistance National strategy framework; a One Health approach 2017 – 2024, Year not stated). Similarly, Nigeria has the following strategic objectives (i) increase awareness and knowledge of AMR and related topics, (ii) build a ‘One Health’ AMR surveillance system, (iii) intensify infection prevention and control in the tripartite sectors, (iv) promote rational access to antibiotic and antimicrobial stewardship and (v) invest in AMR research and development (Federal Ministries of Agriculture and Rural Development, Environment and Health Abuja. National Action Plan for Antimicrobial Resistance 2017-2022, 2017).

1.11 Roles of vaccination in reducing antimicrobial resistance

Vaccines can reduce AMR in two main ways, namely, by decreasing the transmission of resistant and susceptible infections, and/or selective pressure following antibiotic consumption for AMR (Centre for Disease and Dynamics Economics & Policy, Year not stated). Fewer infections mean fewer antibiotics are required, which reduces the selection pressure on pathogenic strains that are resistant to antibiotics (Centre for Disease and Dynamics Economics & Policy, Year not stated). There are vaccines available to prevent many infectious pathogens

such as Diphtheria-Tetanus-Pertussis and meningococcal conjugate vaccines, but low vaccination coverage, drinking of unsafe water and poor sanitation have subjected many people to become vulnerable to infectious agents, thereby increasing the demand for antibiotics (Sriram et al., 2021). Investing resources to expand vaccine coverage especially in LMICs, provision of water and sanitation facilities, and implementation of AMS in hospitals could go a long way to reduce AMR globally (Sriram et al., 2021).

1.12 Antimicrobial stewardship

In 2015, the World Health Assembly recognised AMR as a global public threat and endorsed the Global Action Plan on Antimicrobial Resistance by the member states (WHO, 2015c). Not long after that the Political Declaration of the High-Level Meeting of the General Assembly also declared AMR as a global threat to public health (United Nation General Assembly, 2016). In both settings, it was agreed that overuse and misuse of antibiotics are the main drivers of AMR and acknowledged the need to optimize the use of antibiotics (WHO, 2019d). The Global Action Plan on AMR outlined five strategic objectives as a guide for member states while developing their action plans on AMR:

- Improve awareness and understanding of AMR through effective communication, education and training.
- Strengthen the knowledge and evidence base through surveillance and research.
- Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.
- Optimize the use of antimicrobial medicine in human and animal health.
- Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions (WHO, 2019d).

Objective 4 aims to support the development and implementation of AMS in both human and animal settings. A report from the Organisation for Economic Co-operation and Development (OECD) projected that if implemented AMS programmes along with other initiatives that aim at reducing overconsumption of antimicrobial agents and promote hospital hygiene could help save nearly 1.6 million lives and 4.8 billion US dollars annually by 2050 across the 33 OECD member states (WHO, 2019d).

In a joint policy consensus statement on AMS by the Society for Healthcare Epidemiology of America, the Infectious Diseases Society of America, and the Paediatric Infectious Diseases Society have defined AMS as “coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration” (Fishman, 2012, p.323). In the same vein, the European Society of Clinical Microbiology and Infectious Diseases Study Group for Antimicrobial Stewardship defined AMS as “Antimicrobial stewardship is a coherent set of actions which promote using antimicrobials in ways that ensure sustainable access to effective therapy for all who need them” (Dyar et al., 2017, p. 796).

The main objectives of AMS are to achieve the best clinical outcomes when using antimicrobial agents with minimal toxicity and other adverse events, and also to limit the selective pressure on microbes that drives the emergence of antibiotic-resistant strains (Barlam et al., 2016). AMS programmes may also help reduce excessive costs associated with suboptimal antimicrobial use (Fishman, 2012). The term AMS was first coined in 1996 (McGowan Jr and Gerding, 1996).

AMS is a critical approach in the fight against AMR by decreasing the current problem of AMR and the spread of resistant pathogens in the future (Hulscher and Schouten, 2017). Over the years many documents such as AMS guidelines, policy statements and consensus statements have been issued by national and international organisations that aim at guiding the development of AMS programmes. Some of these documents such as one by Barlam et al., (2016) recommended the formation of an AMS team and the implementation of AMS in a hospital setting. Further, they also describe how to implement AMS interventions aiming to improve responsible antibiotic prescribing practice. However, there is a dearth of literature on how to develop and implement AMS in medical schools, which has the potential to prepare aspiring doctors to become antimicrobial stewards.

AMS programmes are different depending on the antibiotic consumption, available personnel, size and available resources to address AMR (Hulscher and Schouten, 2017). For instance, a Cape Town study that reported a remarkable reduction in antibiotic consumption was conducted in an academic hospital led by infectious disease specialists with other experts in its team. Such a study is difficult to replicate outside of an academic setting because the experts involved are difficult to source (Boyles et al., 2017). In view of this, the Netcare model in South Africa, where the intervention was driven by pharmacists in a hospital environment could be an option

in poor resource settings (Brink et al., 2016). While designing and implementing a robust AMS can be a major challenge especially in non-academic hospitals, such as community hospitals, because of the lack resources involved, AMS strategies can still be designed and implemented in such hospitals to conform with their available resources and staff strength (Septimus and Owens Jr, 2011).

AMS comprises two intrinsically major sets of interventions that fall under the category of either the “what” or the “how” of the **programmes** (Hulscher and Schouten, 2017). The first category of interventions deals with how antibiotic care interventions or antibiotic prescribing practices that describe “appropriate antibiotic use” in hospital inpatients settings relate to antibiotic indication, choice of antibiotic, dose, route of administration, or duration of therapy (Hulscher and Schouten, 2017). Such interventions include “change from intravenous to oral antibiotic treatment” or “streamline treatment” in patients when such decisions are appropriate (Schuts et al., 2016). The second category of interventions consists of strategies to ensure that prescribers actually implement AMS prescribing practices in their daily practice (Hulscher and Schouten, 2017). Some of the interventions that involve behavioural change include providing prescribers with formularies, prospective and retrospective audits and feedback to prescribers; educational meetings; reminders; financial interventions; or the revision of professional roles which all can be done to improve prudent antibiotic prescribing practices (Effective Practice and Organisation of Care Taxonomy, 2015). While the first category of interventions is applied to patients, the second category of interventions is applied to the prescribers (Hulscher and Schouten, 2017).

AMS along with infection prevention and control (IPC), medicine and patient safety are regarded as the three “pillars” of an integrated approach to health systems strengthening (WHO, 2019d). When used effectively along with antimicrobial use surveillance, and the WHO essential medicines list, AMS could help to address AMR by optimising antibiotic utilisation (WHO, 2017b). If the three pillars of an integrated approach to health systems strengthening are implemented along with other key components of infection management and health systems strengthening, such as AMR surveillance and adequate supply of quality-assured medicines, it promotes equitable distribution of quality health care services and helps to achieve universal health coverage.

In 2014, President Barack Obama issued Executive Order 13676: Combating Antibiotic-Resistant Bacteria, which aims to provide a National Action Plan for Combating Antibiotic-resistant Bacteria in the USA (White House, 2015). This encouraged the establishment of AMS in all the critical care hospitals by 2020 and the Centres for Medicare and Medicaid Services to issue a condition of participation requiring participating hospitals to build programmes based on the CDC's guidelines (CDC, 2014). Extension of AMS programmes to other health care facilities such as ambulatory surgery centres, dialysis facilities, nursing homes and wards, and emergency units and outpatient departments are also encouraged (Barlam et al., 2016).

1.13 The goals of an AMS programme are as follows

- To optimize the use of antimicrobials
- To shape the knowledge and behaviour of antibiotic prescribers and change dispensing practices
- To improve the standard of patient care and clinical outcomes
- To reduce health costs without compromising the standard of care
- To decrease the chances of emergence, selection and spread of resistant pathogens
- To prolong the sustainability of existing antibacterial agents
- To reduce the projected burden of the economic impact of AMR on the global economy
- To encourage prescribers to use available evidence-based guidelines while prescribing antibiotics (WHO, 2019d).

1.14 Strategies used in AMS

AMS comprises a wide range of strategies and interventions. A Cochrane review conducted to determine interventions used to optimise antimicrobial prescribing for inpatient settings has categorised the strategies into three main groups as follows:

- Persuasive strategies such as education, prospective audit and feedback, clinical pathways and guidelines.
- Restrictive strategies such as formulary restriction, prior approval or preauthorization from the AMS team, automatic stop orders, antimicrobial cycling and antibiotic order forms.
- Structural strategies such as computerized records and computerized decision support (Davey et al., 2013).

It should be noted that the strategies used in the AMS programme may differ from one institution to another. Some of the commonly used strategies have shown remarkable results in reducing inappropriate antibiotic use in improving patient outcomes (Barlam et al., 2016).

1.14.1 Education

This involves both formal and informal processes to educate the prescribers to improve antibiotic prescribing, as well as antibiotic dispensing and administration practices (Nathwani, 2018). Education training on responsible antibiotic prescribing can be delivered to healthcare providers by trained personnel, for instance to infectious disease physicians during ward rounds. Most of the AMS programmes involve an education strategy, but it is more effective when combined with other strategies (WHO, 2019d). Education strategies take the following forms;

- Educational meetings on basic and prudent antibiotic use, problem-based/case-based discussions, morbidity and mortality meetings, lectures on important topics and significant event analysis,
- Training and delivery of educational content such as clinical guidelines,
- Use of relevant local stakeholders to promote the dissemination of relevant information,
- Reminders provided verbally, on paper or electronically,
- Use of AMS e-learning resources to educate prescribers and
- Incorporating AMS education as a component of continuing medical education (WHO, 2019d).

1.14.2 Treatment guidelines

These are usually designed based on local susceptibility data for the treatment of common infections at an institutional, regional or national level. The WHO has developed a manual to help developing countries to develop their antibiotic treatment guidelines (WHO, 2011a). An antibiotic guideline designed to guide healthcare professionals with empirical antibiotic use should be developed based on susceptibility data and the resultant standard treatment guidelines should help and guide prescribers to commence antibiotic therapy before the results of culture are available (WHO, 2011a).

1.14.3 Formulary restriction

In formulary restriction, the use of certain antibiotics that are associated with *C. difficile* infection or the use of last-resort antibiotics such as carbapenems and colistin are restricted in favour of effective first- and second-generation antibiotics. The formulary restriction is part of most of the AMS programmes. A meta-analysis involving 16 studies that used different interventions such as education, formulary restriction, post-prescription review and prior approval requirement has demonstrated how AMS interventions could reduce the burden of *C. difficile* infection by 52% (Feazel et al., 2014).

1.14.4 Prior approval and justification

A prescriber is expected to get approval from either an infectious disease physician, pharmacist or AMS team before certain antibiotics such as carbapenems and colistin can be released. Prior approval can be obtained via telephone, automatic stop orders, antibiotic order forms, and direct interactions (Fishman, 2006). Prior approval or justification can be seen by the physicians as an intervention where their right to prescribe antibiotics is threatened, but it is likely to be one of the most effective strategies to encourage responsible antibiotic use and reduce antibiotic cost (John Jr and Fishman, 1997).

1.14.5 Streamlining

This involves a change of an initial empiric antibiotic regimen based on the results of the microbiologic laboratory test results. This strategy encourages the use of narrow-spectrum antibiotics which may result in reduction of antibiotic resistance and antibiotic cost saving in favour of broad-spectrum antibiotics that select pressure for the emergence of resistance (Fishman, 2006). It also involves an early conversion from intravenous to oral routes which tend to reduce cost and hospital length of stay (Barlam et al., 2016).

1.14.6 Antibiotic cycling

Antibiotic cycling refers to the planned replacement of one class of antibiotic with one or more antibiotics from a different class for a predetermined period, as opposed to changing one antibiotic with another one from the same class (Brown and Nathwani, 2005). The principle behind antibiotic cycling is that the most commonly used antibiotic is more likely to develop resistance. Hence, the withdrawal of a class of antibiotic(s) for a period will therefore reduce the selective pressures exerted by those agents (Brown and Nathwani, 2005).

1.14.7 Prospective audit with feedback

Here an AMS team assesses the prescribed antibiotics especially during ward rounds and provides recommendations and feedback to prescribers where antibiotic therapy is found to be inappropriate (Akpan et al., 2016). Prospective audits and feedback interventions encourage responsible antibiotic use and are one of the main components of many AMS programmes (Barlam et al., 2016). Prospective audits and feedback implemented at an intensive care unit setting showed improved antibiotic prescription patterns with a favourable impact on the development of AMR (Campbell et al., 2017).

1.14.8 Dose optimization

This is an effort to ensure antibiotic doses are prescribed based on infection, patient characteristics, and available antibiotic treatment guidelines (Cattaneo et al., 2016). It takes into consideration factors such as patient age, weight, organ failure and tissue perfusion. It also involves therapeutic drug monitoring when treating patients with nephrotoxic antibiotics such as linezolid and aminoglycosides (Cattaneo et al., 2016).

1.15 Importance of education in antimicrobial stewardship

Education is regarded as an important component of any AMS programme to help prescribers use antibiotics prudently. Education is central to improving antibiotic prescribing, it shapes the knowledge and attitudes of prescribers and also helps them understand comprehensive contextual and cultural elements that affect antibiotic prescribing behaviours (Dyar and Beović, 2017). Educational intervention may include lectures, distribution of reading material and interactive modules for prescribers. It should be noted that in a clinical setting education is seen as a passive strategy that may not result in a sustained reduction in antibiotic use and should be used in conjunction with other active AMS strategies (Barlam et al., 2016). In the USA, the CDC launched an educational campaign called *Get Smart about Antibiotics*, which at the beginning centred on outpatient healthcare providers and the general public, but was later broadened to incorporate inpatients. The campaign has recorded success (Ohl and Luther, 2014).

Most of the educational AMS interventions target postgraduate students and practising physicians with the hope of changing their behaviour (Gyssens, 2017). However, changing behaviour after graduation from medical school has proven difficult and hence the need to

incorporate AMS into medical school curricula. After graduation and licensing by relevant regulatory bodies, doctors are expected to start prescribing antimicrobials regularly without direct supervision; the same is also expected of pharmacists in some countries (Dyar and Beović, 2017). This underscores the importance of ensuring that medical students receive training on both general and appropriate antibiotic use (Pulcini and Gyssens, 2013). Previous studies across the globe have found that the majority of medical students are not ready for antibiotic prescribing on completion of their studies and desire further training on responsible antibiotic prescribing (Abbo et al., 2013; Dyar et al., 2014; Huang et al., 2013; Minen et al., 2010; Wasserman et al., 2017). More recently, a study involving final year medical and pharmacy students of three East African countries found that the students were not adequately prepared for antibiotic prescribing (Lubwama et al., 2021).

Medical students should graduate with the understanding that they have a duty to optimise their individual patient's antibiotic treatment and also use antibiotics prudently to minimise their chances of developing resistance so that antibiotics can be used for future patients (Pulcini and Gyssens, 2013). Medical schools should equip students with skills to address these responsibilities when they graduate and start practising. A previous study that examined the curricula of the European medical schools demonstrated that many principles of prudent antibiotic use are not adequately covered. It also noted a wide difference in the curricula between countries because of a lack of national frameworks (Pulcini et al., 2015).

Lack of adequate knowledge and skills in prudent antibiotic use among practising physicians and medical students have been attributed to increased misuse of antimicrobial use in the health sector (WHO, 2018). A reasonable approach to tackle the problem of AMR is to ensure rational use of antibiotics by training and educating physicians and aspiring doctors on the relevant competencies necessary to prevent AMR as highlighted by one of the objectives of the WHO Global Action Plan on AMR (WHO, 2018). Currently, there is a remarkable difference in education and training of antimicrobial use across different settings. Considering the lack of sufficient knowledge on prudent antibiotic use, the WHO competency framework for education on AMR could serve as a reference for educators, medical schools, regulatory bodies, accreditation bodies and AMS curriculum developers (WHO, 2018).

1.16 Educating the public on rational antibiotic use

The WHO in its publication released for the World Health Day in 2011 highlighted that in order to encourage prudent use of antibiotic use, the education strategies should involve both prescribers and patients to effectively reduce unnecessary use of antibiotics and their demand by the patients (WHO, 2011b). The Australian Commission on Safety and Quality in Health Care in its national Antimicrobial Stewardship Clinical Care Standard comprises nine competency statements that explained the best quality clinical care in which antibiotic therapy is explained (Vlahović-Palčevski, 2017). It applies to both hospital and community settings and also provides guidelines for patients to understand how their infections are effectively managed and to be able to make an informed choice of the right antibiotic treatment with the support of their clinician (Vlahović-Palčevski, 2017). Patients can help reduce irrational antibiotic use by using advice that is based on evidence-based guidelines, such as not using antibiotics to treat acute viral infections (Vlahović-Palčevski, 2017). Additionally, patients should adhere to the instructions of taking the prescribed antibiotics when they are appropriately prescribed for them (Vlahović-Palčevski, 2017).

A systematic review that involved 24 cross-sectional studies that assessed the general populations' knowledge about antibiotic use and resistance, found that 50% of the participants did not know that antibiotics are not required for the treatment of viral infections, and 27% did not know that inappropriate antibiotic use could lead to AMR (Gualano et al., 2015). The investigators concluded that to improve knowledge on responsible antibiotic use and AMR it is advisable to take the campaign to the community so that they stop pressurising prescribers for antibiotics and change their behaviour towards antibiotics (Gualano et al., 2015). Additionally, another systematic review that examined the public's knowledge and beliefs on AMR, found that the general public has a poor understanding of AMR and misperception on how it comes about (McCullough et al., 2015). The researchers suggested that these findings should be taken into consideration when designing an intervention aiming at changing the public's beliefs about how they can help in tackling this global problem (McCullough et al., 2015). Public health enlightenment campaigns could help to tackle AMR by educating the general public on how bacteria develop resistance. To encourage appropriate antibiotic use at an individual level, clinicians should use strategies like shared decision-making when prescribing antibiotics for patients (McCullough et al., 2015).

1.17 Campaign for responsible use of antibiotics

There are several initiatives to educate the public on the dangers associated with inappropriate antibiotic use (Vlahović-Palčevski, 2017). The WHO is at the forefront of the global campaign “Antibiotics: Handle with Care” educating the public, governments, health and veterinary workers to develop strategies to urgently address the problem of AMR (WHO, 2015d). In 2015, the WHO put on their calendar “World Antibiotic Awareness Week” for the first time. The week aims to create an awareness of global AMR and to encourage responsible antibiotic use among the general public, healthcare providers, opinion- and policy-makers to prevent further development and spread of AMR (WHO, 2015d). In the USA, the 2008 CDC’s *Get Smart: Know When Antibiotics Work* initiative was started to ensure antibiotics are only prescribed when they are indicated and are then used appropriately (Get Smart US Centres for Disease Control Prevention, 2013). It is a one-week event that encourages the importance of responsible antibiotic use (Get Smart US Centres for Disease Control Prevention, 2013). Elsewhere in Australia, the government is funding the National Prescribing Service Medicine Wise to conduct an AMR awareness and education campaign for the general public and healthcare providers, with special consideration for general practitioners who are the major prescribers of antibiotics in the country (Australian Government Department of Health, Antimicrobial Resistance, 2020). The campaign started in 2012, aims to reduce the rate of antibiotic prescribing in general practice by 25% in five years (Australian Government Department of Health, Antimicrobial Resistance, 2020). In Europe, the European Centre for Disease Prevention and Control inaugurated the European Antibiotic Awareness Day in 2008 as an annual event to organise a public awareness campaign on 18 November of every year to encourage the public to use antibiotics responsibly (McNulty and Johnson, 2008). There are many other national or regional activities in different countries (Huttner et al., 2010).

1.18 Antimicrobial stewardship in low- and middle-income countries

AMR will affect the LMICs mostly in Asia and Africa the hardest (Mendelson, 2016). In addition, many LIMCs have significant data gaps on AMR, stressing the need to develop microbiology laboratory capacity and data collection techniques to better understand this important public health problem (Murray et al., 2022). The UK commissioned report predicted that by 2050 there would be an annual 10 million deaths, with the greatest impact on the LMICs in Asia and Africa (O’Neill, 2014; 2016). Mendelson (2016) noted that there are many reasons for this geographical variation, but the primary influence is the high burden of disease in LMICs

that may warrant high levels of antibiotic use. There was a 36% increase in human antibiotic consumption between 2000 and 2010, notably in the so-called BRICS countries (Brazil, Russia, India, China, and South Africa) and French-speaking West African countries (Van Boeckel et al., 2014). Seventy-six percent of the global increase in antibiotic consumption between 2000 to 2010 occurred in the BRICS countries, while only 33% of the global increase in population occurred in these countries (Van Boeckel et al., 2014). In the BRICS countries, 23% of the increase in the retail sales volume was recorded in India and nearly 57% of the increase in the hospital settings was in China (Van Boeckel et al., 2014).

Failure to address social factors such as drinking water and sanitation predisposes poor people in LMICs to become vulnerable to disease. Other factors include overcrowding causing respiratory illness, living with animals causing zoonotic illnesses and weakened immune systems caused by malnutrition as a result of poverty and HIV infection (Mendelson, 2016). Other challenges in LMICs include poor accessibility to infection prevention facilities such as vaccination and some simple interventions such as soap for handwashing that may reduce the need for antibiotics in the first place (Mendelson, 2016).

A study undertaken to examine the level of preparedness of countries in sub-Saharan Africa to address the burden of AMR found that the implementation of AMS was weak across the sub-region (Elton et al., 2020). However, countries in Eastern and Southern Africa are ahead of other countries in the sub-region (Elton et al., 2020). The authors reported that East Africa has the highest number of countries with AMR National Action Plans, as well as human and animal pathogen AMR surveillance programmes (Elton et al., 2020). Conversely, Southern African countries, had the best AMS guidelines with training programmes and legislation in both human and animal health (Elton et al., 2020). In an effort to improve responsible antibiotic use, LMICs should be encouraged to develop a One Health surveillance system that incorporates veterinary and environmental sectors into any clinical programme (One Health Commission, 2022).

One important issue to also consider in AMS is the accessibility to affordable and quality assured antibiotics. As it stands there are more children under the age of 5 years from LMICs who die of pneumonia because they cannot access antibiotic therapy than due to AMR (Laxminarayan et al., 2013). There is a relationship between the financial status of the family and antibiotic accessibility as more children from an affluent family household will receive antibiotics compared to those from a poor family (Johansson et al., 2012).

Financial institutions such as the Global Alliance for Vaccines and Immunizations, Global Fund, and the International Drug Purchase Facility should support LMICs to access good antimicrobials and vaccines. Developing countries with poor health institutions and weak medicines regulatory bodies are often the target of counterfeit antibiotics which drive antibiotic resistance via sub-optimal doses (Kelesidis and Falagas, 2015). A systematic review conducted to assess the implementation of ASPs in Africa included 13 studies that met selection criteria, of which seven were conducted in South Africa, three in Kenya, and one each in Sudan, Tanzania, and Egypt (Akpan et al., 2020). The 13 included studies mostly assessed improved compliance with antibiotic guidelines, the appropriateness of antibiotic prescribing, the reduction in antibiotic use, and cost savings (Akpan et al., 2020). Two of the studies revealed a decrease in the rate of surgical site infections, as well as a non-significant change in mortality and the 30-day readmission rate (Akpan et al., 2020).

Several factors are responsible for an unstable and commercially unattractive market that affects the accessibility and availability of genuine antibiotics in LMICs (Morel et al., 2020). Such factors include high demand for inexpensive generic antibiotics, price control in some countries where the prices of antibiotics are fixed at either too low or too high levels, and a small market that does not demand huge volumes of antibiotics (Morel et al., 2020). Researchers have proposed four models to incentivise research and development of novel antibiotics in Europe to increase returns on investment and reduce uncertainty, but such models may not work in LMICs (Årdal et al., 2020).

The Global Fund partnership, which aimed to accelerate the end of AIDS, tuberculosis and malaria as epidemics, was able to raise US\$12.9 billion for the period of 2017 to 2019, a little less than the US\$13 billion the fund had intended to raise (Lancet, 2016). As of June 2021, the Global Fund had committed US\$22.7 billion in HIV and AIDS prevention and treatment programmes and US\$3.8 billion in tuberculosis and HIV programmes, accounting for 25% of all international funding for HIV programmes (Global Fund, 2021). Additionally, over the same period, the Fund has invested more than US\$14.7 billion in malaria control initiatives and US\$7.8 billion in tuberculosis prevention and care activities (Global Fund, 2021). In an effort to reduce the burden of the coronavirus disease 2019 (COVID-19) pandemic across the globe, the Fund invested more than US\$1 billion to enhance and build diagnostic tools and laboratory facilities, as well as data and surveillance systems, procurement and supply chains, community

systems and responses, and health worker training (Global Fund, 2021). On the other hand, the AMR Action Fund, which aims to bring two to four new antibiotics into the market by 2030, was only able to raise about US\$1 billion to support the research required to achieve this goal (McCall, 2020; Plackett, 2020). Interestingly, with the new fund, many pharmaceutical companies such as GlaxoSmithKline, Pfizer, Novo Holdings and Novartis are returning to research and the development of new antibiotics (McCall, 2020; Plackett, 2020). The Director-General of the International Federation of Pharmaceutical Manufacturers & Associations, Thomas Cueni, noted that “If we want to change the game in the antibiotic field, then the industry needs to step up and collectively bring real money to the table” (McCall, 2020, p. 1017). As the COVID-19 pandemic continues, AMR lurks in the shadows. In recent years, the world has witnessed how government agencies and donor organisations committed huge sums to support COVID-19 vaccine research and development, expansion of manufacturing capacity, and developing an efficient system for distribution (Robinson, 2021). In fact, a recent report predicted that the total global spending on COVID-19 would reach US\$157 billion by 2025 (Mishra, 2021). According to Prof Avison, a bacteriologist at the University of Bristol, stated that unlike COVID-19, “there will never be herd immunity to antibiotic resistant infections, nor a universal vaccine. If we don’t do these things, the impact of antibiotic resistance will dwarf the impact of COVID-19 over the next decade” (McCall, 2020, p. 1017).

1.19 Statement of the problem

Currently there is no published literature regarding educational antibiotic stewardship intervention programmes in the curricula for medical students in Nigeria, South Africa or, indeed, across the whole African continent. It is critical that such programmes are introduced at a student level to provide future prescribers with the knowledge and skills required to combat the threats raised by inappropriate antibiotic prescribing and use. So, whilst evidence suggests that students and newly qualified doctors lack the skills and confidence to engage in ASPs, in South Africa and Nigeria, no specific ASPs appear to exist in the medical school environment.

In order to implement such a programme, it is necessary to first understand what is currently being taught in the medical schools in South Africa. As well as investigate what programmes have been developed and implemented in other countries in order to identify and develop an appropriate educational intervention that is relevant and sustainable in medical school curricula.

1.20 Justification for the study

An AMS programme is more likely to be successful if started at medical school which is the time when knowledge and behaviour are being shaped (Pulcini and Gyssens, 2013). Surgeons are more likely to accept the principles of surgical prophylaxis if courses on responsible antibiotic prescribing and antibiotic stewardship are included in their medical school curricula (Pulcini and Gyssens, 2013). Surprisingly, only a few studies are conducted to find out the effect of teaching basic and prudent antibiotic knowledge and skills among medical students (Pulcini and Gyssens, 2013; Shankar et al., 2011). Nigerian and South African medical schools were selected in this study because of the countries influence on the continent. Further to this, Nigerian medical schools are still using a discipline-based Flexinarian curriculum in the 21st century, whereas in South Africa the AMS programme is still to be well incorporated into the integrated medical curriculum of the University of the Witwatersrand. The South African medical school was chosen because a previous study involving three South African medical schools, including the medical school in this study, to assess their knowledge and perception about prudent antibiotic use, found that the students from this South African medical school performed poorly when compared to the other two South African universities. Involving the school could help in understanding the problem and developing an antibiotic stewardship curriculum to help address it. Because of the low number of medical students in Nigerian medical schools, many schools were invited to participate in the study, but only four responded. The fourth school was not included in the study due to unrest in the region, which could make data collection challenging.

1.21 Research question

What would be an appropriate, relevant and sustainable educational programme for teaching medical students rational antibiotic prescribing in South Africa and Nigeria?

1.22 Aim

This study aims to develop an educational antibiotic stewardship programme that will assist in teaching rational antibiotic prescribing to medical students in Nigeria and South Africa.

1.23 Objectives

1. To explore the content of the Nigerian and South African medical curricula in relation to antibiotic teaching.
2. To determine the perceptions, attitudes and knowledge of Nigerian and South African final year medical students about rational antibiotic prescribing using a questionnaire format.
3. To explore the current educational antibiotic stewardship interventions in Africa and globally.
4. To develop a curriculum for teaching medical students antibiotic stewardship.

1.24 Study design

In order to achieve the above objectives a multimethod study design was used (Hesse-Biber et al., 2015). A multimethod approach may use either qualitative or quantitative methods or both methods in a single research project. The main characteristic of a multimethod study is that each study is complete on its own and is used to achieve a specific objective of the study (Esteves and Pastor, 2004). The multimethod approach was chosen because it allows for both in-depth and positivist inquiries into a single research project (Esteves and Pastor, 2004).

The multimethod design, especially the integrative multimethod design where two or more methods are combined, is found to be more robust than other methods such as the triangulation design (Seawright, 2016). Integrative multimethod designs have several strengths that triangulation lack. Multimethod designs can clearly show the contribution of each method to the general causal inference which is not the case with triangulation (Seawright, 2016). In multimethod research designs, there is no issue of deciding whether two different results agree with each other and having to decide what to do in cases where they do not agree.

Additionally, the multimethod research design allows researchers to test their assumptions and produce better and more empirically grounded causal inferences (Seawright, 2016). Mingers advocated for the use of the multimethod design based on the fact that research and the research process involve complex and multidimensional processes that require a wide range of approaches (Mingers, 2001). Further, Mingers acknowledged that multimethod techniques allowed for a robust understanding of the problem. The multimethod design enables scholars to have a deep understanding of different concepts under study, and also provides a more

comprehensive explanation (Mingers, 2001). Mingers (2001, p. 241) argues that “different research methods (especially from different paradigms) focus on different aspects of reality and therefore a richer understanding of a research topic will be gained by combining several methods together in a single piece of research or research program.”

1.25 Steps in development of antibiotic stewardship curriculum

The six-step approach to curriculum development developed by Kern and colleagues (Kern et al., 1998) was used to guide the process of curriculum development in this thesis. For the purpose of this study the six-step approach of curriculum development in medical education is modified into two phases (Figure 1.1).

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Problem Identification and General Needs Assessment	Targeted Needs Assessment	Goals and Objectives	Education Strategies	Implementation	Evaluation and Feedback
Phase One (Problem analysis and information gathering) Objectives 1, 2 and 3			Phase Two (Development of an ASP programme/ curriculum) Objective 4		

Figure 1.1: Diagrammatic representation of Kern et al.’s six-step approach for curriculum development and alignment with study objectives (Kern et al., 1998).

1.25.1 Step 1: Problem identification and general needs assessment

In this step the educator begins by identifying and critically analysing the health care problem (Kern et al., 1998). In this study, the problem is the need for an antibiotic stewardship curriculum for teaching responsible antibiotic prescribing to medical students in Nigeria and South Africa. This required an analysis of the current approach of the medical education system to ASP (Chen et al., 2019). This was then followed by determining an ideal way to address the identified need. A general needs assessment represents the difference between the ideal approach and the current approach identified by an educator or a clinician (Kern et al., 1998).

1.25.2 Step 2: Targeted needs assessment

The second step requires an assessment of the needs of the targeted category of learners and their learning environment (Kern et al., 1998). It allows the integration of a specific curriculum into the broader curriculum. This step involves the collection of data, which includes characteristics, preferences and needs of the targeted learners and stakeholders, and the type of resources in the learners' environments (Chen et al., 2019).

1.25.3 Step 3: Goals and objectives

As soon as the needs of the targeted students are identified, the goals and objectives of the curriculum are set and include both the general goals and the specific measurable objectives (Kern et al., 1998). These objectives can be categorised into knowledge, attitudes and skill domains for the learner. This stage of developing goals and objectives is critical as it sets the curricular content and teaching and learning methods (Kern et al., 1998).

1.25.4 Step 4: Educational strategies

After defining the objectives, the curricular content is developed and educational strategies that will help to achieve the set educational objectives are determined (Kern et al., 1998).

1.25.5 Step 5: Implementation

This refers to the implementation of both the educational strategy and its evaluation (Kern et al., 1998). It has many components which include getting political support; identifying and obtaining the necessary resources; identifying and solving some of the implementation problems; introducing, administering and refining the curriculum (Kern et al., 1998).

1.25.6 Step 6: Evaluation and feedback

This step evaluates whether the implemented curriculum was successful and how the curriculum can be improved (Chen et al., 2019). This can be achieved through formative evaluation processes (ongoing feedback about the students' performance or that of the curriculum) or summative evaluation processes (which involves issuing a final “grade” or assessment of the students or curriculum performance) (Kern et al., 1998).

Of note in the real world, curriculum development does not necessarily have to follow the six steps in sequence one step at a time, but rather, it is a dynamic and interactive process. Steps 1-4 of the curriculum development process outlined above are addressed in this study. The first three stages of the model informed Phase One of this study (i.e., Problem Analysis and Information Gathering) and objectives 1 – 3 of the study. Stage 4 of the model informed Phase Two of the study (i.e., Development of an AMS curriculum) and addresses objective 4.

This study started with a scoping review to map available evidence on antibiotic stewardship teaching in medical schools and a survey to determine the knowledge and perceptions of final year medical students. This was followed by a curricula content review from the study sites. A modified Delphi study was conducted to obtain the views of experts in relation to the content that should be included in an antibiotic stewardship framework. The different studies addressed the phases of the research project. One phase informed the next phase. The phases of the study, objectives, and the types of studies conducted are presented in Table 1.1 below.

Table 1.1: Study objectives, phases and studies conducted.

Phases	Objectives	Studies conducted
Phase One	1. To explore the current educational antibiotic stewardship interventions in Africa and globally.	Educational antimicrobial stewardship programmes in medical schools: a scoping review protocol
		Educational antimicrobial stewardship programmes in medical schools: a scoping review
	2. To determine the perceptions, attitudes and knowledge of Nigerian and South African final year medical students about rational antibiotic prescribing using a questionnaire format.	A survey: Knowledge and perceptions about antibiotic resistance and prudent antibiotic prescribing among final year medical students in two African countries.
	3. To explore the content of the Nigerian and South African medical curricula in relation to antibiotic teaching.	A summative content analysis of two African medical schools' antibiotic stewardship curricula

Phase Two	4. To develop a curriculum for teaching medical students antibiotic stewardship	Development of an antibiotic stewardship curriculum for medical students: a modified Delphi
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1.26 Conceptual framework

Figure 1.2 shows the conceptual framework for this PhD thesis, which underpins the two phases used to develop an antibiotic stewardship curriculum for teaching prudent antibiotic prescribing. The framework highlights the interaction between the different stages of the model used in the development of the curriculum. The two phases of the thesis are:

1. Phase One: Problem analysis and information gathering
2. Phase Two: Development of an ASP curriculum

1.26.1 Phase One: Problem Analysis and Information Gathering

This phase explored the problems and gathered important information that guided the development of the prototype AMS curriculum. The following three operational steps were used to gather the relevant information:

1.26.1.1 Step 1: Scoping review of educational AMS programmes in Africa and globally

This stage aimed to identify, appraise and synthesise educational antibiotic stewardship interventions in medical schools. A scoping review was conducted using the Joanna Briggs Institute (JBI) methodology to map available evidence on antibiotic stewardship teaching in medical schools locally and internationally.

1.26.1.2 Step 2: Survey

A descriptive, cross-sectional study involving final year medical students of three Nigerian and one South African medical school was conducted to assess their knowledge and perceptions on antibiotic use, AMR and AMS.

1.26.1.3 Step 3: Curricular review

A summative content analysis of the curricula of one Nigerian and one South African medical school was conducted. This allowed us to explore the content of the curricula as they relate to the teaching of prudent antibiotics use.

1.26.2 Phase Two: Development of an ASM curriculum

This phase contextualised the outcomes of the three stages of Phase One. Competency domains and associated descriptors were developed using the findings of Phase One which were then subjected to two rounds of a modified Delphi to refine the developed prototype. A modified Delphi technique involved a panel of experts drawn from the following fields; clinical pharmacology, pharmacy, infectious diseases, microbiology, nursing and medical education.

The experts responded to questionnaires in two rounds (Hsu and Sandford, 2007). A consensus was regarded as a median score of greater than or equal to 5 and an interquartile range of less than or equal to 1.5. The competencies that reached consensus were used to develop an antibiotic stewardship curriculum for training medical students on rational antibiotic prescribing. Figure 1.2 briefly illustrates the two phases of the study. The results obtained from the three Stages of Phase One guided the development of Phase Two. The plan was to do a Phase Three, but due to the pandemic and going to online teaching the objective (To evaluate the effectiveness of the programme by comparing the mean knowledge score of students before and after the training) was not achieved because of poor response to online questionnaires (Eight returned out of 384 sent out).

1.27 Conclusion

This chapter provides an overview of antibiotic discovery, mechanisms of antibiotic resistance and the drivers of antibiotic resistance. The relationship between humans, animals and the environment and how it leads to antibiotic resistance is also discussed. The need for antibiotic stewardship and how it encourages prudent antibiotic prescribing are included in the discussion. The six-step approach for curriculum development by Kern and colleagues is aligned with the study objectives (Kern et al., 1998). The study design is explained. The next chapter provides information on current educational antibiotic stewardship strategies used to teach medical students globally.

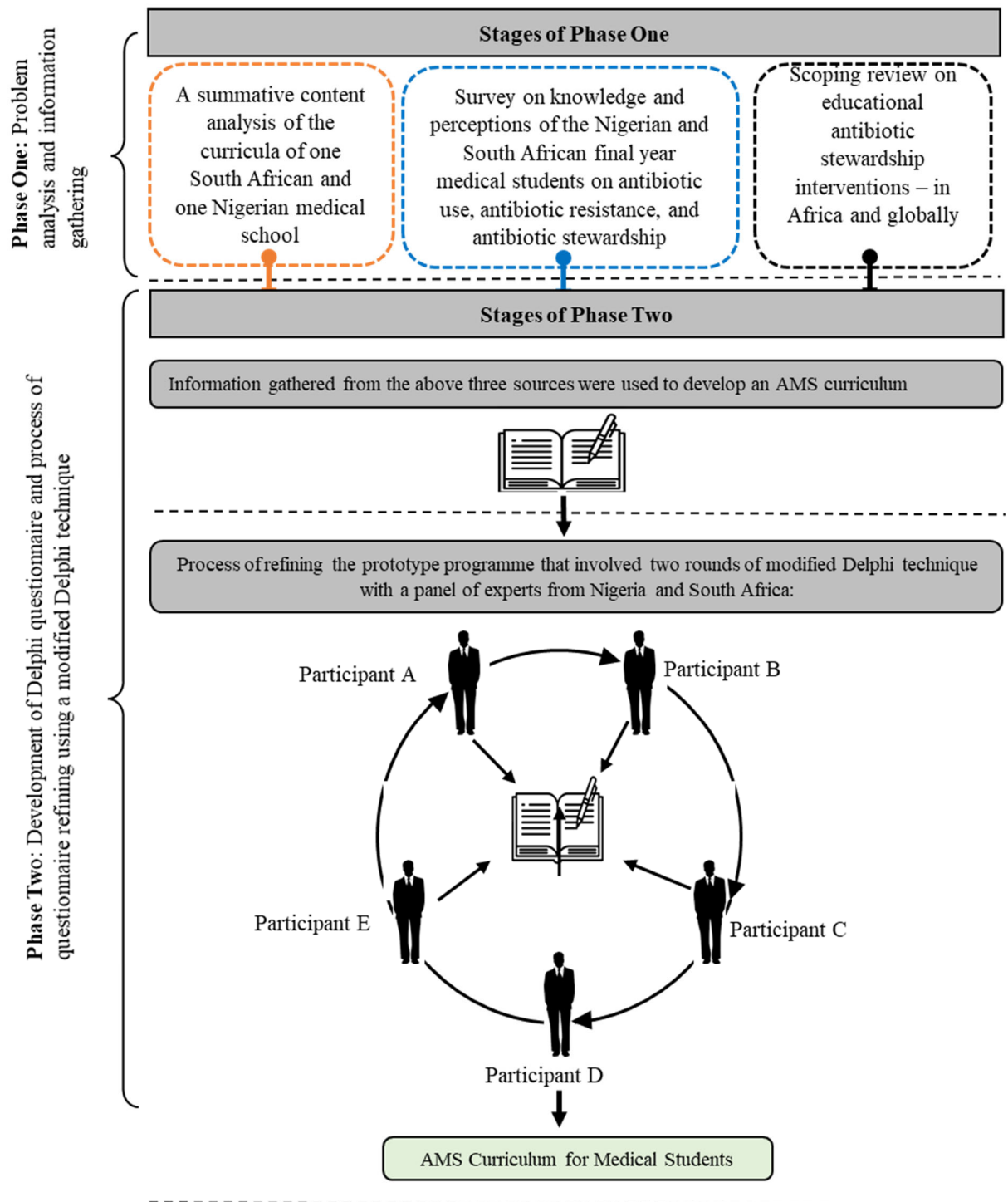


Figure 1.2: A conceptual framework.

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CHAPTER TWO

Antibiotic stewardship programme in medical schools

“Today, antibiotics are rarely prescribed based on a definitive diagnosis. Diagnostic tests can show whether or not an antibiotic is actually needed, and which one. Having rapid, low-cost, and readily available diagnostics is an essential part of the solution to this urgent problem.”

(O’Neil, 2016, p. 37) Dr Margaret Chan,
Former Director General of the World Health Organization

The first step of the study was to develop a protocol for a scoping review for the question: what types of antimicrobial stewardship educational programs are used in medical schools to teach medical students about rational antimicrobial prescribing. The paper was published in *JBIM Evidence Synthesis*. The pdf version of the published article is attached in Appendix A. In the second step, the scoping review was conducted using the methodologies as outlined in the protocol and published in *JBIM Evidence Synthesis*. The pdf version of the published article is attached in Appendix B. The two papers were published to achieve objective 1: To explore the current educational antibiotic stewardship interventions in Africa and globally.

2.1 Educational antimicrobial stewardship programs in medical schools: a scoping review protocol (Augie et al., 2020; Appendix A)

Augie, B. M., McInerney, P. A., van Zyl R. L., and Miot, J.

Abstract

Objective

The objective of this scoping review is to identify the available evidence on antimicrobial stewardship programs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used.

Introduction

Antibiotics are life-saving drugs and their discovery is one of the most important advances of the 20th century. They have transformed modern medicine by playing a critical role in the management of infectious diseases. However, the rapid development of resistance of pathogens to antibiotics is gradually affecting this initial success. Antimicrobial stewardship programs have been shown to reduce the burden of antimicrobial resistance in hospitals.

Inclusion criteria

This scoping review will consider papers conducted in medical school curricula to improve the prescribing of antimicrobial medication. Studies that include other health profession students, such as nursing, pharmacy, or dentistry students, will be excluded. Studies published in English from 1996 onwards will be included.

Methods

Databases to be searched are PubMed, Wiley Online library, CINAHL Complete, Web of Knowledge, Scopus and Education Resources Information Center. Unpublished studies and gray literature will be included. Searching will follow a three-step process and will be conducted by two reviewers. Data will be extracted by two independent reviewers. Any disagreements that arise between the reviewers during the study selection process or data extraction will be resolved through discussion, or with a third reviewer. Results will be presented in tabular or diagrammatic form, together with a narrative summary.

Keywords: Antimicrobial resistance; antimicrobial stewardship; education; medical students; teaching

Introduction

The discovery of penicillin by Alexander Fleming in 1928 has transformed modern medicine.¹ Antibiotics have saved millions of lives since their discovery,² and are currently among the most commonly prescribed medicines in our health facilities.³⁻⁵

It has been reported that 20% to 50% of antibiotic utilization is inappropriate.^{6,7} Inappropriate antimicrobial use is associated with poor patient outcomes such as **AMR**, adverse drug reactions, organ failure, superinfections (especially with *Clostridium difficile*) and increased mortality.⁸⁻¹⁰ It is also associated with increased costs, as a result of prolonged hospital stays and the cost of managing complications.⁸⁻¹⁰ Inappropriate use of antimicrobials has the potential to end the successes achieved by modern medicine.² With the increase in **AMR** has come a slowing in the discovery of new effective antimicrobials due to the dwindling antibiotic pipeline. This has made it difficult to discover new antibiotics that have novel mechanisms of action, thus leading to the emergence of the post-antibiotic era.¹¹ The clinical result of this increased resistance is an increase in the number of deaths from infections that were previously treatable.¹¹

A United Kingdom study reported that the annual global number of deaths due to antibiotic resistance is around 700,000 and predicted that if this situation is not addressed, by 2050 nearly 10 million people will die every year as a result of drug-resistant infections.^{12,13} This would cause the global economy to lose approximately 60 to 100 trillion US dollars.^{12,13} In 2017 the World Bank reported that, if left unchecked, antibiotic resistance would have a cascade effect, such that by 2050, more than 28 million additional people, mostly from developing countries, would be pushed into extreme poverty.¹⁴ The treatment of resistant infections can be prohibitively expensive for people in lower socio-economic sectors and they would be disproportionately affected by a failure to address this issue. Antimicrobial stewardship is an emerging field in medicine and has been described as “coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration”.^{15(p.323)} Antimicrobial stewardship also refers to how the responsible use of antimicrobials can enhance both their current effects and their future sustainability.¹⁶ Antimicrobial stewardship programs (ASPs) are described as one of the most important tools for preserving the value of antimicrobial agents and lowering their inappropriate use.^{17,18} An ASP has many strategies with different approaches that, when conducted properly,

will impact positively on clinical patient outcomes.¹⁹ Education is considered fundamental in any ASP.²⁰

It is a prerequisite for medical students to learn the principles of infection diagnosis and management, and they must understand the link between antibiotic usage and antibiotic resistance.^{20,21} Students are expected to learn to prescribe antibiotics responsibly when they commence their careers as house officers.²² The World Health Organization highlights the need for all healthcare professionals, including medical students, to be educated in the rational use of antimicrobials and stewardship, as a step to address AMR.^{23,24} A survey to assess the teaching of rational antimicrobial prescribing in the curricula of European medical schools has found wide variation among medical schools — even those within the same country — and found that teaching was mainly delivered using passive techniques.²⁵ In Nepal, the use of problem-based learning in small groups of medical students has recorded success in teaching prudent antimicrobial use in clinical pharmacology.²⁶

Medical school is perhaps the only avenue that some doctors have to learn prudent antibiotic prescribing. Apart from the teaching received in medical schools (and perhaps during preparation for internal board examinations), there is barely any requisite teaching after graduation on rational antibiotic prescribing.²⁷ An antimicrobial stewardship program will probably be more successful when initiated at the medical school level, which is when student knowledge and attitudes are being shaped.²¹ For example, surgeons are likely to have a higher acceptance rate of surgical prophylactic guidelines if courses on rational prescribing and antimicrobial stewardship are taught in their medical curriculum.²¹

Understanding the importance of ASP and ensuring their wide implementation is critical to achieving their success. Education in ASP should begin in medical schools to educate future prescribers on the importance of adhering to these programs. While it is acknowledged that medical curricula are often overloaded, the importance of ASP must be addressed by curriculum developers.²¹ In 2009, the General Medical Council in the United Kingdom emphasized the need to incorporate a course on prudent antibiotic prescribing into the medical curriculum.²⁸ Integration of educational programs on prudent antibiotic prescribing into medical school curriculum has been achieved to a certain level in some developed countries such as the United Kingdom^{21,29} and the United States of America.³⁰

A study that assessed the knowledge, attitudes and perceptions of final year medical students in South Africa about rational antibiotic prescribing showed that graduating doctors are not adequately prepared to prescribe antibiotics.³¹ The findings of this study are similar to those of a multicenter study conducted on fourth-year medical students in the United States of America.³² This suggests a deficiency in the curriculum and a need for ASPs to be included in the curriculum to address such deficiencies. Several studies across the globe have revealed that medical students perceive **AMR** as a problem in their professional career and want additional teaching on prudent antimicrobial use.³²⁻³⁵ Several studies show that a wide knowledge gap in rational antibiotic prescribing exists among medical students.³³⁻⁴¹

A search of the literature did not reveal any published studies on educational ASPs in the curricula for medical students in Africa. So, although evidence suggests that students and newly qualified doctors lack the skills and confidence to engage in ASPs, in Africa no such programs appear to exist in the medical school environment. This scoping review serves to determine what programs have been developed and implemented on **AMS**, in order to develop an appropriate educational program that is relevant for teaching medical students in South Africa and Nigeria.

A preliminary search of the *JBIR Database of Systematic Reviews and Implementation Reports*, as well as PubMed, CINAHL, PROSPERO and ERIC databases did not identify any scoping reviews dealing with this topic. A search in Scopus revealed a 2017 published mapping review by Canadian researchers that looked at **AMS** training in medical education.⁴² However, the review only examined the published studies indexed in Ovid MEDLINE and Ovid Embase databases that addressed ASP education for both undergraduate and postgraduate students. This review will focus on studies conducted on medical students in published, unpublished and gray literature. The objective of this scoping review is to identify and synthesize the available evidence on ASPs for teaching medical students about rational antimicrobial use, as well as the content taught and the method of instruction used.

Review question

What types of educational antimicrobial stewardship programs are used in medical school settings to teach medical students about rational antimicrobial prescribing?

Inclusion criteria

Participants

The review will consider studies that include medical students only. For the purpose of this review, a medical student is defined as a student studying for a bachelor degree in medicine. The name of this degree varies between countries, with the more common names being MBBS, MBChB and MBBCh. All these abbreviations refer to a bachelor of medicine and a bachelor of surgery. The review will exclude studies that involve other health profession students.

Concept

The concept of interest in this scoping review is antimicrobial stewardship programs — what is being taught, and how and when it is taught. This will include the content of the program, activities involved during the program, purpose of the activities, duration of the program and time allocated, those delivering the program, evaluation methods, curriculum design and impact of the program. It will also consider the methods of teaching, including online or face-to-face programs.

Context

This review will consider studies that are conducted in medical school settings. It will consider medical school programs that lead to the registration of the student as a beginning medical practitioner.

Types of sources

This scoping review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before-and-after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion. Qualitative studies that examine qualitative data will also be considered. In addition, systematic reviews that meet the inclusion criteria will also be considered. Text and opinion papers will also be considered for inclusion in this scoping review. Only studies published in English will be included because of the cost and time involved in translating non-English studies. The review will include studies published from 1996

onwards; 1996 was chosen as the starting date because it was the year in which the term “antimicrobial stewardship” was first introduced.⁴³

Methods

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews consisting of the following methods: develop review question(s) and review objective(s); determine the eligibility criteria; develop the literature search strategy; extract, analyze, and discuss the findings; and draw conclusions and discuss the implications for practice and further research.⁴⁴

Search strategy

The review will follow a JBI three-phase search strategy approach with an aim to locate both published and unpublished papers. An initial limited search was conducted in PubMed to identify relevant articles on this topic. The text words in the title and abstracts used in the retrieved articles as well as the index terms used to describe the articles were used to develop a full search strategy (Appendix I). The reference lists of all studies selected for inclusion will be screened for additional studies.

Information sources

The databases to be searched include PubMed, Wiley Online library, CINAHL Complete, Web of Knowledge, Education Resources Information Center and *JBI Database of Systematic Reviews and Implementation Reports*. The search for unpublished studies and gray literature will include Scopus and the ProQuest Dissertations and Theses Global database.

Study selection

Following the search, all identified records will be collated and uploaded into EndNote V8.2 (Clarivate Analytics, PA, USA), and duplicates will be removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). The full text of selected citations will be assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection

process will be resolved through discussion, or with a third reviewer. The results of the search will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for scoping reviews.⁴⁵

Data extraction

Data will be extracted from papers included in the scoping review by two independent reviewers using a data extraction tool developed by the reviewers. The data extracted will include specific details about the population, concept, context, study methods, types of educational AMS programs and key findings relevant to the review question. Authors of papers will be contacted to request missing or additional data, where required. A draft data extraction tool (charting table) is provided in Appendix II. This tool will be modified and revised as necessary during the process of extracting data from each included paper. Modifications will be detailed in the full scoping review. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer.

Data presentation

Extracted data will be presented in diagrammatic or tabular form in a manner that aligns with the objective of this scoping review. The charting table will report on: distribution of papers by year of publication, country of origin, study design, research methods and the key findings/outcomes. A narrative summary will accompany the tabulated and/or charted results and will describe how the results relate to the review's objective and question.

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Appendix Ia: Search strategy.

PubMed

Search conducted on 25 October 2019

Search #	Query	Records retrieved
1	"anti-infective agents"[MeSH] OR "antimicrobial stewardship*"[MeSH] OR "drug resistance"[MeSH] OR "antibiotic resistance"[Title/Abstract] OR "antimicrobial resistance"[Title/Abstract] OR antibiotic*[Title/Abstract] OR program*[Title/Abstract] OR "antimicrobial stewardship program"[Title/Abstract]	1842484
2	medical school [MeSH] OR medical schools [MeSH]	24811
3	medical student [MeSH] OR medical students [MeSH]	31497
4	education [MeSH] OR educational [Title/Abstract]	890670
5	1# AND 2# AND 3# AND 4#	847
6	Limit 5 to date range 1996 to onward and English language	718

Appendix IIa: Data extraction instrument.

Study details and characteristics	
Study number	
Authors	
Date/year of publication	
Study design	
Setting	
Population and sample size	
Methodology/methods	
Details/results extracted from study	
Duration of the program	
Outcomes and measures	
Quantitative results	
Qualitative results	
Curriculum design*	
Impact of the program [†]	
Evaluation methods (including timing of evaluation)	
Other findings relevant to review questions	

*The scientific method adopted to train students on rational antibiotic prescribing (for example, problem-based learning curriculum).

[†]Identifies whether or not a measure of knowledge has been used in the study, and the measure used (for example, pre- and post-training assessments).

2.2 Educational antimicrobial stewardship programs in medical schools: a scoping review (Augie et al., 2021; Appendix B)

Augie, B. M., Miot, J., van Zyl R. L., and McInerney, P. A.

Abstract

Objective: The objective of this scoping review was to identify the available evidence on antimicrobial stewardship programs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used.

Introduction: Antibiotics are a precious resource whose discovery have saved millions of lives. They are used extensively in surgical procedures, cancer chemotherapy, and in the treatment of infectious diseases. However, the development of antimicrobial resistance and the slow rate of discovery of new agents with novel mechanisms of actions represent a huge threat to modern medicine.

Inclusion criteria: This scoping review considered papers that described medical school curricula that focused on the teaching and learning of the prescription of antimicrobial medication. Studies that described this concept in the curricula of other health profession students, such as nursing, pharmacy, or dentistry students, were excluded. Only studies published in English from 1996 onwards were included.

Methods: Eight databases were searched for both published and unpublished literature and grey literature. The JBI three-step process was followed and conducted by two reviewers. The scoping review followed an a priori published protocol. Full texts of selected citations were assessed against the inclusion criteria by two independent reviewers. Data were independently extracted by two reviewers. Disagreements were resolved through discussion, and the need for a third reviewer was not required. Data extraction was undertaken using a modified charting table developed for the review objectives. The findings are presented using the narrative synthesis.

Results: Thirteen studies were included in the review, with most of the papers originating from the United States of America and Europe; with one from developing countries. Didactic lectures and web-based distance learning were the most common modes of instruction used in the included papers. Six of the included papers presented the outcomes of their interventions; where

different methods of assessment were used to evaluate students that included baseline and post-instruction assessment or a series of short exams. Some of the concepts included in the teaching material included the use of antimicrobial agents, the prevention of antimicrobial resistance, antimicrobial stewardship, and infection prevention control. The programs (ranging from 75 minutes to 100 hours) were implemented from second to fourth year of study.

Conclusions: A wide range of interventions were used to teach the principles of antimicrobial stewardship to medical students. There is a need to further evaluate these programs through follow-up of students after graduation to determine whether the skills learned are retained.

Keywords: antimicrobial resistance; antimicrobial stewardship; education; medical students; teaching

Introduction

The World Health Organization has identified **AMR** as one of the five major threats to public health¹ and it has emphasized the importance of including appropriate antibiotic prescribing in medical curricula.² Inappropriate antibiotic prescribing is associated with the development of multi-drug-resistant pathogens, adverse events, and increased cost to patients.³ Antimicrobial stewardship programs (ASPs) promote appropriate antimicrobial use and help to achieve good clinical outcomes, minimize adverse events, and reduce selective pressure that encourages the development of resistance.^{4,5} Antimicrobial stewardship programs also reduce the chance of developing *Clostridioides difficile* infection across all settings and in patients of all ages.^{5,6} A 2016 guideline for implementing ASPs recommended medical schools integrate the principles of antimicrobial stewardship into their pre-clinical and clinical curricula.⁵ Education is regarded as a vital tool in changing prescribing behavior and influencing prescribers to accept ASPs.⁷ Antimicrobial stewardship education aims to reduce inappropriate antimicrobial use, such that antimicrobials are only used when indicated, using the appropriate route of delivery, correct dose, and duration of therapy for each infection.⁸

Most of the educational ASPs target postgraduate students and practicing physicians. The same cannot be said about medical students in their undergraduate studies.⁸⁻¹⁰ Little attention is given to teaching medical students appropriate antimicrobial use.¹¹ Conversely, changing the behavior of licensed doctors has proven difficult.⁹ A survey conducted to examine the pre-clinical microbiology curricula in the United States of America (USA) medical schools found that only

65% of schools were including AMS in their courses.¹² A greater percent(74% to 95%) of surveyed medical students across the globe indicated their desire for more education on responsible antimicrobial use.¹³⁻¹⁶ The pedagogical plan in most of the Brazilian medical schools does not address the problem of AMR or AMS to optimize responsible antimicrobial use.⁴ While medical schools in the USA and United Kingdom (UK) are making an effort to develop and incorporate ASP into their medical curricula,^{11,17-21} the same cannot be said of African medical schools, where a literature search did not reveal any ASPs implemented in African medical schools.

Prudent antimicrobial use is an important topic for discussion in medical schools among aspiring doctors who are expected to fulfil their role as advocates on graduation and who should be able to explain to their patients and their patients' relatives the consequences of inappropriate antimicrobial use. Teaching principles of antibiotic prescribing in medical schools can provide a context to deal with issues of health promotion at both the individual and community level. The teaching of prudent antibiotic use in medical schools could be achieved through outcome-based education, which provides unambiguous statements of learning intent, flexibility of delivery, and allows medical schools to develop ways by which the desired outcomes are achieved without having to adhere to a set of standard teaching methods.²⁰ Davenport *et al.*²⁰ developed a set of learning outcomes for medical schools to teach prudent antibiotic prescribing to medical students to help reduce AMR and improve their optimal use.

The objective of this review was to identify and synthesize the available evidence on ASPs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used. The concept of interest in this review included information related to the content of the program, activities involved during the program, method of teaching, year of study, purpose of the activities, ASP training duration, ASP outcomes, student evaluations, and the methods of teaching.

Review question

What types of antimicrobial stewardship educational programs are used in medical schools to teach medical students about rational antimicrobial prescribing?

Inclusion criteria

Participants

The review considered studies that only included medical students, irrespective of their year of study. For the purpose of this review, a medical student is defined as a student studying for a bachelor's degree in medicine. The name of this degree varies between countries, with the more common names being MBBS, MBChB, and MBBCh. All these abbreviations refer to a bachelor of medicine and a bachelor of surgery. The review excluded studies that involved other health profession students.

Concept

The concept of interest in this scoping review was ASPs: what, how, and when it was taught. This included the content of the program, activities involved during the program, method of teaching, year of study, purpose of the activities, ASP training duration, ASP outcomes, and student evaluations. It also considered the methods of teaching, including online or face-to-face programs.

Context

This review considered studies that were conducted in medical school settings. As stated in the protocol,²² all study designs and types of manuscripts were considered for inclusion in the review. It considered medical school programs that led to the registration of the student as a beginning medical practitioner.

Types of studies

The following study designs were included in the review: before-and-after design; case report; quasi-experimental design; prospective cohort study; a mapping review; and descriptive studies, including board game and web-based designs. Surveys, such as those that used cross-sectional study designs to assess students' knowledge, attitudes, and perceptions but not program development, were excluded as they did not meet the inclusion criteria. Only studies published in English were included because of the cost and time involved in translating non-English studies.

Methods

This review was conducted using JBI methodology for scoping reviews.²³ The objectives, inclusion criteria, and data extraction methods for this review were specified in an a priori protocol.²² There were minor deviations from the protocol. The original data extraction tool included in the protocol had to be modified after reviewing two or three papers, as some of the information included in the tool, such as curriculum design and qualitative data, were not reported in the papers.²³ Some of the modifications made included “outcomes and measures” being changed to “ASP outcome” and “evaluation methods” to “student evaluations.” These modifications did not affect the objective, review question, or results of the review.

Search strategy

The JBI three-phase search strategy approach that aimed to locate both published and unpublished papers was followed. An initial limited search of PubMed was conducted to locate articles on this topic, followed by an analysis of the text words contained in the titles, abstracts, and index terms. This led to the development of a search strategy for each database. The emphasis was on ASPs for teaching appropriate antimicrobial prescribing in medical schools using any study design, with none being excluded. The reference lists of all included papers were screened for additional studies. Only papers published in English from 1996 to November 2019, when the search was conducted, were included. The lower limit of 1996 was selected as the starting date because it was the year in which the term “antimicrobial stewardship” was first coined.²⁴

The databases searched include PubMed via OVID, Scopus via Elsevier Science, Web of Science (previously known as Web of Knowledge) via Clarivate Analytics, and *JBI Database of Systematic Reviews and Implementation Reports* via Ovid. Others were searched via EBSCOhost and they include: CINAHL Complete, Wiley Online Library, and ERIC. The search for unpublished studies and gray literature included ProQuest Dissertations and Theses Global database via ProQuest. The search was carried out with the support of a librarian and the search results were uploaded into JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). The full search strategies of the above-listed databases are shown in Appendix I. The search was conducted in November 2019 and the review was submitted to JBI for peer review in July 2020.

Study selection

After searching, all identified records were collated and uploaded into EndNote v.X8.2 (Clarivate Analytics, PA, USA), and duplicates were removed. Titles and abstracts of the identified studies were scrutinized in relation to the review question and objective by two independent reviewers (BMA and PMI). The reviewers met and compared their findings. Disagreements were resolved through discussion and thus a third reviewer was not utilized. Once the list of studies for potential inclusion was developed, the full-text papers were retrieved and read by both reviewers. The full texts that were found to be irrelevant were excluded (Appendix II). A final decision was then made on whether to include or exclude the retrieved papers.

Data extraction

Data extraction was conducted by two independent reviewers (BMA and PMI). Any disagreement that emerged during the data extraction process between the reviewers was settled through discussion and the need of the third reviewer was not necessary. The data extracted included specific details about the population, concept, context, study methods, types of educational ASPs, and key findings relevant to the review question and objective. The concept of interest in this review included information related to the content of the program, activities involved during the program, method of teaching, year of study, purpose of the activities, ASP training duration, ASP outcomes, student evaluations, and the methods of teaching.

Data analysis and presentation

The search process and article selection procedures are presented in a flowchart adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Figure 1).²⁵ Extracted data from the papers that met the selection criteria are presented in Appendix III. The charting table shows the country, authors, year of publication, study details and characteristics, study design, setting, population sample size, methods, ASP training duration, mode of delivery, ASP outcomes, and student evaluations.

Results

Study inclusion

The results of the screening undertaken in the course of this scoping review are presented in Figure 1. A total of 4361 papers were found during the database search (PubMed = 710, CINAHL Complete = 453, ERIC = 352, Scopus = 1793, Web of Science = 801, Wiley Online

Library = 140, JBI SRIR = 29 and ProQuest Dissertations and Theses Global = 83). A total of 1001 duplicates were removed, leaving 3360. An additional 3315 were classified as irrelevant after examining the title and abstract. This left 45 articles, of which 33 did not meet the inclusion criteria and were therefore excluded. Twelve papers were included in the review. A hand search of the reference lists of the 12 included studies was conducted and one additional study was found eligible for inclusion. The 33 papers that were excluded and the reasons for their exclusion are presented in Appendix II. In conclusion, the screening stage resulted in 13 eligible studies for data extraction (Figure 1).

Characteristics of included studies

The characteristics of the included studies are presented in Appendix III. The USA had the highest number of studies with five (38.4%),^{1,17-19,21} followed by the UK with three (23.1%),^{20,26,27} Brazil had two (15.4%),^{4,28} while Canada,²⁹ Europe,¹⁰ and Nepal³⁰ had one paper each. No papers were found from African medical schools (Figure 2). Six of the papers were published between 2016 and 2019.^{4,17-19,21,29} The papers used different study designs. Two studies used a before-and-after design: one with a quasi-experimental design,¹⁹ while the other did not use a control group.⁴ A case report was used in one study,¹⁷ while another one employed a prospective cohort study.¹⁸ Seven papers used a descriptive study design,^{1,10,20,21,26,28,30} of which two papers focused on web-based designs^{10,26} and one described a board game.²⁸ One paper used a cross-sectional design to conduct a postal survey,²⁷ while another one used a mapping review.²⁹ Ten of the papers referred to medical students only,^{1,4,10,17,19-21,26,27,30} two of the papers combined medical and pharmacy students,^{18,28} and the last combined medical students, residents and practicing physicians²⁹ (see Appendix III). The data for each group was reported separately making it possible to extract the medical student data.

Review findings

Elements of ASPs in medical schools are found in the 13 included studies. The summary of key findings is presented with headings including; year of study in which the program was implemented, number of students involved, methods of instruction, ASP training duration, ASP outcomes, and student evaluations (Appendix III).

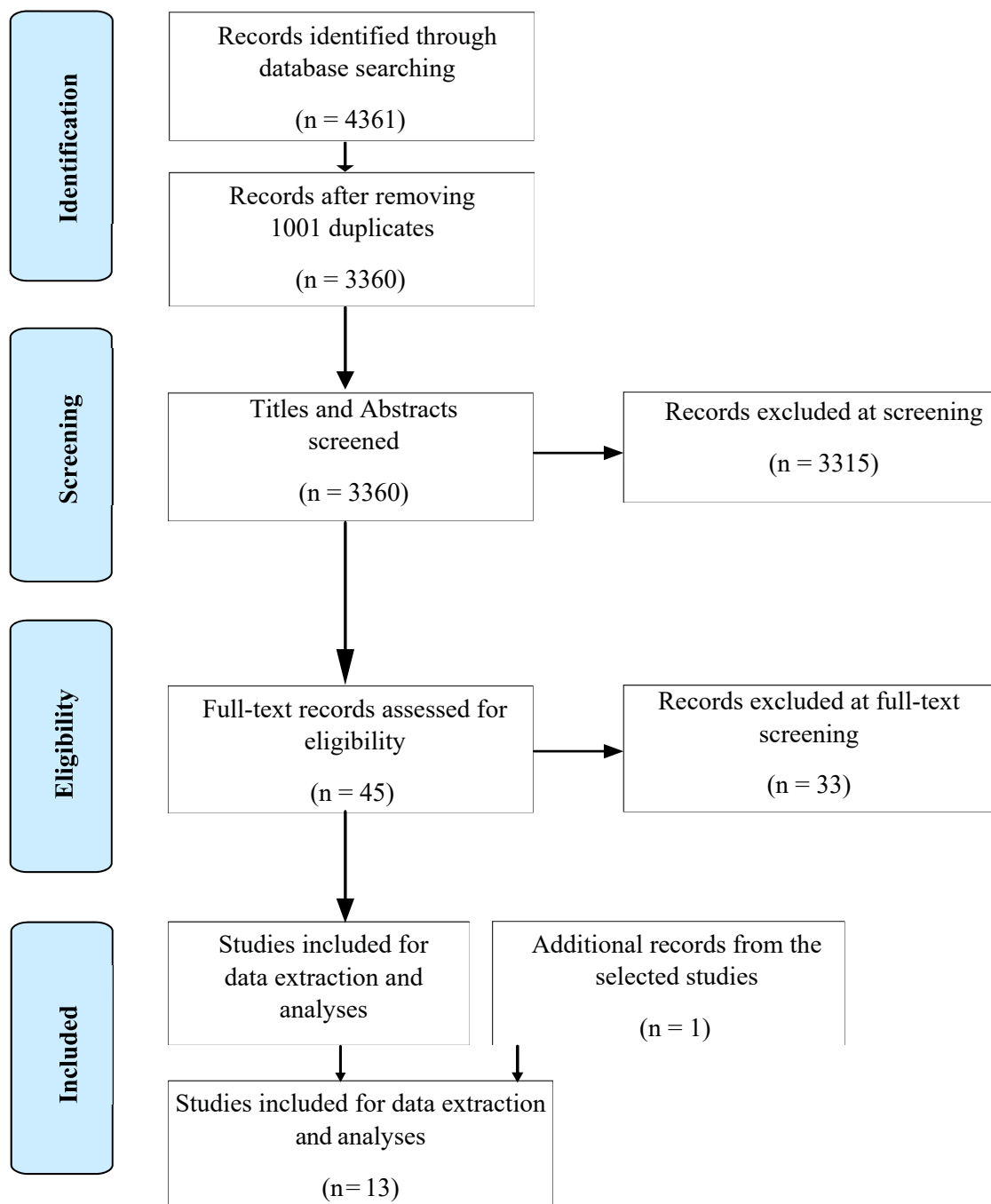


Figure 1: PRISMA flow diagram of study selection and inclusion process (25).

At the Albert Einstein College of Medicine, 183 students took part in an antibiotic stewardship seminar annually from 2014 to 2016, and the same number of students also participated in an infection prevention and patient safety seminar from 2015 to 2016.¹⁹ The University of California, San Francisco Medical School engaged a total of 822 students over three years, of which 470 were medical students and 352 were pharmacy students.¹⁸ In the board game study, 42 medical students, and 36 pharmacy students participated in the program.²⁸

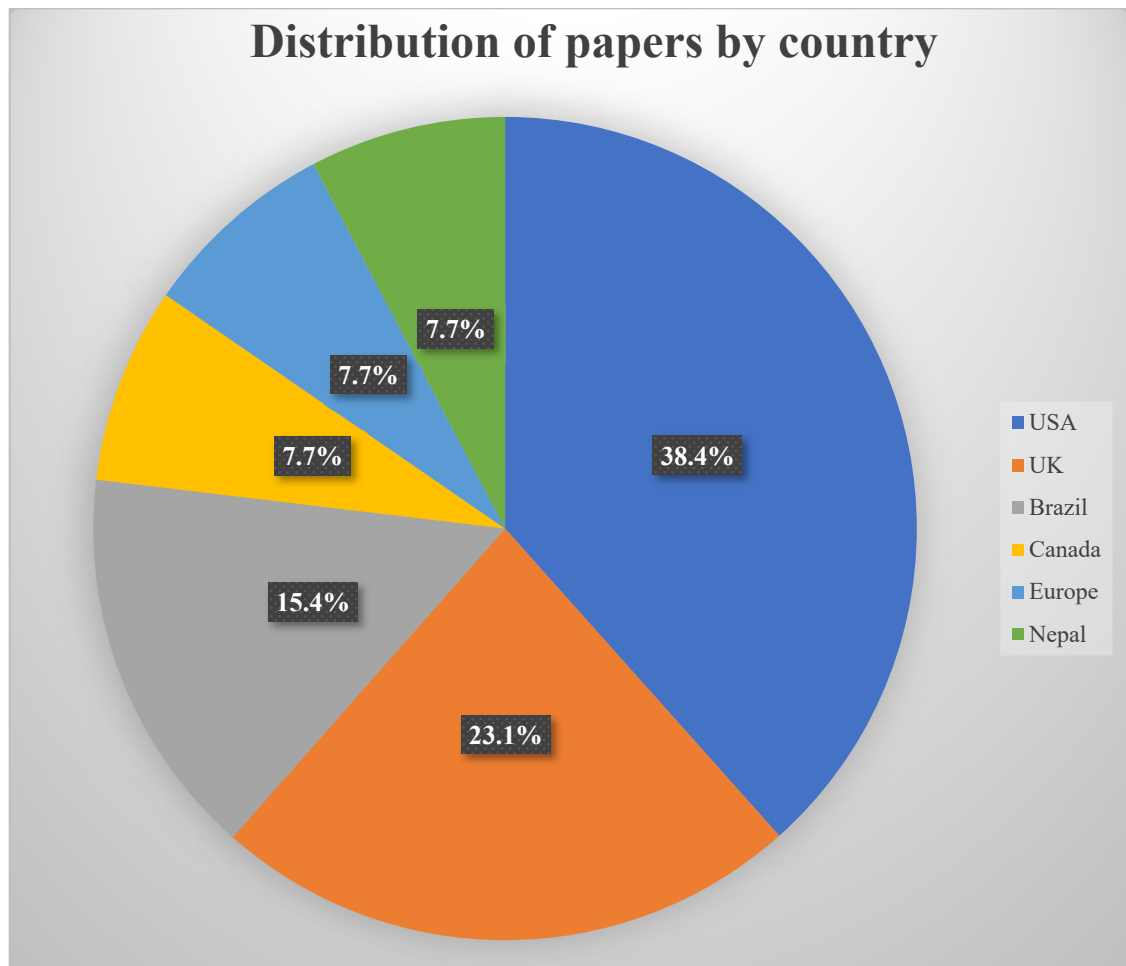


Figure 2: Distribution of papers by country (n = 13).

Number of students involved

Five of the included papers indicated the number of students that participated in the program.^{4,17-19,28} Hsu¹⁷ reports that approximately 150 students were engaged over three years, while at the Brazilian Medical School, 606 medical students completed the **AMS** course over six years.⁴

Year of study in which the program was implemented

Seven of the included papers indicated the year of study in which the program was implemented.^{4,10,17,18,21,26,30} Most of these studies implemented their program in either the second or third year of study.^{10,17,18,30} Shekarchian *et al.*²¹ made use of a spiral curriculum in which the program was taught from the second to the fourth year of study. In one of the papers, the program is implemented in the fourth year of the study.²⁶ The Wake Forest study does not

specify the year of study, but the AMS curriculum is divided into pre-clinical and clinical segments.¹

Methods of instruction

Eleven of the papers stated the mode of instruction used to teach the principles of antimicrobial use.^{1,4,10,17,19,21,24,26,27,29,30} Four studies used a blended approach with didactic lectures and another form of instruction.^{17,21,27,30} Two papers used online/web-based distance-learning programs.^{4,18} One of the papers used a small-group workshop in addition to an online learning program.¹⁸ Paterson Davenport *et al.*²⁰ developed outcomes for a supportive learning resource that could be used in different learning situations, such as self-learning, self-assessment, peer review, small-group discussion, or formal assessment. Silverberg *et al.*²⁹ authored a mapping review that reported different modes of deliveries, which included, amongst others, didactic teaching, web-based teaching, clinical case discussions, workshops/seminars, board games, and guideline promotion.²⁹ This was the only mapping review in AMS in medical education found. It looked at only published literature in two databases on both undergraduate and postgraduate medical education.²⁹ In the Wake Forest program, pre-clinical lectures with facilitator notes and audio recordings were the main modes of instruction, and in the clinical segment, small-group activities with facilitator guides were used.¹

ASP training duration

Seven of the papers stated the amount of time allocated to the program.^{4,17,19,21,27,28,30} One study allocated 75 minutes during a single didactic teaching module in the third-year internal medicine course.¹⁷ A Brazilian study dedicated 100 hours of activities to a web-based distance-learning course.⁴ In another program, two hours were dedicated in the second year and an hour-long interactive, case-based didactic session in the third year; while in the fourth year, two sessions were delivered: one two-hour block at the start of the year and a second 1.5-hour session a week before they graduated.²¹ A USA study provided a two-hour seminar on AMS with an additional two-hour seminar on infection prevention and control to second-year medical students.¹⁹ A Nepal study provided two hours of didactic lectures in the first year of the course and an additional two-hour practical session.³⁰ In the Brazilian program in which a board game was used, one hour and 30 minutes were allocated.²⁸

ASP outcomes

Six of the papers presented the ASP outcomes.^{4,17-19,21,28} The Brazilian paper included more comprehensive coverage on what students thought they had learned about the topic.⁴ Shekarchian *et al.*²¹ reported on student's perceptions on how prepared they felt to initiate empiric antibiotics and when and how to narrow the spectrum of coverage. Students also reported on their satisfaction with the education received on antibiotic stewardship during medical school.²¹ Prescriber confidence, understanding of transmission-based precautions, and related personal protective equipment was assessed in Nori *et al.*¹⁹ MacDougall *et al.*¹⁸ reported on the impact of an interprofessional curriculum between medical and pharmacy students on AMS, on knowledge, attitudes, and interprofessional collaboration. The Brazilian study by Valente *et al.* in which the board game was used reported on whether the students felt the game helped them to understand the subject, and whether it was an important way of enhancing learning.²⁸ Antimicrobial stewardship program outcomes were measured differently across the manuscripts; four of the papers evaluated students' knowledge,^{4,18,19,26} two focused on student satisfaction with the program,^{21,28} one paper conducted a one-minute evaluation of a single didactic teaching module,¹⁷ while six of the papers either did not evaluate their programs or do not report the findings of their evaluations.^{1,10,20,27,29,30}

Student evaluations

Seven of the included studies evaluated whether the intervention influenced students' prescribing behavior,^{4,10,17-19,26,28} of which four of the papers used a before-and-after assessment.^{4,18,19,28} MacDougall *et al.*¹⁸ assessed students' knowledge of AMS using a small number of survey questions before and after implementation of the antimicrobial stewardship curriculum. From this, a more robust assessment tool was planned for use in the future implementation of the curriculum.¹⁸ Another study by Nori *et al.* measured student proficiency in personal protective equipment use in a post-test evaluation, it also measured the number of correct answers in relation to knowledge of hospital-acquired infection.¹⁹ Marwick *et al.*²⁶ used student feedback to evaluate the program and also reported being in the process of evaluating student knowledge through a series of short exams at the beginning and end of each clinical attachment and at the end of the year; however, nothing has been subsequently published.

Discussion

In this scoping review, we examined ASP that targeted medical students. The search was limited to programs from January 1996 onward because the term “antimicrobial stewardship” was coined in 1996.²⁴ Most studies were published in renowned medical journals.

We found a wide range of instructional design methods used to teach medical students the concept of antibiotic prescribing. Most of the interventions in the included papers used the lecture method as the mode of instruction. Lectures are teacher-centered and a passive way of transmitting information to a large group of students.³¹ Of note, none of the programs included a follow-up with the students after their graduation to evaluate the value of the skills learned, or whether they had retained the knowledge. The need to evaluate interventions implemented is something that teachers should be encouraged to undertake as part of the curriculum design process. A university in the USA, in collaboration with the Center for Disease Control and Prevention and the Association of American Medical Colleges, has developed an **AMS** curriculum for pre-clinical and clinical medical students.^{1,11} The curriculum aims to increase understanding of **AMR**, prevention, and control among medical students and is structured to address the microbiological and pharmacological components of antimicrobial use in both outpatient and inpatient settings.¹ The curriculum is intended for use among medical schools in the USA.^{1,11} The pre-clinical segment comprised of lectures with facilitator notes and audio recordings, and nine corresponding exam questions in the United States Medical Licensing Examination format, while the clinical curriculum contained five small-group activities with facilitator guides.¹

Had the papers selected in this review been subjected to critical appraisal, many would have been excluded due to poor methodological quality. There are more quasi-experimental studies or cross-over studies in education and we did not expect to find any studies that utilized a randomized controlled trial (RCT) design. Turner *et al.*³² state that while RCTs are valuable from an evidence-based perspective, they may pose ethical challenges in education in that some students may be denied an opportunity to receive an intervention. Further, they are not always the best method to test a hypothesis in medical education.³³ It is also difficult to directly attribute any success or otherwise to either randomization or non-randomization, especially when there are other confounders.³⁴ According to Norman and Schmidt,³⁵ “Trials of curriculum level interventions, whether they show large, small, zero, or negative effect sizes, whether they are

or are not randomized, whether they are done on large or small samples, whether they are of sound or unsound methodology, are, in our view, a waste of time and resources.”(p.725)

Geographically, most of the included studies were conducted in the USA and Europe, with one conducted in developing countries. Our review did not find any study conducted in Africa and only one was found in Asia.³⁰ There is evidence that medical students are not adequately prepared by their medical schools to engage in appropriate antimicrobial prescribing,³⁶ and this includes South African medical schools that lag behind in including AMS in the curricula for medical students.³⁷ Medical doctors do not normally evaluate the course design and outcomes – as such students may be receiving AMS training but in small courses that are not synchronized or managed throughout their curriculum. But the question of how well this has been done or to what extent has not really been quantified or evaluated. According to South African authors Brink *et al.*³⁷ “A key strategy in facilitating appropriate antibiotic prescribing is the early introduction of the relevant knowledge, concepts and skills into undergraduate curricula.” (p.358)

Educational games are tools that encourage active learning, problem-solving skills, and small-group discussions.³⁸ They are a form of problem-based learning as they provide students with an initial list of problems and expect them to gather information and work on their own to solve the problems.³⁹ Educational games are not a replacement for conventional ways of learning theoretical knowledge, but are complementary learning tools that encourage skills acquisition.⁴⁰ Board games are student centered, which allow them to apply their critical skills.⁴¹ A study in which the game-based technique was used to teach third-year medical students’ breast-related problems reported an improvement in post-game test scores compared to pre-game scores.³⁹ It is documented in the literature that students who have been exposed to problem-based learning and task-based learning curricula are more skilled in terms of interpersonal skills and better prepared for self-directed and life-long learning.^{42,43} Small groups afford learners with an opportunity to freely express their concerns and explore their reactions.⁴⁴ Iranian researchers compared the effectiveness of small-group discussion techniques and traditional lecture-based teaching to teach embryology to medical students. They found that those students in small discussion groups scored higher marks in the mid-term and final exams compared to those in the lecture-based group.⁴⁵

Shekarchian *et al.*²¹ reported that students expressed a high level of satisfaction with the intervention, despite the short period of time allocated to the intervention. Further to this, the intervention utilized a spiral curriculum over three years using different teaching techniques, such as a case-based small-group activity, a case-based didactic session, and an online module. This may be compared with Laks *et al.*⁴ where the level of student satisfaction was low despite a longer period of time allocated to an intervention that utilized only a web-based, distance-learning technique.

Antimicrobial stewardship programs have been shown to improve the appropriate use of antimicrobial agents and have the potential to delay the emergence of the fast-approaching post-antibiotic era.⁴⁶ Antimicrobial stewardship is likely to be successful if started in medical schools when behavior is being shaped.¹⁰ It may be more rewarding to incorporate the AMS principles into the curricula of medical students than waiting till they graduate. Surgeons who were taught the principles of AMS in medical schools are likely to accept antimicrobial prophylactic guidelines in practice.¹⁰

After they graduate and register with the relevant regulatory councils, doctors are expected to start prescribing antimicrobials, hence the need for medical schools to develop AMS curricula to prepare them for appropriate antimicrobial prescribing.¹⁰ In this light, the authors, with the help of a panel of experts, are currently working on another project aimed at developing an antibiotic stewardship curriculum for teaching South African and Nigerian medical students appropriate antibiotic prescribing. An AMS curriculum should provide adequate knowledge, attitudes, and skills to help shape the behavior of aspiring doctors on the basic principles of AMS.¹⁰

Limitations of the review

One of the limitations of this review is that only papers published in the English language were included. Although we searched several databases, unpublished, and gray literature, there is still a possibility that some potentially useful papers published in other languages were excluded. Our review only included studies conducted on medical students, and therefore AMS studies involving other health professional students were excluded. Antimicrobial stewardship is a multidisciplinary program where other health professionals play a critical role. Including students from other professions may have provided us with information about other innovative methods of teaching antimicrobial use. Other limitations are associated with the types of study

designs used in different studies. For instance, although quasi-experimental, before-and-after study design is commonly used in educational programs due to some of the potential problems associated with RCTs in education,^{32,33} it has several limitations, especially when used in small sample sizes. These include threats to internal validity, lack of generalizability of the findings, and robustness of conclusions on the effectiveness of an educational intervention.⁴⁷ Although a wide range of instructional design methods were used in the included studies, none of the studies followed up with the students after graduation to determine retention of knowledge and skills learned.

Conclusions

This scoping review aimed to answer the question: what types of AMS educational programs are used in medical schools to teach medical students about rational antimicrobial prescribing? Our review found that a wide range of AMS interventions are used to teach medical students prudent antimicrobial prescribing in several medical schools across the globe. They included didactic lectures, web-based distance-learning, small-group discussions, and case-based modules. The time allocated to teach principles of AMS differed, ranging from 75 minutes to 100 hours. Antimicrobial stewardship teaching should be managed throughout the medical curriculum. Disciplines such as pharmacology, microbiology, infectious diseases, medical education, and other related disciplines should work synergistically with the relevant stakeholders in medical schools to ensure that the aim of the intervention is achieved.

Recommendation for future research

Although the results from the included studies provided us with useful evidence on teaching prudent antibiotic prescribing, none of these studies followed up with the learners to find out if the knowledge and skills learned are retained after graduation. Further research is required to answer this question – would medical graduates remember the knowledge and skills they learned on responsible antibiotic prescribing after graduation? This can be achieved by using prospective cohort studies where an antibiotic stewardship curriculum that is student-centered is delivered to students. Medical students should be introduced to the principles of prudent antibiotic prescribing in their early years of study and they should continually be reinforced throughout the remaining years of study in a spiral curriculum format. In such interventions, topics such as antibiotic-resistant pathogens, chain of infection, and mechanisms by which antibiotics kill bacteria could be taught in the pre-clinical years through didactic lectures or

problem-based learning. While topics such as the recognition and treatment of sepsis, and antibiotic therapeutic level monitoring could be taught in small-group sessions in the clinical years at a time when students acquire bedside clinical skills, a robust assessment method should be used to evaluate students' AMS knowledge before-and-after program implementation. Students should be followed up during their internship to evaluate the knowledge and skills learned.

Acknowledgments

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Conflicts of interest

The authors declare no conflict of interest.

References

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Appendix Ib: Search strategy.

PubMed

Date searched: 12/11/2019

Set #	Search query	Results retrieved
1	("anti-infective agents"[MeSH] OR "antimicrobial stewardship"[MeSH] OR "drug resistance"[MeSH] OR "antibiotic resistance"[Title/Abstract] OR "antimicrobial resistance"[Title/Abstract] OR antibiotic*[Title/Abstract] OR program*[Title/Abstract] OR "antimicrobial stewardship program"[Title/Abstract])	1,865,631
2	(medical school [MeSH] OR medical schools [MeSH])	25,065
3	(medical student [MeSH] OR medical students [MeSH])	32,102
4	(education [MeSH] OR educational [Title/Abstract])	900,361
5	1# AND 2# AND 3# AND 4#	867
6	Limit 5 to date range 1996 to onward and English language	710

CINAHL Complete (EBSCO)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	AB ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	292,894
2	AB (medical school OR medical schools)	7692
3	AB (medical student OR medical students)	11,044
4	AB (education OR educational)	223,779
5	1# AND 2# AND 3# AND 4#	466
6	Limit 5 to date range 1996 to onward and English language	453

ERIC (EBSCO)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
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1	TX ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	573,889
2	TX (medical school OR medical schools)	5909
3	TX (medical student OR medical students)	6667
4	TX (education OR educational)	1,388,929
5	1# AND 2# AND 3# AND 4#	833
6	Limit 5 to date range 1996 to onward and English language	352
Scopus (Elsevier Science)		
Date searched: 13/11/2019		
Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	672,153
2	TITLE-ABS-KEY (medical school OR medical schools)	170,817
3	TITLE-ABS-KEY (medical student OR medical students)	148,601
4	TITLE-ABS-KEY (education OR educational)	2,204,656
5	1# AND 2# AND 3# AND 4#	2492
6	Limit 5 to date range 1996 to onward and English language	1793
Web of Science (Clarivate Analytics)		
Date searched: 13/11/2019		
Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	501,104
2	TOPIC (medical school OR medical schools)	44,200
3	TOPIC (medical student OR medical students)	64,138
4	TOPIC (education OR educational)	912,615

5	1# AND 2# AND 3# AND 4#	861
6	Limit 5 to date range 1996 to onward and English language	801
Wiley Online Library (EBSCOhost)		
Date searched: 13/11/2019		
Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	86,680
2	ANYWHERE (medical school OR medical schools)	271,886
3	ANYWHERE ("medical student" OR "medical students")	71,464
4	ANYWHERE (education OR educational)	1,630,840
5	1# AND 2# AND 3# AND 4#	620
6	Limit 5 to date range 1996 to onward and English language	140
JB I Systematic Reviews and Implementation Reports (Ovid)		
Date searched: 13/11/2019		
Set #	Search query	Results retrieved
1	All ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	7630
2	All ("medical school" OR "medical schools")	81
3	All ("medical student" OR "medical students")	377
4	All (education OR educational)	8956
5	1# AND 2# AND 3# AND 4#	41
6	Limit 5 to date range 1996 to onward and English language	29
ProQuest Dissertations and Theses Global (ProQuest)		
Date searched: 13/11/2019		
Set #	Search query	Results retrieved

1	ti ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	98,206
2	ab (medical school OR medical schools)	5039
3	ab (medical student OR medical students)	5241
4	ab (education OR educational)	322,338
5	1# AND 2# AND 3# AND 4#	129
6	Limit 5 to date range 1996 to onward and English language	83

Appendix IIb: Studies ineligible following full-text review.

Authors	Reason for exclusion
Merz D, Smaill F, Daneman N, editors. evidence-based Infectious Diseases. Oxford: Wiley Blackwell; 2018.	Ineligible concept
Abbo LM, Cosgrove SE, Pottinger PS, Pereyra M, Sinkowitz Cochran R, Srinivasan A, et al. Medical students' perceptions and knowledge about antimicrobial stewardship: how are we educating our future prescribers? Clin Infect Dis 2013;57(5):631–8	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar OJ, Pulcini C, Howard P, Nathwani D, on behalf of ESGAP (ESCMID Study Group for Antibiotic Policies). European medical students: a first multicentre study of knowledge, attitudes and perceptions of antibiotic prescribing and antibiotic resistance. J. Antimicrob Chemother. 2014;69(3):842–6.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Chuenchom N, Thamlikitkul V, Chaiwarith R, Deoisares R, Rattanaumpawan P. Perception, attitude, and knowledge regarding antimicrobial resistance, appropriate antimicrobial use, and infection control among future medical practitioners: a multicenter study. Infect Control Hosp Epidemiol. 2016;37:603-5.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar O, Howard P, Nathwani D, Pulcini C. Knowledge, attitudes, and beliefs of French medical students about antibiotic prescribing and resistance. Med Mal Infect. 2013;43(10):423-30.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar OJ, Lund M, Lindsjö C, Lundborg CS, Pulcini C. Preparedness to prescribe antibiotics responsibly: a comparison between final year medical students in France and Sweden. Eur J Clin Microbiol Infect Dis. 2019;38(4):711-7.	Ineligible concept
Dyar OJ, Nathwani D, Monnet DL, Gyssens IC, Stålsby Lundborg C, Pulcini C. Do medical students feel prepared to prescribe antibiotics responsibly? Results from a cross-sectional survey in 29 European countries. J Antimicrob Chemother.2018;73(8):2236-42.	Ineligible concept
Haque M, Rahman NIA, Zulkifli Z, Ismail S. Antibiotic prescribing and resistance: knowledge level of medical students of clinical years of University Sultan Zainal Abidin, Malaysia. Ther Clin Risk Manag. 2016;12:413-26.	A survey to determine knowledge and is not about a program development
Jaillon P. Teaching basic and clinical pharmacology to medical students: a 2006 survey in French schools of medicine. Therapie. 2006;61(5):439-46.	Ineligible concept

Hu Y, Wang X, Tucker JD, Little P, Moore M, Fukuda K, et al. Knowledge, attitude, and practice with respect to antibiotic use among Chinese medical students: a multicentre cross-sectional study. <i>Int J Environ Res Public Health</i> . 2018;15(6):1165-79.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Javadi MR, Khezrian M, Sadeghi A, Hajimiri SH, Eslami K. An interprofessional collaboration between medicine and pharmacy schools: designing and evaluating a teaching program on practical prescribing. <i>J Res Pharm Pract</i> . 2017;6(3):178-81.	Ineligible study design
Gupta MK, Vohra C, Raghav P. Assessment of knowledge, attitudes, and practices about antibiotic resistance among medical students in India. <i>J Family Med Prim Care</i> . 2019;8(9):2864-9.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Melber DJ, Teherani A, Schwartz BS. A comprehensive survey of preclinical microbiology curricula among US medical schools. <i>Clin Infect Dis</i> . 2016;63(2):164-8.	Ineligible study design
Minen MT, Duquaine D, Marx MA, Weiss D. A. Survey of knowledge, attitudes, and beliefs of medical students concerning antimicrobial use and resistance. <i>Microb Drug Resist</i> . 2010;16(4):285-9.	A survey on knowledge, attitudes, and beliefs and is not about a program development
O'Brien D, Richards J, Walton K, Phillips M, Humphreys H. Survey of teaching/learning of healthcare-associated infections in UK and Irish medical schools. <i>J Hosp Infect</i> . 2009;73(2):171-5.	Ineligible concept
Ohl CA, Luther VP. Health care provider education as a tool to enhance antibiotic stewardship practices. <i>Infect Dis Clin</i> . 2014;28(2):177-93.	Ineligible concept
Ijeoma O, Chukwuma DU, Onyinyechukwu UO, Azuka SA, Kingsley CO. Knowledge of antibiotic use and resistance among students of a medical school in Nigeria. <i>Malawi Med J</i> . 2019;31(2):133-7.	A survey to determine knowledge and is not about a program development
Phillips C, Henderson PJ, Mandel L, Kim S, Schaad D, Cooper M, et al. Teaching the microscopic examination of urine sediment to second-year medical students using the Urinalysis-Tutor computer program. <i>Clin Chem</i> . 1998;44(8):1692-700.	Ineligible concept
Rattanaumpawan P, Chuenchom N, Thamlikitkul V. Perception, attitude, knowledge and learning style preference on challenges of antimicrobial resistance and antimicrobial overuse among first year doctors in training and final year medical students. <i>Antimicrob Resist Infect Control</i> . 2019;8(1):142-49.	Ineligible concept
Hoque R, Mostafa A, Haque M. Insight of medical students of clinical years to antimicrobials prescribing and resistance in private medical school, Chittagong, Bangladesh. <i>J Young Pharm</i> . 2016;8(4):447-55.	Ineligible study design

Scaioli G, Gualano MR, Gili R, Masucci S, Bert F, Siliquini R. Antibiotic use: a cross-sectional survey assessing the knowledge, attitudes and practices amongst students of a school of medicine in Italy. <i>PloS One</i> . 2015;10(4):e0122476.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Sánchez-Fabra D, Dyar OJ, del Pozo JL, Amiguet JA, de Dios Colmenero J, del Carmen Fariñas M, et al. [Perspective of Spanish medical students regarding undergraduate education in infectious diseases, bacterial resistance and antibiotic use]. <i>Enferm Infecc Microbiol Clin</i> . 2019;37(1):25-30. Spanish.	Ineligible study design
van der Voort T, Brinkman DJ, Benemei S, Böttiger Y, Chamontin B, Christiaens T, et al. Appropriate antibiotic prescribing among final-year medical students in Europe. <i>Int J Antimicrob Agents</i> . 2019;54(3):375-9.	Ineligible concept
Wasserman S, Potgieter S, Shoul E, Constant D, Stewart A, Mendelson M, et al. South African medical students' perceptions and knowledge about antibiotic resistance and appropriate prescribing: are we providing adequate training to future prescribers? <i>S Afr Med J</i> . 2017;107(5):405-10.	A survey on knowledge, attitudes, and perceptions and is not about a program development
World Health Organization. Mapping educational opportunities and resources for health-care workers to learn about antimicrobial resistance and stewardship. 2017 [cited 2020 Mar 08]. Available from: https://apps.who.int/iris/bitstream/handle/10665/259362/9789241512787-eng.pdf?sequence=1 .	Ineligible population; study focuses on healthcare workers
Wright E, Jain P. Survey of antibiotic knowledge amongst final year medical students. <i>J. Antimicrob Chemother</i> . 2004;53(3):550-1.	A survey on knowledge is not about a program development
Huang Y, Gu J, Zhang M, Ren Z, Yang W, Chen Y, et al. Knowledge, attitude and practice of antibiotics: a questionnaire study among 2500 Chinese students. <i>BMC Med Educ</i> . 2013;13(1):163-72.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Zhao A, Xiao S, Kandelaki K, Liu Y, Chen W, Ren R, et al. Knowledge, perception, and educational status of antimicrobial resistance among Chinese medical students. <i>Microb Drug Resist</i> . 2019;25(10):1458-64.	Ineligible concept
Adriana A.B, Magdalena C.S. A gaming approach to learning medical microbiology: students' experiences of flow. <i>Med Teach</i> . 2007;29 (9-10):933-40.	Ineligible study design
Charlier C, Johannessen I, Mackintosh CL, Wilks D, Cauda R, Wolf FI, et al. International infectious diseases teaching to undergraduate medical students: a successful European collaborative experience. <i>Med Teach</i> . 2017;39(9):981-6.	A survey on knowledge, attitudes, and beliefs and is not about a program development

Somwang Danchaivijitr SC, Uapong Jaturatramrong AW, Rachada Cherdungsi SS. Program on nosocomial infection in the curricula of medicine, dentistry, nursing and medical technology in Thailand. J Med Assoc Thai. 2005;88:150-4.	Ineligible population; study focuses on all health science students
Luther VP, Ohl CA, Hicks LA. Antimicrobial stewardship education for medical students. Clin Infect Dis. 2013;57(9):1366-7.	Ineligible study design
Pulcini C, Wencker F, Frimodt-Møller N, Kern WV, Nathwani D, Rodríguez-Baño J, et al. European survey on principles of prudent antibiotic prescribing teaching in undergraduate students. Clin Microbiol Infect. 2015;21(4):354-61.	Ineligible concept

Appendix III: Characteristics of included studies.

Authors year, country	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Hsu 2018, USA ¹⁷	A single didactic teaching module introduced into third-year internal medicine clerkship at the University of South Dakota, Sanford School of Medicine. The teaching module presented included the PowerPoint slide set with instructor notes, student worksheet entitled “Building an Antibiotic Stewardship Program” and one-minute paper evaluation.	Case report	University of South Dakota, Sanford School of Medicine	Approximately 150 (over three years)	Educational intervention – using a single didactic session that included interactive aspects of teaching	75 minutes	Didactic lecture involving large and small groups	Analysis of one-minute paper revealed three themes: concept learned; concept unclear; and concept to try	One-minute paper evaluation
Kerret <i>et al.</i> 2001, United Kingdom ²⁷	A postal survey of UK medical schools and the University of St Andrews that offers a three-year pre-	Postal survey using cross-sectional design	Not stated	Not stated	Not stated	The contact times allocated to teaching about the rational use	All institutions except one reported that lectures, generally in years 2 and 3, were the main method of teaching, but in some	Not stated	No evaluation of learning

	clinical course. Seventeen (71%) of 24 institutions replied.					of antimicrobials (as opposed to pharmacology mode of action, etc) varied greatly (range 0·5–22·0 hours).	cases, lectures were supplemented with tutorials or problem-based learning exercises. One medical school stated that students learned the principles and practice of antimicrobial use through a self-directed learning module throughout the undergraduate course		
MacDougall <i>et al.</i> 2017, USA ¹⁸	The curriculum is designed for second-year medical students and third-year pharmacy students at University of California, San Francisco. The curriculum was embedded in the courses on microbiology and infectious diseases (medical students) or antimicrobial pharmacology (pharmacy students).	Not stated, likely prospective cohort study	University of California, San Francisco	A total of 822 students participated over the three study years (470 medical students, 352 pharmacy students)	Educational intervention	Not stated	Online learning module and interprofessional workshop. The curriculum was designed as follows and delivered through the Moodle learning management system (Moodle Pty Ltd, Perth, Australia): i) students viewed a case vignette online (Case 1) and answered related clinical questions; ii) an online independent learning module on antimicrobial stewardship was subsequently	This has demonstrated how an interprofessional curriculum on antimicrobial stewardship, including medical and pharmacy students can positively impact knowledge and attitudes towards both antimicrobial stewardship and interprofessional collaboration. There was an increase in the	A total of 745 students (425 medical students, 320 pharmacy students) completed both pre- and post-curriculum surveys.

							provided; then, iii) approximately a week later, the students participated in a two-hour workshop on antimicrobial stewardship. Students were subdivided into small groups of 4–5 students comprising mixed-professions. In small groups, students revisited Case 1 from the online module and came to a consensus group answer, which was then discussed with the larger group. The small groups then worked through Case 2 together, again followed by group discussion. The cases used a branched-logic format: the decisions students made in the initial stages of the case determined the subsequent choices and case outcomes. The decisions required in the cases reflected key considerations in antimicrobial stewardship: whether	percent of agree/strongly agree responses after implementation of antimicrobial stewardship curriculum. They hope to use a more robust assessment tool in the future implementation of the curriculum.	
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							to initiate treatment, the impact of patient allergies and drug interactions on antimicrobial selection, adequacy of the empiric spectrum of activity, and de-escalation of therapy based on culture results.		
Marwick and Nathwani, 2007, United Kingdom ²⁶	Clinical infection teaching of medical students	Descriptive study design details in web-based format	University of Dundee Medical School	Fourth-year medical students	Not stated	Time not stated but the teaching is delivered by the infectious disease physicians, microbiologists, infection control nurses, pharmacists, and public health clinicians.	Teaching students how to recognize, diagnose, and manage common infections. It also involves infection control and health protection aspect of infection	Not stated	Learning was evaluated via student feedback and has shown positive results. Currently, evaluating student knowledge through a series of short exams at the beginning and end of each attachment and at the end of the year.
Lakset <i>al.</i> 2019, Brazil ⁴	The authors developed and implemented a Moodle-based, distance-learning course on the use of antimicrobial	Before-and-after with no control group	Federal University of São Paulo Paulista School of Medicine	606 students completed the course: 72 were sixth-year students (2008 only); and 534 were fifth-year	Educational intervention study	100 hours of activities	Web-based, distance-learning course	About 421 (69.5%) of the students reported that they had learned a lot or more than they had expected	Before-and-after evaluation of students' knowledge score

	agents and the prevention of antimicrobial resistance. The students were tutored in their online activities, and some classes were conducted in real-time for live discussions. In addition, students underwent face-to-face assessments of their knowledge of the topic before and after the course. The course was conducted for over seven years. The course consists of five theoretical modules, exercises, and simulations, within a virtual learning environment.			students (2008–2014).				about the topic. The average mean score of all 606 students' initial assessment was 5.78 (5.70–5.86) and this has significantly increased to 8.45 (8.36–8.53) in the final assessment $p < 0.001$. The average mean score of all the 534 fifth-year students was 5.75 (5.66–5.83) in the initial assessment and has increased to 8.46 (8.37–8.54) in the final assessment. These were significant at $p < 0.001$.	
Nori <i>et al.</i> 2017, USA ¹⁹	Pre-clinical Curriculum: antimicrobial stewardship Pre-clinical Curriculum:	Quasi-experimental Before-and-after study design	Albert Einstein College of Medicine	183 students participated in antibiotic stewardship seminar per year (2014–2016).	Educational intervention	Annual two-hour seminar: 2014–2016 on antimicrobial stewardship	Small-group sessions, team-based activities, smartphone app, case-based modules	Improved prescriber confidence: the smart phone app is the preferred source of antibiotic information	Pre- and post-intervention surveys and knowledge assessment questions during antimicrobial stewardship and

	infection prevention control			183 students participated in Infection Prevention and Patient Safety Seminar (2015–2016).		Annual two-hour seminar: since 2015 – 2016 on infection prevention and control		Improved understanding of transmission-based precautions and related personal protective equipment The post-test results showed a significant improvement in personal protective equipment proficiency and knowledge of hospital-acquired infection with an increase in correct responses from 38% to 76% observed for questions involving antibiogram use ($p = 0.02$).	infection prevention control.
Paterson Davenport <i>et al.</i> 2005, United Kingdom ²⁰	This study provides an introduction to understanding outcome-based education and how it has been applied	This is a descriptive paper of outcomes-based education	Not stated	Not stated	Not stated	Not stated	These outcomes provided the trigger for developing a supportive learning resource that could be used in different	Not stated	No evaluation of learning

	in the context of prudent antimicrobial prescribing for undergraduate medical education as defined by an expert working party	and how it can be applied to antibiotic stewardship					learning situations, including for self-learning, self-assessment, peer review, small-group discussion, or formal assessment. <i>How the Appropriate Antimicrobial Prescribing for Tomorrow's Doctor</i> materials are used within individual educational institutes will depend on many issues, including the organization of the curricular program, the available teaching resources, and the level of experience of students, as well as timetabling issues.		
Pulcini and Gyssens, 2013, Europe ¹⁰	Not stated	Not stated; likely descriptive design	University of Rotterdam (The Netherlands)	Second-year medical students	Not stated	Not stated	One-week module on several concepts of antimicrobial resistance, hygiene, and prudent antibiotic prescribing in the core curriculum	Not stated	Not stated
	A module on antibiotic policy on infectious diseases and hygiene. Other	Not stated; likely descriptive design	University of Nijmegen (The	Third-year students	Not stated	Not stated	Elective problem-based learning	Not stated	Not stated

	topics include infection control, antibiotic guidelines, principles of prophylaxis, and laboratory techniques.		Netherlands)						
	In the UK, the Prudent Antibiotic User (PAUSE, www.pause-online.org.uk) is a website of shared standardized teaching materials for prudent antimicrobial prescribing for use in the undergraduate medical curriculum. PAUSE provides standardized teaching aides for all educators of antibiotic prescribing based on patient-focused, reflective learning.	Descriptive study design details in web-based format	UK medical schools	Not stated	Resources are designed to enable students to prepare for interactive sessions to compare standard patient vignettes with their own clinical experience. The structured preparation required of the students is a key to success. The interactive discussion sessions focus on learning prudent	Not stated	The prepared materials about structure and content for each interactive session are available for tutors to use (in a PowerPoint format). These resources include patient histories, clinical signs, investigations and questions on diagnosis, assessing severity, appropriate prescribing, public health issues, and patient management. Best practice statements and core resource lists are also available.	Not stated	Guideline answers to the questions with feedback are provided, including inappropriate responses and the corresponding reasons.

					antibiotic prescribing through reflective practice.				
Shankar <i>et al.</i> 2011, Nepal ³⁰	Teaching in rational use of antibiotics is conducted during the pharmacology practical sessions. Proper antibiotic use is also stressed during the session on analysis of rationality of prescriptions. Students learn not to use antibiotics in predominantly viral infections, and to avoid the use of multiple antibiotics. They are also shown and interpret a video on antibiotic resistance.	The paper outlines how and when to teach this module; likely descriptive design	Kist Medical College medical school in Lalitpur, Nepal	Not stated	Educational intervention	Two hours didactic lectures throughout the first year of the course; two-hour practical session follows the lecture; lectures held in the first two years of study	A problem-based approach within clinical pharmacology teaching using the World Health Organization essential medicine prescribing approach.	Not stated	No evaluation of learning
Shekarchian <i>et al.</i> 2016, USA ²¹	A comprehensive learning experience is developed throughout the second to fourth years of medical	Letter to the editor describing the intervention	University of California, San Francisco	Not stated	Educational intervention	A two-hour session in the second year; an hour interactive case-based	Made use of a spiral curriculum. The second-year component: purposeful integration of	Before graduation, 88% felt at least moderately prepared to initiate empiric	Not stated

	school. The curriculum utilized the concept of spiral learning. The antibiotic stewardship curriculum is initiated in 2013 at the University of California, San Francisco School of Medicine.		School of Medicine			didactic session in the third year; in the fourth year two sessions are delivered: two hours before the start of the year and 1.5 hours a week before graduation. • an interprofessional, case-based small-group activity for medical and pharmacy students on antibiotic stewardship. The third-year component: • an interactive case-based didactic session emphasizing responsible antibiotic use immediately before the start of clerkships; • during the medicine clerkship, an online module on common infections and	stewardship themes throughout the foundations science microbiology block (integrates microbiology, infectious diseases, and pharmacology);	antibiotics and when and how to narrow the spectrum of coverage. Eighty-eight percent felt very or extremely satisfied with the education they received on antibiotic stewardship during medical school.	
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							antimicrobial use, followed by an interactive “Jeopardy”-style chief resident–taught game. The fourth-year component: • during the fourth year of medical school, two sessions are delivered on common infections and responsible antimicrobial use immediately before the start of the fourth year and one week before graduation; • antibiotic cards were developed and disseminated for medical students to use on the wards starting in the third year.		
Silverberg <i>et al.</i> 2017, Canada ²⁹	This is a literature review conducted to compile a summary of the current published	Mapping review	Medical education (undergraduate and	Not stated	Educational review	Not stated	Approaches at the undergraduate level included didactic teaching, web-based teaching, clinical case	Not stated	None of the articles that targeted undergraduate medical students

	research on antimicrobial stewardship training in medical education. Of the 48 articles included in this summary, 14 included only undergraduate medical trainees, 11 included both undergraduate and postgraduate trainees, 20 included only postgraduate trainees, and three did not specify the training level of the participants		postgraduate)				discussions, workshops/seminars, board games, guideline promotion, audits on current stewardship integration in the medical curriculum, and intensive modules.		evaluated whether the intervention influenced their prescribing behavior either as a senior medical student or followed them beyond graduation.
Valente <i>et al.</i> 2009, Brazil ²⁸	The game consists of an illustrated board and is played with dice and pawns. The board has 121 squares, including squares with question marks and antimicrobial agents. Each student receives a card with a clinical case, identification of the bacterium,	Descriptive study design details in board game	Universidade Federal do Rio Grande do Sul, Brazil	78 medical and pharmacy students, of which 42 were medical students while 36 were pharmacy students.	Not stated	1.5 hours	Not stated	An improvement in right answers after board games. More than 90% said the game helped them to understand the subject, and was an important way to enhance learning	Pre-test and a post-test. There was an increase in the number of right answers and a decrease in the number of unknown answers in the post-test after board games.

	and its resistance to antimicrobials.								
Wake Forest Medical School, USA, n.d. ¹	An antibiotic stewardship curriculum was developed by Wake Forest School of Medicine in collaboration with the Centers for Disease Control and Prevention and the Association of American Medical Colleges to increase understanding of antimicrobial resistance prevention and control among medical students. It is structured to address the microbiological and pharmacological components of antimicrobial use in outpatient and inpatient settings.	Not empirical research – a description of the content of the curriculum	Wake Forest Medical School	Not stated	Educational intervention	Three didactic lectures; five small-group activities and nine exam questions. Not stated how long any of these activities lasted	The curriculum is intended for use in US medical schools and intended for pre-clinical and clinical years of instruction. The pre-clinical segment comprised of lectures with facilitator notes and audio recordings, and nine corresponding exam questions in the United States Medical Licensing Examination format. The clinical curriculum contains five small-group activities with facilitator guides.	Not stated – this was a description of a curriculum in terms of content and delivery	No evaluation of learning

CHAPTER THREE

Knowledge and perceptions about antibiotic resistance and prudent antibiotic prescribing among final year medical students in two African countries

Augie, B. M., van Zyl R. L., McInerney, P. A., and Miot, J.

“If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine.” (Raina, 2019, p. 133)

David Cameron,
Former UK Prime Minister

The paper is published in *International Journal of Pharmacy Practice*. The pdf version of the published article is attached as Appendix C. This study was undertaken to achieve objective 2: To determine the perceptions, attitudes and knowledge of Nigerian and South African final year medical students about rational antibiotic prescribing using a questionnaire format.

Abstract

Objectives: The objectives of this study were to assess the knowledge and perceptions of final year medical students about antibiotic resistance and antibiotic use in order to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria the principles of prudent antibiotic prescribing.

Methods: A cross-sectional study was conducted to determine the knowledge and perceptions of final year medical students in one South African and three Nigerian universities about prudent antibiotic use, antibiotic resistance and antibiotic stewardship. A 26-item questionnaire was administered electronically to students in three medical schools and a paper-based copy in the fourth.

Key findings: A difference in the gap in knowledge between the two countries was identified; however, respondents from both countries had a similar understanding of antibiotic use and

antibiotic resistance. Most respondents in South Africa (94.8%) and Nigeria (91.4%) agreed that antibiotics are overused in their countries. There was a significant difference between the number of respondents in the two countries who thought that there are new antibiotics available to treat resistant pathogens; 45.4% of Nigerian respondents agreed with the statement as compared to 9.6% of the South African respondents. Of the 10 vignettes answered correctly, South African respondents scored an average of 62.4% in the knowledge segment compared to 31.9% scored by the Nigerian respondents ($p=0.001$). All of the South African (100%) and 98.3% of the Nigerian respondents indicated their desire for more education on appropriate antibiotic use.

Conclusions: Although students from both countries had the same perception of antibiotic resistance, there was however a difference in their level of knowledge, which could have been improved in both countries. This should be addressed at an undergraduate curriculum level; as well as with continued education to reinforce antibiotic knowledge.

Introduction

Antibiotics represent a miracle of science that have saved millions of lives since the discovery of penicillin by Alexander Fleming in 1928,^[1] resulting in major advancements in modern medicine.^[2] The discovery of antibiotics has undoubtedly changed the way life-threatening bacterial infections, like meningitis and endocarditis, are treated.^[3] Antibiotic resistance is an inevitable evolutionary process, which occurs as a result of exposure of bacteria to antibiotics.^[4] The use of antibiotics, either appropriately or inappropriately, drives selective pressure for the emergence of resistance.^[5] Overuse of antibiotics has dire consequences such as antibiotic resistance, which is one of the major problems affecting public health.^[6-7] There is a direct relationship between antibiotic consumption and the development of antibiotic resistance;^[8-9] whilst responsible antibiotic use delays the development of antibiotic resistance.^[10-11] Antibiotic resistance is a global public health problem requiring a global solution.^[12] In its five-year Antimicrobial Resistance Strategy, the United Kingdom's Department of Health acknowledged that antibiotic resistance occurs mainly as a result of selective pressures from antibiotic use, which can be reduced by optimal antibiotic use, and slow the emergence of resistant bacteria.^[13]

Antibiotic resistance can result in prolonged hospitalisation, increased morbidity and mortality,^[2] and consequently increased costs from consumables and laboratory investigations.^[6,14] A United Kingdom commissioned report predicted that if left unchecked by 2050, 10 million people will die of resistant infections annually which will cost the global economy over 10 trillion US dollars.^[12]

The pipeline for the production of new antibiotics with novel mechanisms of action remains meagre.^[15] This has implications for medical education.^[15] Ganter, a senior advisor on antimicrobial resistance (AMR) at the WHO stated that there is room for improvement in the current antimicrobial teaching of medical students.^[16] He recommended that medical students should be introduced to prudent antibiotic use as early as possible in their careers.^[16] Inappropriate antibiotic use by physicians is a source of concern and could be linked to education on rational antibiotic use in medical schools.^[16]

To encourage appropriate antibiotic prescribing, many medical schools across the globe have developed prudent antibiotic prescribing programmes for their students.^[17-22] Our scoping review did not identify any such programme in African medical schools.^[23] It has been established that to engage in responsible antibiotic prescribing one needs requisite skills, but the decision to prescribe antibiotics is often left to junior staff who may not have the required knowledge, experience or guidance to make an informed choice of optimal antibiotics.^[24] Many patients admitted to hospitals stand a risk of either presenting with or acquiring infections that may require urgent treatment with antibiotics. However, only those with severe or complicated infections may benefit from the expertise of infectious disease specialists. This implies that the majority of patients will be treated by non-specialist doctors,^[24] who have a tendency to use broad-spectrum antibiotics for a longer duration. Hence the need to educate medical students on antibiotic stewardship, so that they are able to undertake rational antibiotic prescribing by making an informed decision regarding the choice of antibiotics.

In an effort to improve rational antibiotic use, South Africa and Nigeria have developed National Action Plans for AMR. The South African AMR National Strategy Framework 2014 – 2024 provides a four-point strategy for managing AMR to reduce the spread of resistant pathogens and improve patient outcomes.^[25] Similarly, Nigeria has a five-point strategy.^[26] Both strategies aim to encourage optimal antibiotic therapy and reduce collateral damage from antibiotic use.^[3] The objectives of this study were to assess the knowledge and perceptions of

final year medical students about antibiotic resistance and antibiotic use in order to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria the principles of prudent antibiotic prescribing.

Methods

Study design, setting and participants

A cross-sectional multicentre survey of final year medical students in one South African and three Nigerian universities was conducted in 2019. The two countries were selected because of their influence on the African continent. The three Nigerian universities use a traditional curriculum, while the South African university uses an integrated curriculum. This provided opportunity to compare and contrast the curriculum type on students' learning of antibiotic prescribing. Three Nigerian medical schools were chosen because their student numbers were small (220 in total) as compared to the South African medical school (328 students). Nigerian universities generally have fewer medical students compared to the South African universities which informed the decision to choose up to four medical schools. Unfortunately, one of the Nigerian universities was excluded from the study because of unrest in the region that affected academic activities. An attempt to include other Nigerian universities was unsuccessful.

Survey development

An existing questionnaire was used with permission of the developer.^[27] A pilot study was conducted on 10 final year medical students in each of the two countries, to assess readability, length, and relevance of items in the questionnaire before it was administered. The survey assessed perceptions and knowledge about antibiotics, antibiotic resistance, and the perceived quality of education regarding preparedness to prescribe antibiotics. The data collected included demographic information, perceptions regarding antibiotic use and resistance; awareness of antibiotic-resistant diseases, sources of antibiotic education, and self-confidence in antibiotic prescribing. Mode of teaching and evaluation of antibiotic knowledge were also studied. In order to determine respondents' actual knowledge, they were asked to respond to vignettes for correctness of action. Responses to the different questions varied from single item responses to a choice on a 5-point Likert scale.

Survey administration

Data were collected between July and November 2019. The questionnaire was administered online using REDCap in three schools and hard copies were administered in one Nigerian medical school, because the survey was conducted at a time when students were preparing for their final examinations and it was anticipated that the electronic response would generate a low response rate. Students were informed that their participation was voluntary and that they had the right to withdraw at any time or decide not to answer any question they wished without penalty. They were also assured that their responses were anonymous and would not be shared with their universities. No incentive was given to respondents as a motivation to participate in the study.

For the online administration, a survey link was emailed to respondents, with the link to the survey being active for equal time periods in both countries. In South Africa this was done by the class coordinator, while in Nigeria it was done by the class representatives. REDCap was set to send weekly reminders.

The hard copies of the questionnaire were distributed to the respondents after a class test by the first author. A box was provided outside the hall for respondents to return their questionnaires. The questionnaire was administered a few weeks before the start of the examinations. Neither the curriculum nor the mode of teaching of antibiotics was changed before or during the survey in any of the schools.

Data management and analysis

Stata software (version 15) was used for data analysis. Data collected using the paper-based survey were manually entered into REDCap, together with the data collected using the REDCap link. All data were exported into an Excel document (version 2019), cleaned, anonymised and imported into Stata. The participating medical schools were anonymised by assigning a numerical ID to enable blinded data analysis. The 5-point Likert scale was condensed into three categories: agree/good, neutral/average, and disagree/poor. Percentages were determined for categorical data and an overall knowledge score was assessed by calculating the total percentage of correct answers for the vignette-based questions for each country. Fischer's exact test was used to determine the association between categorical variables. Variations between observed and expected proportions were tested for significance using the Chi-squared test and

the independent t-test was used to determine significant differences in age and mean knowledge scores between the South African and Nigerian samples.

Ethics

Ethics approval was obtained from the ethics committee of each institution (ref numbers: M1902108; ABUTHZ/HREC/D25/2018; BUK/CHS/REC/VII/52; UDUTH/HREC/2018/NO;756). (Appendices D, E, F, G, H, I, J, K, L, and M are study title approvals, ethical clearances for Phases One and Two of the study, while Appendices N, O, P, Q, and R are letters of permission to conduct the study in four medical schools).

Results

A total of 548 students was invited to participate in the study, 328 from South Africa and 220 from Nigeria. A total of 276 (50.4%) students responded, with 31.7% (104) being from South Africa and 78.2% (172) being from Nigeria. There was some information that was not completed by the respondents in seven of the paper-based questionnaires and four among the online completed surveys, where 72.7% and 27.3% were from Nigeria and South Africa, respectively. The average age of all respondents was 25.7 ± 2.18 years and was similar in both countries. The Nigerian cohort consisted of a greater number of males as compared with the South African sub-sample. Of the total sample, 16.3% had a previous degree, with most being from South Africa. The exposure to AMS was relatively poor especially among Nigerian respondents. The sociodemographic characteristics of both groups of respondents are shown in Table 1.

Knowledge and perceptions of antibiotic use

A similar number of Nigerian (94.8%) and South African (91.4%) respondents agreed that antibiotics are overused in their countries and more than half of the respondents in both countries agreed that antibiotics are overused in the hospitals in which they had completed clinical rotations. More Nigerian respondents (11.0%) disagreed with the statement that antibiotic resistance was a major problem at the teaching hospitals at which they had completed clinical rotations, as compared to 4.8% of the South African respondents. There was a significant difference ($p=0.001$) between Nigerian and South African respondents on the availability of new antibiotics to treat resistant infections; 45.4% of Nigerian respondents agreed compared to 9.6% of the South African respondents. More South African respondents (99.0%) compared to Nigerian respondents (93.0%) agreed that inappropriate antibiotic use

causes resistance and 99.0% of the respondents from both countries agreed that better antibiotic use could reduce the level of resistance. The majority of the South African (91.4%) and Nigerian (84.3%) respondents agreed that the use of broad-spectrum antibiotics, when equally effective narrow spectrum antibiotics are available, may encourage resistance. Just under two-thirds in both countries agreed that lack of hand disinfectant by healthcare providers can lead to the spread of antibiotic resistance, with >20% in both countries being neutral to the statement. The majority of the South African (95.2%) and Nigerian (86.0%) respondents agreed that inappropriate antibiotic use is harmful to patients; however, a statistical difference was found between the Nigerian respondents (12.3%) who were neutral to the statement as compared to the South African respondents (2.9%) ($p=0.02$). Most respondents (99.0%) in both countries agreed that a good knowledge of antibiotics is important for their career as doctors; while all of the South African (100%) and 98.3% of the Nigerian respondents indicated their desire for more education on appropriate antibiotic use.

Table 1: Socio demographic characteristics of South African and Nigerian medical students ($n = 276$).

Sociodemographic (n = 276)	South Africa (n = 104)	Nigeria (n = 172)	p-value
Gender	n (%)	n (%)	
Male	50 (48.1%)	101 (58.7%)	0.11 ^a
Female	54 (51.9%)	71 (41.3%)	
Age			
Age, Mean (SD)	25.7 (1.7)	25.8 (2.4)	0.67 ^c
Age, range (minimum – maximum)	23 - 32	21 - 38	
Previous degree			
Yes	38 (36.5%)	7(4.1%)	0.001 ^a
No	66 (63.5%)	165(95.9%)	
Type of the previous degree	(n = 38)	(n = 7)	
	n (%)	n (%)	
Bachelor only	23 (60.5%)	-	
Bachelor and Honors	13 (34.2%)	7 (100.0%)	
Bachelor, Honors and Masters	2 (5.3%)	-	
Exposure to antimicrobial stewardship teaching in the previous degree.			
Yes	11 (28.9%)	4 (57.1%)	0.20 ^b
No	27 (71.1%)	3 (42.9%)	

^a Chi-squared test; ^b Fischer's exact test; ^c Independent t-test

Learning methods

The respondents felt that formal lectures (93% Nigerian; South Africans 83.7%) and consultant ward rounds (91.8% Nigerian; South African 89.4%) were useful in understanding antibiotic classes and their spectrum of activities and 82.7% and 92.4% of the South African respondents compared to 94.8% and 94.1% of the Nigerian respondents agreed that formal lectures, and consultant ward rounds are useful in learning about antibiotic prescribing and resistance (Table 2). Nigerian respondents were more likely to consult infectious disease specialists compared to the South African respondents. Of note in Table 2 are the differences in relation to formal lectures, formal bedside tutorial and problem-based learning between countries. The South African respondents were either very familiar (34.6%) or familiar (64.4%) with the term antibiotic stewardship, while more than half of the Nigerian respondents were either not familiar (43.8%) or not at all familiar (16.6%).

Table 2: Perceptions about learning methods used (n = 276).

	South Africa n (%)			Nigeria n (%)			Fischer's exact Test p-value
	Useful	Neutral	Not useful	Useful	Neutral	Not useful	
If available, how useful are the following education activities for learning about antibiotic classes and spectrum of activity?							
Formal lectures	87 (83.7)	12 (11.5)	5 (4.8)	159 (93)	10 (5.8)	2 (1.2)	0.04
Formal bedsid es tutorial	93 (89.4)	8 (7.7)	3 (2.9)	166 (97.1)	4 (2.3)	1 (0.6)	0.03
Consultant ward rounds	93 (89.4)	4 (3.9)	7 (6.7)	156 (91.8)	14 (8.2)	-	0.001
Registrar ward rounds	83 (79.8)	13 (12.5)	8 (7.7)	151 (88.3)	13 (7.6)	7 (4.1)	0.15
Problem based learning	83 (79.8)	12 (11.5)	9 (8.7)	150 (87.7)	19 (11.1)	2 (1.2)	0.01
If available, how useful are the following education activities for learning about antibiotic prescribing and resistance?							
Formal lectures	86 (82.7)	12 (11.5)	6 (5.8)	163 (94.8)	8 (4.7)	1 (0.5)	0.00
Formal bedsid es tutorial	96 (92.4)	6 (5.7)	2 (1.9)	167 (97.7)	4 (2.3)	-	0.05
Consultant ward rounds	96 (92.4)	4 (3.8)	4 (3.8)	161 (94.1)	9 (5.3)	1 (0.6)	0.14
Registrar ward rounds	87 (83.6)	11 (10.6)	6 (5.8)	153 (89.4)	16 (9.4)	2 (1.2)	0.10
Problem based learning	85 (81.7)	10 (9.6)	9 (8.7)	149 (87.1)	21 (12.3)	1 (0.6)	0.00

Curricula and antibiotic use

Most of the respondents in both countries felt their medical schools had prepared them to make an accurate diagnosis of infections and know when to start antibiotics, although this was more so amongst the Nigerian respondents (Table 3). Of note are the statistically significant differences that existed between the two cohorts in all the parameters relating to their perceptions of the curricula listed in Table 3. The Nigerian students were significantly more confident in knowing when and how to transition from intravenous to oral antibiotics compared to the South African students.

Teaching and learning methods

Most of the respondents in both countries felt that providing more formal lectures, more formal tutorials, more exposure to infectious disease specialists, provision of a local handbook/guideline on treating common infections to newly qualified doctors could help them to learn how to prescribe antibiotics appropriately (Table 4). Other important differences between the countries were in relation to learning from a microbiologist and a clinical pharmacologist. Surprisingly, most of the respondents in both countries did not agree that exposure to more applications for smart devices and computer-based tutorials would contribute to learning.

Knowledge about antibiotic use

In general, the two cohorts of respondents did not perform well in assessing the vignettes for appropriateness of decision making as shown in Supplementary Table 1. However, the South African respondents correctly answered most of the vignettes, compared to the Nigerian respondents. Of the 10 vignettes answered, South African respondents scored an average of 62.4% in the knowledge segment compared to 31.9% scored by the Nigerian respondents ($p=0.001$). Respondents in both countries did well on vignettes related to the management of HIV patients and respondents in both countries demonstrated a lack of knowledge in methicillin-sensitive *Staphylococcus aureus* and extended beta-lactamase *Escherichia coli* infections.

Table 3: Perceptions of curricula in relation to issues related to antibiotic use (n = 276).

	South Africa n (%)			Nigeria n (%)			Fischer's exact test (p-value)
	Good	Average	Poor	Good	Average	Poor	
How well do you feel that your medical school has prepared you for the following?							
Making an accurate diagnosis of infection	59 (56.7)	41 (39.5)	4 (3.8)	154 (89.5)	17 (9.9)	1 (0.6)	0.001
Knowing when to start antibiotics	51 (49.0)	47 (45.2)	6 (5.8)	144 (83.7)	25 (14.6)	3 (1.7)	0.001
Choosing the correct antibiotic for a specific infection	26 (25.0)	65 (62.5)	13 (12.5)	142 (82.6)	27 (15.7)	3 (1.7)	0.001
Knowledge of dosing and duration of antibiotic therapy for specific infection	26 (25.0)	57 (54.80)	21 (20.2)	128 (74.4)	39 (22.7)	5 (2.9)	0.001
How to de-escalate to narrow spectrum antibiotics	11 (10.6)	36 (34.60)	57 (54.8)	96 (55.8)	63 (36.6)	13 (7.6)	0.001
How and when to transition from intravenous to oral antibiotics	13 (12.5)	42 (40.4)	49 (47.1)	129 (75.0)	38 (22.1)	5 (2.9)	0.001
How to interpret antibiograms	6 (5.8)	30 (28.8)	68 (65.4)	76 (44.4)	50 (29.3)	45 (26.3)	0.001
Understanding the spectrum of activity of commonly used antibiotics	33 (31.7)	44 (42.3)	27 (26.0)	131 (76.2)	30 (17.4)	11 (6.4)	0.001
Understanding basic mechanisms of antibiotic resistance	62 (59.6)	40 (38.5)	2 (1.9)	131 (76.2)	30 (17.4)	11 (6.4)	0.001

Table 4: Ways in which newly qualified doctors could be better prepared to prescribe antibiotics (n = 276).

In what way could newly qualified doctors be better prepared to prescribe antibiotics?	South Africa n (%)	Nigeria n (%)	Chi-Squared Test (p-value)
More formal lectures			
Yes	56 (53.8)	108 (62.8)	0.16
No	48 (46.2)	64 (37.2)	
More formal bedside tutorials			
Yes	60 (57.7)	99 (57.6)	1.00
No	44 (42.3)	73 (42.4)	
More time in microbiology			
Yes	66 (63.5)	57 (33.1)	0.001
No	38 (36.5)	115 (66.9)	
More exposure to infectious diseases specialists			
Yes	70 (67.3)	98 (57.0)	0.10
No	34 (32.7)	74 (43.0)	
A local handbook/guideline on treating common infections			
Yes	65 (62.5)	100 (58.1)	0.53
No	39 (37.5)	72 (41.9)	
More applications for smart devices			
Yes	50 (48.1)	61 (35.5)	0.04
No	54 (51.9)	111 (64.5)	
More computer-based tutorials			
Yes	21 (20.2)	41 (23.8)	0.55
No	83 (79.8)	131 (76.2)	
More exposure to clinical pharmacologist			
Yes	77 (74.0)	86 (50.0)	0.001
No	27 (26.0)	86 (50.0)	

Discussion

The study findings identified a gap in knowledge in both groups, but more so among the Nigerian cohort; whilst both categories of respondents were found to have similar perceptions of antibiotic use and resistance.

Limitations of this study included the low response rate from the South African respondents and that it did not include all medical schools in both countries. There are 51 accredited medical schools in Nigeria and eight in South Africa, which means that the findings of this survey cannot be generalised.

The Nigerian cohort responded confidently that they were competent to prescribe antibiotics but performed poorly in the knowledge segment compared to the South African respondents. Previous studies have identified differences between medical schools.^[15,27] The results of a 2017 South African study by Wasserman *et al*,^[27] involving three South African medical schools including the medical school in this study, found that the students from this South African medical school performed poorly when compared to the other two South African universities. An informal discussion with the relevant stakeholders in medical education at the South African medical school revealed that in recent years, more emphasis on antibiotic prescribing has been included in the curriculum. This may explain why the South African respondents performed better than their Nigerian colleagues. Another possible reason why the Nigerian respondents performed poorly in the knowledge segment may be related to the manner in which the curriculum is taught. The South African curriculum is vertically integrated, while the Nigerian schools still implement a discipline-based curriculum.

Both South African and Nigerian respondents did well in questions that related HIV to tuberculosis and pneumonia; which may be explained by the prevalence of these infections in both countries.^[28-29] On the other hand, the respondents in both countries did poorly in questions involving the management of patients with methicillin-sensitive *Staphylococcus aureus* and extended beta-lactamase *Escherichia coli* infections.

Antibiotics are among the most commonly prescribed class of drugs in healthcare, both in the inpatient and outpatient setting.^[30] Almost all respondents from both countries acknowledged the importance of responsible antibiotic use and agreed that antibiotics are overused in their countries and that antibiotic resistance is a significant problem in their countries. Similarly, almost all the respondents from both countries would have liked further education on prudent antibiotic prescribing; which mirrors that reported in previous studies done in South Africa (95%), Europe (74%) and USA (78%).^[15,27,31]

The study findings suggest that prudent antibiotic prescribing and antibiotic stewardship should begin at the time when behaviour is being shaped. Education is crucial in improving appropriate antibiotic prescribing by changing the attitudes and improving the knowledge of the prescribers.^[30] The ability to prescribe antibiotics is expected of medical doctors immediately after leaving medical school and is a task they will encounter on a daily basis throughout their careers. This means that medical schools must ensure that their graduates are adequately

prepared, not only in general antibiotic use, but also how to use them prudently.^[32] Medical students should finish their undergraduate training with the mindset that antibiotics are a special class of drugs whose inappropriate use could not only affect the index patient, but the entire population.^[30] So, they should understand that their duty as antibiotic prescribers is to optimise the therapy for the patient they are treating; whilst at the same time preserving the efficacy of the drug to delay the development of resistance.^[32]

While the two groups of respondents used medical experts differently to learn, it was noted that healthcare designed apps are used more by the Nigerian respondents. A USA study found that most students referred to Wikipedia rather than text-books or peer-reviewed articles, and only a fraction referred to the Infectious Diseases Society of America guidelines.^[15] (Appendix S: a list of accredited Nigerian medical schools by the National Universities Commission, while Appendix T: a final year medical student's survey questionnaire).

Conclusion

In this study, the knowledge and perceptions of the final year medical students in two African countries was assessed. This was to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria the principles of prudent antibiotic prescribing. The objective of this study was to determine the knowledge and perceptions of the final year South African and Nigerian medical students from four medical schools on prudent antibiotic prescribing and principles of antibiotic stewardship. The respondents from both countries have similar perceptions of antibiotic use and resistance. However, a gap in knowledge is demonstrated between the respondents of the two countries and an effort must be made to bridge these gaps. It is recommended that Nigerian medical schools should consider changing their traditional curriculum to an integrated one, which is student-centred, facilitates life-long learning and the development of skills that will make them become self-directed learners for the rest of their lives.^[33-34]

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Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

Authors' contributions

Dr Bashar Muhammad Augie: Is a PhD candidate under the supervision of Dr Jacqui Miot, Prof Patricia A. McInerney and Prof Robyn L. van Zyl. He was involved in the design of the project, data collection, data analysis and the writing of the manuscript.

Prof Robyn L. van Zyl: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript.

Prof Patricia A. McInerney: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript.

Dr Jacqui Miot: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript.

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Supplementary Table 1: Knowledge about antimicrobial use (n = 267).

Knowledge about antimicrobial use	South Africa	Nigeria	p-value
	Correct answers		
Q1 A 24-year-old previously well woman presents to causality with dysuria and frequency. This is her first episode of this problem, which started about one day earlier. Clinically she is completely well without fever or signs of systemic illness. She has mild suprapubic tenderness, but no renal angle tenderness is elicited. A urine pregnancy is negative. A urine dipstick is positive for 3+ leucocytes and nitrites. Would you: a. Treat with intravenous gentamycin for 10 days b. Give a stat dose of intravenous ceftriaxone and then complete an oral course of antibiotics c. Prescribe 3 days of oral ciprofloxacin d. Send a urine culture and wait for results before prescribing antibiotics e. Treat with cotrimoxazole (Septrin™/Bactrim™) for 5 days	73 (70.2)	47 (27.3)	0.001
Q2 Which of the following antibiotics is appropriate for treating methicillin-sensitive <i>Staphylococcus aureus</i>? a. Vancomycin b. Cloxacillin c. Amoxicillin-clavulanic acid (Augmentin)® d. Ceftriaxone e. All of the above	47 (45.2)	32 (18.6)	0.001
Q3 A 34-year-old HIV-infected man presents to hospital with a 5 days history of productive cough, fever, pleuritic chest pain and shortness of breath. On examination, he is pyrexial, temperature 39.0°C, with a respiratory rate of 35 breaths per minute and bronchial breath sounds in the right middle zone. He is slightly confused but his blood pressure is normal. A chest X-ray confirms your suspicion of right middle lobe consolidation. Blood results show a urea of 10 mmol/L and white cell count of 20 x 10⁹ /L. Would you: a. Send a blood culture and start intravenous ceftriaxone b. Discharge on oral amoxicillin c. Start intravenous ertapenem after performing a blood culture d. Start empiric anti-tuberculous therapy e. Send a blood culture and start intravenous moxifloxacin	80 (76.9)	117 (68.4)	0.17
Q4 A resident of an old age home develops fever, confusion and renal angle tenderness. A urine dipstick shows 3+ leucocytes. You send blood and urine cultures and start empiric ertapenem for healthcare-associated pyelonephritis. After 48 hours your patient is alert and oriented and has been afebrile for a day. The cultures have grown <i>Escherichia coli</i> susceptible to ertapenem, amikacin and ciprofloxacin. Would you: a. Complete a full course of ertapenem because of excellent response b. Switch to oral ciprofloxacin c. Switch to intravenous ciprofloxacin d. Switch to amikacin because of better kidney penetration e. Stop all antibiotics because she has recovered fully	59 (56.7)	44 (25.7)	0.001
Q5 A 27-year-old man comes to your clinic complaining of a sore throat that started the previous day. A few of his colleagues have the same problem. On examination, he is not acutely ill but has a fever of 37.8°C, generalized lymphadenopathy and an inflamed pharynx with no pus on the tonsils. His chest is clear. How would you proceed? a. Prescribe penicillin VK for 10 days to prevent rheumatic fever b. Perform a blood culture and await the result c. Prescribe a 5-day course of amoxicillin	79 (76.0)	28 (16.4)	0.001

d. Perform a throat swab and give an antibiotic while awaiting the result. Treat symptomatically with bed rest, paracetamol and expectant management			
Q6 A patient is receiving intravenous fluids in the surgical ward for pancreatitis. On day 5 of his admission, he spikes a fever of 39°C with tachycardia and you find tenderness and erythema around his drip site. Would you: a. Do a 'septic screen' and await result of cultures b. Send cultures and prescribe empiric amoxicillin-clavulanic acid c. Prescribe cloxacillin for suspected drip site sepsis d. Take a blood culture and give a loading dose of vancomycin e. Take a blood culture and start ertapenem for hospital-acquired infection	53 (51.0)	13 (7.6)	0.001
Q7 An elderly man was recently discharged from hospital where he received clindamycin for cellulitis. He had a complete clinical response and is now on day 7 of this therapy but returns to the hospital with new onset of mucoid diarrhoea and fever. A stool specimen was sent and the microbiology lab calls to confirm your suspicion of <i>Clostridium difficile</i>-associated diarrhoea. He has a normal white cell count and creatinine, and there are no clinical signs of colitis. How would you manage this? a. Stop the clindamycin and add oral metronidazole b. Continue the clindamycin and add oral metronidazole c. Continue the clindamycin and treat symptomatically with loperamide (Imodium®) d. Give a course of ciprofloxacin for bacterial diarrhoea e. Give a combination of intravenous metronidazole and vancomycin	55 (52.9)	61 (35.7)	0.01
Q8 The lab calls with a result of a blood culture for extended beta-lactamase <i>Escherichia coli</i>. Which of the following antibiotics would you prescribe? a. Vancomycin b. Amoxicillin-clavulanic acid c. Ceftriaxone d. Piperacillin-tazobactam e. Ertapenem	49 (47.1)	26 (15.7)	0.001
Q9 A 60-year-old woman with rheumatoid arthritis is admitted for an elective knee replacement. The orthopaedic surgeon has prescribed prophylactic cefazolin for 5 days. He has decided to extend the duration beyond 24 hours "just for extra protection". What are the potential problems with prolonging prophylactic antibiotics? a. Encouraging antibiotic resistance b. Adverse drug reactions c. <i>Clostridium difficile</i> associated diarrhoea d. Increased risk of drip site infection e. All of the above	78 (75.0)	55 (32.7)	0.001
Q10 A 43-year-old male patient, known to be HIV positive with CD4 220. Has been unwell for 2 weeks with fever, loss of appetite and a dry cough. On examination, his temperature is 38.3°C, blood pressure 106/58mmHg, pulse 126, RR 22, oxygen saturations 96% on room air. Chest X-ray shows a subtle reticular-nodular pattern bilaterally. A blood culture is taken and he is started on ceftriaxone 1g per day and clarithromycin. After 3 days he says that he is not feeling better, his temperature and pulse remain elevated. The blood culture remains negative at this point. What would you do next? a. Continue ceftriaxone at current dose b. Change to ertapenem c. Stop antibiotics and investigate for tuberculosis d. Change to ciprofloxacin e. Increase dose of ceftriaxone to 2g 12-hourly	76 (73.1)	118 (70.7)	0.68

CHAPTER FOUR

A summative content analysis of two African medical schools' antibiotic stewardship curricula

Augie, B. M., van Zyl R. L., Miot, J. and McInerney, P. A.

“We have reached a critical point and must act now on a global scale to slow down antimicrobial resistance” (Cruz & Peter, 2020, p. 704)

Professor Dame Sally Davies,
Former UK Chief Medical Officer

An abbreviated version of the manuscript has been submitted to Education for Health for publication on January 31, 2022 (manuscript ID efh_34_22) – still under review. The full version is included here to present the full scope of work undertaken to achieve objective 3: To explore the content of the Nigerian and South African medical curricula in relation to antibiotic teaching.

Abstract

Objective

The objective of this study was to describe the content of South African and Nigerian medical students' curricula with respect to prudent antimicrobial prescribing.

Methods

A summative content analysis framework was used to identify, describe and count the keywords, key phrases and sentences relevant to the teaching of prudent antimicrobial prescribing in the complete curricula content of two African countries medical schools. The courses are taught in the Graduate Entry Medical Programme curriculum of the South African medical school and years 4-6 of the Nigerian medical school. The frequency of keywords/key phrases relevant to prudent antibiotic prescribing such as AMS, mechanisms of bacterial resistance and principles of antibiotic therapy was determined.

Results

The two curricula reviewed were found to be different. While the South African medical school uses an integrated curriculum in MBChB 3-6, the Nigerian medical school operates a traditional (discipline-based) curriculum from MBBS 1-6. There was a difference in the number of keywords between the two countries. There are more keywords and key phrases in the South African curriculum (30) compared to the Nigerian curriculum (9) in relation to prudent antibiotic prescribing and AMS. The key phrase ‘antimicrobial stewardship’ or ‘antibiotic stewardship’ was absent in the Nigerian curriculum but appeared four times in the South African curriculum.

Conclusion

The findings of this summative content analysis suggest a need for revision of the medical curricula of the two countries, to one that will better prepare learners for AMS.

Keywords: Africa; antimicrobial resistance; antimicrobial stewardship; curriculum; medical schools; medical students

Introduction

The discovery of antibiotics is undoubtedly one of the major advancements of science in the 20th century. The discovery of the first antibiotic ‘penicillin’ in 1928 by Alexander Fleming has saved millions of lives, especially during World War II. Antibiotics also transformed medical practice by playing a role in the management of infectious diseases, cancer chemotherapy and organ transplantation (Barlam et al., 2016; Gaynes, 2017). However, the emergence of antimicrobial resistance (AMR), which is one of the major global threats affecting public health and economic stability, is affecting this initial success (Barlam et al., 2016; Nathwani et al., 2019). AMR occurs due to inappropriate antimicrobial use that can result from overuse, underuse, abuse and misuse of antimicrobial agents (Hand, 2013). The United Kingdom (UK) commission report predicted that if left unchecked by 2050, AMR has the potential to cause 10 million deaths annually, of which 4.1 million will come from Africa. It will also result in a loss to the global economy of 100 trillion US dollars by 2050 (O'Neill, 2014; 2016). Similarly, a 2017 World Bank report which examined the economic and development consequences of AMR indicated that, if not addressed, AMR will push more than 28 million additional people into extreme poverty by 2050 (World Bank, 2017). Most of these people will be from low- and middle-income countries (World Bank, 2017). Until something is done urgently, the world is

heading towards a post-antibiotic era where people will die from simple bacterial infections that were previously curable (Wang et al., 2020).

Antimicrobial stewardship programmes (ASPs) are one of the strategies that encourage responsible antibiotic use, thereby reducing AMR. The aim of ASPs is to optimise antimicrobial therapy, reduce inappropriate antibiotic use and collateral damage (Davey et al., 2013). Making an informed decision to use antibiotics appropriately is a complex process that involves among other things understanding the pharmacokinetic and pharmacodynamic (PK/PD) principles of antibiotics (Onufrak et al., 2016). Education is viewed as an important tool in shaping prescribing behaviour and encouraging prescribers to accept and adopt ASPs (Dellit et al., 2007). Most of the educational ASPs are implemented at the postgraduate level and among practising physicians, with the hope of changing their behaviour. Little emphasis has been given to teaching prudent antibiotic prescribing to medical students (Pulcini and Gyssens, 2013). It is suggested that medical schools incorporate courses on antimicrobial stewardship to ensure that aspiring doctors acquire basic skills on prudent antibiotic prescribing at an early stage of their careers (Brinket al., 2017).

The World Health Organization has stressed the importance of incorporating courses on prudent antimicrobial prescribing in medical schools' curricula (WHO, 2001). In order to produce doctors who have a good understanding of both general and prudent antibiotic use, there is a need to incorporate courses on AMS into medical schools' curricula at the time when their knowledge and behaviour is being shaped (Pulcini and Gyssens, 2013). A survey that examined the inclusion of antibiotic stewardship courses across the United States of America (USA) medical schools in their preclinical microbiology curricula showed that only 66% of schools include such courses (Melber et al., 2016). Conversely, surveys conducted across medical schools in different parts of the world on appropriate antibiotic use show that medical students acknowledge antibiotic resistance as a problem in their career and 74% to 95% of them desire further education on prudent antibiotic prescribing (Abbo et al., 2013; Dyar et al., 2014; Wasserman et al., 2017). In its effort to encourage the culture of appropriate antibiotic prescribing among aspiring doctors across medical schools in the UK the General Medical Council in 2009 highlighted the importance of integrating courses on responsible antibiotic prescribing into medical schools' curricula (McNulty et al., 2012). Medical schools across the UK have developed courses on prudent antibiotic prescribing (Davenport et al., 2005) and the USA (Hsu, 2018; MacDougall et al., 2017; Nori et al., 2017; Shekarchian et al., 2016; Wake

Forest School of Medicine, n.d). The same cannot be said about medical schools in Africa, where many countries still use the traditional curriculum adopted from the West decades ago to teach medical students despite innovations in teaching and learning in medicine over the years (Gukas, 2007). South Africa is probably the most advanced nation on the African continent as far as innovations in medical education are concerned (Gukas, 2007). Our scoping review which maps available evidence on AMS in medical schools did not find any literature on an ASP in any African medical school (Augie et al., 2021a). According to South African authors “A key strategy in facilitating appropriate antibiotic prescribing is the early introduction of the relevant knowledge, concepts and skills into undergraduate curricula” (Brink et al., 2017, p. 358).

Medical doctors are expected to start prescribing antibiotics upon graduation and will continue to do so throughout their career (WHO, 2018). Hence, the need to incorporate courses on prudent antibiotic prescribing and AMS into the medical school curriculum. This led the authors to question the content of medical schools’ curricula in relation to the use of keywords and phrases related to responsible antibiotic prescribing such as ‘antimicrobial stewardship’, and ‘principles of antibiotic therapy’. The objective of this study was to describe the content of the South African and Nigerian medical students’ curricula with respect to prudent antimicrobial prescribing. Identifying these concepts in the curricula will help in the development of an educational antibiotic stewardship programme for medical schools.

Materials and methods

Study design

This study used a summative content analysis framework as described by Hsieh and Shannon (2005) to identify and count the keywords, key phrases and sentences relevant to rational antimicrobial teaching in the curricular content of two African medical schools. Four disciplines (pharmacology, microbiology, medicine and surgery) were chosen because they are likely areas where antimicrobials will be taught. The summative content analysis technique involves identifying and counting the number of times a keyword, key phrase or sentence appears in a document or text and interpreting the context in which they were used (Hsieh and Shannon, 2005). For instance, how many times does the phrase ‘antimicrobial stewardship’ appear in a curriculum? This method was used because the curricula texts mostly consist of lists of words and sentences. Our inquiry intended to determine all the keywords in the curricula documents and the presence and frequency of keywords, key phrases and sentences relevant to prudent antibiotic use in the two curricula and attempt to infer meaning for their usage. They include

antibiotic(s), AMS, mode of bacterial resistance, mechanisms of bacterial resistance, mechanisms of antimicrobial resistance, rational choice of antibiotics, principles of antibiotic therapy, principles of anti-infective therapy and principles of dose optimisation in the context of antimicrobial therapy. Four categories, namely medical knowledge, surgical knowledge, practical knowledge and contextual knowledge, were identified beforehand after reviewing the curricula content and were agreed upon by the authors. The keywords were arranged and interpreted based on their affinity to fit into a category. Then the keywords in each category were grouped together based on their similarity to form subcategories (Sjölin et al., 2015). Subsequently, the keywords, key phrases and sentences were counted to show their distribution within the subcategories and categories (Sjölin et al., 2015). The study was based on our assumption that the presence of these keywords, key phrases and sentences in the curriculum is central to an understanding of prudent antibiotic use.

Summative content analysis

Summative content analysis requires more than the counting of keywords. It also involves latent content analysis (Hsieh and Shannon, 2005), which involves a process of interpretation of content (Holsti, 1969). Manifest content analysis refers to the analysis of what the text says and deals with the content aspect and describes the visible, obvious components of the text (Downe-Wamboldt, 1992; Kondracki, et al., 2002). On the other hand, latent content analysis describes what the text talks about and deals with the relationships that exist between keywords and also involves an interpretation of the underlying meaning in the text (Downe-Wamboldt, 1992; Kondracki et al., 2002). Keywords were sorted into categories and subcategories not only because of their similarity, but to create knowledge and understanding of how they were associated (Cavanagh, 1997; Sjölin et al., 2015). The two forms of content analysis refer to interpretation, but at different levels and depth and level of abstraction (Graneheim and Lundman, 2004). Our study involved both types of analysis i.e., determining the presence and frequency of keywords or key phrases such as ‘antimicrobial stewardship’ and ‘principles of antibiotic therapy’ and attempted to interpret their usage in the text. The process helped us to identify the strengths and weaknesses of the curricula with respect to the teaching of responsible antibiotic prescribing to aspiring doctors and what should be included in a proposed antibiotic stewardship curriculum.

Data extraction from the curricula

Data were generated from the review of the medical students’ curricula of one South African and one Nigerian medical school; where there are 51 and 8 accredited medical schools in

Nigeria and South Africa, respectively. The curricula of these medical schools were selected because their final year students had previously participated in a survey that aimed to identify gaps in knowledge of prudent antibiotic use with a view to develop a programme to strengthen undergraduate antibiotic teaching and optimise prescribing practice. Permission was granted to access the curricula of the two medical schools in South Africa and Nigeria. The part of the curricula analysed cut across years 3-6 of the medical school that involved the Graduate Entry Medical Programme (GEMP) of the South African medical school and years 4-6 of the Nigerian medical school. The text reviewed included pharmacology, microbiology, medicine and surgery courses where topics related to antibiotics are taught. In the course content of disciplines such as anatomy, physiology and morbid anatomy, antibiotic related topics are less likely to be discussed and were therefore not included in the analysis.

Data analysis

Content analysis is a flexible method for analysing text data such as a curriculum (Cavanagh, 1997). However, there are no systematic rules for analysing data using content analysis, but the guiding principle of the technique is that several words within the text are classified into much smaller content categories (Burnard, 1996; Weber, 1990). Higher institutions of learning organise their educational programmes into courses and each course has its curriculum, with a segment of the curriculum describing how it will be delivered and assessed. According to the General Medical Council of the UK, “a curriculum is a statement of the intended aims and objectives, content, experiences, learning outcomes and processes of a programme or course of learning, including a description of the structure and expected methods of learning, teaching, assessment, feedback and supervision. The curriculum should set out a programme of learning and specify what learning outcomes the learner will achieve” (General Medical Council, 2017, p. 32-33).

The process of data analysis used in this study is based on that described by Sjölin et al. (2015). The analysis process followed four steps (Figure 1). In the first step, we read the course content several times to understand how the words were used in the curricula. Lecture presentations, text books, tutorials, bedside presentations and methods of teachings used in delivering the content of the curricula to students were not analysed. In the second step, the course content of the curriculum were split into units of analysis (Table 1), which made it easy to identify keywords, key phrases and sentences relevant to prudent antibiotic prescribing if present in the curricula, such as ‘antimicrobial stewardship’ and ‘principles of antibiotic therapy’. The units

of analysis were transferred into a word document. Depending on the research question, the unit of analysis can be a letter, word, sentence, portion of pages or words, the number of participants in discussion or the time used for discussion (Ronson, 1993; Polit and Beck, 2004). In the third step, keywords and key phrases were identified and counted. All the keywords in the curricula were counted regardless of whether they were related to the research question or not (Table 2). Absolute frequency is determined by counting the number of times a keyword or key phrase appeared in the curriculum from each medical school (Edling and Mooney Simmie, 2018). The fourth step of the analysis was conducted by sorting out the keywords. Similar keywords, key phrases or sentences were placed into categories and subcategories irrespective of whether they originally belonged to pharmacology, microbiology, medicine or surgery. The process of sorting and placing keywords into different categories and subcategories involved an iterative process and all authors participated and contributed. There was an agreement between authors on what should go into each category and subcategory and ambiguities that arose during the process were resolved through discussion among authors.

Counting and interpretation of keywords, key phrases, and sentences

Historically, content analysis was used as an objective and neutral method to develop quantitative data from a review of documents or communication and counting the number of times a keyword or a term appeared in a document (Berelson, 1952). However, the process has evolved over time and today it has gone beyond a mere word count to involve interpretation of the counted words. An analysis that stops at counting keywords is a purely quantitative process (Kondracki et al., 2002). As Busch *et al.* notes “researchers quantify and analyse the presence, meanings and relationships of such words and concepts, then make inferences about the messages within the texts, the writer(s), the audience, and even the culture and time of which these are a part” (Busch et al., 2005, p. 2). In content analysis, a text can be defined broadly as books, book chapters, essays, interviews, discussions, newspaper headlines and articles, historical documents, speeches, conversations, advertising, theatre, informal conversation, or any form of communicative language (Busch et al., 2005). This justified the use of this methodology in analysing the curricular content. Counting keywords helps to identify patterns, frequencies, and their distributions in a text document (Marshall and Roman, 2014). Interpretation provides insight, meaning, patterns and coherence to the keywords as they were

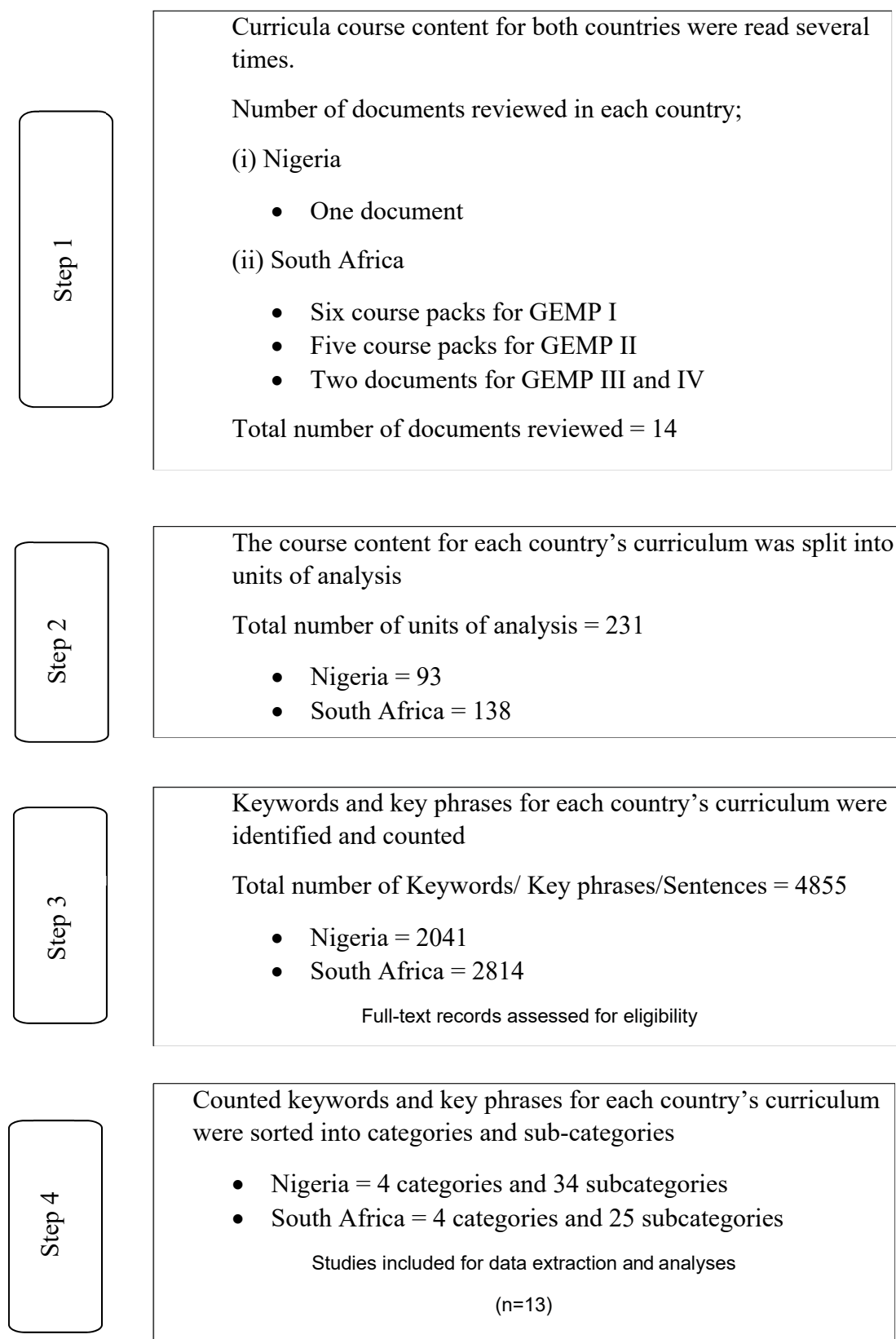


Figure 1: Four steps of data analysis to achieve objective 3.

used in the text (Hsieh and Shannon, 2005). According to Patton “interpretation means attaching significance to what was found, making sense of the findings, offering explanations,

drawing conclusions, extrapolating lessons, making inferences, considering meanings, and otherwise imposing order on an unruly but surely patterned world.” (Patton, 2014, p. 801).

Ethics

The study forms part of a bigger project that received ethics clearance from the University of the Witwatersrand Human Research Ethics Committee (Medical) (Clearance number: M1902108).

Results

The two curricula reviewed were very different. While the South African medical school curriculum is integrated in GEMP, the Nigerian medical school uses a traditional (discipline-based) curriculum throughout the years. The differences between the two curricula are highlighted in Table 4. The courses reviewed are taught in the GEMP curriculum of the South African medical school and in years 4-6 of the Nigerian medical school. In both countries, the medical degree is six years for students coming directly from high schools. The South African medical school has a GEMP stream where candidates with undergraduate degrees are enrolled into the third year of medical school to spend four years. There is no GEMP stream in the Nigerian medical schools but they have a Direct Entry Programme where candidates with an A level organised by the Joint Interim Matriculation Board are admitted into the second year of medical school to spend five years of study. The analysis did not involve the years of internship and speciality training. Table 1 shows an example of how the content of the two curricula was split into units of analysis from which keywords were generated. The analysis of the two curricula shows a difference in the number of keywords. There are more keywords and key phrases in the South African curriculum (2814) compared to the Nigerian curriculum (2041). Similarly, there are more keywords and key phrases relevant to prudent antibiotic prescribing in the South African curriculum compared to the Nigerian curriculum (Table 3). For instance, the key phrases ‘antimicrobial stewardship’ or ‘antibiotic stewardship’ were absent in the Nigerian curriculum.

Categories and their subcategories

The number of keywords, key phrases or sentences in each category and subcategory are summarised in Table 2. There are four categories in each medical school with 25 and 34 subcategories in the South African and Nigerian medical schools, respectively. The medical category contains 1999 and 1307 keywords and phrases in the South African and Nigerian

curricula, respectively. These were used in the curricula to describe the medical knowledge, perceptions and skill domains which medical students should know to be able to effectively manage different medical conditions. In both countries, the medicine subcategory (South Africa, n = 744; Nigeria, n = 452) had the highest number of keywords that were used to describe the different medical conditions, their clinical presentation, diagnoses and management. In both countries, the microbiology subcategory, had the second highest number of keywords (South Africa, n = 599; Nigeria, n = 417). Keywords such as ‘antimicrobial resistance’ and ‘principles of antibiotic therapy’ were found in both countries. In the South African curriculum, the keyword ‘antimicrobial stewardship’ appeared four times in the microbiology curriculum, but none was found in the Nigerian curriculum at all. The pharmacology subcategory is consistent with that of microbiology in terms of the number of keywords (South Africa, n = 523; Nigeria, n = 347). The subcategory contains keywords that explain pharmacokinetic and pharmacodynamic principles, mechanism of actions, interactions and side effects of drugs. Keywords that describe antimicrobial agents and their indication, **AMR** and rational antibiotic use were found, but the keyword ‘antimicrobial stewardship’ was not found. More keywords on clinical skills were found in the South African curriculum (76) compared to the Nigerian curriculum (21). Keywords in clinical skills described competencies such as demonstration of physical examinations, suturing techniques, the ability of students to elicit clinical signs and communication skills.

The surgical category contained 787 and 446 keywords and phrases in the South African and Nigerian curricula, respectively; where they were used in the curricula to describe basic surgical knowledge and skills required of medical students to diagnose and manage surgical conditions. In both countries, the general surgery subcategory had the largest number of keywords (South Africa, n = 154; Nigeria, n = 121). The keywords described principles of diagnoses and management of surgical conditions such as hernia, acute appendicitis, subcutaneous wounds and cholecystitis. Orthopaedic surgery had the second highest number of keywords in both countries (South Africa, n = 127; Nigeria, n = 75) and the keywords were used to describe conditions such as fractures, joint dislocation and how to diagnose and manage orthopaedic conditions conservatively and surgically.

Table 1: Example of units of analysis and identification of keywords and key phrases.

Units of analysis	Keywords	Curriculum
Principles of Anti-infective therapy 2- Antimicrobial Stewardship - Define antimicrobial stewardship and the desired outcomes of this intervention. - Discuss various antimicrobial stewardship strategies. - List and describe the important pharmacodynamic parameters associated with antimicrobial therapy. List and describe the important pharmacokinetic considerations in antimicrobial prescription Discuss the principle of dose optimization in the context of antimicrobial therapy and stewardship	- Principles of Anti-infective therapy - Antimicrobial Stewardship - Define antimicrobial stewardship - Desired outcome of antimicrobial stewardship - Various antimicrobial stewardship strategies - Important pharmacodynamic parameters - Antimicrobial therapy - Important Pharmacokinetic considerations - Antimicrobial prescription - Principle of dose optimization - Antimicrobial therapy - Antimicrobial stewardship	From microbiology curriculum of the South African medical school
The development and cultivation of medically important viruses. Basic properties; and classification of viruses, systemic differences of viruses. Description and identification of the following viruses” Influenza virus, polio virus, Small Pox virus, Measles virus, Yellow fever virus, Lassa fever virus, Bunya-, REO-, Hepadna-, Parvo, Arena, Toga-, Adeno-, Corona-, Picorna-, rhabdo-, myxo-viruses, <i>Rubella</i> virus, Dengue virus, <i>Herpes</i> virus, Hepatitis viruses. DNA virus RNA virus, unclassified viruses, slow virus oncogenic viruses. Viral immunotherapy and prophylaxis, arboviruses. Viral haemorrhagic fevers, viral gastroenteritis viral encephalopathy, paralysis meningitis.	- Development of medically important viruses - Cultivation of medically important viruses - Basic properties of viruses - Classification of viruses - Systemic differences of viruses. - Description of Influenza virus - Identification of Influenza virus - Description of polio virus - Identification of polio virus - Description of Small Pox virus - Identification of Small Pox virus - Description of Measles virus - Identification of Measles virus - Description of Yellow fever virus - Identification of Yellow fever virus - Description of Lassa fever virus - Identification of Lassa fever virus - Description of Bunya viruses - Identification of Bunya viruses - Description of Reoviruses - Identification of Reoviruses - Description of Hepadnaviruses	From microbiology curriculum of the Nigerian medical school

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- Identification of Hepadnaviruses
 - Description of Parvoviruses
 - Identification of Parvoviruses
 - Description of Arenaviruses
 - Identification of Arenaviruses
 - Description of Togaviruses
 - Identification of Togaviruses
 - Description of Adenoviruses
 - Identification of Adenoviruses
 - Description of Coronaviruses
 - Identification of Coronaviruses
 - Description of Picorna-viruses
 - Identification of Picorna-viruses
 - Description of rhabdo-virus
 - Identification of rhabdo-virus
 - Description of myxo-virus
 - Identification of myxo-virus
 - Description of Rubella virus
 - Identification of Rubella virus
 - Description of Dengue virus
 - Identification of Dengue virus
 - Description of Herpes virus
 - Identification of Herpes virus
 - Description of Hepatitis viruses
 - Identification of Hepatitis viruses
 - DNA virus
 - RNA virus
 - Unclassified viruses
 - Slow virus
 - Oncogenic viruses.
 - Viral immunotherapy
 - Viral prophylaxis
 - Arboviruses
 - Viral haemorrhagic fevers
 - Viral gastroenteritis
 - Viral encephalopathy
-

-
- Viral paralysis
 - Viral meningitis
-

Table 2: Comparison of the counted keywords, key phrases and sentences between South African and Nigerian curricula.

South Africa				Nigeria			
Category	n	Subcategory	n	Category	n	Subcategory	n
Medical knowledge				Medical knowledge			
		Pharmacology	523			Pharmacology	347
		Medicine	744			Medicine	452
		Microbiology	599			Microbiology	417
		Haematology	30			Haematology	25
		Ethics	2			Clinical skills	21
		Clinical skills	76			Ethics	45
		Public health	25			-	-
	1999	Sub-Total			1307	Sub-Total	
Surgical knowledge		General surgery	154	Surgical knowledge		General surgery	121
		Trauma	101			Paediatric surgery	16
		Plastic surgery	16			Cardiothoracic surgery	15
		Urology	44			Plastic surgery	11
		Orthopaedics	127			Vascular surgery	8
		Neurosurgery	11			Urology	13
		Anaesthesia	1			Orthopaedics	75
		Otorhinolaryngology	89			Neurosurgery	16
		Ophthalmology	137			Anaesthesia	35
		Radiology	107			Otorhinolaryngology	60
		-	-			Ophthalmology	73
		-	-			Radiology	3
	787	Sub-Total			446	Sub-Total	
Practical knowledge		Pharmacology practical	6	Practical knowledge		Pharmacology practical	10
	6	-	-		147	Microbiology practical	137
Contextual knowledge		Global health	1	Contextual knowledge		Global health	15
		Interprofessional collaboration	2			Interprofessional collaboration	11
		Environment	10			Continuing medical education	5
		Learning	8			Environment	4
		Equality	1			Learning	49
		-	-			Technology	13
		-	-			Disaster management	12
		-	-			Immigration	5
		-	-			Family	8
		-	-			Economics	3
		-	-			Equality	11
	22	-	-		141	Family planning	5
Total	2814				2041		

n = number of keywords / key phrases

Table 3: Comparison between South African (2019) and Nigerian (from Student's Handbook Revised October, 2016) curricula as regards the frequency of the keywords, key phrases and sentences relating to teaching prudent antibiotic use, and their absolute frequency.

Keywords/key phrases/sentences	South Africa	Nigeria
	Absolute frequency	Absolute frequency
Antimicrobial stewardship	3	0
Mode of bacterial resistance, mechanisms of bacterial resistance, mechanisms of antimicrobial resistance	16	1
Rational choice of antibiotics, principle of antibiotic therapy, principle of anti-infective therapy	2	2
Principle of dose optimisation in the context of antimicrobial therapy	1	0
Total	22	3

In South Africa, the subcategories ophthalmology (n = 137) and trauma (n = 101) followed with the largest number of keywords compared to Nigeria where ophthalmology had 73 and otorhinolaryngology had 60 keywords. They were used to describe how to manage eye and ear conditions such as cataracts, glaucoma, conjunctivitis, otitis media, tonsillitis, foreign body removal and trauma cases.

The practical knowledge category contained 6 and 147 keywords and phrases in the South African and Nigerian curricula, respectively. They were used in the curricula to describe how students should be able to demonstrate practical skills such as the preparation of Gram stains. In the Nigerian curriculum, 137 and 10 keywords were used to describe microbiology and pharmacology practical knowledge, respectively; while in the South African curriculum six keywords were found in relation to pharmacology practical knowledge. The keywords were used in the curricula to describe students' ability to demonstrate laboratory skills. The Nigerian contextual category contained 141 keywords compared to 22 keywords in the South African curriculum. The keywords in this category described knowledge and skills students are likely to use outside clinical settings. Subcategories such as disaster management (12 keywords), immigration (five keywords) and economics (three keywords) were found in the Nigerian curriculum, but were not found in the South African curriculum.

Table 4: Nigerian versus South African medical curricula.

Year	Nigerian medical school				South Africa medical school			
	Courses	Nature of curriculum	Assessment	Course name	Courses	Nature of curriculum	Assessment	Course name
Year One	Biology, Chemistry, Physics, Mathematics, Introductory Genetics and Introductory Parasitology	Discipline-based curriculum	Semester examination	MBBS 1	Introduction to Medical Science I Chemistry I Physics I Psychological Foundations of Health Sociological Foundations of Health Medical Thought and Practice I First Aid Computer Literacy	Discipline-based curriculum	Semester examination	MBBCh 1
Year Two	Human Anatomy, Physiology, Medical Biochemistry, Community Health	Discipline-based curriculum	End of course tests and Pre-MBBS promotional examination in Anatomy, Physiology and Medical Biochemistry	MBBS 2	Human Anatomy Physiology and Medical Biochemistry I Molecular Medicine	Discipline-based curriculum	Semester examination	MBBCh 2
Year Three			End of course tests and 1 st Professional MBBS examination in Anatomy, Physiology and Medical Biochemistry after three semesters. Exams include Essay	MBBS 3	GEMP 1 consist of six Blocks: Basic Concepts in Medicine and Health 1 Basic Concepts in Medicine and Health 2 Haematology Respiratory Cardiovascular System Renal. GEMP II consist of five Blocks: Neurosciences, Musculoskeletal,	Vertically integrated	6 blocks tests including MCQ, Part 1 OSCE, and End of Year Exam and Part 2 OSCE. GEMP I have 6 critical medical science subject group tracks: 1. Pathology (Anatomical, Haematological, Chemical, Genetics, Immunology)	MBBCh 3 / GEMP 1

			type/ or short answers, MCQ, Practical examinations and Viva Voce.	Gastrointestinal tract and Nutrition, Endocrine, Reproduction.	2. Microbiology (Bacteriology, Virology, Mycology, Parasitology) 3. Pharmacology (Basic Pharmacology, Clinical Pharmacology) 4. Basic Sciences (Anatomy, Physiology) 5. Clinical Sciences (Medicine, Obstetrics and Gynaecology, Surgery, Paediatrics, Neurosurgery, Neurology, Orthopaedics, Psychiatry, Ophthalmology, Otorhinolaryngology) 6. Themes (PD theme including Clinical Skills, Personal and Professional Development theme including Evidence Base Medicine, Biostatistics, CD theme - Community Health)
Year Four	Introductory Medicine I, Introductory Medicine II, Introductory Surgery, Psychiatry, Medicine I, Surgery I (General Surgery, Trauma and Emergency Surgery, GIT Surgery, Congenital Surgery), Community Health, Rural PHC Rotation, Pharmacology and Therapeutics (General Pharmacology, Systemic Pharmacology),	Discipline-based curriculum	End of course tests and 2nd Professional MBBS examination in Medical Microbiology, Pharmacology and Pathology. Exams include Essay type/ or short answers, MCQ, Practical examinations and Viva Voce.	MBBS 4	5 blocks tests including MCQ, Part 1 OSCE, and End of Year Exam and Part 2 OSCE MBBS Ch 4 / GEMP 2

	Microbiology (Bacteriology, Virology, Mycology, Parasitology, Helminthology, Applied Medical Microbiology, Medical Entomology) Pathology (Chemical Pathology, Morbid Anatomy and Forensic Medicine, Haematology)							
Year Five	Medicine II (Cardiology I, Respiratory Medicine I, Gastroenterology I, Haematology (Clinical), Metabolic and Endocrine Medicine, Neurology I and Nephrology I) Surgery II (Paediatric Surgery, Cardiothoracic Surgery, Burn and Plastic Surgery, Vascular Surgery, Endocrine Surgery), Radiology, Psychiatry, Paediatrics and Obstetrics and Gynaecology, Community Health.	Discipline- based curriculum	End of course tests and Part I Final professional MBBS in Paediatrics, Obstetrics, Gynaecology. Exams include Essay type/ or short answers, MCQ, Clinical examinations and Viva Voce.	MBBS 5	Integrated Clinical Medicine A is divided into seven rotational clinical blocks: Obstetrics APC (Anaesthesia/Trauma/Em ergency Medicine) Surgery Mixed I ((Urology/Ophthalmolog y/ Otorhinolaryngology (ENT)) Internal Medicine Paediatrics Mixed II (Family Medicine, Psychiatry Public Health)	Integrated curriculum	blocks tests and End of Year Exam,	MBBCh 5 / GEMP 3
Year Six	Psychiatry, Community Health and Research Project, Medicine III (Cardiology II,	Discipline- based curriculum	End of course tests and Part II Final professional MBBS in	MBBS 6	Integrated Clinical Medicine B is divided into seven rotational clinical blocks	Integrated curriculum	blocks tests and End of Year Exam	MBBCh 6 / GEMP 4

Respiratory Medicine
II, Gastroenterology II,
Nephrology II,
Rheumatology,
Clinical Immunology,
Tropical Medicine and
Infections, Special
Topics and Neurology
II, Dermatovenereology,
Medical Ethics and
Jurisprudence,
Traditional Medicine
and Telemedicine,
Surgery III (Urology,
Rural Surgery,
Neurosurgery,
Urology, Anaesthesia,
Ophthalmology,
Otorhinolaryngology
(ENT), Orthopaedics,
and Special topics in
Surgery)
Radiology

Medicine,
Surgery and
Community
Health. Exams
include
Essay type/ or
short answers,
MCQ, Clinical
examinations and
Viva Voce.

as well as two learning
components:
Internal Medicine
Paediatrics
Mixed
(Orthopaedics/Internal
Medicine)
Psychiatry
Gynaecology
Integrated Primary Care

Discussion

The objective of this study was to describe the content of the South African and Nigerian medical students' curricula with respect to prudent antimicrobial prescribing. This was to help gather relevant information from the curricula to be used in the development of an antibiotic stewardship curriculum for teaching appropriate antibiotic prescribing to medical students in South Africa and Nigeria. Before transforming antibiotic curricula in medical schools, there is a need for a comprehensive understanding of the content of the curriculum and antibiotic teaching medical students are receiving. The two curricula were different in design, where the South African curriculum was integrated in GEMP 1-4, compared to the Nigerian curriculum one that was traditional (discipline-based) without integration. This difference in curricula may have implications for how students learn the various concepts of prudent antibiotic prescribing. In a discipline-based curriculum, the different disciplines are compartmentalised and students learn content in silos and it encourages rote learning and memorisation of concepts (Dujeepa et al., 2019). The General Medical Council of the UK which used to be the regulator of medical training and supervised the establishment of the first medical school in Nigeria before it got its independence in 1960 (Ibrahim, 2007), advocates for the use of an integrated curriculum in medical schools instead of the traditional one (General Medical Council, 1993). Nigerian medical schools have continued to follow the Flexinarian approach to medical education in the 21st century despite transformations and innovations in the field (Frenk et al., 2010).

As shown in Table 2 there are more keywords related to prudent antibiotic prescribing in the South African curriculum compared to the Nigerian curriculum. Although the number of keywords used does not translate into how the concepts are taught, it provides information on the distribution and emphasis given to such topics in the curriculum. It is not surprising that the key phrase 'antimicrobial stewardship' was not found in the Nigerian curriculum because the phrase was first coined in 1996 (McGowan Jr and Gerding, 1996), and Nigerian medical schools use a curriculum developed by the English academics in the 1940s, with little modification (Ibrahim, 2007). The presence of fewer keywords related to prudent antibiotic prescribing in both curricula could explain the gap in knowledge identified in a recent study that aims to examine the knowledge and attitude among South African and Nigerian final year medical students on antimicrobial use, AMR and antibiotic stewardship (Augie et al., 2021b). In that study, many Nigerian final year medical students are not familiar with the term AMS.

There is a difference in the distribution of keywords across the four categories, with the medical category having the highest number of keywords in both countries, which suggests that more emphasis is given to medical knowledge compared to other concepts that fall within the realm of surgical, practical and contextual knowledge. Subcategories such as medicine, microbiology and pharmacology where topics on prudent antibiotic prescribing are likely to be taught have the highest number of keywords in both countries, but only a few of the keywords are related to topics on responsible antibiotic prescribing. This means that little emphasis is given to teaching prudent antibiotic prescribing in both countries. AMR is one of the factors making pharmaceutical industries shift their attention away from the development of new classes of antibiotics towards research and the development of drugs used in the treatment of chronic conditions (Luepke et al., 2017). Hence, the need for curriculum developers to include topics on **AMS** to equip the medical students with adequate knowledge and skills on rational antibiotic prescribing to be able to manage the available antibiotics.

The South African medical school had more keywords compared to the Nigerian medical school. This is probably because the South African medical school's curriculum has undergone modifications over the years. Some South African medical schools have dedicated Units for Undergraduate Medical Education mostly headed by medical educators, who regularly review and innovate the curriculum. On the other hand, Nigerian medical schools do not have such units (Olasoji, 2014). Nigerian medical schools are mostly headed by clinicians who have little background in teaching and learning in higher education. Ibrahim (2007, p. 904) states that "It would not be an exaggeration to say that the medical teachers in Nigeria are vastly untrained in teaching methods". In an unpublished small survey, he conducted among young academics at Bayero Medical School Nigeria, only about 10% of the respondents had heard of 'medical education' as a field of speciality. Most of them had not heard of newer methods of teaching in health sciences such as problem-based learning, ambulatory teaching, case-based learning, outcome-based education, and task-based learning, and most of them were not familiar with simulated patients or clinical skills centres (Ibrahim, 2007).

Study limitation

One of the limitations of this study is that the reviewed curriculum from each country is not representative of other medical schools in the two countries. However, according to Ibrahim (2007) in Nigeria, almost all medical schools without exception use a traditional curriculum developed by the English academics in the 1940s. Interaction with academics teaching across

Nigerian medical schools revealed that they still use the same type of curriculum. The same cannot be said about South African medical schools that use an integrated curriculum. In spite of that, the reviewed curricula provided us with sufficient relevant information to be able to extract keywords relevant to prudent antibiotic prescribing. While the counted keywords, key phrases and sentences provided us with information about their relative importance in the curricula, they did not explicitly provide us with data related to teaching methods used. The integrated nature of the South African curriculum made it difficult to separate it into different disciplines during analysis. Another limitation is the way AMS is reported or worded in the curriculum outline, where it may be included but not clearly identifiable. Medical students on rural rotations may be presenting a case with infection that includes antibiotic issues. As such students may be receiving AMS training but in small courses that are not captured in the curricular course content.

Conclusions

A summative content analysis that sought to identify, describe and count keywords relevant to prudent antibiotic prescribing in the curricula of two African medical schools found few such keywords. The two countries implement different curricula. The South African medical school uses an integrated curriculum, while the Nigerian medical school has adopted a traditional curriculum. Based on the sample analysis of the two medical schools' curricula, there might be concerns regarding the training of prudent antibiotic use in medical schools. Nigerian medical schools should reconsider their teacher-centred discipline-based curriculum for a student-centred vertically integrated one, that encourages life-long learning, critical thinking and the development of skills that will prepare them for self-directed learning throughout their career (Brauer and Ferguson, 2015; Malik and Malik, 2011). Medical schools should aim to produce doctors with the required knowledge and skills to face the health challenges of the 21st century, such as AMR.

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Declaration

This is to declare that the manuscript has not been published previously and is not under simultaneous review elsewhere, and it has been edited for language.

Disclosure statement

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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CHAPTER FIVE

Development of an antibiotic stewardship curriculum for medical students: a modified Delphi

Augie, B. M., van Zyl R. L., Miot, J. and McInerney, P. A.

"Without urgent, coordinated action by many stakeholders, the world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill."

(Stephens, 2014)

Dr Keiji Fukuda, the Director General's Special Representative for Antimicrobial Resistance at the WHO

An abbreviated version of the manuscript has been submitted to Education for Health for publication (on January 31, 2022, Manuscript ID efh_31_22) – under review. The full version is included here to present the full scope of work undertaken to achieve objective 4: Development of an antibiotic stewardship curriculum for medical students: a modified Delphi.

Abstract

Objective

The objective of this study was to develop an antibiotic stewardship curriculum for teaching responsible antibiotic prescribing and therapeutic use to medical students in South African and Nigerian medical schools.

Methods

A modified Delphi technique was used in this study to reach a consensus between a panel of experts. Purposive and snowball sampling techniques were used to select the panel of experts to participate in this study. The instrument used was piloted on three local experts before it was sent out to the panellists. They were asked to critique the instrument using the following criteria; form, content, context, length, adequacy of instruction, clarity of question, comprehensiveness, content domains, and scaling method. The median and interquartile range were used to determine consensus.

Results

Thirty-three experts from six different disciplines in South Africa and Nigeria were invited to participate, of which twenty-seven indicated their willingness to participate. In the first round 23 of the 27 (85.2%) responded. After two rounds of Delphi, 88 of the 105 competencies reviewed by the panellists reached consensus and outcomes were categorized into knowledge, attitudes and skills domains.

Conclusion

Two rounds of Delphi were conducted, after an initial review of the competencies by three validators. The competencies that reached consensus were then categorized into three domains of learning, namely knowledge, skills and attitudes. This list will contribute towards the development of a curriculum for antibiotic stewardship in undergraduate medical programs in two African countries.

Keywords: antibiotics; antibiotic stewardship; antibiotic resistance; medical Students; Africa; curriculum

Introduction

The rapid development of antibiotic resistance across the globe is jeopardizing the sustainability of antibiotics, which have transformed modern medicine and saved millions of lives since their discovery (Golkar et al., 2014; Gould and Bal, 2013; Sengupta et al., 2013). This poses an increasing challenge to public health, aggravated by the lack of effective antibiotics to treat resistant pathogens (Holmes et al., 2016), which has been recognized by the World Health Organisation (WHO) (WHO, 2014). The development of antibiotic resistance is a natural evolutionary phenomenon as a result of exposure to antibiotics (Holmes et al., 2016). Antibiotic resistance occurs primarily because of selective pressures from antibiotic use. It can be reduced by prudent antibiotic use to delay the emergence of resistant pathogens (Department of Health, 2013). A United Kingdom study forecasted that if left unchecked antibiotic resistance would cause 10 million people to die annually across the globe and result in a loss of 100 trillion US dollars to the global economy by 2050 (O'Neill, 2016).

Unlike some other health problems, antibiotic resistance affects both rich and poor countries, where resistant organisms do not respect international borders (O'Neill, 2016; WHO, 2014). The WHO in its 2014 report acknowledged Africa and South East Asia as the two regions with poor antibiotic resistance surveillance (WHO, 2014). The lack of surveillance data in Africa results in antibiotic guidelines that are inadequate for the local context (Tadesse et al., 2017).

There is a high rate of inappropriate use of antibiotics among doctors, which is a source of concern and could be related to the level of education they received on prudent antibiotic use at medical school (Vickers, 2011). According to Jacob “The misuse and abuse of antibiotics by physicians is serious. Inadequacy of training in prescribing rational antibiotic therapy is a major gap.” (Vickers, 2011, p. 1).

The Infectious Diseases Society of America has identified the antibiotic stewardship programme as a panacea to antibiotic resistance (Fridkin and Srinivasan, 2014). Antibiotic stewardship is described as “coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration.” (Fishman et al., 2012, p. 15). Antibiotic stewardship is best started in medical school at the time when knowledge and behaviour are being shaped (Pulcini and Gyssens, 2013). Concerted efforts are required from all stakeholders to manage the crisis of antibiotic resistance (Gould and Bal, 2013; Spellberg and Gilbert, 2014). In 2009, the General Medical Council of the United Kingdom called on medical schools to develop courses to teach medical students prudent antibiotic prescribing (McNulty et al., 2012). Some medical schools especially in the USA and Europe have developed courses on prudent antibiotic prescribing to encourage aspiring doctors to develop skills on rational antibiotic prescribing (Hsu, 2018; MacDougall et al., 2017; Nori et al., 2017; Paterson Davenport et al., 2005; Shekarchian et al., 2016).

In Africa, aspiring doctors, newly qualified doctors and even practicing physicians often do not have the requisite skills to engage in antibiotic stewardship and many of the medical schools do not have such programmes in their curriculum. Even where the elements of prudent antibiotic prescribing are available as we recently found when we undertook a review of the South African and Nigerian medical curricula, they are taught in short courses that are not synchronous or managed throughout the curriculum (unpublished). We recently undertook a scoping review to map available antibiotic stewardship programmes across the globe, but we did not find any such programmes on the African continent (Augie et al., 2021). In that light, we decided to engage clinical pharmacologists, clinical microbiologists, pharmacists, nurses, infectious disease specialists and experts in medical education from South Africa and Nigeria to help develop an antibiotic stewardship curriculum for medical schools in these two countries through a Delphi technique. South Africa and Nigeria were selected because of their influence on the African continent. The objective of this study was to develop an antibiotic stewardship

curriculum for teaching responsible antibiotic prescribing and therapeutic use to medical students in South African and Nigerian medical schools.

Methods

We conducted a modified Delphi to reach consensus between experts. The Delphi is a well-organised method of communication that is commonly used to obtain a consensus on an issue under consideration (Jones and Hunter, 1995; Vernon, 2009). This technique involves a review of the literature and a series of rounds where a panel of experts help to refine and fine-tune the Delphi questionnaire **competencies** and finally obtain a consensus (Masud et al., 2014). One of the advantages of the process is that it can be conducted online where experts can freely express their view without the influence of others (Masud et al., 2014). The technique was developed by Olaf Helmer and colleagues while working on a defence project in the early 1950s at the Rand Corporation (Yousuf, 2007). Three main characteristics differentiate Delphi techniques from conventional face-to-face group interactions such as the focus group discussion. They are anonymous and allow for iteration with controlled and statistical feedback (Martino, 1993). Round one of the Delphi allows for the determination of participants' opinions about the **competencies**. The measure of central tendency and variability are used to describe their opinions, which in turn results in the removal of some **competencies** from the list and subsequent rounds (Rayens and Hahn, 2000). **Competencies** have reached consensus are not included in subsequent rounds, while those **competencies** in which consensus has not been reached are carried forward to the next round (Rayens and Hahn, 2000).

Sampling

Purposive and snowball sampling were used to select the panel of experts to participate in this Delphi study. There is no consensus on the maximum number of panellists that can participate in a Delphi study (Keeney et al., 2011). It is suggested that the sample size is dependent on the homogeneity and heterogeneity of the participants, and the nature of the problem being investigated (Keeney et al., 2011). However, it has been suggested that 10 to 15 experts are sufficient for a homogenous sample (Skulmoski et al., 2007). The sample used in this study was considered to be homogenous as all were academics and several were also clinicians.

Delphi Questionnaire Development and Piloting

We adopted a 53-competencies instrument with six domains developed by UK researchers for health professional students, with the permission of the lead author (Courtenay et al., 2018). Those competencies that reached consensus were to be used to develop an antibiotic stewardship curriculum for teaching medical students responsible antibiotic use. The 53-competencies were modified to meet the local context. A review of the literature resulted in an additional 29-competencies, giving a total of 88-competencies. The instrument was piloted on three local experts, who were requested to critique the instrument using the following criteria; form, content, context, length, adequacy of instruction, clarity of question, comprehensiveness, content domains, and scaling method. They were also requested to suggest missing competencies for possible inclusion. After a series of modifications as recommended by the three validators, the instrument was sent to a panel of experts. The instrument was divided into six domains; infection and prevention and control (22 competencies); antibiotics and antibiotic resistance (9 competencies); the diagnosis of infection and the use of antibiotics (25 competencies); the practice of prescribing antibiotics (13 competencies), patient-centred care (7 competencies) and inter-professional collaborative practice (6 competencies).

Selection of Panel of Experts

A critical stage in the Delphi technique is the identification and selection of the panel of experts who will express a view and provide feedback (Martino, 1993; Turner et al., 2013). According to Martino, an ideal panel member should have vast experience and knowledge in the field under study and be willing and available to participate as a panellist and should be able to represent their discipline (Martino, 1993). The panellists were experts from nine medical schools in South Africa and Nigeria and represented six disciplines. Selection was based on the following criteria:

- Should have a minimum of three years teaching or clinical supervision of medical students or health science students.
- Willing and have time to participate as a panellist.
- Familiar with the medical curriculum of their schools.

The experts were from different disciplines that included infectious diseases, medical microbiology, clinical pharmacology, pharmacy, nursing and medical education. Of 33 experts

invited to participate as panellists, 27 accepted the invitation and were sent the questionnaire in round one. Of these 23 (85.2%) responded. These 23 were sent the questionnaire in round two, and 20 (86.9%) responded.

Data Collection

The Delphi was conducted via two rounds. The instrument was sent to the panellists online using Research Electronic Data Capture (REDCap). The COVID-19 pandemic necessitated an extended duration for data collection such that the survey link was left active for six weeks in each round. The two rounds took place between March and July 2020. In round one, 82 competency items formed the content of the survey instrument. The panellists were asked to rate each competency item on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree. At the end of each domain, provision was made for experts to give their feedback, interpretation and recommend any missing competency. Before the commencement of round two, the results of round one were circulated to panellists and they were requested to send their feedback and recommendations. As in round one, the round two questionnaire was administered online. Only competencies that had not reached a consensus, those that were amended on recommendation by the panellists and those generated from the analysis of the qualitative input from the experts were included in round two. The qualitative input derived from round one were analysed using a qualitative content analysis approach (Hsieh and Shannon, 2005).

Data Analysis

The median and interquartile ranges (IQRs) for each response to **competencies** were calculated to sort **competencies** above or below 50% (Courtenay et al., 2018). The IQR that forms the distance between the 25th and the 75th percentile quantifies the spread of data and determines the degree of consensus. A narrow IQR indicates considerable agreement, while a wide IQR indicates considerable disagreement (Martino, 1993; Shepherd et al., 2017). Those **competencies** with a median score of greater than or equal to 5 and a narrow IQR were considered to have reached consensus. Those **competencies** with a median score of less than 5 were excluded after round one. There is no agreement in the literature on the best method to determine consensus in the Delphi technique. However, the common statistics used in the Delphi are measures of central tendency (mean, median and mode) and measures of dispersion (standard deviation and interquartile range) to determine the judgements of the panellists (Hasson et al., 2000). The use of the median and IQR when a Likert scale is used, is strongly favoured to give feedback to the panellists (Hill and Fowles, 1975).

Ethics

The study was approved by the University of the Witwatersrand Human Research Ethics Committee (Medical) (Certificate Clearance: M190864).

Results

Round One

The profile of the panel of experts who participated in Delphi round one is presented in Table 1. Most of the experts were from South Africa (60.9%); one of the experts is a South African, but currently working in the United Kingdom. The average years of experience, as tertiary educators, was 16.57 ± 8.59 years. Six competencies were excluded after round one, while one was recommended by the panellists to be amended and taken to second round. Competencies removed after round one are presented in Table 2.

Table 1: Distribution of Experts by Discipline and Country.

Expert Panel Details (N = 23)	Round One N (%)	Round Two N (%)
Disciplines		
Clinical microbiology	4 (17.4)	4 (20.0)
Clinical pharmacology	8 (34.9)	7 (35.0)
Infectious diseases	6 (26.1)	6 (30.0)
Medical education	3 (13.0)	2 (10.0)
Pharmacy	1 (4.3)	1 (5.0)
Nursing	1 (4.3)	-
Total	23 (100.0)	20 (100.0)
Distribution of Experts by Country of Residence		
South Africa	14 (60.9)	11 (55.0)
Nigeria	8 (34.8)	8 (40.0)
Other	1 (4.3)	1 (5.0)
Total	23 (100.0)	20 (100.0)
Average years of experience of experts as tertiary educators, (SD), range	16.57 ± 8.59 , 5 - 35	

Table 2: Competencies Removed After Round One and Two (N = 17).

	Competency Items	Median	IQR
	Round One		
*1.	Explain the four main mechanisms of antibiotic resistance	4.0	1.0
2.	Describe what is meant by "delayed prescribing"	4.5	1.0
3.	Identify the presence of an intra-abdominal abscess on plain abdominal X-ray film	3.5	3.0
4.	Use a serum inflammatory marker such as procalcitonin and a C-reactive protein to help differentiate between viral and bacterial infections when the diagnosis is unclear	4.0	1.25
5.	Explain how a biomarker such as procalcitonin can be used as a tool in guiding the decision to discontinue antibiotics in a patient	4.0	1.0
6.	Explain why it is essential to ensure that an accurate diagnosis of an allergy to an antibiotic is based on the medical history of the patient and laboratory tests	4.0	1.0
7.	Explain the appropriateness of antibiotic administration models such as outpatient parenteral antibiotic therapy (OPAT)	4.0	1.0
	Round Two		
8.	Describe the principles of pathogenesis of infectious disease based on the pathogenetic triad and damage response framework is fundamental to understanding how to prevent and control infections	4.0	1.0
9.	Should be able to provide first aid for exposed cuts/puncture wounds, or the exposure of the eyes, nose or mouth to fluids	4.5	2.0
10.	Describe the concept of the basic reproductive number of an infectious pathogen and how it influences spread and control	4.0	1.0
11.	Explain the importance of waste segregation	4.0	1.0
12.	Explain the importance of screening colonized patients and the principles of decolonization	4.0	1.0
13.	Explain the challenges associated with culture-sample techniques such as lack of alcohol swab, lack of training, lack of speedy services etc.	4.0	1.0
14.	Explain the importance of using an appropriate medium to prevent samples from drying	4.0	1.0
15.	Explain why consideration of Ideal Body Weight and body surface area is important when dosing antibiotics	4.0	1.0
16.	Explain the appropriate channels of reporting adverse drug reactions resulting from antibiotic therapy, e.g. National Adverse Drug Reactions or Hospital Essential Drugs Lists Committees	4.0	1.0
17.	Should avoid revealing sensitive information like adverse drug reactions from antibiotic therapy on social media, which can lead to litigation and job loss	5.0	2.0

*competency was carried forward to round two as recommended by the experts; median score of less than 5 indicate a high level of agreement that the competency is not important; IQR value of more than 1.5 indicate lack of agreement between experts.

Round Two

The Delphi was sent to the 23 experts who participated in round one of whom 20 (86.9%) responded. Two of the experts that participated in the first round did not respond to the second round invitation despite several weekly reminders that were sent via REDCap. The third expert died before the second round commenced. Most of the respondents were clinical pharmacologists (35.0%) and infectious diseases specialists (30.0%) followed by clinical microbiologists (20.0%), where more than half of the experts were from South Africa (55.0%) (Table 1). Twenty-three competencies were generated from the analysis of the qualitative data from the experts' feedback in round one. The panellists requested that one of the competencies with a median of less than 5 - *Explain the four main mechanisms of antibiotic resistance* should be amended and it was changed to *Explain mechanisms of antibiotic resistance*. These formed the 24 competencies that were sent to the panel of experts in round two. Competencies removed after round two are presented in Table 2.

Some of the panellists suggested that instead of reporting the findings based on the six domains as used during data collection in the two rounds that the competencies be grouped into knowledge, attitudes and skills. As such the final results of the two rounds were summed up into these three latter domains and consisted of 66 (Table 3), nine (Table 4) and 13 (Table 5) competencies in each respective domains (Appendices U and V are modified Delphi questionnaires for Rounds One and Two, respectively).

Table 3: Proposed Knowledge Component for Antibiotic Stewardship Curriculum (N = 66).

	Curriculum Item	Median	IQR
1.	Describe what a bacterium is	5.0	1.0
2.	Describe the different types of bacteria that may cause infections and how they contribute to healthcare-associated infections	5.0	0.0
3.	Explain what an antibiotic-resistant organism is	5.0	0.0
4.	Explain the 'Chain of Infection'	5.0	1.0
5.	Define the components required for the transmission of an infection (i.e., the presence of an organism, the route of transmission of the organism from one person to another, the host who would be susceptible to the infection)	5.0	0.0
6.	Describe the routes of transmission of infectious organisms (i.e., contact, droplets, and airborne routes)	5.0	0.0
7.	Explain the role played by the environment in the transmission of bacteria	5.0	1.0
8.	Present and recognize the characteristics of a susceptible host	5.0	1.0
9.	Explain an understanding of the importance of surveillance	5.0	1.0
10.	Describe how vaccines can prevent infections in susceptible persons	5.0	1.0
11.	Explain the application of standard precautions in healthcare environments	5.0	0.0
12.	Explain how to appropriately use the following products, namely soap and water, antibacterial soap, surgical scrubs, waterless alcohol agents, for hand hygiene, and the conditions under which to apply each of the methods	5.0	1.0
13.	Differentiate between the cleaning, disinfecting and sterilization of hospital equipment	5.0	1.0
14.	Describe safe handling methods and the disposal of sharp objects	5.0	1.0
15.	Describe techniques to safely handle blood and body fluids to prevent exposure.	5.0	0.0
16.	Describe at least two different ways in which antibiotics may kill bacteria	5.0	1.0
17.	Explain the concept of bacterial killing by either concentration-dependent or time-dependent antibiotics	5.0	1.0
18.	Differentiate between bactericidal and bacteriostatic antibiotics	5.0	1.0
19.	Differentiate between latent tuberculosis infection and active tuberculosis disease	5.0	1.0
20.	Discuss how the inappropriate use of antibiotics (including non-adherence to a treatment regime) may lead to resistance to antibiotics	5.0	0.0
21.	Identify approaches to support the optimal prescription of antibiotics	5.0	0.0
22.	Explain how the inappropriate use of broad-spectrum antibiotics increases the risk of <i>Clostridium difficile</i> colitis	5.0	1.0
23.	Describe how antibiotic use drives the emergence of drug-resistant bacteria	5.0	0.0
24.	Recognize the symptoms of infection	5.0	0.25
25.	Explain how microbiology samples may be of assistance in the diagnosis of infections	5.0	1.0
26.	Describe the appropriate way of taking samples following local procedures for taking samples	5.0	0.25
27.	Interpret microbiology results/reports from the laboratory at a basic level	5.0	0.0

28.	Discuss how the identification of bacteria and their susceptibility to antibiotics from a specific culture are important in antibiotic therapy	5.0	0.0
29.	Explain the concept of Minimum Inhibitory Concentration (MIC) in terms of bacterial killing	5.0	1.0
30.	Explain why self-limiting bacterial or viral infections are unlikely to benefit from the dispensing of antibiotics	5.0	0.0
31.	Describe the required management strategies to treat self-limiting infections (i.e. the administration of analgesics/rest /fluid intake)	5.0	1.0
32.	Understand the importance of following local antibiotic policies (i.e. in that their development is based on local resistance patterns), and adhere to these policies in practice	5.0	0.25
33.	Explain the importance of documenting the following parameters in antibiotic therapy route of administration, dosage, duration, intervals between dosages, and the review date in clinical notes and of demonstrating these aspects in practice	5.0	0.0
34.	Explain an understanding of the factors that need to be considered when choosing an antibiotic (including the site of infection and the type of bacteria likely to cause an infection at that particular site)	5.0	0.0
35.	Describe the use of broad and narrow-spectrum antibiotics and the role of broad-spectrum antibiotics in contributing to antibiotics resistance	5.0	0.0
36.	Describe and be able to recognize the common side-effects associated with commonly-administered antibiotics	5.0	0.0
37.	Explain an understanding as to why the documentation of a patient's allergy to an antibiotic is important	5.0	0.0
38.	Explain why it is important to consider certain physiological conditions (e.g. renal function) in patients who receive an antibiotic	5.0	0.25
39.	Explain how the removal or drainage of material from the focus of infection, such as an abscess (often called source control) would facilitate a clinical cure	5.0	0.25
40.	Identify the likely source of infection and likely pathogens	5.0	1.0
41.	Explain how to recognize and manage sepsis	5.0	0.0
42.	Describe why it is important to use local guidelines to initiate prompt and effective antibiotic treatment in patients with life-threatening infections	5.0	0.0
43.	Describe why it is important to switch from intravenous antibiotics to oral therapy	5.0	0.5
44.	Describe how to alter the route of administration from IV to oral antibiotic therapy	5.0	1.5
45.	Explain an understanding of the rationale and use of perioperative prophylactic antibiotics to prevent surgical-site infections	5.0	0.0
46.	Discuss factors that could influence the prescription of antibiotics (e.g. availability of resources, diagnostic uncertainty, peer practice, patient expectations, and financial interests) and the implications for antibiotic stewardship programmes	5.0	0.0
47.	Describe national guidance in respect to the completion of a course of antibiotics	5.0	1.0

48.	Describe some of the medicines with which antibiotics can sometimes interact	5.0	1.0
49.	Describe how switching to oral antibiotics when appropriate can reduce costs, facilitate discharge and prevent complications associated with indwelling catheters and clots	5.0	1.0
50.	Establish that source control (incision and drainage) is often the most critical intervention in the management of purulent skin and soft tissue infections, and that antibiotics should be reserved for a patient with a severe disease	5.0	0.5
51.	Establish that some antibiotics, such as aminoglycosides and vancomycin, should be dosed according to the patient's weight in order to minimize complications	5.0	1.0
52.	Discuss the patient's/carer's expectations or demands in respect of antibiotics and the need to use antibiotics appropriately	5.0	1.0
53.	Explain an understanding of the roles, responsibilities, and competencies of other health professionals involved in policy decisions concerning antibiotic treatment	5.0	1.0
54.	Explain why it is important that healthcare professionals, involved in the delivery of antibiotic therapy (including the prescription, delivery and supply), have a common understanding of antibiotic treatment policy decisions, the quantities involved in antibiotic use, and effective patient/client outcomes	0.5	0.5
*55.	Recognize the symptoms of infections like fever, pain, cough and rashes as a guidance that will trigger empirical antibiotic therapy versus those that could wait for a culture-based antibiotic therapy	5.0	0.0
*56.	Explain the importance of personal protective equipment and when to use them to prevent infections	5.0	0.0
*57.	Describe the need for precaution when prescribing antibiotics in populations at risk e.g. children, the elderly, pregnant women and lactating mothers.	5.0	0.0
*58.	Explain mechanisms of antibiotic resistance	5.0	1.0
*59.	Describe the different ways in which antibiotics may kill bacteria	5.0	1.0
*60.	Explain the importance of prompt submission of swab specimens to the laboratory to preserve the organisms during transportation	5.0	1.0
*61.	Explain how to de-escalate to narrow-spectrum antibiotics after initial broad-spectrum antibiotics use	5.0	1.0
*62.	Describe the importance of bioavailability and non-inferiority of oral versus parenteral formulations when doing some antibiotics	5.0	1.0
*63.	Explain principles for selection of antibiotics which includes pathogen type (suspected or confirmed)	5.0	1.0
*64.	Explain pharmacokinetic parameters such as MIC and ability to dose optimize using PK-PD principles	5.0	1.0
*65.	Explain the importance of medical decisions about dosing strategies, interactions and the treatment of patients with specific disease conditions e.g., interaction between clarithromycin and digoxin	5.0	1.0

*66.	Explain the need for therapeutic drug level monitoring in antibiotic stewardship programmes, e.g., in patients on vancomycin, linezolid and aminoglycosides therapy	5.0	1.0
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*Competencies that reached consensus during round two

Table 4: Proposed Attitudes Component for Antibiotic Stewardship Curriculum (N = 8).

	Curriculum Items	Median	IQR
1.	Implement work practices that reduce the risk of infection (e.g., undergoing appropriate immunization or not coming to work when sick) to ensure the protection of the patient and other healthcare workers	5.0	0.0
2.	Appreciate that healthcare workers should show accountability and commit to follow infection control protocols as part of their contract of employment	5.0	1.0
3.	Act as a role model to healthcare workers and members of the public by adhering to the principles to prevent and control infections	5.0	0.0
4.	Consider drug allergies, vaccination history and severity of illness before starting empiric antibiotic therapy	5.0	1.0
5.	Support the participation of patients/carers, as integral partners, when planning/delivering their care	5.0	1.0
6.	Ensure that appropriate education and support is provided by learners to patients/carers, and others involved with their care or service	5.0	1.0
7.	Raise public awareness of the problems associated with antibiotic resistance and explain to the patients their role in promoting appropriate antibiotic use	5.0	0.0
8.	Establish a trusting relationship with patients/carers and other health/social care professionals	5.0	0.0

Table 5: Proposed Skills Component of Antibiotic Stewardship Curriculum (N = 14).

	Curriculum Items	Median	IQR
1.	Demonstrate ideal hand hygiene practices	5.0	0.0
2.	Demonstrate the appropriate way of taking laboratory samples following local procedures	5.0	1.0
3.	Acquire communication skills to be able to counsel their patients on appropriate antibiotic use and discourage them from purchasing antibiotics without prescription	5.0	0.0
4.	Establish collaborative communication principles and actively listen to other professionals and patients/carers involved in the delivery of antibiotic therapy	5.0	0.0
5.	Communicate effectively to ensure a common understanding of care decisions	5.0	0.0
6.	Effectively use information and communication technology to improve interprofessional patient-centered care	5.0	1.0
7.	Share information with patients/carers in a respectful manner and in such a way that it is understandable, encourages discussion, and enhances participation in decision-making	5.0	1.0
8.	Apply appropriate policies/procedures and guidelines for the collection and handling of specimens	5.0	1.0
9.	Apply policies, procedures and guidelines relevant to the control of infection when infection control cases and situations present themselves	5.0	1.0
10.	Communicate with respect and express needs of all parties in shaping and delivering care or services	5.0	1.0
11.	Demonstrate the correct technique for performing a blood culture	5.0	0.25
12.	Demonstrate the correct technique for performing a pus swab	5.0	1.0
*13.	Demonstrate the WHO concept of 'My five moments for hand hygiene'	5.0	1.0
*14.	Interpret and use MIC provided in AST report in informing dosing decisions and attempts to dose optimize	5.0	1.0

*Competencies that reached consensus during round two

Discussion

The objective of this study was to achieve consensus among a group of experts in infectious diseases, medical microbiology, clinical pharmacology, pharmacy, nursing and medical education about content for an antibiotic stewardship curriculum for medical schools. The experts reached consensus on 88 of the competencies required to adequately practice AMS. A critical step to encourage appropriate antibiotic prescribing is the inclusion of relevant knowledge and skills in the medical curriculum (Paterson Davenport et al., 2005). According to Brink et al. the prescribing of antibiotics is dependent on many factors which include the availability of local antibiotic prescribing guidelines, familiarity with the concept of antibiotic stewardship and regular seeking of advice from infectious disease physicians and

microbiologists on prudent antibiotic use (Brink et al., 2017). It is hoped that the developed competencies may help future prescribers to become antibiotic stewards and also help to bridge the gap we identified in the medical curriculum of the two countries. South African experts have called on South African medical schools to standardize prudent antibiotic prescribing teaching and furnish aspiring doctors with the necessary skills to engage in responsible antibiotic prescribing (Brink et al., 2017).

Antibiotics are among the most widely used class of drugs in a healthcare setting to treat infections in both inpatient and outpatient settings (Dyar and Beović, 2017). Education is critical in improving antibiotic prescribing, as well as improve knowledge and attitudes (Dyar and Beović, 2017). Apart from medical students, this antibiotic stewardship framework may be useful for newly qualified doctors starting their career, especially those who have not had adequate training on responsible antibiotic prescribing. Doctors are expected to be able to prescribe antibiotics appropriately after exiting medical school and will continue to do so, often daily with or without direct supervision (Dyar and Beović, 2017). This emphasizes the need to incorporate courses on both general and appropriate antibiotic prescribing into the medical curriculum (Pulcini and Gyssens, 2013).

These competencies could be taught in a spiral fashion, where competencies such as antibiotic-resistant pathogens, chain of infection, ways by which antibiotics kill bacteria could be taught in the preclinical years. Others such as the recognition and treatment of sepsis, antibiotic therapeutic level monitoring and communication skills could be taught in the clinical years at a time when students have acquired bedside clinical skills. Shekarchian et al. (2016) have developed an antibiotic stewardship spiral curriculum at the University of California, San Francisco School of Medicine to teach medical students prudent antibiotic prescribing from second to fourth year. Spiral learning encourages mastery, reinforces and deepens previously learnt concepts. After completing the three-year antibiotic stewardship spiral curriculum and just before graduation more than (80%) of the learners reported they were competent to initiate empiric antibiotic and also know when and how to de-escalate from broad-spectrum to narrow-spectrum antibiotics (Shekarchian et al., 2016).

The curriculum developers in South Africa and Nigeria should consider reviewing the antibiotic teaching component of their curriculum, and may also consider adopting these competencies into their curriculum. Medical schools should aim to produce doctors with the understanding

that antibiotics are a special class of drugs which, if not used appropriately, could lead to the selection of resistant bacteria that may not only affect the index patient, but the entire population (Dyar and Beović, 2017). Antibiotic stewardship educational programmes tend to target postgraduates and practicing physicians, with little effort being made to incorporate it into undergraduate medical curricula in most countries (Pulcini et al., 2015). Although it is acknowledged that medical curricula are overloaded, there is need of support from medical schools to agree that antibiotic stewardship should be considered core knowledge so that graduating doctors are able to make informed choices when prescribing antibiotics (Pulcini and Gyssens, 2013).

Curricula require clearly stated learning outcomes and competencies and appropriate assessment methods to evaluate learning outcomes (Pulcini and Gyssens, 2013). The competencies developed in this study are a step towards improving the teaching of rational antibiotic prescribing in medical schools. It is critical for relevant stakeholders in undergraduate medical education to consider incorporating competencies on prudent antibiotic prescribing into medical curricula, and the use of interactive teaching methods (Ohl and Luther, 2014; Pulcini and Gyssens, 2013). It is hoped that regulatory bodies should consider adopting these competencies to standardize prudent antibiotic teaching in medical schools.

Building consensus is a critical component of a Delphi process (Rayens and Hahn, 2000). One of the main attributes of the Delphi technique is to bring together experts with divergent views to systematically try to reach a consensus and also point out divergence of opinion (Strauss and Zeigler, 1975). One of the main strengths of our study is the multi-disciplinary composition of the panel of experts and the years of experience the panel had as tertiary educators. A limitation to this study was that competencies that reached consensus in round one were not carried to round two which might have reduced the iteration. However, the results were circulated to the panellists and were requested to send feedback and recommendations to improve iteration.

Conclusion

Two rounds of Delphi were conducted, after an initial review of the competencies by three validators drawn from the Faculty of Health Sciences, University of the Witwatersrand. The final 88 competencies were then categorized, into three domains of learning – knowledge, skills and attitudes. This list will contribute towards the development of a curriculum for antibiotic stewardship in undergraduate medical programmes in two African countries.

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Declaration

This is to declare that the manuscript has not been published previously and is not under simultaneous review elsewhere, and it has been edited for language.

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CHAPTER SIX

Antibiotic stewardship curriculum for medical students

"We see horrendous rates of antibiotic resistance wherever we look in our field operations, including children admitted to nutritional centres in Niger, and people in our surgical and trauma units in Syria".

(Stephens, 2014)

Dr Jennifer Cohn,

Medical Director of Medecins sans Frontiers' Access Campaign

6.1 Introduction

In this chapter, the researcher describes how the competencies that reached consensus during the two rounds of the modified Delphi with medical teachers were used to develop an antibiotic stewardship framework for teaching prudent antibiotic prescribing in medical schools. It also describes how the three domains: knowledge, attitudes and skills are used to develop a spiral curriculum for antibiotic stewardship, the methods of teaching to be used in delivering the curriculum and how knowledge will be assessed.

6.2 Antibiotic stewardship curriculum

According to the General Medical Council of the UK, "a curriculum is a statement of the intended aims and objectives, content, experiences, learning outcomes and processes of a programme or course of learning, including a description of the structure and expected methods of learning, teaching, assessment, feedback and supervision. The curriculum should set out a programme of learning and specify what learning outcomes the learner will achieve" (General Medical Council 2017, p. 32-33). The lack of a defined antibiotic stewardship curriculum for both Nigerian and South African cohorts of students that clearly outlines the learning objectives for prudent antibiotic prescribing could be the reason for the poor performance of the students in this study (Chapter four: Table 3). The knowledge and perceptions demonstrated by the sampled Nigerian and South African medical students on rational antibiotic use are a source of concern (Chapter three: Table 2 and Supplementary Table 1). This necessitates the need for the development of an antibiotic stewardship curriculum. The core of this curricular framework is to guide medical schools in Nigeria and South Africa on what to include in their antibiotic

stewardship curriculum. In this study curriculum refers to an academic document that guides teachers to the content that should be taught for general and prudent antibiotic prescribing to medical students. The curriculum was developed using competencies that reached consensus during the modified Delphi study with a panel of experts drawn from different disciplines.

A summative content analysis of the South African and Nigerian medical students' curricula that sought to identify, describe and count keywords relevant to prudent antibiotic prescribing in the curricula of two African medical schools found that the two countries operate a different curriculum. The South African medical school uses an integrated curriculum, while the Nigerian medical schools have adopted a traditional, discipline-based curriculum. The key phrase 'antimicrobial stewardship' or 'antibiotic stewardship' was absent in the Nigerian curriculum, but appeared four times in the South African curriculum.

The findings of the summative content analysis suggest a need for revision of the medical curricula of the two countries, as currently there is little emphasis on prudent antibiotic prescribing that will produce graduates who are competent as antimicrobial stewards. A survey to determine the knowledge and perceptions of final year Nigerian and South African medical students about antibiotic resistance, prudent antibiotic use and antibiotic stewardship identified a gap in knowledge in both groups. However, the gap is more so among the Nigerian cohort; whilst both categories of respondents were found to have similar perceptions of antibiotic use and resistance (Chapter three: Supplementary Table 1). The survey findings suggest that prudent antibiotic prescribing and antibiotic stewardship should begin at the time when knowledge and behaviour are being shaped. A scoping review was conducted to map the evidence relating to the teaching of antibiotic stewardship in medical schools globally (Chapter two).

The scoping review did not identify any ASPs in African medical schools. The findings of the three studies (Figure 6.1) described above, informed the modified Delphi study. Medical teachers from different disciplines reached a consensus on what to include in the curriculum for teaching prudent antibiotic prescribing to medical students (Chapter five: Tables 3-5).

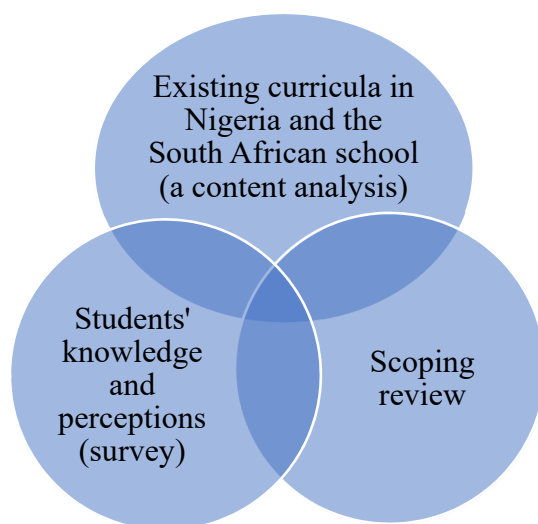


Figure 6.1: Diagrammatic representation of the three studies in Phase One of the study.

6.3 Current context

According to Stabback (2007), the current context deals with the socioeconomic setting where the developed antibiotic stewardship curriculum is to be implemented. Nigeria and South Africa, are the two most influential countries on the African continent because of the size of their economies and the roles they have been assigned to play in their sub regions and the continent in general (Odubajo and Akinboye, 2017). The United Nations Population Fund estimated that in 2021 Nigeria has a population of 211.4 million people, while South Africa has 60 million people (United Nations Population Fund, 2021). In 1999 the two countries signed a bilateral agreement in Abuja to strengthen and deepen cooperation in the fields of defence and security, science and technology and infrastructure, as well as education and culture (Odubajo and Akinboye, 2017). Nigeria is regarded as the most populous country and also has the largest economy on the African continent, while South Africa is considered the most industrialised country on the continent (Odubajo and Akinboye, 2017). Gukas (2007, p. 888) notes that “South Africa is arguably way ahead of most of Africa as far as medical education and innovations in education is concerned”. Currently, there are 51 accredited medical schools in Nigeria and eight in South Africa.

6.4 Educational policy statements

Educational policy statements in curriculum development express the objectives for education, which include universal literacy and numeracy, the development of relevant skills required for economic prosperity and the development of a stable society (Stabback, 2007). The WHO

highlights the need for all healthcare professionals including medical students to be sensitised to responsible antibiotic use and antibiotic stewardship as a step towards addressing antibiotic resistance (Vickers, 2011). Ganter, a senior advisor on AMR at the WHO Regional Office for Europe, stated that there is room for improvement in the current antimicrobial teaching of medical students (Vickers, 2011). Ganter recommended that medical students should be introduced to prudent antibiotic use in bacteriology or pharmacology – “the principles of prudent use of antibiotics, it should start as early as possible” (Vickers, 2011, p 1). The goal of this antibiotic stewardship framework is to provide medical students with the required knowledge, attitudes and skills to engage in appropriate antibiotic prescribing.

6.5 Antibiotic stewardship competencies

Medical teachers reached a consensus on 66 competencies in the knowledge domain (Chapter five: Table 3), 14 competencies in the skills domain (Chapter five: Table 5) and eight competencies in the attitude domain (Chapter five: Table 4). The framework is designed to be implemented in an integrated curriculum and makes use of the concept of spiral learning where it can be taught from the third to the sixth year of study. An integrated curriculum is defined as “a fully synchronous, trans-disciplinary delivery of information between the foundational sciences and the applied sciences throughout all years of a medical school curriculum” (Brauer and Ferguson, 2015, p. 318). According to the Pennsylvania Department of Education, a curriculum framework involves “big ideas, concepts, competencies, and essential questions aligned to standards and assessment anchors and, where appropriate, eligible content” while competencies “describe what students should be able to do (key skills) as a result of this instruction, specific to grade level” (Pennsylvania Department of Education, 2022). The competencies in this framework will support medical students in their journey to becoming antibiotic stewards and in so doing will help patients get the best from their prescribed antibiotics.

6.5 Statement of broad learning objectives and outcomes

This describes what learners are required to know and be able to do after completing the school curriculum and outcomes should be presented in a wide range of domains such as knowledge, attitudes, understanding, values, skills and competencies (Stabback, 2007). The broad learning objectives and outcomes of this framework stipulate what medical students should know and be able to do when they complete the curriculum. The outcomes are expressed in three domains

- knowledge, attitudes and skills (See Tables 6.1-6.3). Moon (2003, p. 56), defined a learning outcome as “a statement of what a learner is expected to know, understand and be able to do at the end of a period of learning and of how that learning is to be demonstrated. Learning outcomes are linked to the relevant level and since they should generally be assessable, they should be written in terms of how the learning is represented”.

6.6 Structure of the education system

This provides a background on the school system through which the curriculum is to be delivered which includes the duration of the programme, learning phases and their durations (Stabback, 2007). In spiral learning, the same concepts are revisited regularly, but with increasing complexity (Harden et al., 1997). Additionally, in a spiral curriculum, as the learners move to each new level, a new concept is introduced that links directly back to the information they received from the previous year (Dowding, 1993) (Figure 6.2). Learners build on and elaborate on previous knowledge as they work through the three phases in the curriculum. The concept of the spiral curriculum was proposed by Jerome Bruner of Harvard University in 1960 (Bruner, 1960).

In 1975 Jerome Bruner explained the idea behind the spiral curriculum as follows:

“...I was struck by the fact that successful efforts to teach highly structured bodies of knowledge like mathematics, physical sciences, and even the field of history often took the form of a metaphoric spiral in which at some simple level a set of ideas or operations were introduced in a rather intuitive way and, once mastered in that spirit, were then revisited and reconstrued in a more formal or operational way, then being connected with other knowledge, the mastery at this stage then being carried one step higher to a new level of formal or operational rigour and to a broader level of abstraction and comprehensiveness. The end state of this process was eventual mastery of the connexity and structure of a large body of knowledge...” (Dowding, 1993, p. 18).

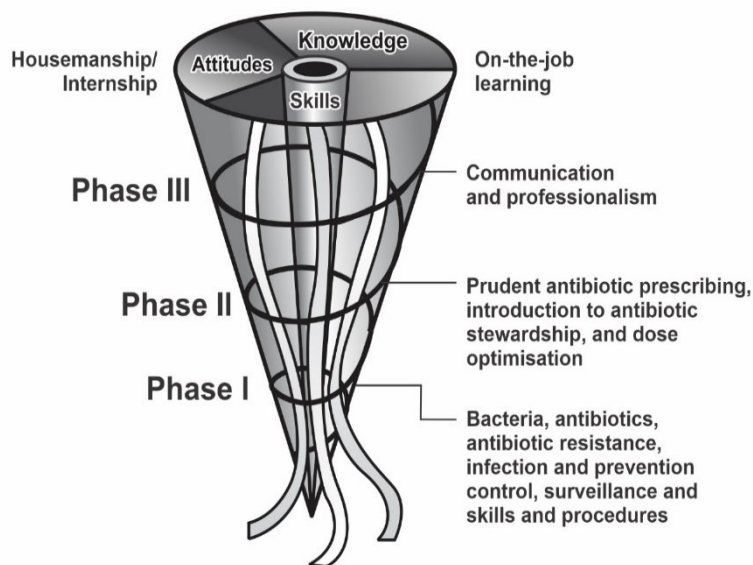


Figure 6.2: The antibiotic stewardship spiral integrated curriculum model. (Adapted from the spiral curriculum of the University of Dundee Medical School, Dundee, UK (Harden et al., 1997).

The distribution of the learning objectives in the three domains knowledge, attitudes and skills and how knowledge and skills are built is presented in Figure 6.3.

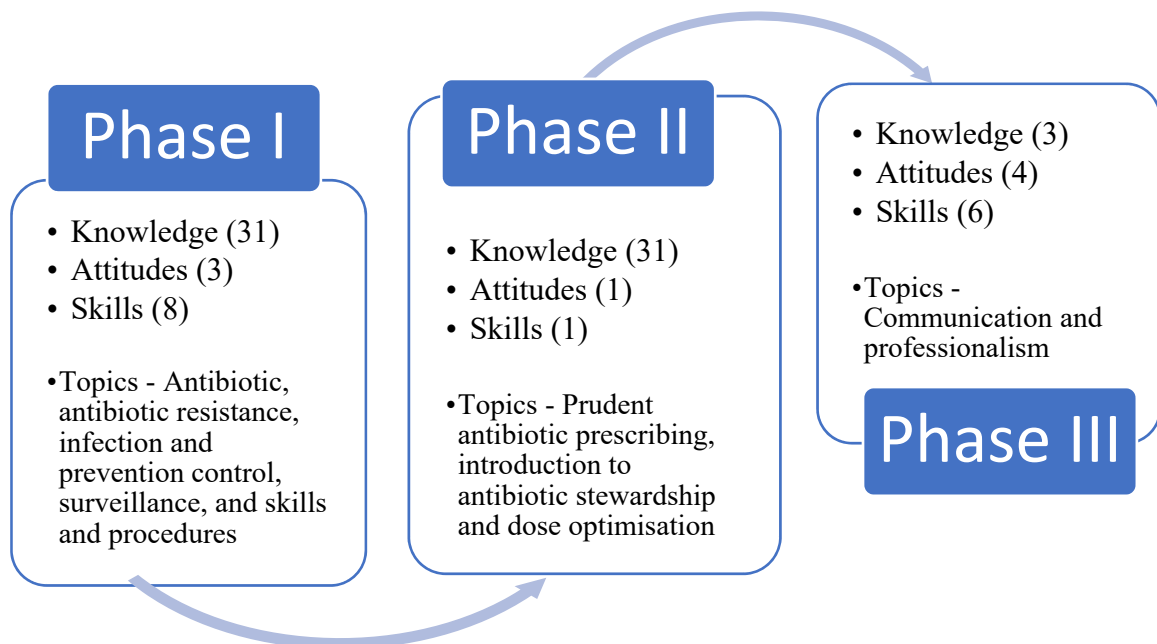


Figure 6.3: A spiral curriculum for prudent antibiotic prescribing in medical schools designed to be delivered in three Phases.

Harden (1999) outlines the following as the main features of a spiral curriculum; topics are revisited, there are increasing levels of complexity, new learning is linked to previous learning, and the competence of learners increases. In this curriculum, Phase I involves the integration

of antibiotic stewardship principles throughout microbiology, pharmacology and medicine curricula. It introduces students to bacteria, antibiotics, antibiotic resistance, infection and prevention control, surveillance of resistant pathogens and skills and procedures. In Phase II, students build on their knowledge by applying the skills they learned in Phase I. New learning topics include prudent antibiotic prescribing, introduction to antibiotic stewardship, and dose optimisation. In Phase III, emphasis is given to the practice of medicine and interprofessional collaboration. Topics included in this phase are communication and professionalism. The learners also explore new ideas and apply the skills learnt in Phases I and II. Depending on the resources available at a medical school the following modes of delivery could be used; didactic teaching, web-based teaching, clinical case discussions, workshops/seminars and board games.

At the bottom of the spiral curriculum (Figure 6.2) students should be introduced to fundamental topics such as “describing what a bacterium is” and “describing the different types of bacteria that may cause infections and how they contribute to healthcare-associated infections”. These topics should be covered in the early years (Phase I) at the time when students are learning the basic concepts. Didactic lectures can be used to teach these basic concepts. Board games which could be developed by the teachers or students can be used to teach concepts such as “explain mechanisms of antibiotic resistance” and “differentiating between bactericidal and bacteriostatic antibiotics”. In the later years (Phases II and III) at the time when students have acquired basic clinical skills, the core concepts of AMS in the top spiral curriculum should be taught. Some of these concepts include “describing how to alter the route of administration from intravenous to oral antibiotic therapy” or “raising public awareness of the problems associated with antibiotic resistance and explaining to the patients their role in promoting appropriate antibiotic use”. Teaching methods that encourage critical thinking and problem-solving ability such as small group teaching and flipped classroom learning models are considered as the teaching approaches at this stage.

6.7 Methods of teaching to be used in teaching the curriculum

The spiral curriculum should be embedded into microbiology, pharmacology, medicine (infectious diseases), public health and paediatrics’ curricula and be implemented over three to four years in a spiral model. The scoping review identified different teaching methods used to teach responsible antibiotic prescribing in medical schools across the globe. Different teaching methods such as case-based small group activity, case-based didactic sessions, and online

learning should be used to deliver the curriculum. The lecture method can be used to teach concepts that introduce students to bacteria, mechanisms of antibiotic resistance, mechanisms by which antibiotics kill bacteria and surveillance in the third or fourth year (Table 6.1). In years 4-5 when students have acquired more clinical skills, small group problem-based and case-based teaching should be used to teach students competencies such as how inappropriate use of broad-spectrum antibiotics increases the risk of *Clostridioides difficile* colitis, the rationale and use of perioperative prophylactic antibiotics to prevent surgical-site infections and pharmacokinetic parameters such as minimum inhibitory concentration (MIC) and ability to dose optimize using PK-PD principles (Table 6.2).

In years 5-6 when students are about to graduate and start working together with other health professionals, they should be taught competencies such as communication skills and professionalism along with other health professional students using small group learning or the flipped classroom learning model (Table 6.3). These competencies include acquiring communication skills to be able to counsel their patients on appropriate antibiotic use and discourage them from purchasing antibiotics without prescription and establishing collaborative communication principles and actively listening to other professionals and patients/carers involved in the delivery of antibiotic therapy. The flipped classroom learning model engages students in a learning process that stimulates deep and self-directed learning. In flipped learning Bloom's taxonomy is reversed so that the learners are engaged in the simplest tasks at home i.e., remembering and understanding, and when they are in the class they work on the tasks that are higher in Bloom's taxonomy i.e., application, analysis, synthesis and evaluation (Brame, 2013; Brinks, 2014).

Table 6.1: Proposed integration of learning objectives, disciplines, teaching and assessment methods for an antibiotic stewardship programme using a spiral curriculum – third/fourth years of a medical programme.

Learning objectives - Knowledge	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Describe what a bacterium is	Microbiology	Didactic lecture	A-type MCQs
Describe the different types of bacteria that may cause infections and how they contribute to healthcare-associated infections	Microbiology	Didactic lecture	A-type MCQs
Explain the role played by the environment in the transmission of bacteria	Microbiology	Didactic lecture	A-type MCQs
Differentiate between latent tuberculosis infection and active tuberculosis disease	Microbiology/ Pharmacology	Board games	A-type MCQs
Describe at least two different ways in which antibiotics may kill bacteria	Microbiology/ Pharmacology	Board games	A-type MCQs
Differentiate between bactericidal and bacteriostatic antibiotics	Pharmacology	Board games	A-type MCQs
Explain the concept of bacterial killing by either concentration-dependent or time-dependent antibiotics	Pharmacology/ Medicine	Small group discussion	A-type MCQs
Explain the concept of Minimum Inhibitory Concentration (MIC) in terms of bacterial killing	Microbiology/ Pharmacology	Flipped classroom learning model	A-type MCQs
Describe and be able to recognize the common side-effects associated with commonly administered antibiotics	Pharmacology/ Medicine	Small group discussions/ ward round teaching	A-type MCQs

Describe the different ways in which antibiotics may kill bacteria	Microbiology/ Pharmacology	Didactic lecture	A-type MCQs
Explain what an antibiotic-resistant organism is	Microbiology/ Pharmacology	Flipped classroom learning model	A-type MCQs
Discuss how the inappropriate use of antibiotics (including non-adherence to a treatment regime) may lead to resistance to antibiotics	Pharmacology /Medicine	Small group discussion	A-type MCQs
Describe how antibiotic use drives the emergence of drug-resistant bacteria	Microbiology /Pharmacology/ Medicine	Flipped classroom learning model	A-type MCQs
Describe the use of broad and narrow-spectrum antibiotics and the role of broad-spectrum antibiotics in contributing to antibiotics resistance	Pharmacology/ Medicine	Small group discussion	A-type MCQs
Explain mechanisms of antibiotic resistance	Microbiology/ Pharmacology	Board games	A-type MCQs
Explain the 'Chain of Infection'	Microbiology	Board games	A-type MCQs
Define the components required for the transmission of an infection (i.e., the presence of an organism, the route of transmission of the organism from one person to another, the host who would be susceptible to the infection)	Microbiology	Flipped classroom learning model	A-type MCQs
Describe the routes of transmission of infectious organisms (i.e., contact, droplets, and airborne routes)	Microbiology	Flipped classroom learning model	A-type MCQs
Present and recognize the characteristics of a susceptible host	Microbiology	Board games	A-type MCQs
Describe how vaccines can prevent infections in susceptible persons	Microbiology	Flipped classroom learning model	A-type MCQs
Explain the application of standard precautions in healthcare environments	Microbiology	Small group discussion	A-type MCQs

Explain how to appropriately use the following products, namely soap and water, antibacterial soap, surgical scrubs, waterless alcohol agents, for hand hygiene, and the conditions under which to apply each of the methods	Microbiology	Flipped classroom learning model	A-type MCQs
Differentiate between the cleaning, disinfecting and sterilization of hospital equipment	Microbiology	Small group discussion	A-type MCQs
Describe safe handling methods and the disposal of sharp objects	Microbiology	Flipped classroom learning model	A-type MCQs
Describe techniques to safely handle blood and body fluids to prevent exposure	Microbiology	Practical	A-type MCQs
Recognize the symptoms of infection	Microbiology	Small group discussion	A-type MCQs
Identify the likely source of infection and likely pathogens	Medicine	Small group problem-based teaching/ Flipped classroom learning model	A-type MCQs or clinical scenarios
Explain how to recognize and manage sepsis	Medicine	Small group case-based teaching	A-type MCQs or clinical scenarios
Explain the importance of personal protective equipment and when to use them to prevent infections	Microbiology	Flipped classroom learning model	A-type MCQs or extended matching item or short answer questions
Explain the importance of surveillance	Microbiology	Small group discussion	A-type MCQs

Explain how the removal or drainage of material from the focus of infection, such as an abscess (often called source control) would facilitate a clinical cure	Surgery	Ward round teaching	A-type MCQs or clinical scenarios
Learning Objectives - Skills	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Apply policies, procedures and guidelines relevant to the control of infection when infection control cases and situations present themselves	Microbiology/ Public Health	Practical	mini-CEX or DOPS or portfolio or log book
Demonstrate the appropriate way of taking samples following local procedures for taking samples	Clinical skills	Ward round teaching/ practical	OSCE
Interpret and use MIC provided in AST report clinically in informing dosing decisions and attempts to dose optimize	Microbiology	Practical	mini-CEX or DOPS or portfolio or logbook
Demonstrate ideal hand hygiene practices	Clinical skills	Practical	OSCE
Demonstrate the appropriate way of taking laboratory samples following local procedures	Clinical skills	Ward round teaching/ practical	OSCE
Demonstrate the correct technique for performing a blood culture	Clinical skills	Ward round teaching/ practical	OSCE
Demonstrate the correct technique for taking a pus swab	Clinical skills	Ward round teaching/ practical	OSCE
Demonstrate the WHO concept of 'My five moments for hand hygiene'	Clinical skills	Practical	OSCE

Learning Objectives - Attitudes	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Implement work practices that reduce the risk of infection (e.g., undergoing appropriate immunization or not coming to work when sick) to ensure the protection of the patient and other healthcare workers	Public Health	Small group discussion	A-type MCQs
Appreciate that healthcare workers should show accountability and commit to following infection control protocols as part of their contract of employment	Public Health	Small group discussion	A-type MCQs
Act as a role model to healthcare workers and members of the public by adhering to the principles to prevent and control infections	Microbiology/ Public Health	Small group discussion	A-type MCQs

MCQs: Multiple Choice Questions, OSCE: Objective structured clinical examination, mini-CEX (Mini Clinical Evaluation Exerciser), Directly Observed Procedural Skills (DOPS)

Table 6.2: Proposed integration of learning objectives, disciplines, teaching and assessment methods for an antibiotic stewardship programme using a spiral curriculum – fourth/fifth years of a medical programme.

Learning objectives - Knowledge	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Identify approaches to support the optimal prescription of antibiotics	Pharmacology/ Medicine	Flipped classroom learning model	A-type MCQs
Explain how the inappropriate use of broad-spectrum antibiotics increases the risk of <i>Clostridioides difficile</i> colitis	Medicine	Small group case-based teaching	A-type MCQs

Discuss how the identification of bacteria and their susceptibility to antibiotics from a specific culture are important in antibiotic therapy	Medicine	Small group problem-based teaching	A-type MCQs
Explain why self-limiting bacterial or viral infections are unlikely to benefit from the dispensing of antibiotic	Medicine/ Paediatrics	Small group case-based teaching	A-type MCQs
Describe the required management strategies to treat self-limiting infections (i.e. the administration of analgesics/rest /fluid intake)	Medicine/ Paediatrics	Small group case-based teaching	A-type MCQs
Explain the importance of following local antibiotic policies (i.e. in that their development is based on local resistance patterns), and adhere to these policies in practice	Medicine/ Paediatrics	Small group discussion	A-type MCQs
Explain the importance of documenting the following parameters in antibiotic therapy route of administration, dosage, duration, intervals between dosages, and the review date in clinical notes and demonstrate this in practice	Medicine	Ward round teaching/Flipped classroom learning model	A-type MCQs
Explain the factors that need to be considered when choosing an antibiotic (including the site of infection and the type of bacteria likely to cause an infection at that particular site)	Medicine	Ward round teaching	A-type MCQs
Explain the importance of documenting a patient's allergy to an antibiotic	Pharmacology/ Medicine	Ward round teaching	A-type MCQs
Describe why it is important to use local guidelines to initiate prompt and effective antibiotic treatment in patients with life-threatening infections	Medicine	Small group problem-based teaching	A-type MCQs
Describe why it is important to switch from intravenous antibiotics to oral therapy	Medicine	Small group problem-based teaching/ward round teaching	A-type MCQs
Describe how to alter the route of administration from IV to oral antibiotic therapy	Medicine	Ward round teaching/Small group problem-based teaching	A-type MCQs
Explain the rationale and use of perioperative prophylactic antibiotics to prevent surgical-site infections	Surgery/ Anaesthesia	Ward round teaching/Small group problem-based teaching	A-type MCQs
Discuss factors that could influence the prescription of antibiotics (e.g. availability of resources, diagnostic uncertainty, peer practice, patient	Medicine	Small group discussion	A-type MCQs

expectations, and financial interests) and the implications for antibiotic stewardship programmes			
Describe national guidance in respect to the completion of a course of antibiotics	Medicine	Small group discussion	A-type MCQs
Describe some of the medicines with which antibiotics can sometimes interact	Pharmacology/ Medicine	Flipped classroom learning model / ward round teaching	A-type MCQs
Describe how switching to oral antibiotics when appropriate can reduce costs, facilitate discharge and prevent complications associated with indwelling catheters and clots	Medicine	Ward round teaching	A-type MCQs
Explain the importance of source control (incision and drainage) in the management of purulent skin and soft tissue infections	Surgery	Ward round teaching	A-type MCQs
Recognize the symptoms of infections like fever, pain, cough and rashes as a guidance that will trigger empirical antibiotic therapy versus those that could wait for a culture-based antibiotic therapy	Medicine/ Paediatrics	Flipped classroom learning model/ ward round teaching	A-type MCQs
Describe the need for precaution when prescribing antibiotics in populations at risk e.g., children, the elderly, pregnant women and lactating mothers.	Medicine/ Paediatrics/ Obstetrics	Small group problem-based teaching/ ward round teaching	A-type MCQs
Explain the importance of prompt submission of swab specimens to the laboratory to preserve the organisms during transportation	Microbiology/ Medicine		A-type MCQs
Explain how to de-escalate to narrow-spectrum antibiotics after initial broad-spectrum antibiotic use	Medicine	Flipped classroom learning model/ward round teaching	A-type MCQs
Describe the importance of bioavailability and non-inferiority of oral versus parenteral formulations when doing some antibiotics	Pharmacology/ Medicine	Flipped classroom learning model	A-type MCQs
Explain principles for selection of antibiotics which includes pathogen type (suspected or confirmed)	Microbiology	Flipped classroom learning model	A-type MCQs

Explain the importance of medical decisions about dosing strategies, interactions and the treatment of patients with specific disease conditions e.g. interaction between clarithromycin and digoxin	Medicine	Ward round teaching	A-type MCQs
Explain the need for therapeutic drug level monitoring in antibiotic stewardship programmes, e.g., in patients on vancomycin, linezolid and aminoglycosides therapy	Medicine	Ward round teaching	A-type MCQs
Explain how microbiology samples may be of assistance in the diagnosis of infections	Microbiology	Small group discussion	A-type MCQs
Interpret microbiology results/reports from the laboratory at a basic level	Microbiology/ Medicine	Ward round teaching/Flipped classroom learning model	A-type MCQs
Explain why it is important to consider certain physiological conditions (e.g., renal function) in patients who receive an antibiotic	Medicine	Ward round teaching/Small group problem-based teaching	A-type MCQs
Establish that some antibiotics, such as aminoglycosides and vancomycin, should be dosed according to the patient's weight in order to minimize complications	Pharmacology/ Medicine	Small group problem-based teaching	A-type MCQs
Explain pharmacokinetic parameters such as MIC and ability to dose optimize using PK-PD principles	Microbiology/ Pharmacology/ Medicine	Small group problem-based teaching	A-type MCQs
Learning Objectives - Skills	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Apply appropriate policies/procedures and guidelines for the collection and handling of specimens	Microbiology	Practical	mini-CEX or DOPS or portfolio or logbook

Learning Objectives - Attitudes	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Consider drug allergies, vaccination history and severity of illness before starting empiric antibiotic therapy	Medicine	Ward round teaching/Small group problem-based teaching	A-type MCQs

MCQs: Multiple Choice Questions, mini-CEX (Mini Clinical Evaluation Exerciser), Directly Observed Procedural Skills (DOPS)

Table 6.3: Proposed integration of learning objectives, disciplines, teaching and assessment methods for an antibiotic stewardship programme using a spiral curriculum – fifth/sixth years of a medical programme.

Learning objectives - Knowledge	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Explain the patient's/carer's expectations or demands in respect of antibiotics and the need to use antibiotics appropriately	Medicine	Flipped classroom learning model	A-type MCQs
Explain the roles, responsibilities, and competencies of other health professionals involved in policy decisions concerning antibiotic treatment	Medicine	Flipped classroom learning model	A-type MCQs
Explain why it is important that healthcare professionals, involved in the delivery of antibiotic therapy (including the prescription, delivery and supply), have a common understanding of antibiotic treatment policy decisions, the quantities involved in antibiotic use, and effective patient/client outcomes	Medicine	Flipped classroom learning model	A-type MCQs
Learning Objectives - Skills	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Communicate with respect and express needs of all parties in shaping and delivering care or services	Medicine	Flipped classroom learning model	mini-CEX or DOPS or portfolio or logbook
Acquire communication skills to be able to counsel patients on appropriate antibiotic use and discourage them from purchasing antibiotics without prescription	Medicine	Flipped classroom learning model	mini-CEX or DOPS or portfolio or logbook
Communicate effectively to ensure a common understanding of care decisions	Medicine	Flipped classroom learning model	mini-CEX or DOPS or

			portfolio or logbook
Establish collaborative communication principles and actively listen to other professionals and patients/carers involved in the delivery of antibiotic therapy	Medicine	Flipped classroom learning model	mini-CEX or DOPS or portfolio or logbook
Effectively use information and communication technology to improve interprofessional patient-centred care	ICT Department	Flipped classroom learning model	mini-CEX or DOPS or portfolio or logbook
Share information with patients/carers in a respectful manner and in such a way that it is understandable, encourages discussion, and enhances participation in decision-making	Medicine	Flipped classroom learning model	mini-CEX or DOPS or portfolio or logbook
Learning Objectives - Attitudes	Suggested disciplines to deliver the learning objectives	Teaching method	Assessment of and for learning
Support the participation of patients/carers, as integral partners, when planning/delivering their care	Medicine	Flipped classroom learning model	A-type MCQs
Ensure that appropriate education and support is provided by learners to patients/carers, and others involved with their care or service	Medicine	Flipped classroom learning model	A-type MCQs
Raise public awareness of the problems associated with antibiotic resistance and explain to the patients their role in promoting appropriate antibiotic use	Public Health	Flipped classroom learning model	A-type MCQs
Establish a trusting relationship with patients/carers and other health/social care professionals	Public Health	Flipped classroom learning model	A-type MCQs

MCQs: Multiple Choice Questions, mini-CEX (Mini Clinical Evaluation Exerciser), Directly Observed Procedural Skills (DOPS)

Competencies explaining how to de-escalate to narrow-spectrum antibiotics after initial broad-spectrum antibiotic use, how the removal or drainage of material from the focus of infection, such as an abscess (often called source control) would facilitate a clinical cure and describing why it is important to switch from intravenous antibiotics to oral treatment should be taught at the bedside during ward rounds. Other competencies that could be taught during ward rounds include describing how to alter the route of administration from intravenous to oral antibiotic therapy and how switching to oral antibiotics when appropriate can reduce costs, facilitate discharge and prevent complications associated with indwelling catheters and clots.

6.8 Evaluation of the curriculum

Assessment and feedback are important in shaping knowledge, behaviours, skills and attitudes and life-long learning (Dougall et al., 2014). The scoping review found the ASP in medical schools were evaluated differently, while some studies evaluated student's knowledge others evaluated student's satisfaction with the programme. They used strategies such as a before and after assessment and a post-test evaluation. Different methods of assessments can be used to evaluate the antibiotic stewardship learning in this curriculum. Examinations such as clinical scenarios, multiple choice questions, essays and objective structured clinical examinations can be used to evaluate many learning objectives in this curriculum (Tables 6.1-6.3).

There is a need for a wide range of assessment methods to assess different clinical competencies, however, it should be noted that no one assessment method can adequately assess all the different clinical competencies (Miller, 1990). For assessment of the knowledge, knowledge application and concepts of 'Knows' (knowledge) and 'Knows How' (competence) of Miller's framework for clinical assessment is best assessed with Multiple Choice Questions (MCQs), short answer questions and extended matching items (Tabish, 2008). The use of single best answer MCQs (A-type MCQs) is advocated in assessing this antibiotic stewardship curriculum. They are ideal for testing decision making, making a diagnosis, selecting special investigations, deciding on management, and choosing an appropriate method (Personal communication: McInerney). A-type items are the most widely used MCQs format. They consist of a stem (e.g., a clinical case presentation) and a lead-in question, followed by a series of choices, typically one correct answer and four distractors (Case and Swanson, 2000). For assessment of practical skills that involve 'Shows How' (performance) in Miller's framework

for clinical assessment, the multi-station objective structured clinical examination (OSCE) is appropriate (Tabish, 2008). The Mini Clinical Evaluation Exercise (mini-CEX), Directly Observed Procedural Skills (DOPS), portfolios or logbooks can be used to assess performance-based assessments targeting ‘Does’ (action) of Miller’s framework for clinical assessment (Tabish, 2008; Yousuf, 2012). The American Board of Internal Medicine developed a mini-CEX assessment method to assess competencies such as physical examination skills, clinical judgment, humanistic qualities/professionalism, counselling skills, medical interviewing skills, organization and efficiency (Tabish, 2008; Yousuf, 2012). There are some emergency procedures such as analgesia, aseptic technique, and post-procedure management that cannot be assessed with the OSCE, but can be assessed with DOPS (Naeem, 2013). Other limitations of the OSCE include cost and difficulty in assessing examinee attitudes (Naeem, 2013). The DOPS involve the use of a structured rating scale to evaluate practical procedures (Naeem, 2013). Some of the competencies that can be assessed with DOPS include general knowledge regarding a procedure, counselling and communication, informed consent, and pre-procedure preparation (Tabish, 2008).

The antibiotic stewardship framework developed in this thesis is designed to be taught and assessed in line with the concept of constructive alignment. Biggs (2014, p. 1) defined constructive alignment as “an outcomes-based approach to teaching in which the learning outcomes that students are intended to achieve are defined before teaching takes place. Teaching and assessment methods are then designed to best achieve those outcomes and to assess the standard at which they have been achieved.”

6.9 Conclusion

This chapter described how the competencies that reached consensus during the two rounds of the modified Delphi with medical teachers were used to develop an antibiotic stewardship framework for teaching prudent antibiotic prescribing in medical schools. It also provided an overview on how the three domains: knowledge, attitudes and skills are used to develop a spiral curriculum for antibiotic stewardship, the proposed methods of teaching to be used in delivering the curriculum and how knowledge will be assessed. The next chapter discusses the outcome of the project.

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CHAPTER SEVEN

Discussion of findings and conclusion

"What we urgently need is a solid global plan of action which provides for the rational use of antibiotics so quality-assured antibiotics reach those who need them but are not overused or priced beyond reach"

(Stephens, 2014)

Dr Jennifer Cohn,

Medical Director of Medecins Sans Frontiers' Access Campaign

7.1 Introduction

This thesis highlighted the importance of incorporating an antibiotic stewardship curriculum into the curricula of the Nigerian and South African medical schools to encourage the teaching of prudent antibiotic prescribing. This is important considering the consequences of antibiotic resistance and the role of antibiotic stewardship in improving prudent antibiotic use. Therefore, this study aimed to develop an educational antibiotic stewardship programme that will assist in teaching medical students in Nigeria and South Africa rational antibiotic prescribing.

The study was divided into two phases. Phase One involved the problem identification. This phase was subdivided into three stages, while Phase Two involved the development of an antibiotic stewardship framework for medical schools with a panel of experts. To meet the research objectives related to Phase One the following studies were conducted; a scoping review to map the available evidence on teaching prudent antibiotic prescribing in medical schools, a summative content analysis of the sampled Nigerian and South African medical schools' curricula and a survey on the knowledge and perceptions of final year Nigerian and South African medical students on prudent antibiotic use. The survey identified a knowledge gap among the respondents of both countries and the scoping review did not reveal any papers on educational antibiotic stewardship conducted in an African medical school. The data collected in the three stages of the Phase One informed the Phase Two of the study. In Phase Two, medical teachers involved in teaching prudent antibiotic prescribing participated in a modified Delphi study that led to the development of an antibiotic stewardship framework for

teaching prudent antibiotic prescribing. The panel of experts reached consensus on 88 competencies which are divided into knowledge, attitudes and skills domains.

7.2 Educational ASPs in African medical schools

The scoping review did not reveal any papers on ASPs from African medical schools and only one was found from Asia (Shankar et al., 2011). Most of the included studies were conducted in the USA and Europe. According to Brink et al. (2017, p. 358) “A key strategy in facilitating appropriate antibiotic prescribing is the early introduction of the relevant knowledge, concepts and skills into undergraduate curricula”. In view of the lack of effective antibiotics to treat emerging infections and uncertainty in getting them in the near future, there is a need for African medical schools to develop antibiotic stewardship programmes to prepare aspiring medical doctors on responsible antibiotic prescribing. The scoping review identified a wide range of teaching methods used to teach medical students the concept of antibiotic stewardship. However, most of the antibiotic stewardship strategies in the included papers used the lecture method as the mode of instruction. Lectures are a traditional way of disseminating information to learners and it is a teacher-centred method that allows an educator to pass large amounts of information to a large group of students, but its disadvantage is that it results in passive students (McInerney and Green-Thompson, 2020). According to Frost (1965) as cited in Verner and Dickinson (1967, p. 90).

“In a lecture given by a brilliant scholar with an outstanding topic and a highly competent audience, ten per cent of the audience displayed signs of inattention within fifteen minutes. After eighteen minutes one-third of the audience and ten per cent of the platform guests were fidgeting. At 35 minutes everyone was inattentive; at 45 minutes, trance was more noticeable than fidgeting; and at 47 minutes some were asleep and at least one was reading. A casual check twenty-four hours later revealed that the audience recalled only insignificant details, and these were generally wrong.”

The use of active learning methods that are student-centred could enhance students’ learning experience. The principles of education in the 21st century are to encourage collaboration, critical thinking, communication skills and creativity and these can not be achieved with traditional didactic lectures. In the antibiotic stewardship curriculum developed in this study, we propose the use of a wide range of teaching methods such as small group problem-based

teaching, small group case-based teaching, the flipped classroom learning model, board games and ward round teaching to encourage critical thinking. Some of these pedagogical approaches encourage active learning. The use of the flipped classroom is increasingly becoming popular in medical education (Prober and Heath, 2012). The use of newer learning methods such as the flipped classroom allows students to use technology to guide their learning (Prober and Heath, 2012). While millennial learners prefer the use of digital resources and interfaces to improve their learning, it was interesting to find that most of the respondents that participated in the survey (51.9% and 79.8%) of the South African and (64.5% and 76.2%) of the Nigerian respondents did not agree that the use of applications for smart devices and computer-based tutorials respectively, by newly qualified doctors would improve appropriate antibiotic prescribing.

In the traditional method of teaching students, information is passed to the students in class and homework is given to do after the class. While in the flipped classroom, students are given a problem to work on such as an out-of-class activity before the class, and in the class they actively discuss the concepts usually in small groups (McInerney and Green-Thompson, 2020). Small group learning may enhance the in-class activities in the flipped classroom concept. The scoping review found that some of the papers included in the scoping review reported an evaluation of student knowledge after implementation of the antibiotic stewardship programme, while others did not. In this study, a wide range of assessment methods are proposed to assess the different competencies. These include multiple-choice questions, objective structured clinical examination, mini clinical evaluation exercise, directly observed procedural skills, student portfolios, or logbook keeping.

7.3 Knowledge and in relation to appropriate antibiotic prescribing

In Phase One, a survey on the knowledge and perceptions of final year medical students of the sampled Nigerian and South African medical schools was conducted. The respondents in both countries did poorly in questions involving the management of patients with methicillin-sensitive *Staphylococcus aureus* and extended beta-lactamase *Escherichia coli* infections. Of the 10 vignettes answered correctly, South African respondents scored an average of 62.4% in the knowledge segment compared to 31.9% scored by the Nigerian respondents. Conversely, respondents from both countries had similar perceptions of antibiotic use and antibiotic

resistance. An effort should be made to bridge the gaps identified. A recent study conducted among final year medical and pharmacy students of three East African countries found that the students were not adequately prepared for antibiotic prescribing after graduation (Lubwama et al., 2021). It should be noted that this problem is not only limited to African medical students. Previous studies across the globe have found that most medical students are not ready for antibiotic prescribing on completion of their studies and desire further training on responsible antibiotic prescribing (Abbo et al., 2013; Dyar et al., 2014; Huang et al., 2013; Minen et al., 2010). The antibiotic stewardship competencies in this thesis were developed with the help of medical teachers drawn from different disciplines. Teachers were chosen from different disciplines because for antibiotic stewardship to succeed, a multidisciplinary approach is essential.

7.4 Curricula content in relation to prudent antibiotic prescribing and stewardship

A summative content analysis of two African medical schools' antibiotic stewardship curricula to describe the content of South African and Nigerian medical students' curricula with respect to prudent antimicrobial prescribing was undertaken. While the South African medical school uses an integrated curriculum, the Nigerian medical school has adopted a traditional discipline-based curriculum. The teaching of prudent antibiotic stewardship is not well coordinated in either curriculum reviewed. The term "antimicrobial stewardship" appeared a few times in the curriculum of the South African medical school, but it is completely absent in the curriculum of the Nigerian medical school. The Nigerian curriculum was designed by English academics when the medical degree was initiated and it has undergone little modification over the years. It was not altogether surprising to find no information related to AMS in the Nigerian curriculum because it is an emerging field in medicine and antibiotic resistance was not thought to be a serious problem when the curriculum was designed. Whereas now AMR is considered one of the major health challenges in the 21st century and medical schools should aim to produce doctors with the required knowledge and skills to help reduce this problem. The findings of the content analysis suggest a need for revision of the medical curricula of both medical schools reviewed with an emphasis on responsible antibiotic prescribing that will produce doctors with the required knowledge and skills to engage in antibiotic stewardship. Additionally, Nigerian medical schools should consider changing their teacher-centred discipline-based curriculum to

a student-centred vertically integrated one. This will help the student to develop life-long learning, critical thinking and the development of skills that will prepare them for self-directed learning throughout their careers (Brauer and Ferguson, 2015; Malik and Malik, 2011). An antibiotic stewardship framework was developed in this thesis to be taught in a spiral curriculum over 3-4 years. A spiral curriculum encourages mastery, reinforces and deepens previously learnt concepts. Further, in spiral learning, as the students move to each new level, a new concept is introduced that links directly back to the information they received from the previous year (Dowding, 1993).

In the proposed curriculum developed in this thesis students should be introduced to fundamental topics such as “describing what a bacterium is” and “describing the different types of bacteria that may cause infections and how they contribute to healthcare-associated infections”. These topics should be covered in the early years in Phase I at the time when students are learning the basic concepts and these can be delivered using didactic lectures while board games can be used to teach concepts such as “explain mechanisms of antibiotic resistance” and “differentiating between bactericidal and bacteriostatic antibiotics”. In the later years in Phases II and III at the time when students have acquired basic clinical skills, the core concepts of AMS should be taught. Some of these competencies include “describing how to alter the route of administration from intravenous to oral antibiotic therapy” or “raising public awareness of the problems associated with antibiotic resistance and explaining to the patients their role in promoting appropriate antibiotic use”. Teaching methods that encourage critical thinking and problem-solving ability such as small group teaching and the flipped classroom can be used as the teaching approaches at this stage.

7.5 The use of a panel of experts to develop an antibiotic stewardship curriculum

In the Delphi study, a panel of experts was used to reach a consensus among a group of experts in infectious diseases, clinical pharmacology, medical microbiology, nursing, pharmacy and medical education about content for an antibiotic stewardship curriculum for medical schools in Nigeria and South Africa. The experts reached consensus on 88 of the competencies required to adequately practice AMS. The competencies were categorised into three domains; knowledge, attitudes and skills, to be taught in a spiral curriculum. A similar study conducted

in the UK to develop an antibiotic stewardship framework for healthcare professional students reached consensus on 55 competencies following two rounds of the modified Delphi technique (Courtenay et al., 2018). It is hoped that the developed curriculum, if incorporated into the existing curricula, may help the future prescribers to acquire basic knowledge and skills to engage in antibiotic stewardship and bridge the gap in knowledge identified in the survey and deficiencies in the content of the medical curriculum of the two countries studied in the summative content analysis. This highlights the need to integrate courses on both general and prudent antibiotic prescribing into the medical curriculum (Pulcini and Gyssens, 2013). African medical schools should consider developing and integrating antibiotic stewardship competencies or adopting the ones developed in this study because antibiotics are among the most widely used class of pharmaceuticals in a healthcare setting.

7.5 Antibiotic stewardship curriculum

In spite of all efforts to implement antibiotic stewardship in different healthcare settings, most antibiotic stewardship teaching efforts are presently directed at the postgraduate level (Centres for Medicare and Medicaid Services, 2016; Pulcini and Gyssens, 2013). The antibiotic stewardship competencies that reached consensus with the help of the panel of experts were used to develop an antibiotic stewardship framework. The framework will help in teaching principles of antibiotic stewardship in medical schools which will add value to the limited published studies in antibiotic stewardship education. Recently a multifaceted antibiotic stewardship curriculum for teaching responsible antibiotic stewardship to medical students using small group didactic teaching was developed in the USA to address the growing need for a dedicated stewardship programme in medical schools (Wang et al., 2021). For each of the learning objectives developed with the help of the panel of experts in this thesis, the best method to teach and assess it was proposed, it is hoped that this will help in the delivery of the curriculum. If effectively implemented constructed alignment can improve the quality of teaching and learning (Biggs, 2014).

7.6 Limitations of the study

One of the main limitations of this thesis was the fact that I was unable to conduct the third phase of the study as outlined in the study proposal. The study was scheduled for 2020 however, due to the COVID-19 pandemic changes to the medical school curriculum were necessitated.

Some of these changes to the curriculum include the cancellation of the spiral weeks and face-to-face teaching. The arrangement made with the Unit for Undergraduate Medical Education of the University of the Witwatersrand at the beginning of the academic year before the pandemic was to conduct the third phase of the study during spiral weeks. An attempt to do it online was not welcomed by the unit as students were struggling to cope with the transition from face-to-face to online and had a lot of work to be covered. An attempt in 2021 to measure knowledge scores before and after an intervention through an online presentation was unsuccessful as there was a poor response rate to the questionnaire.

One of the limitations of the scoping review was that only papers published in the English language were included. Even though several databases were searched, including unpublished, and grey literature, there is still a possibility that some potentially useful articles published in other languages were excluded. The review only included studies conducted on medical students, and therefore **AMS** studies involving other health professional students such as nursing, pharmacy, and dentistry were excluded. Although these health professional students have a role to play in encouraging prudent antibiotic use when they graduate, they were excluded because the PhD aimed to develop an antibiotic stewardship curriculum for medical students.

Limitations of the survey were the low response rate (31.7%) from the South African respondents and that it did not include all medical schools in both countries. Attempts to improve the response rate included extending the survey period and sending weekly reminders. The findings of the survey cannot be generalised as only four universities were included and there are 51 accredited medical schools in Nigeria and eight in South Africa. The survey findings are similar to a South African study by Wasserman et al. (2017) on final year medical students that included three medical schools. To the best of my knowledge, this is the first study conducted in Nigerian medical schools to examine the knowledge and perceptions of final year medical students on prudent antibiotic use. Similarly, a limitation to the summative content analysis is that the reviewed curriculum from each country is not representative of other medical schools in the two countries. However, Ibrahim (2007) notes that almost all Nigerian medical schools without exception use a traditional discipline-based curriculum developed by the English academics in the 1940s. Further, a recent discussion with lecturers teaching across Nigerian medical schools shows that they still use the same type of curriculum. This cannot be

said about the South African curriculum because it is arguably the most advanced country in terms of innovation in medical education (Gukas, 2007). The eight South African medical schools use some sort of integrative curriculum, such as problem-based or case/theme-based in preclinical years and clinical block rotations during clinical years (Botha and Adefolalu, 2020).

A limitation of the Modified Delphi conducted in this thesis is that items that reached consensus in round one were not carried to round two which might have reduced the iteration of the process. However, the results of each round were sent to the experts for input which improved iteration.

7.7 Recommendations for future research

Some recommendations emerged from this study which should inform future research. There is a need to implement and evaluate the competencies developed in this thesis. The research should aim to answer a question - would medical graduates remember the knowledge and skills they learned of responsible antibiotic prescribing after graduation? This can be achieved by using prospective cohort studies where an antibiotic stewardship curriculum that is student-centred is delivered to students with follow-up after graduation to evaluate the value of the skills learned, and whether they had retained the knowledge. A similar survey should be conducted in other African medical schools to evaluate medical student's knowledge and perceptions about prudent antibiotic use. Further research should also be conducted in primary, secondary, and tertiary healthcare settings in Africa about antibiotic prescribing and the outcomes should guide the development of ASPs in such settings.

7.8 Conclusion

In conclusion, I highlighted further insights into many aspects of teaching responsible antibiotic prescribing in medical schools. In this regard, I demonstrated a gap in knowledge in prudent antibiotic prescribing among both samples of Nigerian and South African respondents which is more evident among the Nigerian cohort. Secondly, I showed that no literature from African medical schools is published on antibiotic stewardship for teaching prudent antibiotic prescribing among medical students. Thirdly, I demonstrated that the content of the curricula of the two countries is inadequate to prepare aspiring doctors to acquire basic knowledge and skills to engage in appropriate antibiotic prescribing. These data, therefore, suggest the need for

revision of antibiotic teaching in both countries. In view of these, I engaged medical teachers drawn from different disciplines related to antibiotic stewardship from different medical schools in both countries as panellists to recommend and reach a consensus on what should be included in the medical curriculum for teaching responsible antibiotic prescribing to medical schools. The competencies that reached consensus were grouped into three domains – knowledge, attitude and skill and were used to develop a spiral antibiotic stewardship curriculum which should be incorporated into the existing curricula to be taught in three different phases over three years.

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Appendix A: Educational antimicrobial stewardship programs in medical schools: a scoping review protocol (Augie et al., 2020).

Educational antimicrobial stewardship programs in medical schools: a scoping review protocol

Bashar M. Augie¹ • Patricia A. McInerney^{2,3} • Robyn L. van Zyl¹ • Jacqui Miot⁴

¹ Pharmacology Division, Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, ²Centre for Health Science Education, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, ³The Wits-JBI Centre for Evidenced-Based Practice: A JBI Affiliated Group, and ⁴Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

ABSTRACT

Objective: The objective of this scoping review is to identify the available evidence on antimicrobial stewardship programs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used.

Introduction: Antibiotics are life-saving drugs and their discovery is one of the most important advances of the 20th century. They have transformed modern medicine by playing a critical role in the management of infectious diseases. However, the rapid development of resistance of pathogens to antibiotics is gradually affecting this initial success. Antimicrobial stewardship programs have been shown to reduce the burden of antimicrobial resistance in hospitals.

Inclusion criteria: This scoping review will consider papers conducted in medical school curricula to improve the prescribing of antimicrobial medication. Studies that include other health profession students, such as nursing, pharmacy, or dentistry students, will be excluded. Studies published in English from 1996 onwards will be included.

Methods: Databases to be searched are PubMed, Wiley Online library, CINAHL Complete, Web of Knowledge, Scopus and Education Resources Information Center. Unpublished studies and gray literature will be included. Searching will follow a three-step process and will be conducted by two reviewers. Data will be extracted by two independent reviewers. Any disagreements that arise between the reviewers during the study selection process or data extraction will be resolved through discussion, or with a third reviewer. Results will be presented in tabular or diagrammatic form, together with a narrative summary.

Keywords Antimicrobial resistance; antimicrobial stewardship; education; medical students; teaching

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Introduction

The discovery of penicillin by Alexander Fleming in 1928 has transformed modern medicine.¹ Antibiotics have saved millions of lives since their discovery,² and are currently among the most commonly prescribed medicines in our health facilities.^{3–5}

It has been reported that 20% to 50% of antibiotic utilization is inappropriate.^{6,7} Inappropriate antimicrobial use is associated with poor patient outcomes such as antimicrobial resistance, adverse drug reactions, organ failure, superinfections (especially with *Clostridium difficile*) and increased mortality.^{8–10}

It is also associated with increased costs, as a result of prolonged hospital stays and the cost of managing complications.^{8–10} Inappropriate use of antimicrobials has the potential to end the successes achieved by modern medicine.² With the increase in antimicrobial resistance has come a slowing in the discovery of new effective antimicrobials due to the dwindling antibiotic pipeline. This has made it difficult to discover new antibiotics that have novel mechanisms of action, thus leading to the emergence of the post-antibiotic era.¹¹ The clinical result of this increased resistance is an increase in the number of deaths from infections that were previously treatable.¹¹

A United Kingdom study reported that the annual global number of deaths due to antibiotic resistance is around 700,000 and predicted that if this situation

Correspondence: Bashar M. Augie, muhammad.bashar1@students.wits.ac.za

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is not addressed, by 2050 nearly 10 million people will die every year as a result of drug-resistant infections.^{12,13} This would cause the global economy to lose approximately 60 to 100 trillion US dollars.^{12,13} In 2017 the World Bank reported that, if left unchecked, antibiotic resistance would have a cascade effect, such that by 2050, more than 28 million additional people, mostly from developing countries, would be pushed into extreme poverty.¹⁴ The treatment of resistant infections can be prohibitively expensive for people in lower socio-economic sectors and they would be disproportionately affected by a failure to address this issue. Antimicrobial stewardship is an emerging field in medicine and has been described as “coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration”.^{15(p.323)} Antimicrobial stewardship also refers to how the responsible use of antimicrobials can enhance both their current effects and their future sustainability.¹⁶ Antimicrobial stewardship programs (ASPs) are described as one of the most important tools for preserving the value of antimicrobial agents and lowering their inappropriate use.^{17,18} An ASP has many strategies with different approaches that, when conducted properly, will impact positively on clinical patient outcomes.¹⁹ Education is considered fundamental in any ASP.²⁰

It is a prerequisite for medical students to learn the principles of infection diagnosis and management, and they must understand the link between antibiotic usage and antibiotic resistance.^{20,21} Students are expected to learn to prescribe antibiotics responsibly when they commence their careers as house officers.²² The World Health Organization highlights the need for all healthcare professionals, including medical students, to be educated in the rational use of antimicrobials and stewardship, as a step to address antimicrobial resistance.^{23,24} A survey to assess the teaching of rational antimicrobial prescribing in the curricula of European medical schools has found wide variation among medical schools — even those within the same country — and found that teaching was mainly delivered using passive techniques.²⁵ In Nepal, the use of problem-based learning in small groups of medical students has recorded success in teaching prudent antimicrobial use in clinical pharmacology.²⁶

Medical school is perhaps the only avenue that some doctors have to learn prudent antibiotic prescribing. Apart from the teaching received in medical schools (and perhaps during preparation for internal board examinations), there is barely any requisite teaching after graduation on rational antibiotic prescribing.²⁷ An antimicrobial stewardship program will probably be more successful when initiated at the medical school level, which is when student knowledge and attitudes are being shaped.²¹ For example, surgeons are likely to have a higher acceptance rate of surgical prophylactic guidelines if courses on rational prescribing and antimicrobial stewardship are taught in their medical curriculum.²¹

Understanding the importance of ASP and ensuring their wide implementation is critical to achieving their success. Education in ASP should begin in medical schools to educate future prescribers on the importance of adhering to these programs. While it is acknowledged that medical curricula are often overloaded, the importance of ASP must be addressed by curriculum developers.²¹ In 2009, the General Medical Council in the United Kingdom emphasized the need to incorporate a course on prudent antibiotic prescribing into the medical curriculum.²⁸ Integration of educational programs on prudent antibiotic prescribing into medical school curriculum has been achieved to a certain level in some developed countries such as the United Kingdom^{21,29} and the United States of America.³⁰

A study that assessed the knowledge, attitudes and perceptions of final year medical students in South Africa about rational antibiotic prescribing showed that graduating doctors are not adequately prepared to prescribe antibiotics.³¹ The findings of this study are similar to those of a multicenter study conducted on fourth-year medical students in the United States of America.³² This suggests a deficiency in the curriculum and a need for ASPs to be included in the curriculum to address such deficiencies. Several studies across the globe have revealed that medical students perceive antimicrobial resistance as a problem in their professional career and want additional teaching on prudent antimicrobial use.³²⁻³⁵ Many studies show that a wide knowledge gap in rational antibiotic prescribing exists among medical students.³³⁻⁴¹

A search of the literature did not reveal any published studies on educational ASPs in the curricula for medical students in Africa. So, although

evidence suggests that students and newly qualified doctors lack the skills and confidence to engage in ASPs, in Africa no such programs appear to exist in the medical school environment. This scoping review serves to determine what programs have been developed and implemented on antimicrobial stewardship, in order to develop an appropriate educational program that is relevant for teaching medical students in South Africa and Nigeria.

A preliminary search of the *JBIR Database of Systematic Reviews and Implementation Reports*, as well as PubMed, CINAHL, PROSPERO and ERIC databases did not identify any scoping reviews dealing with this topic. A search in Scopus revealed a 2017 published mapping review by Canadian researchers that looked at antimicrobial stewardship training in medical education.⁴² However, the review only examined the published studies indexed in Ovid MEDLINE and Ovid Embase databases that addressed ASP education for both undergraduate and postgraduate students. This review will focus on studies conducted on medical students in published, unpublished and gray literature. The objective of this scoping review is to identify and synthesize the available evidence on ASPs for teaching medical students about rational antimicrobial use, as well as the content taught and the method of instruction used.

Review question

What types of educational antimicrobial stewardship programs are used in medical school settings to teach medical students about rational antimicrobial prescribing?

Inclusion criteria

Participants

The review will consider studies that include medical students only. For the purpose of this review, a medical student is defined as a student studying for a bachelor degree in medicine. The name of this degree varies between countries, with the more common names being MBBS, MBChB and MBBCh. All these abbreviations refer to a bachelor of medicine and a bachelor of surgery. The review will exclude studies that involve other health profession students.

Concept

The concept of interest in this scoping review is antimicrobial stewardship programs — what is

being taught, and how and when it is taught. This will include the content of the program, activities involved during the program, purpose of the activities, duration of the program and time allocated, those delivering the program, evaluation methods, curriculum design and impact of the program. It will also consider the methods of teaching, including online or face-to-face programs.

Context

This review will consider studies that are conducted in medical school settings. It will consider medical school programs that lead to the registration of the student as a beginning medical practitioner.

Types of sources

This scoping review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before-and-after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion. Qualitative studies that examine qualitative data will also be considered. In addition, systematic reviews that meet the inclusion criteria will also be considered. Text and opinion papers will also be considered for inclusion in this scoping review. Only studies published in English will be included because of the cost and time involved in translating non-English studies. The review will include studies published from 1996 onwards; 1996 was chosen as the starting date because it was the year in which the term “antimicrobial stewardship” was first introduced.⁴³

Methods

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews consisting of the following methods: develop review question(s) and review objective(s); determine the eligibility criteria; develop the literature search strategy; extract, analyze, and discuss the findings; and draw conclusions and discuss the implications for practice and further research.⁴⁴

Search strategy

The review will follow a JBI three-phase search strategy approach with an aim to locate both published and unpublished papers. An initial limited search was conducted in PubMed to identify relevant articles on this topic. The text words in the title and abstracts used in the retrieved articles as well as the index terms used to describe the articles were used to develop a full search strategy (Appendix I). The reference lists of all studies selected for inclusion will be screened for additional studies.

Information sources

The databases to be searched include PubMed, Wiley Online library, CINAHL Complete, Web of Knowledge, Education Resources Information Center and *JBI Database of Systematic Reviews and Implementation Reports*. The search for unpublished studies and gray literature will include Scopus and the ProQuest Dissertations and Theses Global database.

Study selection

Following the search, all identified records will be collated and uploaded into EndNote V8.2 (Clarivate Analytics, PA, USA), and duplicates will be removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). The full text of selected citations will be assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with a third reviewer. The results of the search will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for scoping reviews.⁴⁵

Data extraction

Data will be extracted from papers included in the scoping review by two independent reviewers using a data extraction tool developed by the reviewers. The data extracted will include specific details about the

population, concept, context, study methods, types of educational antimicrobial stewardship programs and key findings relevant to the review question. Authors of papers will be contacted to request missing or additional data, where required. A draft data extraction tool (charting table) is provided in Appendix II. This tool will be modified and revised as necessary during the process of extracting data from each included paper. Modifications will be detailed in the full scoping review. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer.

Data presentation

Extracted data will be presented in diagrammatic or tabular form in a manner that aligns with the objective of this scoping review. The charting table will report on: distribution of papers by year of publication, country of origin, study design, research methods and the key findings/outcomes. A narrative summary will accompany the tabulated and/or charted results and will describe how the results relate to the review's objective and question.

Acknowledgments

Devind Peter, librarian at the Health Sciences Library, University of the Witwatersrand, for his assistance in developing a search strategy and conducting the initial search of PubMed and Scopus.

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Appendix I: Search strategy

PubMed

Search conducted on 25 October 2019

Search	Query	Records retrieved
#1	anti-infective agents[MeSH] OR antimicrobial stewardship[MeSH] OR drug resistance[MeSH] OR “antibiotic resistance”[Title/Abstract] OR “antimicrobial resistance”[Title/Abstract] OR antibiotic*[Title/Abstract] OR program*[Title/Abstract] OR “antimicrobial stewardship program”[Title/Abstract]	1,842,484
#2	medical school[MeSH] OR medical schools[MeSH]	24,811
#3	medical student[MeSH] OR medical students[MeSH]	31,497
#4	education[MeSH] OR educational[Title/Abstract]	890,670
#5	1# AND 2# AND 3# AND 4#	847
#6	Limit 5 to date range 1996 to onward and English language	718

Appendix II: Data extraction instrument

Study details and characteristics	
Study number	
Authors	
Date/year of publication	
Study design	
Setting	
Population and sample size	
Methodology/methods	
Details/results extracted from study	
Duration of the program	
Outcomes and measures	
Quantitative results	
Qualitative results	
Curriculum design*	
Impact of the program [†]	
Evaluation methods (including timing of evaluation)	
Other findings relevant to review questions	

*The scientific method adopted to train students on rational antibiotic prescribing (for example, problem-based learning curriculum).

[†]Identifies whether or not a measure of knowledge has been used in the study, and the measure used (for example, pre- and post-training assessments).

Appendix B: Educational antimicrobial stewardship programs in medical schools: a scoping review (Augie et al., 2021).

Educational antimicrobial stewardship programs in medical schools: a scoping review

Bashar M. Augie¹ • Jacqui Miot² • Robyn L. van Zyl¹ • Patricia A. McInerney^{3,4}

¹ Pharmacology Division, Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, ²Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, ³Centre for Health Science Education, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, and ⁴The Wits-JBI Centre for Evidenced-Based Practice: A JBI Centre of Excellence, Johannesburg, South Africa

ABSTRACT

Objective: The objective of this scoping review was to identify the available evidence on antimicrobial stewardship programs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used.

Introduction: Antibiotics are a precious resource whose discovery have saved millions of lives. They are used extensively in surgical procedures, cancer chemotherapy, and in the treatment of infectious diseases. However, the development of antimicrobial resistance and the slow rate of discovery of new agents with novel mechanisms of actions represent a threat to modern medicine.

Inclusion criteria: This scoping review considered papers that described medical school curricula that focused on the teaching and learning of the prescription of antimicrobial medication. Studies that described this concept in the curricula of other health profession students, such as nursing, pharmacy, or dentistry students, were excluded.

Methods: The JBI three-step process was followed and conducted by two reviewers. The scoping review followed an a priori published protocol. Eight databases were searched for both published and unpublished literature and gray literature. Only studies published in English from 1996 onwards were included. Full texts of selected citations were assessed against the inclusion criteria by two independent reviewers. Data were independently extracted by two reviewers. Disagreements were resolved through discussion, and the need for a third reviewer was not required. Data extraction was undertaken using a modified charting table developed for the review objectives. The findings are presented using the narrative synthesis.

Results: Thirteen studies were included in the review, with most of the papers originating from the United States of America and Europe, with one from developing countries. Didactic lectures and web-based distance learning were the most common modes of instruction used in the included papers. Six of the included papers presented the outcomes of their interventions; different methods of assessment were used to evaluate students, which included baseline and post-instruction assessment or a series of short exams. Some of the concepts in the teaching material included the use of antimicrobial agents, prevention of antimicrobial resistance, antimicrobial stewardship, and infection prevention control. The programs (ranging from 75 minutes to 100 hours) were implemented from second to fourth year of study.

Conclusions: A wide range of interventions were used to teach the principles of antimicrobial stewardship to medical students. There is a need to further evaluate these programs through follow-up of students after graduation to determine whether the skills learned are retained.

Keywords: antimicrobial resistance; antimicrobial stewardship; education; medical students; teaching

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Correspondence: Bashar M. Augie, muhammad.bashar1@students.wits.ac.za

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Introduction

The World Health Organization has identified antimicrobial resistance as one of the five major threats to public health,¹ and it has emphasized the importance of including appropriate antibiotic prescribing in medical curricula.² Inappropriate antibiotic prescribing is associated with the development of multi-drug-resistant pathogens, adverse events, and increased cost to patients.³ Antimicrobial stewardship programs (ASPs) promote appropriate antimicrobial use and help to achieve good clinical outcomes, minimize adverse events, and reduce selective pressure that encourages the development of resistance.^{4,5} Antimicrobial stewardship programs also reduce the chance of developing *Clostridioides difficile* infection across all settings and in patients of all age groups.^{5,6} A 2016 guideline for implementing ASPs recommended medical schools integrate the principles of antimicrobial stewardship into their pre-clinical and clinical curricula.⁵ Education is regarded as a vital tool in changing prescribing behavior and influencing prescribers to accept ASPs.⁷ Antimicrobial stewardship education aims to reduce inappropriate antimicrobial use, such that antimicrobials are only used when indicated, using the appropriate route of delivery, correct dose, and duration of therapy for each infection.⁸

Most of the educational ASPs target postgraduate students and practicing physicians rather than medical students in their undergraduate studies.⁸⁻¹⁰ Little attention is given to teaching medical students appropriate antimicrobial use.¹¹ Conversely, changing the behavior of licensed doctors has proven difficult.⁹ A survey conducted to examine the pre-clinical microbiology curricula in the United States of America (USA) medical schools found that only 65% of schools were including antimicrobial stewardship in their courses.¹² A greater percentage (74% to 95%) of surveyed medical students across the globe indicated their desire for more education on responsible antimicrobial use.¹³⁻¹⁶ The pedagogical plan in most of the Brazilian medical schools does not address the problem of antimicrobial resistance or antimicrobial stewardship to optimize responsible antimicrobial use.⁴ While medical schools in the USA and United Kingdom (UK) are making an effort to develop and incorporate ASP into their medical curricula,^{11,17-21} a literature search did not reveal any ASPs implemented in African medical schools.

Prudent antimicrobial use is an important topic for discussion in medical schools among aspiring doctors who are expected to fulfill their role as advocates on graduation and who should be able to explain to their patients and their patients' relatives the consequences of inappropriate antimicrobial use. Teaching principles of antibiotic prescribing in medical schools can provide a context to address issues of health promotion at both the individual and community level. The teaching of prudent antibiotic use in medical schools could be achieved through outcome-based education, which provides unambiguous statements of learning intent, allows flexibility of delivery, and allows medical schools to develop ways by which the desired outcomes are achieved without having to adhere to a set of standard teaching methods.²⁰ Paterson Davenport *et al.*²⁰ developed a set of learning outcomes for medical schools to teach prudent antibiotic prescribing to medical students to help reduce antimicrobial resistance and improve optimal use.

The objective of this review was to identify and synthesize the available evidence on ASPs for teaching medical students about rational antimicrobial use, including the content taught and the method of instruction used.

Review question

What types of educational ASPs are used in medical schools to teach medical students about rational antimicrobial prescribing?

Inclusion criteria

Participants

The review considered studies that only included medical students, irrespective of their year of study. For the purpose of this review, a medical student is defined as a student studying for a bachelor's degree in medicine. The name of this degree varies between countries, with the more common names being MBBS, MBChB, and MBBCh. All these abbreviations refer to a Bachelor of Medicine and a Bachelor of Surgery. The review excluded studies that involved other health profession students.

Concept

The concept of interest in this scoping review was ASPs: what, how, and when antimicrobial stewardship was taught. This included the content of the program, activities involved during the program, method of teaching, year of study, purpose of the

activities, ASP training duration, ASP outcomes, and student evaluations. It also considered the methods of teaching, including online or face-to-face programs.

Context

This review considered studies that were conducted in medical school settings. It considered medical school programs that led to the registration of the student as a beginning medical practitioner.

Types of studies

The following study designs were included in the review: before-and-after, case report, quasi-experimental, prospective cohort, mapping review, and descriptive. Surveys, such as those that used cross-sectional study designs to assess students' knowledge, attitudes, and perceptions but not program development, were excluded as they did not meet the inclusion criteria.

Methods

The objectives, inclusion criteria, and data extraction methods for this review were specified in an *a priori* protocol.²² This review was conducted using JBI methodology for scoping reviews.²³ There were minor deviations from the protocol. The original data extraction tool included in the protocol was modified after reviewing two or three papers, because some of the information included in the tool, such as curriculum design and qualitative data, was not reported in the papers.²³ Some of the modifications included changing “outcomes and measures” to “ASP outcome” and “evaluation methods” to “student evaluations.” These modifications did not affect the objective, review question, or results of the review.

Search strategy

The JBI three-phase search strategy approach that aimed to locate both published and unpublished papers was followed. An initial limited search of PubMed was conducted to locate articles on this topic, followed by an analysis of the text words contained in the titles, abstracts, and index terms. This led to the development of a search strategy for each database. The emphasis was on ASPs for teaching appropriate antimicrobial prescribing in medical schools using any study design. The reference lists of all included papers were screened for additional studies. Only papers published in English from 1996 to November 2019, when the search was conducted, were included. The language restriction was due to the

cost and time involved in translating non-English studies. The lower limit of 1996 was selected as the starting date because it was the year in which the term “antimicrobial stewardship” was first coined.²⁴

The databases searched include PubMed (Ovid), Scopus (Elsevier), Web of Science (Clarivate Analytics), and *JBI Database of Systematic Reviews and Implementation Reports* (Ovid). Other databases searched via EBSCO included CINAHL Complete, Wiley Online Library, and ERIC. The search for unpublished studies and gray literature included ProQuest Dissertations and Theses Global database. The search was carried out with the support of a librarian, and the search results were uploaded into JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). The full search strategies of the above-listed databases are shown in Appendix I.

Study selection

After searching, all identified records were collated and uploaded into EndNote v.X8.2 (Clarivate Analytics, PA, USA), and duplicates were removed. Titles and abstracts of the identified studies were scrutinized in relation to the review question and objective by two independent reviewers (BMA and PM). The reviewers met and compared their findings. Disagreements were resolved through discussion and thus a third reviewer was not utilized. Once the list of studies for potential inclusion was developed, the full-text papers were retrieved and read by both reviewers. The full texts that were found to be irrelevant were excluded (Appendix II). A final decision was then made on whether to include or exclude the retrieved papers. The search results and article selection process are presented in a flowchart adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR; Figure 1).²⁵

Data extraction

Data extraction was conducted by two independent reviewers (BMA and PM). Any disagreement that emerged during the data extraction process between the reviewers was settled through discussion and the need of the third reviewer was not necessary. The data extracted included specific details about the population, concept, context, study methods, types of educational ASPs, and key findings relevant to the review question and objective. The concept of interest in this

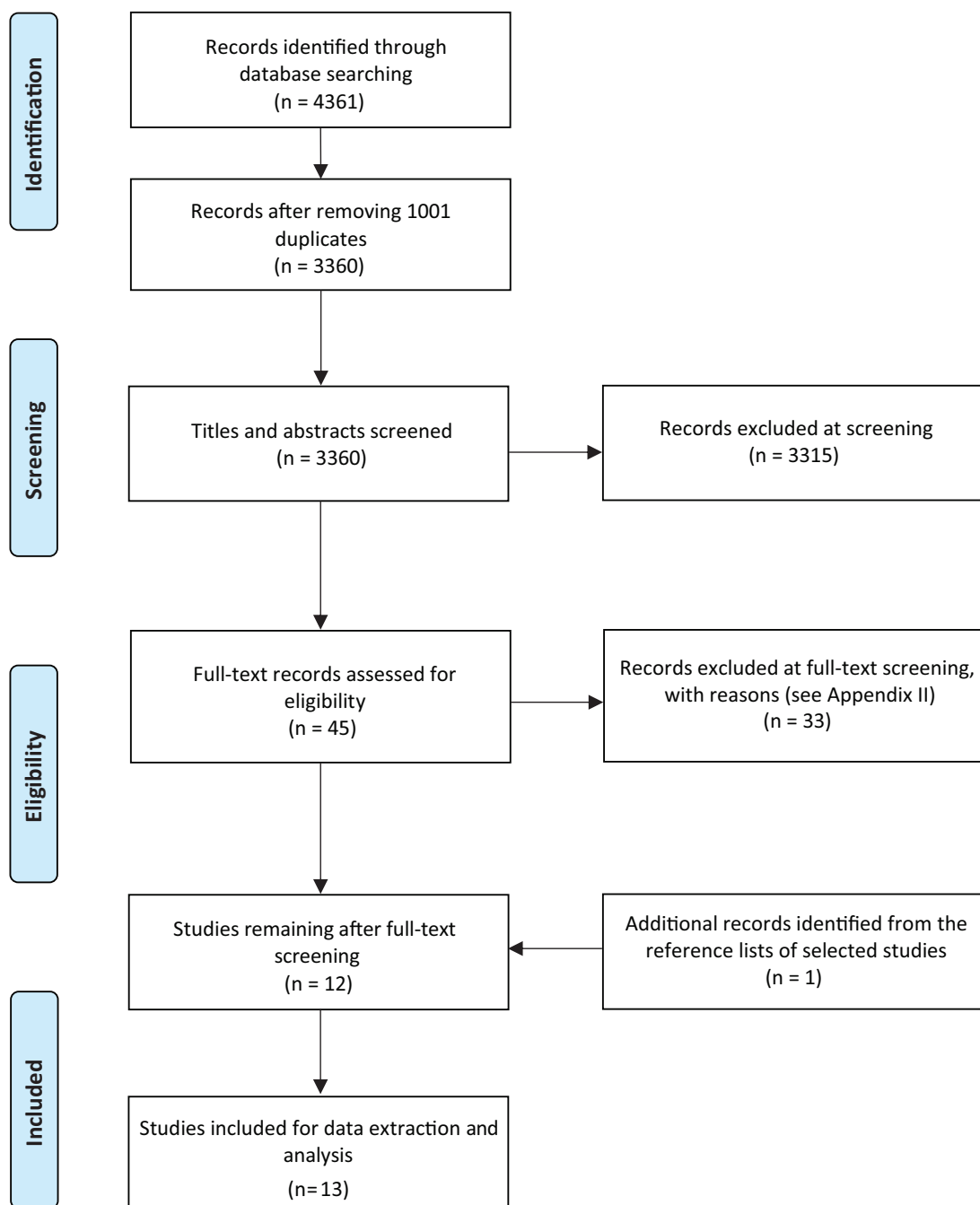


Figure 1: Search results and article selection and inclusion process²⁵

review included information related to the content of the program, activities involved during the program, method of teaching, year of study, purpose of the activities, ASP training duration, ASP outcomes, and student evaluations.

Data analysis and presentation

Extracted data from the papers that met the selection criteria are presented in Appendix III. The charting table shows the country, authors, year of publication, study details and characteristics, study design,

setting, population sample size, teaching methods, ASP training duration, mode of delivery, ASP outcomes, and student evaluations.

Results

Study inclusion

The results of the screening undertaken during this scoping review are presented in Figure 1.²⁵ A total of 4361 papers were found during the database search (PubMed = 710, CINAHL Complete = 453, ERIC = 352, Scopus = 1793, Web of Science = 801, Wiley Online Library = 140, JBI SRIR = 29 and ProQuest Dissertations and Theses Global = 83). A total of 1001 duplicates were removed, leaving 3360 titles and abstracts to screen. An additional 3315 were classified as irrelevant after examining the title and abstract. This left 45 articles, of which 33 did not meet the inclusion criteria and were therefore excluded. The 33 excluded papers and the reasons for their exclusion are presented in Appendix II. Twelve papers were identified as eligible for inclusion. A hand search of the reference lists of the 12 included studies was conducted, and one additional

study was found eligible for inclusion. In conclusion, the screening stage resulted in 13 eligible articles for data extraction.

Characteristics of included articles

The characteristics of the included articles are presented in Appendix III. The USA had the highest number of studies with five (38.5%),^{1,17-19,21} followed by the UK with three (23.1%),^{20,26,27} Brazil had two (15.4%),^{4,28} while Canada,²⁹ Europe,¹⁰ and Nepal³⁰ had one paper each. No papers were found from African medical schools (Figure 2). Six of the papers were published between 2016 and 2019.^{4,17-19,21,29} The papers used different study designs. Two studies used a before-and-after design: one with a quasi-experimental design,¹⁹ while the other did not use a control group.⁴ A case report was used in one study,¹⁷ while another one employed a prospective cohort study.¹⁸ Seven papers used a descriptive study design,^{1,10,20,21,26,28,30} of which two papers focused on web-based designs^{10,26} and one described a board game.²⁸ One paper used a cross-sectional design to conduct a postal

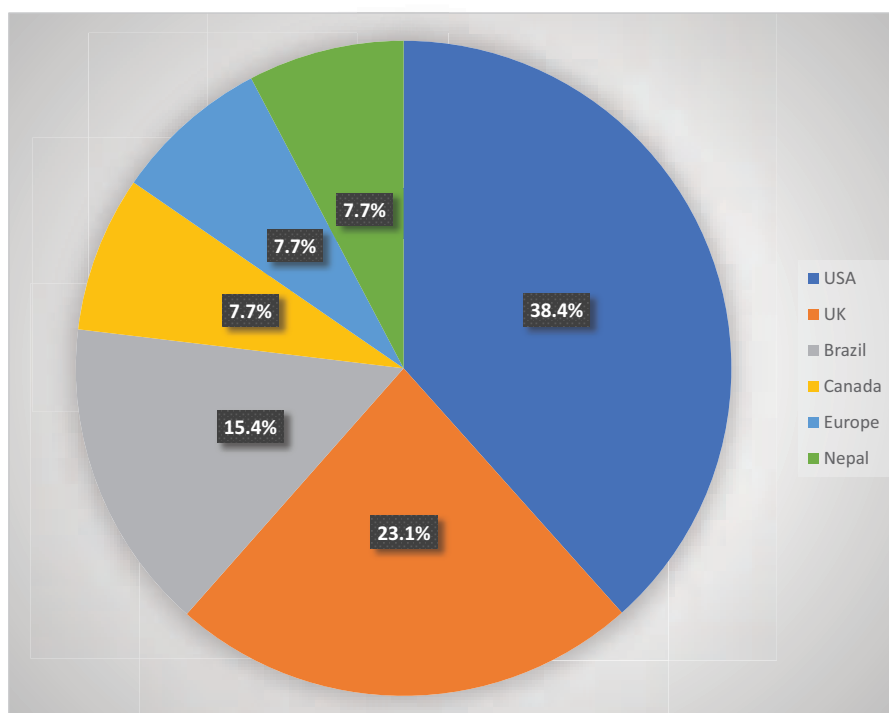


Figure 2: Distribution of papers by geographical location (n = 13)

survey,²⁷ while another one used a mapping review.²⁹ Ten of the papers referred to medical students only,^{1,4,10,17,19-21,26,27,30} two of the papers combined medical and pharmacy students,^{18,28} and the last combined medical students, residents, and practicing physicians²⁹ (see Appendix III). The data for each group were reported separately, making it possible to extract the medical student data.

Review findings

Elements of ASPs in medical schools are found in the 13 included studies. The summary of key findings is presented with headings, including number of students involved, year of study in which the program was implemented (where available), methods of instruction, ASP training duration, ASP outcomes, and student evaluations (Appendix III).

Number of students involved

Five of the included papers indicated the number of students who participated in the program.^{4,17-19,28} Hsu¹⁷ reports that approximately 150 students participated over three years, while at the Brazilian Medical School, 606 medical students completed the antimicrobial stewardship course over six years.⁴

At the Albert Einstein College of Medicine, 183 students took part in an antibiotic stewardship seminar annually from 2014 to 2016, and the same number of students also participated in an infection prevention and patient safety seminar from 2015 to 2016.¹⁹ The University of California, San Francisco Medical School engaged a total of 822 students over three years, of which 470 were medical students and 352 were pharmacy students.¹⁸ In the board game study, 42 medical students and 36 pharmacy students participated in the program.²⁸

Year of study in which the program was implemented

Seven of the included papers indicated the year of study in which the program was implemented.^{4,10,17,18,21,26,30} Most of these studies implemented their program in either the second or third year of study.^{10,17,18,30} Shekarchian *et al.*²¹ made use of a spiral curriculum in which the program was taught from the second to the fourth year of study. In one of the papers, the program was implemented in the fourth year of the study.²⁶ The Wake Forest study did not specify the year of study, but the

antimicrobial stewardship curriculum was divided into pre-clinical and clinical segments.¹

Methods of instruction

Eleven of the papers stated the mode of instruction for teaching the principles of antimicrobial use.^{1,4,10,17,19,21,24,26,27,29,30} Four studies used a blended approach with didactic lectures and another form of instruction.^{17,21,27,30} Two papers used online/web-based distance-learning programs.^{4,18} One of the papers used a small-group workshop in addition to an online learning program.¹⁸ Paterson Davenport *et al.*²⁰ developed outcomes for a supportive learning resource that could be used in different learning situations, such as self-learning, self-assessment, peer review, small-group discussion, or formal assessment. Silverberg *et al.*²⁹ authored a mapping review that reported different modes of deliveries, which included, amongst others, didactic teaching, web-based teaching, clinical case discussions, workshops/seminars, board games, and guideline promotion.²⁹ This was the only mapping review that was identified on antimicrobial stewardship in medical education. It looked at published literature in two databases on both undergraduate and postgraduate medical education.²⁹ In the Wake Forest program, pre-clinical lectures with facilitator notes and audio recordings were the main modes of instruction, and in the clinical segment, small-group activities with facilitator guides were used.¹

Antimicrobial stewardship program training duration

Seven of the papers stated the amount of time allocated to the program.^{4,17,19,21,27,28,30} One program allocated 75 minutes during a single didactic teaching module in the third-year internal medicine course.¹⁷ A Brazilian program dedicated 100 hours of activities to a web-based distance-learning course.⁴ In another program, two hours were dedicated in the second year and an hour-long interactive, case-based didactic session in the third year; while in the fourth year, two sessions were delivered: one two-hour block at the start of the year and a second 1.5-hour session a week before graduation.²¹ One US program provided a two-hour seminar on antimicrobial stewardship with an additional two-hour seminar on infection prevention and control to second-year medical students.¹⁹ The program in Nepal provided two hours of didactic lectures in the first year of the course and an

additional two-hour practical session.³⁰ In the Brazilian program in which a board game was used, 1.5 hours were allocated.²⁸

Antimicrobial stewardship program outcomes

Six of the papers presented the ASP outcomes.^{4,17-19,21,28} The Brazilian paper included more comprehensive coverage on what students thought they had learned about the topic.⁴ Shekarchian *et al.*²¹ reported on students' perceptions on how prepared they felt to initiate empiric antibiotics, and when and how to narrow the spectrum of coverage. Students also reported on their satisfaction with the education received on antibiotic stewardship during medical school.²¹ Prescriber confidence, understanding of transmission-based precautions, and related personal protective equipment were assessed in Nori *et al.*¹⁹ MacDougall *et al.*¹⁸ reported the impact of an interprofessional curriculum on antimicrobial stewardship, assessing students' knowledge, attitudes, and interprofessional collaboration. The Brazilian study by Valente *et al.*²⁸ in which the board game was used reported on whether the students felt the game helped them to understand the subject, and whether it was an important way of enhancing learning. Antimicrobial stewardship program outcomes were measured differently across the manuscripts; four of the papers evaluated students' knowledge,^{4,18,19,26} two focused on student satisfaction with the program,^{21,28} one paper conducted a one-minute evaluation of a single didactic teaching module,¹⁷ while six of the papers either did not evaluate their programs or did not report the findings of their evaluations.^{1,10,20,27,29,30}

Student evaluations

Seven of the included studies evaluated whether the intervention influenced students' prescribing behavior,^{4,10,17-19,26,28} of which four of the papers used a before-and-after assessment.^{4,18,19,28} MacDougall *et al.*¹⁸ assessed students' knowledge of antimicrobial stewardship using a small number of survey questions before and after implementation of the antimicrobial stewardship curriculum. From this, a more robust assessment tool was planned for use in the future implementation of the curriculum.¹⁸ Another study by Nori *et al.*¹⁹ measured student proficiency in personal protective equipment use in a post-test evaluation; it also measured the number of correct answers in relation to knowledge of

hospital-acquired infection. Marwick *et al.*²⁶ used student feedback to evaluate the program. The authors also reported being in the process of evaluating student knowledge through a series of short exams at the beginning and end of each clinical attachment and at the end of the year; however, nothing has been subsequently published.

Discussion

In this scoping review, we examined ASP that targeted medical students. The search was limited to programs from January 1996 onward because the term "antimicrobial stewardship" was coined in 1996.²⁴ Most studies were published in renowned medical journals.

We found a wide range of instructional design methods used to teach medical students the concept of antibiotic prescribing. Most of the interventions in the included papers used lectures as the mode of instruction. Lectures are teacher-centered and a passive way of transmitting information to a large group of students.³¹ Of note, none of the programs included a follow-up with the students after their graduation to evaluate the value of the skills learned, or whether they had retained the knowledge. The need to evaluate interventions implemented is something that teachers should be encouraged to undertake as part of the curriculum design process. A university in the USA, in collaboration with the Centers for Disease Control and Prevention and the Association of American Medical Colleges, has developed an antimicrobial stewardship curriculum for pre-clinical and clinical medical students.^{1,11} The curriculum aims to increase understanding of antimicrobial resistance, prevention, and control among medical students and is structured to address the microbiological and pharmacological components of antimicrobial use in both outpatient and inpatient settings.¹ The curriculum is intended for use among medical schools in the USA.^{1,11} The pre-clinical segment comprises lectures with facilitator notes and audio recordings, and nine corresponding exam questions in the United States Medical Licensing Examination format, while the clinical curriculum includes five small-group activities with facilitator guides.¹

Had the papers selected in this review been subjected to critical appraisal, many would have been excluded due to poor methodological quality. There are more quasi-experimental studies or crossover

studies in education, and we did not expect to find any studies that utilized a randomized controlled trial (RCT) design. Turner *et al.*³² state that while RCTs are valuable from an evidence-based perspective, they may pose ethical challenges in education in that some students may be denied an opportunity to receive an intervention. Further, they are not always the best method to test a hypothesis in medical education.³³ It is also difficult to directly attribute success or failure to either randomization or non-randomization, especially when there are other confounders.³⁴ According to Norman and Schmidt,³⁵ “Trials of curriculum level interventions, whether they show large, small, zero, or negative effect sizes, whether they are or are not randomized, whether they are done on large or small samples, whether they are of sound or unsound methodology, are, in our view, a waste of time and resources.”^(p.725)

Geographically, most of the included studies were conducted in the USA and Europe, with one conducted in a developing country. Our review did not find any study conducted in Africa and only one was found in Asia.³⁰ There is evidence that medical students are not adequately prepared by their medical schools to engage in appropriate antimicrobial prescribing,³⁶ and this includes South African medical schools that lag behind in including antimicrobial stewardship in the curricula for medical students.³⁷ Medical doctors do not normally evaluate the course design and outcomes because such students may be receiving antimicrobial stewardship training but in small courses that are not synchronized or managed throughout their curriculum. But the question of how well this has been done or to what extent has not been quantified or evaluated. According to South African authors Brink *et al.*,³⁷ “A key strategy in facilitating appropriate antibiotic prescribing is the early introduction of the relevant knowledge, concepts and skills into undergraduate curricula.”^(p.358)

Educational games are tools that encourage active learning, problem-solving skills, and small-group discussions.³⁸ They are a form of problem-based learning as they provide students with an initial list of problems and require students to gather information and work on their own to solve the problems.³⁹ Educational games are not a replacement for conventional ways of learning theoretical knowledge, but are complementary learning tools

that encourage skills acquisition.⁴⁰ Board games are student-centered, which allows students to apply their critical skills.⁴¹ A study in which the game-based technique was used to teach third-year medical students about breast disease reported an improvement in post-game test scores compared to pre-game scores.³⁹ It is documented in the literature that students who have been exposed to problem-based learning and task-based learning curricula have improved interpersonal skills and are better prepared for self-directed and life-long learning.^{42,43} Small groups afford learners with an opportunity to freely express their concerns and explore their reactions.⁴⁴ Iranian researchers compared the effectiveness of small-group discussion techniques and traditional lecture-based teaching to teach embryology to medical students. They found that those students in small discussion groups scored higher marks in the mid-term and final exams compared to those in the lecture-based group.⁴⁵

Shekarchian *et al.*²¹ reported that students expressed a high level of satisfaction with the intervention, despite the short period of time allocated to the intervention. Further to this, the intervention utilized a spiral curriculum over three years using different teaching techniques, such as a case-based small-group activity, a case-based didactic session, and an online module. This may be compared with Laks *et al.*⁴ where the level of student satisfaction was low despite a longer period allocated to an intervention that utilized only a web-based, distance-learning technique.

Antimicrobial stewardship programs have been shown to improve the appropriate use of antimicrobial agents and have the potential to delay the emergence of the fast-approaching post-antibiotic era.⁴⁶ Antimicrobial stewardship is likely to be successful if started in medical schools when behavior is being shaped.¹⁰ It may be more rewarding to incorporate the antimicrobial stewardship principles into the curricula of medical students than waiting until they graduate. Surgeons who were taught the principles of antimicrobial stewardship in medical schools are likely to accept antimicrobial prophylactic guidelines in practice.¹⁰

After they graduate and register with the relevant regulatory councils, doctors are expected to start prescribing antimicrobials, hence the need for medical schools to develop antimicrobial stewardship curricula to prepare them for appropriate

antimicrobial prescribing.¹⁰ In this light, the authors, with the help of a panel of experts, are currently working on another project aimed at developing an antibiotic stewardship curriculum for teaching South African and Nigerian medical students appropriate antibiotic prescribing. An antimicrobial stewardship curriculum should provide adequate knowledge, attitudes, and skills to help shape the behavior of aspiring doctors regarding the basic principles of antimicrobial stewardship.¹⁰

Limitations of the review

One of the limitations of this review is that only papers published in the English language were included. Although we searched several databases, unpublished literature, and gray literature, there is still a possibility that some potentially useful papers published in other languages were excluded. Our review only included articles with medical students, and antimicrobial stewardship articles involving other health professional students were excluded. Antimicrobial stewardship is a multidisciplinary program where other health professionals play a critical role. Including students from other professions may have provided information about other innovative methods of teaching antimicrobial use. Other limitations are associated with the types of study designs used in different studies. For instance, although quasi-experimental, before-and-after study design is commonly used in educational programs due to some of the potential problems associated with RCTs in education,^{32,33} it has several limitations, especially when used in small sample sizes. These include threats to internal validity, lack of generalizability of the findings, and robustness of conclusions on the effectiveness of an educational intervention.⁴⁷ Although a wide range of instructional design methods were used in the included studies, none of the studies followed up with the students after graduation to determine retention of knowledge and skills learned.

Conclusions

This scoping review aimed to answer the question: what types of educational ASPs are used in medical schools to teach medical students about rational antimicrobial prescribing? Our review found that a wide range of interventions are used to teach medical students prudent antimicrobial prescribing in several medical schools across the globe. They

included didactic lectures, web-based distance-learning, small-group discussions, and case-based modules. The time allocated to teach principles of antimicrobial stewardship differed, ranging from 75 minutes to 100 hours. Antimicrobial stewardship teaching should be managed throughout the medical curriculum. Disciplines such as pharmacology, microbiology, infectious diseases, medical education, and other related disciplines should work synergistically with the relevant stakeholders in medical schools to ensure that the aim of the intervention is achieved.

Implications for future research

Although the results from the included studies provided us with useful evidence on teaching prudent antibiotic prescribing, none of these studies followed up with the learners to find out if the knowledge and skills learned are retained after graduation. Further research is required to answer this question – do medical graduates remember the knowledge and skills they learned on responsible antibiotic prescribing after graduation? This can be achieved by using prospective cohort studies where an antibiotic stewardship curriculum that is student-centered is delivered to students. Medical students should be introduced to the principles of prudent antibiotic prescribing in their early years of study, and they should continually be reinforced throughout the remaining years of study in a spiral curriculum format. In such interventions, topics such as antibiotic-resistant pathogens, chain of infection, and mechanisms by which antibiotics kill bacteria could be taught in the pre-clinical years through didactic lectures or problem-based learning. While topics such as the recognition and treatment of sepsis, and antibiotic therapeutic-level monitoring could be taught in small-group sessions in the clinical years when students acquire clinical skills, a robust assessment method should be used to evaluate students' antimicrobial stewardship knowledge before and after program implementation. Students should be followed up during their internship to evaluate the knowledge and skills learned.

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Appendix I: Search strategy

PubMed (Ovid)

Date searched: 12/11/2019

Set #	Search query	Results retrieved
1	("anti-infective agents"[MeSH] OR "antimicrobial stewardship"[MeSH] OR "drug resistance"[MeSH] OR "antibiotic resistance"[Title/Abstract] OR "antimicrobial resistance"[Title/Abstract] OR antibiotic*[Title/Abstract] OR program*[Title/Abstract] OR "antimicrobial stewardship program"[Title/Abstract])	1,865,631
2	(medical school [MeSH] OR medical schools [MeSH])	25,065
3	(medical student [MeSH] OR medical students [MeSH])	32,102
4	(education [MeSH] OR educational [Title/Abstract])	900,361
5	1# AND 2# AND 3# AND 4#	867
6	Limit 5 to date range 1996 to onward and English language	710

CINAHL Complete (EBSCO)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	AB ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	292,894
2	AB (medical school OR medical schools)	7692
3	AB (medical student OR medical students)	11,044
4	AB (education OR educational)	223,779
5	1# AND 2# AND 3# AND 4#	466
6	Limit 5 to date range 1996 to onward and English language	453

ERIC (EBSCO)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	TX ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	573,889

(Continued)		
Set #	Search query	Results retrieved
2	TX (medical school OR medical schools)	5909
3	TX (medical student OR medical students)	6667
4	TX (education OR educational)	1,388,929
5	1# AND 2# AND 3# AND 4#	833
6	Limit 5 to date range 1996 to onward and English language	352

Scopus (Elsevier Science)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	672,153
2	TITLE-ABS-KEY (medical school OR medical schools)	170,817
3	TITLE-ABS-KEY (medical student OR medical students)	148,601
4	TITLE-ABS-KEY (education OR educational)	2,204,656
5	1# AND 2# AND 3# AND 4#	2492
6	Limit 5 to date range 1996 to onward and English language	1793

Web of Science (Clarivate Analytics)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	501,104
2	TOPIC (medical school OR medical schools)	44,200
3	TOPIC (medical student OR medical students)	64,138
4	TOPIC (education OR educational)	912,615
5	1# AND 2# AND 3# AND 4#	861
6	Limit 5 to date range 1996 to onward and English language	801

Wiley Online Library (EBSCO)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	TITLE ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	86,680
2	ANYWHERE (medical school OR medical schools)	271,886
3	ANYWHERE ("medical student" OR "medical students")	71,464
4	ANYWHERE (education OR educational)	1,630,840
5	1# AND 2# AND 3# AND 4#	620
6	Limit 5 to date range 1996 to onward and English language	140

JBIR Database of Systematic Reviews and Implementation Reports (Ovid)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	All ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	7630
2	All ("medical school" OR "medical schools")	81
3	All ("medical student" OR "medical students")	377
4	All (education OR educational)	8956
5	1# AND 2# AND 3# AND 4#	41
6	Limit 5 to date range 1996 to onward and English language	29

ProQuest Dissertations and Theses Global (ProQuest)

Date searched: 13/11/2019

Set #	Search query	Results retrieved
1	ti ("anti-infective agents" OR "antimicrobial stewardship" OR "drug-resistance" OR "antibiotic resistance" OR "antimicrobial resistance" OR antibiotic* OR program* OR "antimicrobial stewardship program")	98,206
2	ab (medical school OR medical schools)	5039
3	ab (medical student OR medical students)	5241
4	ab (education OR educational)	322,338
5	1# AND 2# AND 3# AND 4#	129
6	Limit 5 to date range 1996 to onward and English language	83

Appendix II: Studies ineligible following full-text review

Authors	Reason for exclusion
Merz D, Smaill F, Daneman N, editors. Evidence-based infectious diseases. Oxford: Wiley Blackwell; 2018.	Ineligible concept
Abbo LM, Cosgrove SE, Pottinger PS, Pereyra M, Sinkowitz-Cochran R, Srinivasan A, <i>et al.</i> Medical students' perceptions and knowledge about antimicrobial stewardship: how are we educating our future prescribers? Clin Infect Dis. 2013;57(5):631–8.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar OJ, Pulcini C, Howard P, Nathwani D, on behalf of ESGAP (ESCMID Study Group for Antibiotic Policies). European medical students: a first multicentre study of knowledge, attitudes and perceptions of antibiotic prescribing and antibiotic resistance. J Antimicrob Chemother. 2014;69(3):842–6.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Chuenchom N, Thamlikitkul V, Chaiwarith R, Deoisares R, Rattanaumpawan P. Perception, attitude, and knowledge regarding antimicrobial resistance, appropriate antimicrobial use, and infection control among future medical practitioners: a multicenter study. Infect Control Hosp Epidemiol. 2016;37:603–5.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar O, Howard P, Nathwani D, Pulcini C. Knowledge, attitudes, and beliefs of French medical students about antibiotic prescribing and resistance. Med Mal Infect. 2013;43(10):423–30.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Dyar OJ, Lund M, Lindsjö C, Lundborg CS, Pulcini C. Preparedness to prescribe antibiotics responsibly: a comparison between final year medical students in France and Sweden. Eur J Clin Microbiol Infect Dis. 2019;38(4):711–7.	Ineligible concept
Dyar OJ, Nathwani D, Monnet DL, Gyssens IC, Stålsby Lundborg C, Pulcini C. Do medical students feel prepared to prescribe antibiotics responsibly? Results from a cross-sectional survey in 29 European countries. J Antimicrob Chemother. 2018;73(8):2236–42.	Ineligible concept
Haque M, Rahman NIA, Zulkifli Z, Ismail S. Antibiotic prescribing and resistance: knowledge level of medical students of clinical years of University Sultan Zainal Abidin, Malaysia. Ther Clin Risk Manag. 2016;12:413–26.	A survey to determine knowledge and is not about a program development
Jaillon P. Teaching basic and clinical pharmacology to medical students: a 2006 survey in French schools of medicine. Therapie. 2006;61(5):439–46.	Ineligible concept
Hu Y, Wang X, Tucker JD, Little P, Moore M, Fukuda K, <i>et al.</i> Knowledge, attitude, and practice with respect to antibiotic use among Chinese medical students: a multicentre cross-sectional study. Int J Environ Res Public Health. 2018;15(6):1165–79.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Javadi MR, Khezrian M, Sadeghi A, Hajimiri SH, Eslami K. An interprofessional collaboration between medicine and pharmacy schools: designing and evaluating a teaching program on practical prescribing. J Res Pharm Pract. 2017;6(3):178–81.	Ineligible study design

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Authors	Reason for exclusion
Gupta MK, Vohra C, Raghav P. Assessment of knowledge, attitudes, and practices about antibiotic resistance among medical students in India. <i>J Family Med Prim Care</i> . 2019;8(9):2864–9.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Melber DJ, Teherani A, Schwartz BS. A comprehensive survey of preclinical microbiology curricula among US medical schools. <i>Clin Infect Dis</i> . 2016;63(2):164–8.	Ineligible study design
Minen MT, Duquaine D, Marx MA, Weiss D. A. Survey of knowledge, attitudes, and beliefs of medical students concerning antimicrobial use and resistance. <i>Microb Drug Resist</i> . 2010;16(4):285–9.	A survey on knowledge, attitudes, and beliefs and is not about a program development
O'Brien D, Richards J, Walton K, Phillips M, Humphreys H. Survey of teaching/learning of healthcare-associated infections in UK and Irish medical schools. <i>J Hosp Infect</i> . 2009;73(2):171–5.	Ineligible concept
Ohl CA, Luther VP. Health care provider education as a tool to enhance antibiotic stewardship practices. <i>Infect Dis Clin</i> . 2014;28(2):177–93.	Ineligible concept
Ijeoma O, Chukwuma DU, Onyinyechukwu UO, Azuka SA, Kingsley CO. Knowledge of antibiotic use and resistance among students of a medical school in Nigeria. <i>Malawi Med J</i> . 2019;31(2):133–7.	A survey to determine knowledge and is not about a program development
Phillips C, Henderson PJ, Mandel L, Kim S, Schaad D, Cooper M, <i>et al.</i> Teaching the microscopic examination of urine sediment to second-year medical students using the Urinalysis-Tutor computer program. <i>Clin Chem</i> . 1998;44(8):1692–700.	Ineligible concept
Rattanaumpawan P, Chuenchom N, Thamlikitkul V. Perception, attitude, knowledge and learning style preference on challenges of antimicrobial resistance and antimicrobial overuse among first year doctors in training and final year medical students. <i>Antimicrob Resist Infect Control</i> . 2019;8(1):142–49.	Ineligible concept
Hoque R, Mostafa A, Haque M. Insight of medical students of clinical years to antimicrobials prescribing and resistance in private medical school, Chittagong, Bangladesh. <i>J Young Pharm</i> . 2016;8(4):447–55.	Ineligible study design
Scaiola G, Gualano MR, Gili R, Masucci S, Bert F, Siliquini R. Antibiotic use: a cross-sectional survey assessing the knowledge, attitudes and practices amongst students of a school of medicine in Italy. <i>PLoS One</i> . 2015;10(4):e0122476.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Sánchez-Fabra D, Dyar OJ, del Pozo JL, Amiguet JA, de Dios Colmenero J, del Carmen Fariñas M, <i>et al.</i> [Perspective of Spanish medical students regarding undergraduate education in infectious diseases, bacterial resistance and antibiotic use]. <i>Enferm Infecc Microbiol Clin</i> . 2019;37(1):25–30. Spanish.	Ineligible study design
van der Voort T, Brinkman DJ, Benemei S, Böttiger Y, Chamontin B, Christiaens T, <i>et al.</i> Appropriate antibiotic prescribing among final-year medical students in Europe. <i>Int J Antimicrob Agents</i> . 2019;54(3):375–9.	Ineligible concept

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Authors	Reason for exclusion
Wasserman S, Potgieter S, Shoul E, Constant D, Stewart A, Mendelson M, <i>et al.</i> South African medical students' perceptions and knowledge about antibiotic resistance and appropriate prescribing: are we providing adequate training to future prescribers? <i>S Afr Med J.</i> 2017;107(5):405–10.	A survey on knowledge, attitudes, and perceptions and is not about a program development
World Health Organization. Mapping educational opportunities and resources for health-care workers to learn about antimicrobial resistance and stewardship. 2017 [cited 2020 Mar 08]. Available from: https://apps.who.int/iris/bitstream/handle/10665/259362/9789241512787-eng.pdf .	Ineligible population; study focuses on health care workers
Wright E, Jain P. Survey of antibiotic knowledge amongst final year medical students. <i>J. Antimicrob Chemother.</i> 2004;53(3):550–1.	A survey on knowledge is not about a program development
Huang Y, Gu J, Zhang M, Ren Z, Yang W, Chen Y, <i>et al.</i> Knowledge, attitude and practice of antibiotics: a questionnaire study among 2500 Chinese students. <i>BMC Med Educ.</i> 2013;13(1):163–72.	A survey on knowledge, attitudes, and perceptions and is not about a program development
Zhao A, Xiao S, Kandelaki K, Liu Y, Chen W, Ren R, <i>et al.</i> Knowledge, perception, and educational status of antimicrobial resistance among Chinese medical students. <i>Microb Drug Resist.</i> 2019;25(10):1458–64.	Ineligible concept
Adriana AB, Magdalena CS. A gaming approach to learning medical microbiology: students' experiences of flow. <i>Med Teach.</i> 2007;29(9–10):933–40.	Ineligible study design
Charlier C, Johannessen I, Mackintosh CL, Wilks D, Cauda R, Wolf FI, <i>et al.</i> International infectious diseases teaching to undergraduate medical students: a successful European collaborative experience. <i>Med Teach.</i> 2017;39(9):981–6.	A survey on knowledge, attitudes, and beliefs and is not about a program development
Somwang Danchaivijitr SC, Uapong Jaturatramrong AW, Rachada Cherdungsi SS. Program on nosocomial infection in the curricula of medicine, dentistry, nursing and medical technology in Thailand. <i>J Med Assoc Thai.</i> 2005;88:150–4.	Ineligible population; study focuses on all health science students
Luther VP, Ohl CA, Hicks LA. Antimicrobial stewardship education for medical students. <i>Clin Infect Dis.</i> 2013;57(9):1366–7.	Ineligible study design
Pulcini C, Wencker F, Frimodt-Møller N, Kern WV, Nathwani D, Rodríguez-Baño J, <i>et al.</i> European survey on principles of prudent antibiotic prescribing teaching in undergraduate students. <i>Clin Microbiol Infect.</i> 2015;21(4):354–61.	Ineligible concept

Appendix III: Characteristics of included studies

Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Hsu, 2018, USA ¹⁷	A single didactic teaching module introduced into third-year internal medicine clerkship at the University of South Dakota, Sanford School of Medicine. The teaching module presented included the PowerPoint slide set with instructor notes, student worksheet entitled "Building an Antibiotic Stewardship Program" and one-minute paper evaluation.	Case report	University of South Dakota, Sanford School of Medicine	Approximately 150 students (over three years)	Educational intervention – using a single didactic session that included interactive aspects of teaching	75 minutes	Didactic lecture involving large and small groups	Analysis of one-minute paper revealed three themes: concept learned, concept unclear, and concept to try	One-minute paper evaluation
Kerr <i>et al.</i> , 2001, United Kingdom ²⁷	A postal survey of UK medical schools and the University of St Andrews that offers a three-year pre-clinical course. Seventeen (71%) of 24 institutions replied.	Postal survey using cross-sectional design	Not stated	Not stated	Not stated	The contact times allocated to teaching about the rational use of antimicrobials (as opposed to pharmacology mode of action, etc.) varied greatly (range 0.5–22.0 hours).	All institutions except one reported that lectures, generally in years 2 and 3, were the main method of teaching, but in some cases, lectures were supplemented with tutorials or problem-based learning exercises. One medical school stated that students learned the principles and practice of antimicrobial use through a self-directed learning module throughout the undergraduate course.	Not stated	No evaluation of learning
Laks <i>et al.</i> , 2019, Brazil ⁴	The authors developed and implemented a Moodle-based, distance-learning course on the use of antimicrobial agents and the prevention of antimicrobial resistance. The students were tutored in their online activities, and some classes were conducted in real-time for live discussions. In addition, students underwent face-to-face assessments of their knowledge of the topic before and after the course. The course was conducted over seven years. The course consists of five theoretical modules, exercises, and simulations, within a virtual learning environment.	Before-and-after with no control group	Federal University of São Paulo Paulista School of Medicine	606 students completed the course: 72 were sixth-year students (2008 only); and 534 were fifth-year students (2008–2014)	Educational intervention study	100 hours of activities	Web-based, distance-learning course	About 421 (69.5%) of the students reported that they had learned a lot or more than they had expected about the topic. The average mean score of all 606 students' initial assessment was 5.78 (5.70–5.86) and this significantly increased to 8.45 (8.36–8.53) in the final assessment ($p < 0.001$). The average mean score of all the 534 fifth-year students was 5.75 (5.66–5.83) in the initial assessment and increased to 8.46 (8.37–8.54) in the final assessment ($p < 0.001$).	Before-and-after evaluation of students' knowledge score

(Continued)									
Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
MacDougall et al., 2017, USA ⁴⁸	The curriculum is designed for second-year medical students and third-year pharmacy students at University of California, San Francisco. The curriculum was embedded in the courses on microbiology and infectious diseases (medical students) or antimicrobial pharmacology (pharmacy students).	Not stated, likely prospective cohort study	University of California, San Francisco	A total of 822 students participated over the three study years (470 medical students, 352 pharmacy students)	Educational intervention	Not stated	Online learning module and interprofessional workshop. The curriculum was designed as follows and delivered through the Moodle learning management system (Moodle Pty Ltd, Perth, Australia): i) students viewed a case vignette online (Case 1) and answered related clinical questions; ii) an online independent learning module on antimicrobial stewardship was subsequently provided; then, iii) approximately a week later, the students participated in a two-hour workshop on antimicrobial stewardship. Students were subdivided into small groups of 4–5 students comprising mixed-professions. In small groups, students revisited Case 1 from the online module and came to a consensus group answer, which was then discussed with the larger group. The small groups then worked through Case 2 together, again followed by group discussion. The cases used a branched logic format: the decisions students made in the initial stages of the case determined the subsequent choices and case outcomes. The decisions required in the cases reflected key considerations in antimicrobial stewardship: whether to initiate treatment, the impact of patient allergies and drug interactions on antimicrobial selection, adequacy of the empiric spectrum of activity, and deescalation of therapy based on culture results.	This has demonstrated how an interprofessional curriculum on antimicrobial stewardship including medical and pharmacy students can positively impact knowledge and attitudes towards both antimicrobial stewardship and interprofessional collaboration. There was an increase in the percentage of agree/strongly agree responses after implementation of antimicrobial stewardship curriculum. They hope to use a more robust assessment tool in the future implementation of the curriculum.	A total of 745 students (425 medical students, 320 pharmacy students) completed both pre- and post-curriculum surveys.
Marwick and Nathwani, 2007, United Kingdom ²⁶	Clinical infection teaching of medical students	Descriptive study design details in web-based format	University of Dundee Medical School	Fourth-year medical students	Not stated	Time not stated but the teaching is delivered by infectious disease physicians, microbiologists, infection control nurses, pharmacists, and public health clinicians.	Teaching students how to recognize, diagnose, and manage common infections. It also involves infection control and health protection aspect of infection.	Not stated	Learning was evaluated via student feedback and has shown positive results. Currently, evaluating student knowledge through a series of short exams at the beginning and end of each attachment and at the end of the year.

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Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Nori et al., 2017, USA ¹⁹	Pre-clinical curriculum: antimicrobial stewardship Pre-clinical curriculum: infection prevention control	Quasi-experimental Before-and-after study design	Albert Einstein College of Medicine, New York	183 students participated in antibiotic stewardship seminar per year (2014–2016) 183 students participated in Infection Prevention and Patient Safety Seminar (2015–2016)	Educational intervention	Annual two-hour seminar: 2014–2016 on antimicrobial stewardship Annual two-hour seminar: 2015–2016 on infection prevention and control	Small-group sessions, team-based activities, smartphone app, case-based modules	Improved prescriber confidence: the smart phone app is the preferred source of antibiotic information. Improved understanding of transmission-based precautions and related personal protective equipment. The post-test results showed a significant improvement in personal protective equipment proficiency and knowledge of hospital-acquired infection with an increase in correct responses from 38% to 76% observed for questions involving antibiogram use ($p = 0.02$).	Pre- and post-intervention surveys and knowledge assessment questions during antimicrobial stewardship and infection prevention control.
Paterson Davenport et al., 2005, United Kingdom ²⁰	This study provides an introduction to understanding outcome-based education and how it has been applied in the context of prudent antimicrobial prescribing for undergraduate medical education as defined by an expert working party.	This is a descriptive paper of outcomes-based education and how it can be applied to antibiotic stewardship	Not stated	Not stated	Not stated	Not stated	These outcomes provided the trigger for developing a supportive learning resource that could be used in different learning situations, including for self-learning, self-assessment, peer review, small-group discussion, or formal assessment. How the <i>Appropriate Antimicrobial Prescribing for Tomorrow's Doctor</i> materials are used within individual educational institutes will depend on many issues, including the organization of the curricular program, the available teaching resources, and the level of experience of students, as well as timetabling issues.	Not stated	No evaluation of learning

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Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Pulcini and Gyssens, 2013, Europe (multiple countries) ¹⁰	Not stated	Not stated; likely descriptive design	University of Rotterdam (The Netherlands)	Second-year medical students	Not stated	Not stated	One-week module on several concepts of antimicrobial resistance, hygiene, and prudent antibiotic prescribing in the core curriculum	Not stated	Not stated
	A module on antibiotic policy on infectious diseases and hygiene. Other topics include infection control, antibiotic guidelines, principles of prophylaxis, and laboratory techniques.	Not stated; likely descriptive design	University of Nijmegen (The Netherlands)	Third-year students	Not stated	Not stated	Elective problem-based learning	Not stated	Not stated
	In the UK, the Prudent Antibiotic User (PAUSE, www.pause-online.org.uk) is a website of shared standardized teaching materials for prudent antimicrobial prescribing for use in the undergraduate medical curriculum. PAUSE provides standardized teaching aides for all educators of antibiotic prescribing based on patient-focused, reflective learning.	Descriptive study design details in web-based format	UK medical schools	Not stated	Resources are designed to enable students to prepare for interactive sessions to compare standard patient vignettes with their own clinical experience. The structured preparation required of the students is a key to success. The interactive discussion sessions focus on learning prudent antibiotic prescribing through reflective practice.	Not stated	The prepared materials about structure and content for each interactive session are available for tutors to use (in a PowerPoint format). These resources include patient histories, clinical signs, investigations and questions on diagnosis, assessing severity, appropriate prescribing, public health issues, and patient management. Best practice statements and core resource lists are also available.	Not stated	Guideline answers to the questions with feedback are provided, including inappropriate responses and the corresponding reasons.

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Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Shankar <i>et al.</i> , 2011, Nepal ³⁰	Teaching in rational use of antibiotics is conducted during the pharmacology practical sessions. Proper antibiotic use is also stressed during the session on analysis of rationality of prescriptions. Students learn not to use antibiotics in predominantly viral infections, and to avoid the use of multiple antibiotics. They are also shown and interpret a video on antibiotic resistance.	The paper outlines how and when to teach this module; likely descriptive design	Kist Medical College medical school in Lalitpur	Not stated	Educational intervention	Two hours didactic lectures throughout the first year of the course; two-hour practical session follows the lecture; lectures held in the first two years of study	A problem-based approach within clinical pharmacology teaching using the World Health Organization essential medicine prescribing approach.	Not stated	No evaluation of learning
Shekarchian <i>et al.</i> , 2016, USA ⁴¹	A comprehensive learning experience is developed throughout the second to fourth years of medical school. The curriculum utilized the concept of spiral learning. The antibiotic stewardship curriculum is initiated in 2013 at the University of California, San Francisco School of Medicine.	Letter to the editor describing the intervention	University of California, San Francisco School of Medicine	Not stated	Educational intervention	A two-hour session in the second year; an hour interactive case-based didactic session in the third year; in the fourth year two sessions are delivered: two hours before the start of the year and 1.5 hours a week before graduation.	Made use of a spiral curriculum. The second-year component: • purposeful integration of stewardship themes throughout the foundations science microbiology block (integrates microbiology, infectious diseases, and pharmacology); • an interprofessional, case-based, small-group activity for medical and pharmacy students on antibiotic stewardship. The third-year component: • an interactive case-based didactic session emphasizing responsible antibiotic use immediately before the start of clerkships; • during the medicine clerkship, an online module on common infections and antimicrobial use, followed by an interactive "Jeopardy"-style chief resident-taught game. The fourth-year component: • during the fourth year of medical school, two sessions are delivered on common infections and responsible antimicrobial use immediately before the start of the fourth year and one week before graduation; • Antibiotic cards were developed and disseminated for medical students to use on the wards starting in the third year.	Before graduation, 88% felt at least moderately prepared to initiate empiric antibiotics and when and how to narrow the spectrum of coverage. 88% felt very or extremely satisfied with the education they received on antibiotic stewardship during medical school.	Not stated

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Authors, year, location	Study details and characteristics	Study design	Setting	Population sample size	Methods	ASP training duration	Mode of delivery	ASP outcomes	Student evaluations (including the timing of evaluation)
Silverberg et al., 2017, Canada ²⁹	This is a literature review conducted to compile a summary of the current published research on antimicrobial stewardship training in medical education. Of the 48 articles included in this summary, 14 included only undergraduate medical trainees, 11 included both undergraduate and postgraduate trainees, 20 included only postgraduate trainees, and three did not specify the training level of the participants.	Mapping review	Medical education (undergraduate and postgraduate)	Not stated	Educational review	Not stated	Approaches at the undergraduate level included didactic teaching, web-based teaching, clinical case discussions, workshops/seminars, board games, guideline promotion, audits on current stewardship integration in the medical curriculum, and intensive modules.	Not stated	None of the articles that targeted undergraduate medical students evaluated whether the intervention influenced their prescribing behavior either as a senior medical student or followed them beyond graduation.
Valente et al., 2009, Brazil ²⁸	The game consists of an illustrated board and is played with dice and pawns. The board has 121 squares, including squares with question marks and antimicrobial agents. Each student receives a card with a clinical case, identification of the bacterium, and its resistance to antimicrobials.	Descriptive study design details in board game	Universidade Federal do Rio Grande do Sul	78 medical and pharmacy students, of which 42 were medical students and 36 were pharmacy students.	Not stated	1.5 hours	Not stated	An improvement in right answers after board games. More than 90% said the game helped them to understand the subject, and was an important way to enhance learning.	Pre-test and a post-test. There was an increase in the number of right answers and a decrease in the number of unknown answers in the post-test after board games.
Wake Forest Medical School, n.d., USA ¹	An antibiotic stewardship curriculum was developed by Wake Forest School of Medicine in collaboration with the Centers for Disease Control and Prevention and the Association of American Medical Colleges to increase understanding of antimicrobial resistance prevention and control among medical students. It is structured to address the microbiological and pharmacological components of antimicrobial use in outpatient and inpatient settings.	Not empirical research – a description of the content of the curriculum	Wake Forest School of Medicine, North Carolina	Not stated	Educational intervention	Three didactic lectures; five small-group activities and nine exam questions. Not stated how long any of these activities lasted.	The curriculum is intended for use in US medical schools and intended for pre-clinical and clinical years of instruction. The pre-clinical segment comprises lectures with facilitator notes and audio recordings, and nine corresponding exam questions in the United States Medical Licensing Examination format. The clinical curriculum contains five small-group activities with facilitator guides.	Not stated – this was a description of a curriculum in terms of content and delivery.	No evaluation of learning

ASP, antimicrobial stewardship program

Research Paper

Knowledge and perceptions about antibiotic resistance and prudent antibiotic prescribing among final year medical students in two African countries

Bashar M. Augie^{1,2, }, Robyn L. van Zyl¹, Patricia A. McInerney³ and Jacqui Miot^{4, }

¹Pharmacology Division, Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

²Department of Pharmacology and Therapeutics, College of Health Sciences, Federal University, Birnin Kebbi, Nigeria

³Centre for Health Science Education, Faculty of Health Science, University of the Witwatersrand, Johannesburg, South Africa

⁴Health Economics and Epidemiology Research Office, Department Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

*Correspondence: Bashar Muhammad Augie, Pharmacology Division, Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, 7 York Rd, Parktown, 2193, South Africa. Tel: +27-11-717-2542; Email: muhammad.bashar1@students.wits.ac.za

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Abstract

Objectives The objectives of this study were to assess the knowledge and perceptions of final year medical students about antibiotic resistance and antibiotic use to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria and the principles of prudent antibiotic prescribing.

Methods A cross-sectional study was conducted to determine the knowledge and perceptions of final year medical students in one South African and three Nigerian universities about prudent antibiotic use, antibiotic resistance and antibiotic stewardship. A 26-item questionnaire was administered electronically to students in three medical schools and a paper-based copy in the fourth.

Key findings A difference in the gap in knowledge between the two countries was identified; however, respondents from both countries had a similar understanding of antibiotic use and antibiotic resistance. Most respondents in South Africa (94.8%) and Nigeria (91.4%) agreed that antibiotics are overused in their countries. There was a significant difference between the number of respondents in the two countries who thought that there are new antibiotics available to treat resistant pathogens; 45.4% of Nigerian respondents agreed with the statement as compared to 9.6% of the South African respondents. Of the 10 vignettes answered correctly, South African respondents scored an average of 62.4% in the knowledge segment compared to 31.9% scored by the Nigerian respondents ($P = 0.001$). All of the South African (100%) and 98.3% of the Nigerian respondents indicated their desire for more education on appropriate antibiotic use.

Conclusions Although students from both countries had the same perception of antibiotic resistance, there was, however, a difference in their level of knowledge, which could have been improved

in both countries. This should be addressed at an undergraduate curriculum level; as well as with continued education to reinforce antibiotic knowledge.

Keywords: Africa; antibiotic; inappropriate prescribing; antibiotic resistance; antibiotic stewardship; education; medical students

Introduction

Antibiotics represent a miracle of science that has saved millions of lives since the discovery of penicillin by Alexander Fleming in 1928,^[1] resulting in major advancements in modern medicine.^[2] The discovery of antibiotics has undoubtedly changed the way life-threatening bacterial infections, like meningitis and endocarditis, are treated.^[3] Antibiotic resistance is an inevitable evolutionary process, which occurs as a result of exposure of bacteria to antibiotics.^[4] The use of antibiotics, either appropriately or inappropriately, drives selective pressure for the emergence of resistance.^[5] Overuse of antibiotics has dire consequences such as antibiotic resistance, which is one of the major problems affecting public health.^[6–7] There is a direct relationship between antibiotic consumption and the development of antibiotic resistance,^[8–9] whilst responsible antibiotic use delays the development of antibiotic resistance.^[10–11] Antibiotic resistance is a global public health problem requiring a global solution.^[12] In its five-year Antimicrobial Resistance Strategy, the United Kingdom's Department of Health acknowledged that antibiotic resistance occurs mainly as a result of selective pressures from antibiotic use, which can be reduced by optimal antibiotic use, and slow the emergence of resistant bacteria.^[13]

Antibiotic resistance can result in prolonged hospitalisation, increased morbidity and mortality,^[2] and consequently increased costs from consumables and laboratory investigations.^[6,14] A United Kingdom commissioned report predicted that if left unchecked by 2050, 10 million people will die of resistant infections annually which will cost the global economy over 10 trillion US dollars.^[12]

The pipeline for the production of new antibiotics with novel mechanisms of action remains meagre.^[15] This has implications for medical education.^[15] Ganter, a senior advisor on antimicrobial resistance (AMR) at the WHO stated that there is room for improvement in the current antimicrobial teaching of medical students.^[16] He recommended that medical students should be introduced to prudent antibiotic use as early as possible in their careers.^[16] Inappropriate antibiotic use by physicians is a source of concern and could be linked to education on rational antibiotic use in medical schools.^[16]

To encourage appropriate antibiotic prescribing, many medical schools across the globe have developed prudent antibiotic prescribing programmes for their students.^[17–22] Our scoping review did not identify any such programme in African medical schools.^[23] It has been established that to engage in responsible antibiotic prescribing one needs requisite skills, but the decision to prescribe antibiotics is often left to junior staff who may not have the required knowledge, experience or guidance to make an informed choice of optimal antibiotics.^[24] Many patients admitted to hospitals stand a risk of either presenting with or acquiring infections that may require urgent treatment with antibiotics. However, only those with severe or complicated infections may benefit from the expertise of infectious disease specialists. This implies that the majority of patients will be treated by non-specialist doctors,^[24] who tend to use broad-spectrum antibiotics for a longer duration. Hence the need to educate medical students on antibiotic stewardship, so that they are able to undertake rational antibiotic prescribing by making an informed decision regarding the choice of antibiotics.

To improve rational antibiotic use, South Africa and Nigeria have developed National Action Plans for AMR. The South African AMR National Strategy Framework 2014–2024 provides a four-point strategy for managing AMR to reduce the spread of resistant pathogens and improve patient outcomes.^[25] Similarly, Nigeria has a five-point strategy.^[26] Both strategies aim to encourage optimal antibiotic therapy and reduce collateral damage from antibiotic use.^[3] The objectives of this study were to assess the knowledge and perceptions of final year medical students about antibiotic resistance and antibiotic use to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria the principles of prudent antibiotic prescribing.

Methods

Study design, setting and participants

A cross-sectional multicentre survey of final year medical students in one South African and three Nigerian universities was conducted in 2019. The two countries were selected because of their influence on the African continent. The three Nigerian universities use a traditional curriculum, while the South African university uses an integrated curriculum. This provided an opportunity to compare and contrast the curriculum type on students' learning of antibiotic prescribing. Three Nigerian medical schools were chosen because their student numbers were small (220 in total) as compared to the South African medical school (328 students). Nigerian universities generally have fewer medical students compared to the South African universities which informed the decision to choose up to four medical schools. Unfortunately, one of the Nigerian universities was excluded from the study because of unrest in the region that affected academic activities. An attempt to include other Nigerian universities was unsuccessful.

Survey development

An existing questionnaire was used with the permission of the developer.^[27] A pilot study was conducted on 10 final year medical students in each of the two countries, to assess the readability, length, and relevance of items in the questionnaire before it was administered. The survey assessed perceptions and knowledge about antibiotics, antibiotic resistance, and the perceived quality of education regarding preparedness to prescribe antibiotics. The data collected included demographic information, perceptions regarding antibiotic use and resistance; awareness of antibiotic-resistant diseases, sources of antibiotic education, and self-confidence in antibiotic prescribing. The mode of teaching and evaluation of antibiotic knowledge were also studied. To determine respondents' actual knowledge, they were asked to respond to vignettes for the correctness of the action. Responses to the different questions varied from single item responses to a choice on a 5-point Likert scale.

Survey administration

Data were collected between July and November 2019. The questionnaire was administered online using REDCap in three schools and hard copies were administered in one Nigerian medical school

because the survey was conducted at a time when students were preparing for their final examinations and it was anticipated that the electronic response would generate a low response rate. Students were informed that their participation was voluntary and that they had the right to withdraw at any time or decide not to answer any question they wished without penalty. They were also assured that their responses were anonymous and would not be shared with their universities. No incentive was given to respondents as a motivation to participate in the study.

For the online administration, a survey link was emailed to respondents, with the link to the survey being active for equal time periods in both countries. In South Africa, this was done by the class coordinator, while in Nigeria it was done by the class representatives. REDCap was set to send weekly reminders.

The hard copies of the questionnaire were distributed to the respondents after a class test by the first author. A box was provided outside the hall for respondents to return their questionnaires. The questionnaire was administered a few weeks before the start of the examinations. Neither the curriculum nor the mode of teaching of antibiotics was changed before or during the survey in any of the schools.

Data management and analysis

Stata software (version 15) was used for data analysis. Data collected using the paper-based survey were manually entered into REDCap, together with the data collected using the REDCap link. All data were exported into an Excel document (version 2019), cleaned, anonymised and imported into Stata. The participating medical schools were anonymised by assigning a numerical ID to enable blinded data analysis. The 5-point Likert scale was condensed into three categories: agree/good, neutral/average and disagree/poor. Percentages were determined for categorical data and an overall knowledge score was assessed by calculating the total percentage of correct answers for the vignette-based questions for each country. Fischer's exact test was used to determine the association between categorical variables. Variations between observed and expected proportions were tested for significance using the Chi-squared test and the independent t-test was used to determine significant differences in age and mean knowledge scores between the South African and Nigerian samples.

Ethics

Ethics approval was obtained from the ethics committee of each institution (ref numbers: M1902108; ABUTHZ/HREC/D25/2018; BUK/CHS/REC/VII/52; UDUTH/HREC/2018/NO;756).

Results

A total of 548 students was invited to participate in the study, 328 from South Africa and 220 from Nigeria. A total of 276 (50.4%) students responded, with 31.7% (104) being from South Africa and 78.2% (172) being from Nigeria. There was some information that was not completed by the respondents in seven of the paper-based questionnaires and four among the online completed surveys, where 72.7% and 27.3% were from Nigeria and South Africa, respectively. The average age of all respondents was 25.7 ± 2.18 years and was similar in both countries. The Nigerian cohort consisted of a greater number of males as compared with the South African subsample. Of the total sample, 16.3% had a previous degree, with most being from South Africa. The exposure to antimicrobial stewardship

Table 1 Sociodemographic characteristics of South African and Nigerian medical students ($n = 276$)

Sociodemographic ($n = 276$)	South Africa ($n = 104$)	Nigeria ($n = 172$)	P-value
Gender	n (%)	n (%)	
Male	50 (48.1%)	101 (58.7%)	0.11 ^a
Female	54 (51.9%)	71 (41.3%)	
Age			
Age, Mean (SD)	25.7 (1.7)	25.8 (2.4)	0.67 ^b
Age, range (minimum–maximum)	23–32	21–38	
Previous degree			
Yes	38 (36.5%)	7 (4.1%)	0.001 ^a
No	66 (63.5%)	165 (95.9%)	
Type of the previous degree	($n = 38$)	($n = 7$)	
	n (%)	n (%)	
Bachelor only	23 (60.5%)	-	
Bachelor and Honors	13 (34.2%)	7 (100.0%)	
Bachelor, Honors and Masters	2 (5.3%)	-	
Exposure to antimicrobial stewardship teaching in the previous degree.			
Yes	11 (28.9%)	4 (57.1%)	0.20 ^c
No	27 (71.1%)	3 (42.9%)	

^aChi-squared test

^bIndependent t-test

^cFischer's exact test

was relatively poor, especially among Nigerian respondents. The sociodemographic characteristics of both groups of respondents are shown in Table 1.

Knowledge and perceptions of antibiotic use

A similar number of Nigerian (94.8%) and South African (91.4%) respondents agreed that antibiotics are overused in their countries and more than half of the respondents in both countries agreed that antibiotics are overused in the hospitals in which they had completed clinical rotations. More Nigerian respondents (11.0%) disagreed with the statement that antibiotic resistance was a major problem at the teaching hospitals at which they had completed clinical rotations, as compared to 4.8% of the South African respondents. There was a significant difference ($P = 0.001$) between Nigerian and South African respondents on the availability of new antibiotics to treat resistant infections; 45.4% of Nigerian respondents agreed compared to 9.6% of the South African respondents. More South African respondents (99.0%) compared to Nigerian respondents (93.0%) agreed that inappropriate antibiotic use causes resistance and 99.0% of the respondents from both countries agreed that better antibiotic use could reduce the level of resistance. The majority of the South African (91.4%) and Nigerian (84.3%) respondents agreed that the use of broad-spectrum antibiotics when equally effective narrow-spectrum antibiotics are available may encourage resistance. Just under two-thirds in both countries agreed that lack of hand disinfectant by healthcare providers can lead to the spread of antibiotic resistance, with >20% in both countries being neutral to the statement. The majority of the South African (95.2%) and Nigerian (86.0%) respondents agreed that inappropriate antibiotic use is harmful to patients; however, a statistical difference was found between the Nigerian respondents (12.3%) who were neutral to the

statement as compared to the South African respondents (2.9%) ($P = 0.02$). Most respondents (99.0%) in both countries agreed that a good knowledge of antibiotics is important for their career as doctors; while all of the South African (100%) and 98.3% of the Nigerian respondents indicated their desire for more education on appropriate antibiotic use.

Learning methods

The respondents felt that formal lectures (93% Nigerian; South Africans 83.7%) and consultant ward rounds (91.8% Nigerian; South African 89.4%) were useful in understanding antibiotic classes and their spectrum of activities and 82.7% and 92.4% of the South African respondents compared to 94.8% and 94.1% of the Nigerian respondents agreed that formal lectures and consultant ward rounds are useful in learning about antibiotic prescribing and resistance (Table 2). Nigerian respondents were more likely to consult infectious disease specialists compared to the South African respondents. Of note in Table 2 are the differences in relation to formal lectures, formal bedside tutorials and problem-based learning between countries. The South African respondents were either very familiar (34.6%) or familiar (64.4%) with the term antibiotic stewardship, while more than half of the Nigerian respondents were either not familiar (43.8%) or not at all familiar (16.6%).

Curricula and antibiotic use

Most of the respondents in both countries felt their medical schools had prepared them to make an accurate diagnosis of infections and know when to start antibiotics, although this was more so amongst the Nigerian respondents (Table 3). Of note are the statistically significant differences that existed between the two cohorts in all the parameters relating to their perceptions of the curricula listed in Table 3. The Nigerian students were significantly more confident in knowing when and how to transition from intravenous to oral antibiotics compared to the South African students.

Teaching and learning methods

Most of the respondents in both countries felt that providing more formal lectures, more formal tutorials, more exposure to infectious disease specialists, provision of a local handbook/guideline on treating common infections to newly qualified doctors could help them to learn how to prescribe antibiotics appropriately (Table 4). Other important differences between the countries were in relation

to learning from a microbiologist and a clinical pharmacologist. Surprisingly, most of the respondents in both countries did not agree that exposure to more applications for smart devices and computer-based tutorials would contribute to learning.

Knowledge about antibiotic use

In general, the two cohorts of respondents did not perform well in assessing the vignettes for appropriateness of decision making as shown in Supplementary Table 1. However, the South African respondents correctly answered most of the vignettes, compared to the Nigerian respondents. Of the 10 vignettes answered, South African respondents scored an average of 62.4% in the knowledge segment compared to 31.9% scored by the Nigerian respondents ($P = 0.001$). Respondents in both countries did well on vignettes related to the management of HIV patients and respondents in both countries demonstrated a lack of knowledge in methicillin-sensitive *Staphylococcus aureus* and extended beta-lactamase *Escherichia coli* infections.

Discussion

The study findings identified a gap in knowledge in both groups, but more so among the Nigerian cohort; whilst both categories of respondents were found to have similar perceptions of antibiotic use and resistance.

Limitations of this study included the low response rate from the South African respondents and that it did not include all medical schools in both countries. There are 51 accredited medical schools in Nigeria and eight in South Africa, which means that the findings of this survey cannot be generalised.

The Nigerian cohort responded confidently that they were competent to prescribe antibiotics, but performed poorly in the knowledge segment compared to the South African respondents. Previous studies have identified differences between medical schools.^[15,27] The results of a 2017 South African study by Wasserman *et al.*,^[27] involving three South African medical schools including the medical school in this study, found that the students from this South African medical school performed poorly when compared to the other two South African universities. An informal discussion with the relevant stakeholders in medical education at the South African medical school revealed that in recent years more emphasis on antibiotic prescribing has been included in the curriculum. This may explain why the South African respondents performed better than their Nigerian

Table 2 Perceptions about learning methods used ($n = 276$)

	South Africa <i>n</i> (%)			Nigeria <i>n</i> (%)			Fischer's exact Test <i>P</i> -value
	Useful	Neutral	Not useful	Useful	Neutral	Not useful	
If available, how useful are the following education activities for learning about antibiotic classes and spectrum of activity?							
Formal lectures	87 (83.7)	12 (11.5)	5 (4.8)	159 (93.0)	10 (5.8)	2 (1.2)	0.04
Formal bedsidess tutorial	93 (89.4)	8 (7.7)	3 (2.9)	166 (97.1)	4 (2.3)	1 (0.6)	0.03
Consultant ward rounds	93 (89.4)	4 (3.9)	7 (6.7)	156 (91.8)	14 (8.2)	-	0.001
Registrar ward rounds	83 (79.8)	13 (12.5)	8 (7.7)	151 (88.3)	13 (7.6)	7 (4.1)	0.15
Problem based learning	83 (79.8)	12 (11.5)	9 (8.7)	150 (87.7)	19 (11.1)	2 (1.2)	0.01
If available, how useful are the following education activities for learning about antibiotic prescribing and resistance?							
Formal lectures	86 (82.7)	12 (11.5)	6 (5.8)	163 (94.8)	8 (4.7)	1 (0.5)	0.00
Formal bedsidess tutorial	96 (92.4)	6 (5.7)	2 (1.9)	167 (97.7)	4 (2.3)	-	0.05
Consultant ward rounds	96 (92.4)	4 (3.8)	4 (3.8)	161 (94.1)	9 (5.3)	1 (0.6)	0.14
Registrar ward rounds	87 (83.6)	11 (10.6)	6 (5.8)	153 (89.4)	16 (9.4)	2 (1.2)	0.10
Problem based learning	85 (81.7)	10 (9.6)	9 (8.7)	149 (87.1)	21 (12.3)	1 (0.6)	0.00

Table 3 Perceptions of curricula in relation to issues related to antibiotic use ($n = 276$)

How well do you feel that your medical school has prepared you for the following?	South Africa n (%)			Nigeria n (%)			Fischer's exact test (P -value)
	Good	Average	Poor	Good	Average	Poor	
Making an accurate diagnosis of infection	59 (56.7)	41 (39.5)	4 (3.8)	154 (89.5)	17 (9.9)	1 (0.6)	0.001
Knowing when to start antibiotics	51 (49.0)	47 (45.2)	6 (5.8)	144 (83.7)	25 (14.6)	3 (1.7)	0.001
Choosing the correct antibiotic for a specific infection	26 (25.0)	65 (62.5)	13 (12.5)	142 (82.6)	27 (15.7)	3 (1.7)	0.001
Knowledge of dosing and duration of antibiotic therapy for specific infection	26 (25.0)	57 (54.8)	21 (20.2)	128 (74.4)	39 (22.7)	5 (2.9)	0.001
How to de-escalate to narrow spectrum antibiotics	11 (10.6)	36 (34.6)	57 (54.8)	96 (55.8)	63 (36.6)	13 (7.6)	0.001
How and when to transition from intravenous to oral antibiotics	13 (12.5)	42 (40.4)	49 (47.1)	129 (75.0)	38 (22.1)	5 (2.9)	0.001
How to interpret antibiograms	6 (5.8)	30 (28.8)	68 (65.4)	76 (44.4)	50 (29.3)	45 (26.3)	0.001
Understanding the spectrum of activity of commonly used antibiotics	33 (31.7)	44 (42.3)	27 (26.0)	131 (76.2)	30 (17.4)	11 (6.4)	0.001
Understanding basic mechanisms of antibiotic resistance	62 (59.6)	40 (38.5)	2 (1.9)	131 (76.2)	30 (17.4)	11 (6.4)	0.001

Table 4 Ways in which newly qualified doctors could be better prepared to prescribe antibiotics ($n = 276$)

In what way could newly qualified doctors be better prepared to prescribe antibiotics?	South Africa n (%)	Nigeria n (%)	Chi-Squared Test (P -value)
More formal lectures			
Yes	56 (53.8)	108 (62.8)	0.16
No	48 (46.2)	64 (37.2)	
More formal bedside tutorials			
Yes	60 (57.7)	99 (57.6)	1.00
No	44 (42.3)	73 (42.4)	
More time in microbiology			
Yes	66 (63.5)	57 (33.1)	0.001
No	38 (36.5)	115 (66.9)	
More exposure to infectious diseases specialists			
Yes	70 (67.3)	98 (57.0)	0.10
No	34 (32.7)	74 (43.0)	
A local handbook/guideline on treating common infections			
Yes	65 (62.5)	100 (58.1)	0.53
No	39 (37.5)	72 (41.9)	
More applications for smart devices			
Yes	50 (48.1)	61 (35.5)	0.04
No	54 (51.9)	111 (64.5)	
More computer-based tutorials			
Yes	21 (20.2)	41 (23.8)	0.55
No	83 (79.8)	131 (76.2)	
More exposure to a clinical pharmacologist			
Yes	77 (74.0)	86 (50.0)	0.001
No	27 (26.0)	86 (50.0)	

colleagues. Another possible reason why the Nigerian respondents performed poorly in the knowledge segment may be related to the manner in which the curriculum is taught. The South African curriculum is vertically integrated, while the Nigerian schools still implement a discipline-based curriculum.

Both South African and Nigerian respondents did well in questions that related HIV to tuberculosis and pneumonia; which may be explained by the prevalence of these infections in both countries.^[28–29] On the other hand, the respondents in both countries did poorly in questions involving the management of patients with methicillin-sensitive *Staphylococcus aureus* and extended beta-lactamase *Escherichia coli* infections.

Antibiotics are among the most commonly prescribed class of drugs in healthcare, both in the inpatient and outpatient setting.^[30] Almost all respondents from both countries acknowledged the importance of responsible antibiotic use and agreed that antibiotics are overused in their countries and that antibiotic resistance is a significant problem in their countries. Similarly, almost all the respondents from both countries would have liked further education on prudent antibiotic prescribing; which mirrors that reported in previous studies done in South Africa (95%), Europe (74%) and the USA (78%).^[15,27,31]

The study findings suggest that prudent antibiotic prescribing and antibiotic stewardship should begin at the time when behaviour

is being shaped. Education is crucial in improving appropriate antibiotic prescribing by changing the attitudes and improving the knowledge of the prescribers.^[30] The ability to prescribe antibiotics is expected of medical doctors immediately after leaving medical school and is a task they will encounter on a daily basis throughout their careers. This means that medical schools must ensure that their graduates are adequately prepared, not only in general antibiotic use but also in how to use them prudently.^[32] Medical students should finish their undergraduate training with the mindset that antibiotics are a special class of drugs whose inappropriate use could not only affect the index patient but the entire population.^[30] So, they should understand that their duty as antibiotic prescribers is to optimise the therapy for the patient they are treating; whilst at the same time preserving the efficacy of the drug to delay the development of resistance.^[32]

While the two groups of respondents used medical experts differently to learn, it was noted that healthcare-designed apps are used more by the Nigerian respondents. A USA study found that most students referred to Wikipedia rather than textbooks or peer-reviewed articles, and only a fraction referred to the Infectious Diseases Society of America guidelines.^[15]

Conclusion

In this study, the knowledge and perceptions of the final-year medical students in two African countries were assessed. This was to assist in the development of an antibiotic stewardship curriculum for teaching medical students in South Africa and Nigeria the principles of prudent antibiotic prescribing. The objective of this study was to determine the knowledge and perceptions of the final year South African and Nigerian medical students from four medical schools on prudent antibiotic prescribing and principles of antibiotic stewardship. The respondents from both countries have similar perceptions of antibiotic use and resistance. However, a knowledge gap is demonstrated between the respondents of the two countries and an effort must be made to bridge these gaps. It is recommended that Nigerian medical schools should consider changing their traditional curriculum to an integrated one, which is student-centred, facilitates life-long learning and the development of skills that will make them become self-directed learners for the rest of their lives.^[33–34]

Supplementary material

Supplementary data are available at *International Journal of Pharmacy Practice* online.

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Conflict of interest

The author(s) declare(s) that they have no conflicts of interest to disclose.

Authors' contributions

Dr. Bashar Muhammad Augie: Is a PhD candidate under the supervision of Dr. Jacqui Miot, Associate Prof Patricia A. McInerney and Prof Robyn L. van Zyl. He was involved in the design of the project, data collection, data analysis and the writing of the manuscript. Prof Robyn L. van Zyl: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript. Associate Prof Patricia A. McInerney: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript. Dr. Jacqui Miot: She was involved in the design of the project, she guided the student in the data analysis and had complete access to the data, participated in the manuscript writing and has approved the final version of the manuscript.

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Appendix D: Approval of study title.



Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

11 February 2019
Person No: 1332258
PAG

Dr MA Bashar
Department Of Pharmacology, College Of Health Sciences
Federal University Birnin Kebbi, Pmb 1157
Kebbi State
8000
Nigeria

Dear Dr Muhammad Bashar

Doctor of Philosophy: Approval of Title

We have pleasure in advising that your proposal entitled *Empowering medical students to join the drive for improved antibiotic stewardship* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely



Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix E: Approval of change of research title.

The final title of the project does not reflect the title on the ethics documents. This is because the title has to be changed to reflect the refocusing of the project as a result of COVID-19 pandemic requiring some changes.



Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

07 July 2021
Person No: 1332258
TAA

Dr MA Bashar
Department of Pharmacology, College of Health Sciences
Federal University Birnin Kebbi, PMB 1157
Kebbi State
8000
Nigeria

Dear Dr Muhammad Bashar

Doctor of Philosophy: Change of title of research

I am pleased to inform you that the following change in the title of your Thesis for the degree of **Doctor of Philosophy** has been approved:

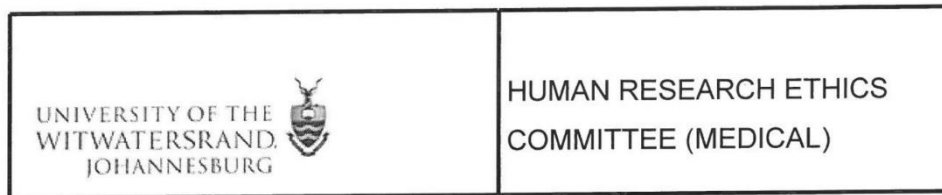
From: **Empowering medical students to join the drive for improved antibiotic stewardship**
To: **Development of an undergraduate antibiotic stewardship training programme for medical students**

Yours sincerely

A handwritten signature in black ink, appearing to read "Sandra Benn".

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix F: Phase One ethics approval from WITS University.



Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr MA Bashar
School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

E-mail: 1332258@students.wits.ac.za

CC: Supervisor: Profs R van Zyl & P McInerney; Dr J Miot
<Robyn.Vanzyl@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2019/07/01

REF: R14/49

PROTOCOL NO: M1902108 *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Empowering medical students to join the drive for improved antibiotic stewardship
Phase 1*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.



MSWorks2000/Iain0007/Clearscan.wps

R14/49 Dr MA Bashar

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M1902108**

NAME: Dr MA Bashar
(Principal Investigator)
DEPARTMENT: School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

PROJECT TITLE: Empowering medical students to join the drive for improved
antibiotic stewardship
Phase 1

DATE CONSIDERED: Ad hoc

DECISION: Approved unconditionally

CONDITIONS: Separate applications will be required for Phases 2/3

SUPERVISOR: Profs R van Zyl & P McNerney; Dr J Miot

APPROVED BY: 
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2019/07/01

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

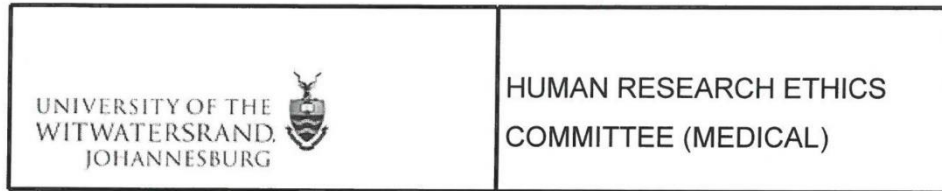
To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and will therefore reports and re-certification will be due early in the month of **February** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature

02/07/2019
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix G: Phase Two ethics approval from WITS University.



Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr MA Bashar
School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

E-mail: 1332258@students.wits.ac.za

CC: Supervisor: Profs R van Zyl & P McInerney; Dr J Miot
<Robyn.VanZyl@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2019/10/28

REF: R14/49

PROTOCOL NO: M190864 (This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)

PROJECT TITLE: *Empowering medical students to join the drive for improved antibiotic stewardship Phase II*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.



MSWorks2000/Iain0007/Clearscan.wps

R14/49 Dr MA Bashar

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190864**

NAME: Dr MA Bashar
(Principal Investigator)
DEPARTMENT: School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

PROJECT TITLE: Empowering medical students to join the drive for
improved antibiotic stewardship
Phase II

DATE CONSIDERED: 2019/08/30

DECISION: Approved unconditionally

CONDITIONS: Follows M1902108 - Phase I

SUPERVISOR: Profs R van Zyl & P McInerney; Dr J Miot

APPROVED BY: 
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2019/10/28

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **August** and will therefore reports and re-certification will be due early in the month of **August** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature

28/10/2019
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix H: Ethics approval from Usmanu Danfodiyo University Sokoto.

USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.

PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

Chairman Board

Chief Osaro Idah (Obazelu of Benin)

Director of Administration

Salim Ibrahim Jafar, B.Sc (Sociology) PGDPA, AIHAN



Chief Medical Director

Dr. Anas A. Sabir MBBS, FMCP

Chairman M.A.C

Dr. Nasir Muhammad MBBS, DO, PGDA, PHEC, FMCoph

UDUTH/HREC/2018/No. 756

Our Ref:

Your Ref:

January 18, 2019

Dr. Bashir Muhammad Augie
Department of Pharmacy and Pharmacology,
Faculty of Health Sciences,
7 York Rd, Parktown 2193, South Africa

RE: REQUEST FOR ETHICAL CLEARANCE TO ADMINISTER A QUESTIONNAIRE TO FINAL YEAR MEDICAL STUDENTS

With reference to your application on the above subject dated 04th October, 2018 on research topic titled *"Empowering Medical Students to Join the Drive for Improved Antibiotic Stewardship"* I hereby acknowledge its receipt and convey Ethical Committee's approval to you.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

You should submit a copy of your research to the Ethics Committee after the study might have been completed

Thank you.


Dr. Karima A. Tunau, MBBS, FWACS, MPH, FMS
Chairperson, HREC

Appendix I: Extended ethics approval from Usmanu Danfodiyo University Sokoto.

USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO.
PRIVATE MAIL BAG 2370, SOKOTO - NIGERIA.

Chairman Board
Chief Osaro Idah (Obazelu of Benin)
Director of Administration
Salim Ibrahim Jafar B.Sc (Sociology), PGDPA, AIHAN



Chief Medical Director
Dr. Anas A. Sabir MBBS, FMCP
Chairman Medical Advisory Committee
Dr. Nasiru Muhammad MBBS, DO, PGDPA, PDE, MSc, PHEC, FMCPh

Our Ref: UDUTH/HREC/2018/No. 756 Your Ref: _____ Date: October 9, 2019

Dr. Bashar Muhammad Augie
Department of Pharmacy and Pharmacology,
Faculty of Health Sciences,
7 York Rd, Parktown 2193, South Africa

RE: REQUEST FOR EXTENSION OF THE VALIDITY OF MY ETHICS CLEARANCE CERTIFICATE

With reference to your application on the above subject dated 26th September, 2016 on research topic titled **"Empowering Medical Students to Join the Drive for Improved Antibiotic Stewardship"** I hereby acknowledge its receipt and convey Ethical Committee's approval to you. The time validity of the approval dates from January, 2020 to January, 2021.

The approval is given with the understanding that the data obtained would be used to substantiate the above topic.

Please ensure that the study is guided by the methodology presented in the proposal.

You should submit a copy of your research to the Ethics Committee after the study might have been completed

Thank you.


Dr. Karima A. Tunau, MBBS, FWACS, MPH, FMAS
Chairperson, HREC

Appendix J: Ethics approval from Bayero University Kano.



BAYERO UNIVERSITY, KANO.

COLLEGE OF HEALTH SCIENCES,

Office of the Provost

VICE CHANCELLOR: Prof. Muhammad Yahuza Bello Bsc, MSc.(BUK), Ph.D (Arkansas)
REGISTRAR: Fatimah Binta Muhammad B A (Ed), MPPA (BUK) MNI
PROVOST: Prof. Ibrahim Adamu Yakasai MBBS (ABU), MRCPG(London), FWACS, FRCOG(UK), FMCOG, FICS M.A. Med Edu(Winchester)

P.M.B. 3011 Kano, Nigeria
+234-8055827576, 9096230271
e-mail: deanmed@med.buk.edu.ng

BUK/CHS/REC/VII/52

Dr. Bashir Muhammad Augie,
Department of Pharmacology,
College of Health Sciences,
University of Witwatersrand,
Johannesburg.

6th November, 2018

RESEARCH ETHICS APPROVAL

With regards to your letter dated 30th September, 2018 seeking for approval to carry out this titled research: **EMPOWERING MEDICAL STUDENTS TO JOIN THE DRIVE FOR IMPROVED ANTIBIOTIC STEWARDSHIP.**

The College of Health Sciences Research Ethics Committee (CHS-REC) has reviewed your proposal and no ethical correction observed.

In line with the above, Ethics Approval is hereby granted to conduct the research. You are required to submit report on the progress of the study and its completion to the CHS-REC.

Accept the assurance of committee's highest regard.

Best wishes.

A handwritten signature in black ink, appearing to read 'Ummi M. Gwadabe'.

Ummi M. Gwadabe
Committee Secretary
For: Chairman

Appendix K: Extended ethics approval from Bayero University Kano.



BAYERO UNIVERSITY, KANO
COLLEGE OF HEALTH SCIENCES
OFFICE OF THE PROVOST

VICE-CHANCELLOR: Prof. Muhammad Y. Bello B.Sc., MSc (BUK); Ph.D. (Arkansas) PMB 3011, BUK, KANO. NIGERIA
REGISTRAR: Fatima Bintu Mohammed B.A. (Ed) MPPA (BUK) MNI
PROVOST: Prof. Ibrahim Adamu Yakasai MBBS (ABU), MRCOG (London) FWACS, FRCOG (UK), FMCOG, FICS, MA Med. Educ. (Winchester)
☎ +2347061540362, +2348095606666 email: provost.chs@buk.edu.ng

BUK/CHS/REC/101

8th October, 2019

TO: Dr. Bashar Muhammad Augie,
Department of Pharmacy and Pharmacology,
Faculty of Health Sciences,
University of the Witwatersrand Johannesburg,
South Africa.

Dear Sir,

**RE- REQUEST FOR EXTENSION OF THE VALIDITY OF ETHICS CLEARANCE
CERTIFICATE**

Sequel to your letter dated 26th September, 2019 seeking for extension of your research ethical approval on a research titled, **Empowering medical students to join the drive for improved antibiotic stewardship**. The College of Health Sciences Research Ethics Committee has resolved to extend your ethical approval to 31st December, 2021.

In view of the above, you are required to submit progress report on the study to the committee on regular basis and also a full report upon completion.

Please accept the kinds assurances of the Committee.

Best wishes

Umami M. Gwadabe
Committee Secretary
For: Chairman.

Appendix L: Ethics approval from Ahmadu Bello University Zaria.

HEALTH RESEARCH ETHICS COMMITTEE



**AHMADU BELLO UNIVERSITY TEACHING HOSPITAL SHIKA,
ZARIA, NIGERIA.**

E- mail: abuthshika@yahoo.com

website: www.abuth.org

Chief Medical Director: Prof. Lawal Khalid, MBBS, FMCS, FWACS, FRCS(ED) mni

Chairman, Medical Advisory Committee: Prof Adamu Ahmed, MBBS, (ABU) LLB (ABU), BL, FWACS, FICS, FACS.

Director of Administration: Alh. Abdulraheem Sallau, BA(Pub. Admin) PGDPA, MPA, (ABU) AHAN, ACIPM.

Ag. Chairperson : HREC Prof Aisha I. Mamman MBBS, FMCPATH

NHREC/10/12/2015

D-U-N-S NUMBER: 954524802

ABUTH/HREC/ CL/05

19th October, 2018

ABUTH HREC FULL ETHICAL CLEARANCE CERTIFICATE

Empowering Medical Students to Join the Drive for Improved Antibiotic Stewardship.

ABUTH Ethics Committee assigned number: - ABUTHZ/HREC/D25/2018

Name of the principal Investigator: - Dr. Bashar Muhammad Augie

Address of the Principal Investigator: - Dept. of Pharmacy and Pharmacology
University of Witwatersrand
Johannesburg, South Africa.

Date of receipt of valid application: - 10th July, 2018

Date of meeting when final determination
On ethical approval was made: - 19th September, 2018

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and **given full approval by the Health Research Ethics Committee.**

Please note: this approval dates from 19th October, 2018 - 19th October, 2019

No participant recruitment into this research may be conducted outside these dates.

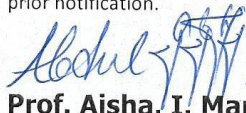
All informed consent forms in this study must carry the ABUTH HREC number assigned to this research and the duration of ABUTH HREC approval of the study.

This HREC expects that you submit your application as well as an annual report for ethical clearance renewal 3 months prior to expiration of study dates. This is to enable you obtain renewal of your approval and avoid interruption of your research.

If there is delay in starting the research, please inform the ABUTH HREC so that starting dates can be adjusted accordingly.

No changes are permitted in the research without prior approval by ABUTH HREC, except in circumstances outlined in national code for Health Research Ethics: <http://www.nhrec.net>.

ABUTH HREC reserves the right to conduct compliance assessment visits to your research site without prior notification.

for  26/10/2018
Prof. Aisha I. Mamman MBBS, FMCPATH
Chairperson

Appendix M: Extended ethics approval from Ahmadu Bello University Zaria.

 **HEALTH RESEARCH ETHICS COMMITTEE**
AHMADU BELLO UNIVERSITY TEACHING HOSPITAL SHIKA,
ZARIA, NIGERIA
E-mail: abuthshika@yahoo.com website: www.abuth.org

Chairman of Board: **ALH. AHMADU RUFAI MACHIKA**
Chief Medical Director: **PROF. HAMIDU A.U.**, MBBS, FWACS, MVUS (USA)
Chairman, Medical Advisory Committee: **PROF. ADAMU AHMED**, MBBS, (ABU), LLB, (ABU), BL, FWACS, FICS, FACS.
Director of Administration: **ALH. ABDULRAHEEM SALLAU**, BA (Pub. Admin) PGDPA, MPA, (ABU) AHAN, ACIPM
Ag. Chairperson: **HREC Prof. Aisha I. Mamman** MBBS, FMCPath

NHREC/10/12/2015 D-U-N-S NUMBER: 954524802
ABUTH/HREC/ CL/05 4th October, 2019

ABUTH HREC FULL ETHICAL CLEARANCE CERTIFICATE

Empowering Medical Students to join the drive for Improved Antibiotic Stewardship.

ABUTH Ethics Committee assigned number: - ABUTHZ/HREC/D25/2018

Name of the principal Investigator: - Dr. Bashar Muhammad Augie
Address of the Principal Investigator: - Dept. of Pharmacy & Pharmacology

Date of receipt of valid application: - 10th July, 2018

Date of meeting when final determination
On ethical approval was made: - 19th September, 2018

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and **given full approval by the Health Research Ethics Committee.**

Please note: this approval dates from **4th October, 2019 - 4th October, 2020**

No participant recruitment into this research may be conducted outside these dates.

All informed consent forms in this study must carry the ABUTH HREC number assigned to this research and the duration of ABUTH HREC approval of the study.

This HREC expects that you submit your application as well as an annual report for ethical clearance renewal 3 months prior to expiration of study dates. This is to enable you obtain renewal of your approval and avoid interruption of your research.

If there is delay in starting the research, please inform the ABUTH HREC so that starting dates can be adjusted accordingly.

No changes are permitted in the research without prior approval by ABUTH HREC, except in circumstances outlined in national code for Health Research Ethics: <http://www.nhrec.net>.

ABUTH HREC reserves the right to conduct compliance assessment visits to your research site without prior notification.

Appendix N: Letter of permission from the University of the Witwatersrand.



OFFICE OF THE DEPUTY REGISTRAR

01 February 2019

Mr. Muhammad Augie Bashar
Student Number: 1332258

TO WHOM IT MAY CONCERN

"Empowering medical students to join the drive for improved antibiotic stewardship"

This letter serves to confirm that the above project has received permission to be conducted on University premises, and/or involving staff and/or students of the University as research participants. In undertaking this research, you agree to abide by all University regulations for conducting research on campus and to respect participants' rights to withdraw from participation at any time.

If you are conducting research on certain student cohorts, year groups, courses or with academic staff within specific Schools and within the teaching term, permission must be sought from Heads of School or individual academics.

No research can commence until ethical clearance has been obtained. Please forward a copy of your ethical clearance certificate once it has been obtained.

A handwritten signature in black ink, appearing to read "Nicoleen Potgieter".

Nicoleen Potgieter

UNIVERSITY DEPUTY REGISTRAR

Appendix O: Letter of permission from the Unit of the Undergraduate medical Education University of the Witwatersrand.



23 January 2019

To: Prof Robyn van Zyl
Head of Pharmacology Division
School of Therapeutic Sciences
Faculty of Health Sciences
University of the Witwatersrand

RE: Support of PhD project regarding antibiotic stewardship education in GEMP

Dear Prof van Zyl,

This letter serves to confirm the support of my unit to conduct this research project with the students in the Graduate Entry Medical Programme (GEMP) here at Wits medical school.

We recognise that this includes a) the extra antibiotic stewardship training and assessments/questionnaires and b) access to the GEMP questions/marks involving this topic.

I look forward to the outcome of this study.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'FHS Schoeman'.

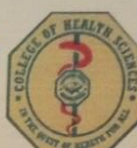
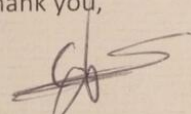
Adj Prof FHS Schoeman

Director: UUME (Wits Medical School)

MBChB (Stell), M.MEd (Medical Education) (Dundee, UK), PhD (Health Professions Education) (UFS), FHEA (UK)

Director - Unit for Undergraduate Medical Education | Wits Medical School | Faculty of Health Science
Private Bag 3, Wits, 2050, South Africa | T: +27 11 717 2756 | E: scarpa.schoeman@wits.ac.za | M: +27 82 378 7333
3rd floor, Wits Medical School, 7 York Road, Parktown, 2193, South Africa |
www.wits.ac.za/health

Appendix P: Letter of permission from Usmanu Danfodiyo University Sokoto.

 COLLEGE OF HEALTH SCIENCES  USMANU DANFODIYO UNIVERSITY, SOKOTO P.M.B. 02254, Sokoto-Nigeria, G.S.M: 08066024503, 07031596126 E-mail: chs@udusok.edu.ng, chsudusok@gmail.com	
Vice Chancellor Prof. A.A. ZURU Bsc. (BUK), Msc (Unisok), Ph.D (Salford, UK) DSCN, FICCON, FSESAN, FSAN.	Provost: Prof. S.O. BELLO Bsc, MB.ChB, Ph.D, FACSc, FWAMS, FAIMER Fellow (Phil)
Dean Fac. Clinical Sciences Prof. S.A. Saidu MBBS, FWACS, FMCr	Ref: UDUS/CHS/SP. Date: 12 th February, 2019
Dean Fac. Basic Medical Sciences Prof. A.D Zagga MBBS, Msc, Ph.D (ANAT) UDUS	Dr. Bashir Muhammad Augie Department of Pharmacy and Pharmacology School of Therapeutic Science, Faculty of Health Sciences University of the Witwatersrand Johannesburg Republic of South Africa
Ag. Dean Fac. Basic Clinical Sciences Dr. Aminu Chika MBBS, Msc, Ph.D	Request for Permission to Administer Questionnaire to Final Year Medical Students and Review Anti-Biotic Training in Medical Curriculum of Your Institution
Director Institute of Urology & Nephrology Prof. I.A. Mungadi, MBBS, FRCSed, FWACS	Yours on the above dated 4 th February, 2019 refers.
Ag. Director School of Medical Lab. Sciences Dr. M.K. Dallatu B.Sc, M.Sc, Ph.D, AMLSCN	I write at the instance of the Provost to convey his approval for you to administer the above subject to final year students.
Coordinator Cent. Adv. Med. Res. & Training (CAMRET) Dr. Ndodo N.D B.Sc, M.Sc, (Ant) M.Sc (Mol. Bioengr.), Ph.D	The Provost had also directed that you have to include Dr. Kasimu Ghandi Ibrahim as per your attachment.
College Secretary Alh. Aminu B. Tukur B.A Eng. Cert. Masscom	Thank you,  Alh. A. B. Tukur College Secretary For: Provost

Appendix Q: Letter of permission from Bayero University Kano.



BAYERO UNIVERSITY, KANO COLLEGE OF HEALTH SCIENCES FACULTY OF CLINICAL SCIENCES

VICE- CHANCELLOR: Prof. Muhammad Y. Bello Bsc,Msc (BUK), PhD (Arkansas)

REGISTRAR: Fatima Binta Mohammed Bsc MPPA (BUK)

Provost: Prof. Ibrahim AdamuYakasai MBBS (ABU), MA (UK), FRCOG, FWACS, FICS, FMCOG

Dean: Prof.Mahmoud U. Sani (MBBS,PhD, FWACP, FACP, FACC, FRCPE

P.M.B. 3011, Kano-Nigeria

Telex: 77189 UNIBAYERO NG

Telegrams UniBAYERO Kano

e-mail dean.clinical@buk.edu.ng

Telephone: 09030631843

OFFICE OF THE DEAN

26th February, 2019

Dr. Bashar Muhammad Augie

Department Of Pharmacy and Pharmacology

Faculty of Health Sciences

University Of Witwatersrand

Johannesburg, South Africa

PERMISSION TO ADMINISTER QUESTIONNAIRE TO MEDICAL STUDENTS

The letter issued to you by the CHS-REC dated 6th November, 2018 conveying the approval to conduct the study titled **EMPOWERING MEDICAL STUDENTS TO JOIN THE DRIVE FOR IMPROVED ANTIBIOTIC STEWARDSHIP** is referred.

Subsequently, you are hereby granted approval to administer the study questionnaire to Medical Students in the Faculty while adhering to the ethical requirements of the research.

Best Wishes.

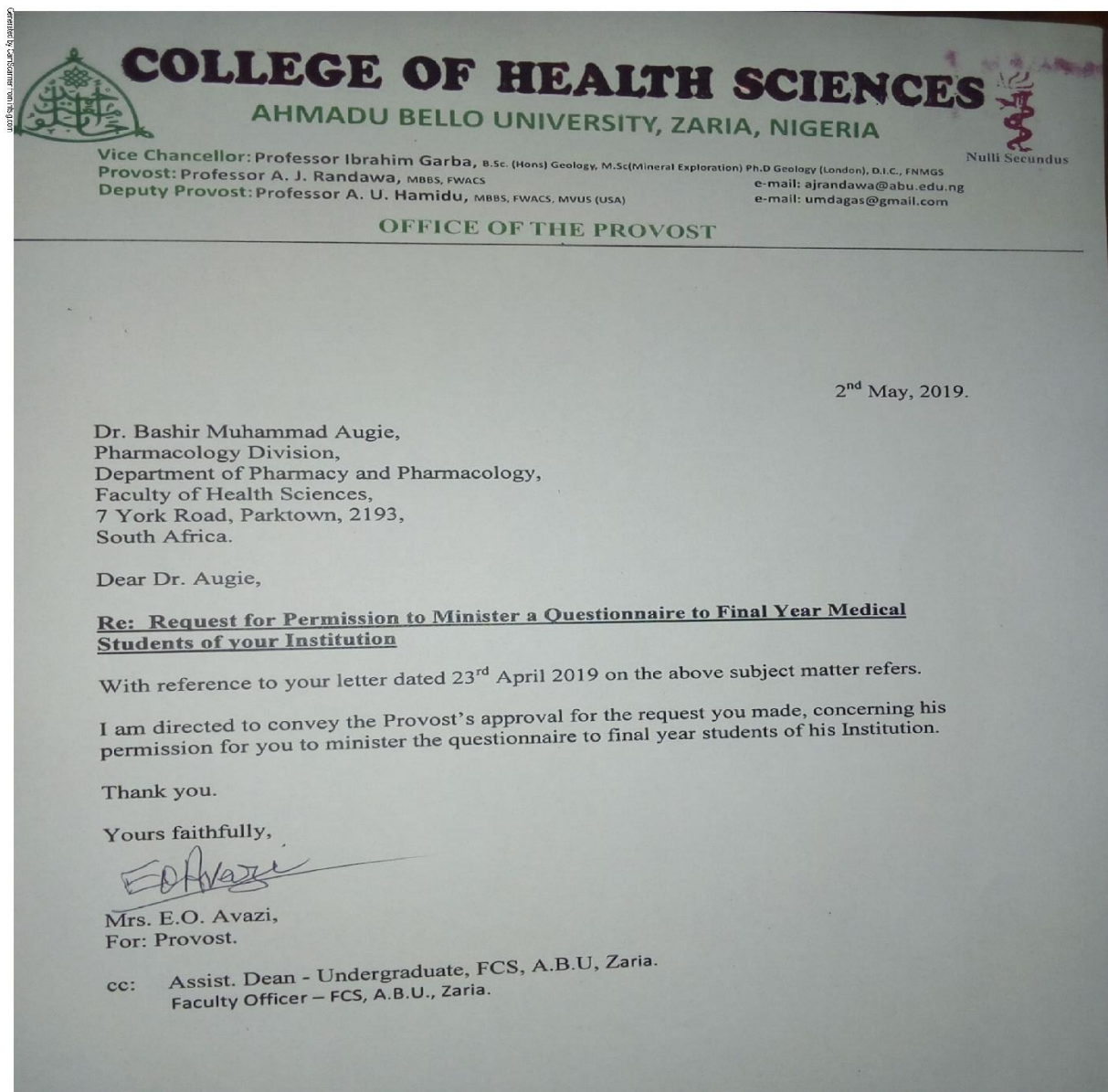
A handwritten signature in black ink, appearing to read 'Dr. Mohammed I.Y.'.

Dr Mohammed I.Y.

SUB DEAN

FOR DEAN, FCS

Appendix R: Letter of permission from Ahmadu Bello University Zaria.



Appendix S: List of Nigerian Medical Schools by National Universities Commission.

NATIONAL UNIVERSITIES COMMISSION

SECRETARIAT

PROF. ABUBAKAR RASHEED, mni, MFR

EXECUTIVE SECRETARY

TEL: +234 802 7455412-13, 703 9254081-2

FAX: 07098212004



AJA NWACHUKWU HOUSE,
NO 26, AGUIYI IRONSI STREET,
MAITAMA DISTRICT,
P.M.B 237, GARKI G.P.O.,
ABUJA-NIGERIA.

NUC/AP/Intl/Vol.III/05

25th August, 2020

School of Therapeutic Science
Faculty of Health Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology
Private Bag 3, Wits 2050
South Africa

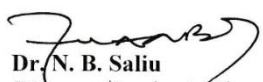
Attention: Dr. Bashar Muhammad Augie

Dear Sir,

RE: REQUEST FOR A LIST OF NIGERIAN MEDICAL SCHOOLS

Please refer to your letter dated 20 July, 2020 on the above subject. Attached herewith is the list of Nigerian Medical Schools.

Please accept the assurances of the Executive Secretary's highest regards.


Dr. N. B. Salio
Director, Academic Planning
For: Executive Secretary

Website: <http://www.nuc.edu.ng>

Appendix T: Medical students survey questionnaire.

Confidential

Page 1

NIGERIAN AND SOUTH AFRICAN MEDICAL STUDENTS' PERCEPTIONS, ATTITUDES AND KNOWLEDGE ABOUT ANTIBIOTIC USE AND RESISTANCE

My name is Dr Bashar Muhammad Augie, and I am registered for a PhD in Pharmacology at the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. This is one of a series of studies that form my PhD thesis. It involves developing an educational antibiotic stewardship programme that will assist in training medical students in South Africa and Nigeria, on rationale antibiotic prescribing. The project is under the supervision of Dr Jacqui Miot, Prof Patricia McInerney and Prof Robyn van Zyl.

The purpose of this survey is to assess South African and Nigerian final year medical students' perceptions, attitudes and knowledge about antibiotic prescribing, as well as the perceived quality of education about antibiotics in general. We ultimately hope to identify ways to improve medical school curricula in order to promote better antibiotic prescribing by medical graduates.

All information collected is completely anonymous. Only me and my supervisors will have access to your individual responses, and this will not be shared with your university. Participation is voluntary and there will be no penalty for not participating. To ensure anonymity your email address will not be shared, divulged, or otherwise sent to third parties.

Please take the survey only once. It will take about 15 minutes to complete. Answer honestly the best you can without discussing questions or looking up the answers. At the end of the study period I will send you a detailed explanation of the correct answers for each scenario. The results of this study may be published in scientific journals and presented at academic meetings.

This study has been approved by the ethics committee of your institution, and permission was also granted by your university. If you have any questions or feedback on this survey please contact me, Dr Bashar Muhammad Augie (email: muhammad.bashar1@students.wits.ac.za).

Thank you for your time and participation!

Biographic information

University/medical school

- ☐ University of the Witwatersrand
☐ Usmanu Danfodiyo University Sokoto
☐ Ahmadu Bello University Zaria
☐ Bayero University Kano

Gender

- ☐ Male ☐ Female

Age (in years)

(e.g. 23)

Previous degrees

- ☐ Bachelors degree
☐ Honours degree
☐ Masters degree
☐ PhD degree
☐ Other
☐ None

Bachelor of

Honours degree in

Masters in

15-11-2021 17:59

projectredcap.org



PhD in _____

Please specify other degree _____

Were you exposed to concept of antimicrobial stewardship in your previous degree?

☐ Yes ☐ No

Perceptions

How much do you agree with the following statements?

	Strongly Agree	Agree	Neutral	Disagree	Strongly disagree
Antibiotics are overused in Nigeria/South Africa	☐	☐	☐	☐	☐
Antibiotics are overused at the teaching hospital where I have rotated	☐	☐	☐	☐	☐
Antibiotic resistance is a significant problem in Nigeria/South Africa	☐	☐	☐	☐	☐
Antibiotic resistance is a significant problem at hospitals where I have rotated	☐	☐	☐	☐	☐
New antibiotics are available to deal with the problem of resistance	☐	☐	☐	☐	☐
Inappropriate use of antibiotics causes antibiotic resistance	☐	☐	☐	☐	☐
Better use of antibiotics will reduce levels of antibiotics resistance	☐	☐	☐	☐	☐
Use of broad spectrum antibiotics when equally effective narrower spectrum antibiotics are available can increase antibiotic resistance	☐	☐	☐	☐	☐
Lack of hand disinfection by healthcare providers causes the spread of antibiotic resistance	☐	☐	☐	☐	☐
Inappropriate use of antibiotics is directly harmful to patients	☐	☐	☐	☐	☐

A good knowledge of antibiotics is important to my work as a doctor	☐	☐	☐	☐	☐
I would like more education on antibiotic resistance	☐	☐	☐	☐	☐
I would like more education on the appropriate antibiotics use	☐	☐	☐	☐	☐

Education

If available, how useful are the following education activities for learning about antibiotic classes and spectrum of activity?

	Very useful	Useful	Neutral	Not useful	Not at all useful
Formal lectures	☐	☐	☐	☐	☐
Formal bedside tutorials	☐	☐	☐	☐	☐
Consultant ward rounds	☐	☐	☐	☐	☐
Registrar ward rounds	☐	☐	☐	☐	☐
Problem-based learning groups	☐	☐	☐	☐	☐

If available, how useful are the following educational activities for learning about antibiotics prescribing and resistance?

	Very useful	Useful	Neutral	Not useful	Not at all useful
Formal lectures	☐	☐	☐	☐	☐
Formal bedside tutorials	☐	☐	☐	☐	☐
Consultant ward rounds	☐	☐	☐	☐	☐
Registrar ward rounds	☐	☐	☐	☐	☐
Problem-based learning groups	☐	☐	☐	☐	☐

How often do you use the following resources to learn about antimicrobial prescribing and resistance?

	Often	Sometimes	Rarely	Never	Not familiar
Infectious diseases specialists	☐	☐	☐	☐	☐
Clinical Pharmacologists	☐	☐	☐	☐	☐
Microbiologists	☐	☐	☐	☐	☐
Consultants	☐	☐	☐	☐	☐
Registrars	☐	☐	☐	☐	☐
Textbooks	☐	☐	☐	☐	☐
Medical journals	☐	☐	☐	☐	☐
iPad or smartphone apps	☐	☐	☐	☐	☐
Other students	☐	☐	☐	☐	☐

Other _____

Do any of the hospitals where you have rotated have antibiotic guidelines? ☐ Yes ☐ No

Have you ever personally used or consulted antibiotic guidelines when considering an antibiotic for a patient? ☐ Yes ☐ No

Topics

Have you attended lectures or tutorials that specifically address the following topics?

	Yes	No	Don't remember
Diagnosis of infection	☐	☐	☐
Indications for starting antibiotics	☐	☐	☐
Dosing and duration of antibiotic therapy for specific infections	☐	☐	☐
Indication for intravenous antibiotics	☐	☐	☐
Rational use of antibiotics in general	☐	☐	☐
Basic principles of infection prevention and control	☐	☐	☐

Are you familiar with the term "antibiotic stewardship?"

- ☐ Very familiar (I've received formal teaching on the subject)
☐ Familiar (It's been mentioned in lectures/tutorials but not explained)
☐ Not familiar (I've heard the term but not sure what it's about)
☐ Not at all familiar (I've never heard it before)

Overall rating

How would you rate your education regarding appropriate use of antibiotics?

- ☐ Very useful
☐ Useful
☐ Neutral
☐ Not useful
☐ Not at all useful
☐ I have not received any education on this subject so far

How confident do you feel to prescribe antibiotics?

- ☐ Very confident
☐ Confident
☐ Neutral
☐ Not confident
☐ Completely unprepared

How well do you feel that your medical school has prepared you for the following?

	Very good	Good	Average	Poor	Very poor
Making an accurate diagnosis of infection	☐	☐	☐	☐	☐

Knowing when to start antibiotics	☐	☐	☐	☐	☐
Choosing the correct antibiotic for a specific infection	☐	☐	☐	☐	☐
Knowledge of dosing and duration of antibiotic therapy for specific infections	☐	☐	☐	☐	☐
How to de-escalate to narrower spectrum antibiotics	☐	☐	☐	☐	☐
How and when to transition from intravenous to oral antibiotics	☐	☐	☐	☐	☐
How to interpret antibiograms	☐	☐	☐	☐	☐
Understanding the spectrum of activity of commonly used antibiotics	☐	☐	☐	☐	☐
Understanding basic mechanisms of antibiotic resistance	☐	☐	☐	☐	☐

In what way could newly qualified doctors be better prepared to prescribe antibiotics? (select one or more options)

- ☐ More formal lectures
- ☐ More formal bedside tutorials
- ☐ More time in microbiology
- ☐ More exposure to infectious diseases specialists
- ☐ A local handbook/guideline on treating common infections
- ☐ More applications for smart devices
- ☐ More computer-based tutorials
- ☐ More exposure to clinical pharmacologist

Knowledge

Please answer the following questions and case scenarios on antibiotic use and resistance (select the correct answer)

A 24-year-old previously well woman presents to casualty with dysuria and frequency. This is her first episode of this problem, which started about one day earlier. Clinically she is completely well without fever or signs of systemic illness. She has mild suprapubic tenderness, but no renal angle tenderness is elicited. A urine pregnancy is negative. A urine dipstick is positive for 3+ leucocytes and nitrites. Would you:

- ☐ Treat with intravenous gentamycin for 10 days
- ☐ Give a stat dose of intravenous ceftriaxone and then complete an oral course of antibiotics
- ☐ Prescribe 3 days of oral ciprofloxacin
- ☐ Send a urine culture and wait for results before prescribing antibiotics
- ☐ Treat with cotrimoxazole (Septrin™/Bactrim™) for 5 days

Which of the following antibiotics is appropriate for treating methicillin-sensitive *Staphylococcus aureus*?

- ☐ Vancomycin
- ☐ Cloxacillin
- ☐ Amoxicillin-clavulanic acid (Augmentin)
- ☐ Ceftriaxone
- ☐ All of the above

A 34-year-old HIV-infected man presents to hospital with a 5 days history of productive cough, fever, pleuritic chest pain and shortness of breath. On examination, he is pyrexial, temperature 39.0°C, with a respiratory rate of 35 breaths per minute and bronchial breath sounds in the right middle zone. He is slightly confused but his blood pressure is normal. A chest X-ray confirms your suspicion of right middle lobe consolidation. Blood results show a urea of 10 mmol/L and white cell count of 20×10^9 /L. Would you:

- ☐ Send a blood culture and start intravenous ceftriaxone
- ☐ Discharge on oral amoxicillin
- ☐ Start intravenous ertapenem after performing a blood culture
- ☐ Start empiric anti-tuberculous therapy
- ☐ Send a blood culture and start intravenous moxifloxacin

A resident of an old age home develops fever, confusion and renal angle tenderness. A urine dipstick shows 3+ leucocytes. You send blood and urine cultures and start empiric ertapenem for health care-associated pyelonephritis. After 48 hours your patient is alert and oriented and has been afebrile for a day. The cultures have grown *Escherichia coli* susceptible to ertapenem, amikacin and ciprofloxacin. Would you:

- ☐ Complete a full course of ertapenem because of excellent response
- ☐ Switch to oral ciprofloxacin
- ☐ Switch to intravenous ciprofloxacin
- ☐ Switch to amikacin because of better kidney penetration
- ☐ Stop all antibiotics because she has recovered fully

A 27-year-old man comes to your clinic complaining of a sore throat that started the previous day. A few of his colleagues have the same problem. On examination, he is not acutely ill but has a fever of 37.8°C, generalised lymphadenopathy and an inflamed pharynx with no pus on the tonsils. His chest is clear. How would you proceed?

- ☐ Prescribe penicillin VK for 10 days to prevent rheumatic fever
- ☐ Perform a blood culture and await the result
- ☐ Prescribe a 5-day course of amoxicillin
- ☐ Perform a throat swab and give an antibiotic while awaiting the result
- ☐ Treat symptomatically with bed rest, paracetamol and expectant management

A patient is receiving intravenous fluids in the surgical ward for pancreatitis. On day 5 of his admission, he spikes a fever of 39°C with tachycardia and you find tenderness and erythema around his drip site. Would you:

- ☐ Do a 'septic screen' and await result of cultures
- ☐ Send cultures and prescribe empiric amoxicillin-clavulanic acid
- ☐ Prescribe cloxacillin for suspected drip site sepsis
- ☐ Take a blood culture and give a loading dose of vancomycin
- ☐ Take a blood culture and start ertapenem for hospital-acquired infection

An elderly man was recently discharged from hospital where he received clindamycin for cellulitis. He had a complete clinical response and is now on day 7 of this therapy, but returns to the hospital with new onset of mucoid diarrhoea and fever. A stool specimen was sent and the microbiology lab calls to confirm your suspicion of *Clostridium difficile*-associated diarrhoea. He has a normal white cell count and creatinine, and there are no clinical signs of colitis. How would you manage this?

- ☐ Stop the clindamycin and add oral metronidazole
- ☐ Continue the clindamycin and add oral metronidazole
- ☐ Continue the clindamycin and treat symptomatically with loperamide (Imodium)
- ☐ Give a course of ciprofloxacin for bacterial diarrhoea
- ☐ Give a combination of intravenous metronidazole and vancomycin

The lab calls with a result of a blood culture for extended beta lactamase (ESBL) *Escherichia coli*. Which of the following antibiotics would you prescribe?

- ☐ Vancomycin
- ☐ Amoxicillin-clavulanic acid
- ☐ Ceftriaxone
- ☐ Piperacillin-tazobactam
- ☐ Ertapenem

A 60-year-old woman with rheumatoid arthritis is admitted for an elective knee replacement. The orthopaedic surgeon has prescribed prophylactic cefazolin for 5 days. He has decided to extend the duration beyond 24 hours "just for extra protection". What are the potential problems with prolonging prophylactic antibiotics?

- ☐ Encouraging antibiotic resistance
- ☐ Adverse drug reactions
- ☐ *Clostridium difficile*-associated diarrhoea
- ☐ Increased risk of drip site infection
- ☐ All of the above

A 43-year-old male patient, known to be HIV positive with CD4 220. Has been unwell for 2 weeks with fever, loss of appetite and a dry cough. On examination his temperature is 38.3°C, blood pressure 106/58mmHg, pulse 126, RR 22, oxygen saturations 96% on room air. Chest X-ray shows a subtle reticular-nodular pattern bilaterally. A blood culture is taken and he is started on ceftriaxone 1g per day and clarithromycin. After 3 days he says that he is not feeling better, his temperature and pulse remain elevated. The blood culture remains negative at this point. What would you do next?

- ☐ Continue ceftriaxone at current dose
- ☐ Change to ertapenem
- ☐ Stop antibiotics and investigate for tuberculosis
- ☐ Change to ciprofloxacin
- ☐ Increase dose of ceftriaxone to 2g 12-hourly

Feedback

If you would like to receive feedback on the answers at the end of the study, please enter your email address

Appendix U: Modified Delphi questionnaire – Round One.

Confidential

Page 1

Antibiotic Stewardship - expert panel

My name is Dr Muhammad Augie Bashar, and I am registered for a PhD in Pharmacology at the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. This is one of a series of studies that constitutes my PhD thesis. It involves developing an educational antibiotic stewardship programme that will assist in training medical students in South Africa and Nigeria in terms of the rational prescription of antibiotics. The project is under the supervision of Dr Jacqui Miot, Prof. Patricia McInerney and Prof. Robyn van Zyl. This aspect of my study is a modified Delphi study. The objectives of the study are to suggest and recommend an international standard that could be applied in medical schools in these two countries. Experts in infectious diseases, medical microbiology, clinical pharmacology, medical education, infectious diseases, nursing and pharmacy across these two countries will be asked to use a Likert Scale to rank the developed antibiotic stewardship competencies. Provision will be made for these experts to recommend some missing competencies. Any competency that does not reach an acceptable level on the Likert scale through consensus by the panel of experts will be removed. As an expert in one of these fields, and in participating in this study, you would be performing a tremendous service to the practice of medicine. It is anticipated that the Delphi study will progress through a minimum of two rounds. If the expert group has not reached consensus by the second round, a third and even subsequent rounds will then be included. It may take 30 to 40 minutes to complete the questionnaire. You will be requested to complete the questionnaire within two weeks to enable the study to progress according to schedule. Based on the results of the first round, a new questionnaire will be compiled for the subsequent round. The results of a previous round of the Delphi study will be communicated to you along with the dispatch of the questionnaire for the subsequent round. Please select the option from the following: strongly disagree (1) to strongly agree (5) to each statement as indicated. Thank you for your time and participation!

Biographic information

Name:

Title:

Email address

Degree(s)/Qualification(s):

Institute where you currently work

Country:

☐ South Africa ☐ Nigeria ☐ Other

Experience as a tertiary educator (in number of years):

15-11-2021 18:01

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DOMAIN ONE: INFECTION PREVENTION AND CONTROL

COMPETENCY STATEMENT: All qualified medical doctors must understand the core knowledge underpinning the prevention and control of infection, and use this knowledge appropriately to prevent the spread of infection.

DESCRIPTORS

To support antibiotic stewardship, learners must demonstrate their impressions of the necessary means for the prevention and control of infection by means of the following:

- 1 Describe what a bacterium is
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 2 Describe the different types of bacteria that may cause infections and how they contribute to healthcare-associated infections
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 3 Explain what an antibiotic-resistant organism is
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 4 Explain the 'Chain of Infection'
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 5 Define the components required for the transmission of an infection (i.e. the presence of an organism, the route of transmission of the organism from one person to another, the host who would be susceptible to the infection)
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 6 Describe the routes of transmission of infectious organisms (i.e., contact, droplets, and airborne routes)
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 7 Explain the role played by the environment in the transmission of bacteria
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 8 Present and recognize the characteristics of a susceptible host
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 9 Demonstrate an understanding of the importance of surveillance
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

- 10 Describe how vaccines can prevent infections in susceptible persons
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

-
- 11 Demonstrate the application of standard precautions in healthcare environments
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 12 Apply appropriate policies/procedures and guidelines for the collection and handling of specimens
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 13 Apply policies, procedures and guidelines relevant to the control of infection when infection control cases and situations present themselves
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 14 Implement work practices that reduce the risk of infection (e.g. undergoing appropriate immunization or not coming to work when sick) to ensure the protection of the patient and other healthcare workers
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 15 Appreciate that healthcare workers should show accountability and commit to follow infection control protocols as part of their contract of employment
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 16 Act as a role model to healthcare workers and members of the public by adhering to the principles to prevent and control infections
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 17 Demonstrate ideal hand hygiene practices
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 18 Explain the first aid for exposed cuts/puncture wounds, or the exposure of the eyes, nose or mouth to fluids
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 19 Explain how to appropriately use the following products, namely soap and water, antibacterial soap, surgical scrubs, waterless alcohol agents, for hand hygiene, and the conditions under which to apply each of the methods
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 20 Differentiate between the cleaning, disinfecting and sterilization of hospital equipment
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 21 Describe safe handling methods and the disposal of sharp objects
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 22 Describe techniques to safely handle blood and body fluids to prevent exposure.
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

Further initiatives would be to demonstrate how information can be accessed and how awareness can be fostered of international/national strategies on infection prevention and control, and antibiotic resistance campaigns, such as the Global Action Plan for Antimicrobial Resistance and the SAVE LIVES: Clean Your Hands initiatives (accessed from <http://www.who.int/gpsc/5may/en/>). Recommendations could also be made to consult a pocket guide to antibiotic prescribing for adults in South Africa (2015).

DOMAIN TWO: ANTIBIOTICS AND ANTIBIOTIC RESISTANCE

COMPETENCY STATEMENT: All qualified medical doctors need to understand the core knowledge underpinning the concept of resistance to antibiotics and the application of this knowledge to help prevent antibiotic resistance.

Descriptors

To support antibiotic stewardship, learners must be able to do the following:

- 23 Describe at least two different ways in which antibiotics may kill bacteria
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 24 Explain the concept of bacterial killing by either concentration-dependent or time-dependent antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 25 Differentiate between bactericidal and bacteriostatic antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 26 Differentiate between latent tuberculosis infection and active tuberculosis disease
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 27 Discuss how the inappropriate use of antibiotics (including non-adherence to a treatment regime) may lead to resistance to antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 28 Identify approaches to support the optimal prescription of antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 29 Explain how the inappropriate use of broad-spectrum antibiotics increases the risk of Clostridium difficile colitis
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 30 Describe how antibiotics use drives the emergence of drug-resistant bacteria
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 31 Explain the four main mechanisms of antibiotic resistance
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

DOMAIN THREE: THE DIAGNOSIS OF INFECTION AND THE USE OF ANTIBIOTICS

COMPETENCY STATEMENT: All qualified medical doctors need to demonstrate their knowledge of the manner in which infections are diagnosed and the appropriate use of antibiotics, as well as the proper application of this knowledge to support the accurate diagnosis of infections and the appropriate use of antibiotics.

DESCRIPTORS

To support antibiotic stewardship, learners must be able to do the following:

- 32 Recognise the symptoms of infection
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 33 Explain how microbiology samples may be of assistance in the diagnosis of infections
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 34 Describe the appropriate way of taking samples following local procedures for taking samples
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 35 Describe the correct technique for performing a blood culture
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 36 Describe the correct technique for performing a pus swab
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 37 Demonstrate the appropriate way of taking samples following local procedures
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 38 Interpret microbiology results/reports from the laboratory at a basic level
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 39 Discuss how the identification of bacteria and their susceptibility to antibiotics from a specific culture are important in antibiotic therapy
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 40 Explain the concept of Minimum Inhibitory Concentration (MIC) in terms of bacterial killing
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 41 Explain why self-limiting bacterial or viral infections are unlikely to benefit from the dispensing of antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

-
- 42 Describe the required management strategies to treat self-limiting infections (i.e. the administration of analgesics /rest /fluid intake)
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 43 Understand the importance of following local antibiotic policies (i.e. in that their development is based on local resistance patterns), and adhere to these policies in practice
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 44 Explain the importance of documenting the following parameters in antibiotic therapy route of administration, dosage, duration, intervals between dosages, and the review date in clinical notes and of demonstrating these aspects in practice
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 45 Demonstrate an understanding of the factors that need to be considered when choosing an antibiotic (including the site of infection and the type of bacteria likely to cause an infection at that particular site)
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 46 Describe the use of broad and narrow-spectrum antibiotics and the role of broad-spectrum antibiotics in contributing to antibiotics resistance
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 47 Describe and be able to recognize the common side-effects associated with commonly-administered antibiotics
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 48 Demonstrate an understanding as to why the documentation of a patient's allergy to an antibiotic is important
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 49 Explain why it is important to consider certain physiological conditions (e.g. renal function) in patients who receive an antibiotic
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 50 Describe what is meant by "delayed prescribing"
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 51 Explain how the removal or drainage of material from the focus of infection, such as an abscess (often called source control) would facilitate a clinical cure
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 52 Identify the presence of an intra-abdominal abscess on plain abdominal X-ray film
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

-
- 53 Identify the likely source of infection and likely pathogens
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 54 Use a serum inflammatory marker such as procalcitonin and a C-reactive protein to help differentiate between viral and bacterial infections when the diagnosis is unclear
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 55 Explain how a biomarker such as procalcitonin can be used as a tool in guiding the decision to discontinue antibiotics in a patient
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 56 Explain why it is essential to ensure that an accurate diagnosis of an allergy to an antibiotic is based on the medical history of the patient and laboratory tests
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

DOMAIN FOUR: THE PRACTICE OF PRESCRIBING ANTIBIOTICS

COMPETENCY STATEMENT: All qualified medical doctors need to be aware of the way in which antibiotics are used in practice in terms of their dosage, timing, duration and the appropriate route of administration. They should be able to apply this knowledge as part of their routine practice.

Descriptors

To support antibiotic stewardship, learners must be able to do the following:

- 57 Explain how to recognize and manage sepsis
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 58 Describe why it is important to use local guidelines to initiate prompt and effective antibiotic treatment in patients with life-threatening infections
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 59 Describe why it is important to switch from intravenous antibiotics to oral therapy
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 60 Describe how to alter the route of administration from IV to oral antibiotic therapy
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 61 Explain the appropriateness of antibiotic administration models such as outpatient parenteral antibiotic therapy (OPAT)
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 62 Demonstrate an understanding of the rationale and use of perioperative prophylactic antibiotics to prevent surgical-site infections
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 63 Discuss factors that could influence the prescription of antibiotics (e.g. availability of resources, diagnostic uncertainty, peer practice, patient expectations, and financial interests) and the implications for antibiotic stewardship programmes
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 64 Describe national guidance in respect to the completion of a course of antibiotics
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 65 Describe some of the medicines with which antibiotics can sometimes interact
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree

-
- 66 Describe how switching to oral antibiotics when appropriate can reduce costs, facilitate discharge and prevent complications associated with indwelling catheters and clots
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 67 Establish that source control (incision and drainage) is often the most critical intervention in the management of purulent skin and soft tissue infections, and that antibiotics should be reserved for a patient with a severe disease
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 68 Establish that some antibiotics, such as aminoglycosides and vancomycin, should be dosed according to the patient's weight in order to minimize complications
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 69 Consider drug allergies, vaccination history and severity of illness before starting empiric antibiotic therapy
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

DOMAIN FIVE: PATIENT-CENTRED CARE

COMPETENCY STATEMENT: All qualified medical doctors must seek out, integrate and value as a partner the input and engagement of the patient /carer in designing and implementing care

DESCRIPTORS

To support antibiotic stewardship that is patient-centred, learners need to do the following:

- 70 Support the participation of patients/carers, as integral partners, when planning/delivering their care
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 71 Share information with patients/carers in a respectful manner and in such a way that it is understandable, encourages discussion, and enhances participation in decision-making
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 72 Ensure that appropriate education and support is provided by learners to patients/carers, and others involved with their care or service
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 73 Listen respectfully to the expressed needs of all parties in shaping and delivering care or services
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 74 Discuss the patient's/carer's expectations or demands in respect of antibiotics and the need to use antibiotics appropriately
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 75 Raise public awareness of the problems associated with antibiotic resistance and explain to the patients their role in promoting appropriate antibiotic use
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 76 Acquire communication skills to be able to counsel their patients on appropriate antibiotic use and discourage them from purchasing antibiotics without prescription
☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

DOMAIN SIX: INTERPROFESSIONAL COLLABORATIVE PRACTICE

COMPETENCY STATEMENT: All qualified medical doctors need to understand how different professions collaborate in relation to how they contribute to antibiotic stewardship.

DESCRIPTORS

To support antibiotic stewardship, learners should be able to do the following:

- 77 Demonstrate an understanding of the roles, responsibilities, and competencies of other health professionals involved in policy decisions concerning antibiotic treatment
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 78 Explain why it is important that healthcare professionals, involved in the delivery of antibiotic therapy (including the prescription, delivery and supply), have a common understanding of antibiotic treatment policy decisions, the quantities involved in antibiotic use, and effective patient/client outcomes
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 79 Establish collaborative communication principles and actively listen to other professionals and patients/carers involved in the delivery of antibiotic therapy
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 80 Communicate effectively to ensure a common understanding of care decisions
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 81 Develop trusting relationships with patients/carers and other health/social care professionals
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-
- 82 Effectively use information and communication technology to improve interprofessional patient-centred care
- ☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly Agree
-

Please add if you have any recommendations for competencies that have not been addressed in this section

Appendix V: Modified Delphi questionnaire – Round Two.

Confidential

Page 1

Antibiotic Stewardship - expert panel round 2

My name is Dr Muhammad Augie Bashar, and I am registered for a PhD in Pharmacology at the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. This is one of a series of studies that constitutes my PhD thesis. It involves developing an educational antibiotic stewardship programme that will assist in training medical students in South Africa and Nigeria in terms of the rational prescription of antibiotics. The project is under the supervision of Dr Jacqui Miot, Prof. Patricia McInerney and Prof. Robyn van Zyl.

This aspect of my study is a modified Delphi study. The objectives of the study are to suggest and recommend an international standard that could be applied in medical schools in these two countries. Experts in infectious diseases, medical microbiology, clinical pharmacology, medical education, infectious diseases, nursing and pharmacy across these two countries will be asked to use a Likert Scale to rank the developed antibiotic stewardship competencies.

I would like to thank you for participating in round one of this study despite your busy schedules. The level of consensus in this study is considered as a median score of greater than or equal to 5 and interquartile range of less than or equal to 1.5. All competencies that have not reached an acceptable level on the Likert scale through consensus by the panel of experts in round one will be dropped.

As an expert in one of these fields, and in participating in this study, you would be performing a tremendous service to the practice of medicine.

It may take 20 to 25 minutes to complete the questionnaire. You will be requested to complete the questionnaire within three weeks to enable the study to progress according to schedule.

Please select the option from the following: strongly disagree (1) to strongly agree (5) to each statement as indicated

Thank you for your time and participation!

Your Information

Name:

Title:

Email address

Degree(s)/Qualification(s):

Institute where you currently work

Country:

☐ South Africa ☐ Nigeria ☐ Other

Experience as a tertiary educator (in number of years):

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DOMAIN ONE: INFECTION PREVENTION AND CONTROL

COMPETENCY STATEMENT: All qualified medical doctors must understand the core knowledge underpinning the prevention and control of infection, and use this knowledge appropriately to prevent the spread of infection.

DESCRIPTORS

To support antibiotic stewardship, learners must demonstrate their impressions of the necessary means for the prevention and control of infection by means of the following:

- 1 Describe the principles of pathogenesis of infectious disease based on the pathogenetic triad and damage response framework is fundamental to understanding how to prevent and control infections
☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
- 2 Should be able to provide first aid for exposed cuts/puncture wounds, or the exposure of the eyes, nose or mouth to fluids
☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
- 3 Explain the importance of personal protective equipment and when to use them to prevent infections
☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
- 4 Describe the need for precaution when prescribing antibiotics in populations at risk e.g. children, the elderly, pregnant women and lactating mothers.
☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
- 5 Describe the concept of the basic reproductive number of an infectious pathogen and how it influences spread and control
☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree

-
- 6 Should be able to demonstrate the WHO concept of 'My five moments for hand hygiene'
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 7 Explain the importance of waste segregation
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 8 Explain the importance of screening colonised patients and the principles of decolonisation
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree

DOMAIN TWO: ANTIBIOTICS AND ANTIBIOTIC RESISTANCE

COMPETENCY STATEMENT: All qualified medical doctors need to understand the core knowledge underpinning the concept of resistance to antibiotics and the application of this knowledge to help prevent antibiotic resistance.

Descriptors

To support antibiotic stewardship, learners must be able to do the following:

- 9 Explain mechanisms of antibiotic resistance
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 10 Describe the different ways in which antibiotics may kill bacteria
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree

DOMAIN THREE: THE DIAGNOSIS OF INFECTION AND THE USE OF ANTIBIOTICS

COMPETENCY STATEMENT: All qualified medical doctors need to demonstrate their knowledge of the manner in which infections are diagnosed and the appropriate use of antibiotics, as well as the proper application of this knowledge to support the accurate diagnosis of infections and the appropriate use of antibiotics.

DESCRIPTORS

To support antibiotic stewardship, learners must be able to do the following:

- 11 Should be able to interpret and use MIC provided in AST report clinically in informing dosing decisions and attempts to dose optimize
- ☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
-
- 12 Recognise the symptoms of infections like fever, pain, cough and rashes as a guidance that will trigger empirical antibiotic therapy versus those that could wait for a culture-based antibiotic therapy
- ☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
-
- 13 Explain the challenges associated with culture-sample techniques such as lack of alcohol swab, lack of training, lack of speedy services e.t.c.
- ☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
-
- 14 Explain the importance of prompt submission of swab specimens to the laboratory to preserve the organisms during transportation
- ☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree
-
- 15 Explain the importance of using an appropriate medium to prevent samples from drying
- ☐ Strongly disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly Agree

-
- 16 Explain how to de-escalate to narrow-spectrum antibiotics after initial broad-spectrum antibiotics use
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 17 Describe the importance of bioavailability and non-inferiority of oral versus parenteral formulations when doing some antibiotics
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree

DOMAIN FOUR: THE PRACTICE OF PRESCRIBING ANTIBIOTICS

COMPETENCY STATEMENT: All qualified medical doctors need to be aware of the way in which antibiotics are used in practice in terms of their dosage, timing, duration and the appropriate route of administration. They should be able to apply this knowledge as part of their routine practice.

Descriptors

To support antibiotic stewardship, learners must be able to do the following:

- 18 Explain principles for selection of antibiotics which includes pathogen type (suspected or confirmed)
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 19 Explain pharmacokinetic parameters such as MIC and ability to dose optimize using Pk-Pd principles
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 20 Explain the importance of medical decisions about dosing strategies, interactions and the treatment of patients with specific disease conditions e.g. interaction between clarithromycin and digoxin
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 21 Explain why consideration of Ideal Body Weight and body surface area is important when dosing antibiotics
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree
-
- 22 Explain the need for therapeutic drug level monitoring in antibiotic stewardship programmes, e.g. in patients on vancomycin, linezolid and aminoglycosides therapy
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree

-
- 23 Explain the appropriate channels of reporting adverse drug reactions resulting from antibiotic therapy, e.g. National Adverse Drug Reactions or Hospital Essential Drugs Lists Committees
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree

DOMAIN FIVE: PATIENT-CENTRED CARE

COMPETENCY STATEMENT: All qualified medical doctors must seek out, integrate and value as a partner the input and engagement of the patient /carer in designing and implementing care

DESCRIPTORS

To support antibiotic stewardship that is patient-centred, learners need to do the following:

- 24 Should avoid revealing sensitive information like adverse drug reactions from antibiotic therapy on social media, which can lead to litigation and job loss
- ☐ Strongly disagree
 - ☐ Disagree
 - ☐ Neutral
 - ☐ Agree
 - ☐ Strongly Agree