An evaluation of knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in South Africa

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DECLARATION

I, Mrs Sholene Ballaram, hereby declare that:

- The research reported in this thesis, except where otherwise indicated, is the result of my own investigation and research.
- This thesis has not been submitted in part or full for any degree or examination at any other university.
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LIST OF ACRONYMS

AMR – Antimicrobial Resistance

CDDEP - The Centre for Disease Dynamics, Economics and Policy

DDDs – Defined Daily Doses

EML – Essential medicine List

FISSA – Federation of infectious diseases societies of Southern Africa

GARP-SA – Global Antibiotic Resistance Partnership – South Africa

GDP – Gross domestic product

HIV – Human immunodeficiency virus

HIV/AIDS – Human immunodeficiency virus and acquired immune deficiency syndrome

HPCSA – Health Professionals Council for South Africa

IMS – Intercontinental Marketing Services

LMIC – Low-middle income countries

OTC – Over-the-counter

PHC – Primary Healthcare Centres

SAASP – South African Antibiotic Stewardship

STGs – Standard Treatment Guidelines

SU – Standard Unit

TB – Tuberculosis

USA – United States of America

WHO – World Health Organisation

ABSTRACT

Background: Antibiotic misuse is a global problem that presents a threat to public health. Antibiotic misuse and overuse are responsible for the increase and spread of antibiotic resistance. The community plays a fundamental role in the appropriate antibiotic use and the increase and spread of antibiotic resistance. Hence, public knowledge and attitude regarding antibiotic use are imperative in treatment success.

Method: A quantitative approach was performed using a descriptive cross-sectional design. The data were collected by a self-administered questionnaire completed by patients accessing the pharmacy. The data was analysed using descriptive statistics, namely Microsoft Excel and the Statistical Package for the Social Sciences (SPSS).

Results: From a total of 135 respondents, the majority (n = 108; 80%) of the respondents were aware that different antibiotics were needed to treat different diseases. However, over two-thirds (n = 98; 73%) of the respondents agreed that antibiotics are effective against viruses. More than half of the respondents (n = 82; 61%) considered that antibiotic resistance is a global problem. The vast majority of the sample population (n = 104; 77%) agreed that the pharmacists often tell them how to use their antibiotics during the dispensing process. However, a high number of respondents (n = 97; 72%) agreed that doctors take time to inform them during the consultation on using the antibiotics that s/he prescribed, but this number is lower (n = 104; 77%) when compared to the pharmacists.

Conclusion: The results demonstrate that the community frequently uses antibiotics. These findings indicate misunderstanding related to the antibiotics' role and their cause of the disease (bacterial or viral). The multifaceted educational interventions and patient-healthcare provider communication tools should focus on the specific socio-demographic factors and misconceptions of antibiotics to promote rational antibiotic use. Community-based interventions will help prevent the development of antibiotic resistance, cross-resistance and anticipated future events of treatment failure.

Keywords: knowledge, attitude, behaviour, antibiotic use, antibiotic misuse, antibiotic resistance, self-medication, South Africa.

CHAPTER 1: INTRODUCTION

1.1 Background of Research

The significant challenges faced with the inappropriate use of antimicrobial agents and the consequences of the spread of antimicrobial resistance (AMR) is a soaring global health problem. Antimicrobial resistance arises when viruses, bacteria, parasites, and fungi alter and no longer respond to medicines, making these infections difficult to treat with a drastic increase in disease spread, severe illnesses and death (WHO, 2020).

The misuse and overuse of antimicrobials (antibiotics, antivirals, antifungals and antiparasitic) are critical factors in the development of drug-resistant pathogens (WHO, 2020). When an antibiotic's effectiveness is compromised by antibiotic misuse and overuse on a certain strain of bacteria, those bacteria are known to be antibiotic resistant. Subsequently, infections become more difficult to treat and on the long run, its impact on societies worldwide is immense, resulting in loss of human life and money (Paphitou, 2013).

Among the most commonly purchased medicine worldwide, antibiotics are ranked high (Morgan et al., 2011). The newer antibiotics produced are modifications of existing classes of antibiotics, offering short-term solutions. Despite serving as short-term solutions; they are not readily available in the market, to arrest the decline in the effectiveness of the older options (WHO, 2017).

The global risk report used the United States of America (USA) as a case study in 2013. It cited an estimate of one hundred thousand AMR-related deaths in the USA hospitals alone. The report also cited eighty thousand AMR-related deaths in China's hospitals (Anonymous, 2018). Thereby, placing the potential economic impact at 0.4% to 1.6% of gross domestic profit (GDP) (Anonymous, 2018).

These figures mean that the world is gradually moving towards a stage where antibiotics and other antimicrobial medicines will no longer treat infectious diseases and microorganisms will no longer respond to these medicines (Palan and Hermoso, 2016). The lack of response of microorganisms to antibiotics will result in increased infection rate, increasing morbidity and mortality, and this could cause low-income countries to lose more than five percent of their GDP. Thus, by 2050 about twenty-eight million people universally will be impoverished, and most people involved will be in developing countries (Palan and Hermoso, 2016).

Antibiotic resistance patterns of pathogens to medicines differ from country to country. These differences are related to the various antibiotic uses and practices, various country disease burdens and

first and second-line treatment disparities. In South Africa, another new cofounding issue is the strain created by co-infections such as human immunodeficiency virus (HIV), malaria and tuberculosis (TB) (O'Neill, 2014). In addition, antibiotic resistance is a major public health threat driven by inappropriate prescribing and dispensing patterns (Farley, et al., 2018).

1.2 The Significance of the Research

1.2.1 The magnitude of the Research Problem

The human antibiotic consumption is increasing with an exceptional rise noticed between the years 2000 – 2020 around the world, especially in low-middle income countries (LMICs). Although, the high-income and developed countries still use more antibiotics per capita. It was estimated that eighty percent of all antibiotic consumption within the communities are often without prescriptions, especially in LMICs (Van Boeckel et al., 2014 and Elmasry et al., 2013).

Antibiotic misuse may arise from a complex interaction between numerous determinants namely the doctor's knowledge and experiences, diagnostic uncertainty, perceptions of patients concerning the patient-doctor interaction, and insufficient patient education by the doctor (Awad and Aboud, 2015). Also, the benefits of antibiotics are threatened by other factors such as patient socio-demographic characteristics (age and gender), the patients' knowledge, beliefs and attitudes towards antibiotic use, self-medication, patients' and parents expectations, and patients' experience with antibiotics (Awad and Aboud, 2015).

Antibiotic self-medication remains a universal problem. Antibiotic misuse and overuse are further complicated by the spread of infectious diseases resulting in multi-drug resistant bacteria that limits the drug activity that was previously highly effective and the shortage of novel antibiotics (Elong Ekambi et al., 2019). In Africa, studies revealed a high distress (30-85%) of self-medication that are often due to antibiotic misuse, and patients, doctors and pharmacist bad habits (Elong Ekambi et al., 2019). Also, the self-medication amongst the adult adolescent and adults patients are favoured by over-the-counter (OTC) medications, which, are readily available in the local retail outlets and pharmacy frontshops. Besides, even doctors and pharmacists have incentives to misuse and overuse antibiotics (Llor and Bjerrum, 2014).

The risks associated with antibiotic overuse and antibiotic overprescribing leads to increased AMR, severe diseases with more extended disease period, longer hospital stays, higher medical care costs, increased risk of adverse effects (some life-threatening), increased medicalisation of self-limiting infectious conditions and increased rate of morbidity and mortality (Llor and Bjerrum, 2014). Thus, the

control of antibiotic utilisation in communities requires multifaceted educational interventions by combining knowledgeable and engaged doctors and pharmacists.

In the World Health Organisation (WHO) report on overcoming AMR, three critical issues were identified for public involvement in antibiotic misuse that leads to resistance (McNulty et al., 2007). These were (1) improving access to medical services, (2) reducing unnecessary use of antimicrobial medicines and (3) not sharing antibiotics with other people or keeping part of the course for another occasion.

Antibiotic misuse and overuse are public health issues, and they affect the community at large. Therefore, the public need to play their role and the government ought to provide an enabling environment to make this achievable. Furthermore, there is a need for research that investigates the community's knowledge, attitude and behaviour of antibiotic use, to determine what the community understands about antibiotics and how these are used, to curb the proliferation of antibiotic misuse, overuse and resistance (Awad and Aboud, 2015).

1.2.2 Justification of the Problem

Social factors including patient misconceptions about antibiotics, views on infectious diseases, doctor inappropriate prescribing methods and irrational use of antibiotics, patient demand, self-medication and noncompliance are responsible for the development of antibiotic resistance (Harbath and Samore, 2005).

Most educational campaigns against antibiotic misuse have not been designed as trials that could be easily evaluated for intended action, to assess knowledge, attitude and behaviour. Also, understanding how changing these factors influence antibiotic use can assist in reducing antibiotic resistance. However, in countries like France and Belgium, a reduction was noted in resistance to macrolide and penicillin following a reduction in their use following educational campaigns (Sabuncu et al., 2009 and Goosens et al., 2005). Subsequent campaigns should be the basis of good education and understanding of which, interventions and approaches are most effective in rational antibiotic use.

The study in Lithuania showed that the demographic characteristics associated with the patient knowledge of antibiotics comprised of gender, age, education level, family income and place of residence and other factors such as the lack of advice regarding rational antibiotic use, given by the doctor and pharmacist are directly or indirectly involved in influencing the patient's attitude towards the antibiotic usage (Pavyde et al., 2015). Therefore, it is imperative to determine the community's

understanding regarding their knowledge on the role of antibiotics and its use. Also, to educate them on bacteria versus virus aspects, side effects of antibiotics, antibiotic resistance and rational antibiotic use.

1.3 Global, African and South African Burden

1.3.1 The Burden of Antibiotic Misuse

It is imperative to emphasise that studies have shown, over time, twenty to fifty percent of the total consumption of antibiotics to be inappropriately used (Cizman, 2003). "Inappropriate" can mean either:

- The suboptimal antibiotic use for responsive conditions which, can include: an incorrect dosage or duration, the choice of medicines with an unnecessarily broad-spectrum, or poor patient adherence to the prescribed treatment (Cizman, 2003).
- The antibiotic use when no health benefit is possible, such as to treat infections caused by viruses such as upper respiratory tract infections (Starrels et al., 2009).

Also, antibiotic misuse results from substandard use, either when used when it is not needed or in lower quality than what is required.

When antibiotics are necessary for treating an infective process, and they are not used, this is classified as inappropriate use. As a result, rather than improving health, morbidity and mortality can be increased, for example in 2013, when pneumonia was responsible for an estimated 935,000 deaths in children under five years old worldwide which, could have resulted from delayed or lack of access to antibiotics (Liu et al., 2015).

A higher prevalence of self-medication with antibiotics was reported in South Europe (19%) compared with northern Europe (3%) and central Europe (6%). In some countries in Africa, 100% of antimicrobial use is without a prescription, and in Asia, it reaches 58% (Morgan et al., 2011). Hence, an increase in self-medication and a low rate of primary and private healthcare utilisation may result from low diagnostic ability compounded by limited knowledge of appropriate management.

This current practice cuts across the following attributes: culture, gender, health and social status, race, occupation or any other socio-medical or demographic factors (Afolabi, 2008). Many people still resort to this practice instead of contacting healthcare professionals which, may be due to long waiting periods in hospitals and healthcare facilities, minor ailments, high medical costs, lack of availability and accessibility and shortage of doctors and pharmacists (Afolabi, 2008).

The Jordanian study in 2012, concluded that the respondents need to be educated on how to take antibiotics prescribed and the storage of all medications including antibiotics in a designated medicine cabinet (Shehadeh et al., 2012). It was observed that education plays a pivotal role in this emerging crisis since several researchers had confirmed that low-level knowledge of the public on antibiotic usage had been the primary challenge in stopping the misuse of antibiotics (Awad and Aboud, 2015; Pereko et al., 2015 and Shehadeh et al., 2012).

The lack of education on antibiotic misuse has been presented in studies conducted on proper use and treatment of antibiotics for common respiratory tract infections (Emeka et al., 2014; Shehadeh et al., 2012 and Elmasry et al., 2013). The findings of these studies had reported inappropriate antibiotic use and non-adherence to directives given for antibiotics which, are strongly associated with public awareness and knowledge of antibiotics (Pavyde et al., 2015).

Furthermore, AMR has been further promoted by individual acts by patients, themselves especially in cases where signs and symptoms of infections begin to subside. In other patients, after an initial favourable therapeutic response witnessed by them, they miss doses either by mistake or deliberately (Pavyde et al., 2015).

Finally, patients end up presenting at healthcare facilities when an infection has taken place with infecting organisms that are more virulent and carrying resistant strains (Ayukekbong et al., 2017). Various factors contribute to AMR, in South Africa; for instance, the most significant contributing factors include inadequate diagnostic coverage, medicine stock-outs and patient adherence challenges (Albert, H., 2018).

The problem of inappropriate use of antibiotics is undoubtedly complex and multifactorial. The way to solve this problem is for developing countries and developed countries to have a proper understanding of the problem for effective control (Pereko et al., 2015). The appropriate use of antibiotics is essential, to ensure treatment efficacy as well as to prevent resistance (Awad and Aboud, 2015). The development of AMR is a threat to the collective existence of all because as this progresses, the standard treatment of infections is becoming ineffective, complicating patient management and increasing patient morbidity and mortality (Harbath et al., 2015).

A way to manage this crisis is for countries around the world, most especially developing countries, to ensure that medicines are not just given to patients solely on signs and symptoms. Instead, specific individual prescriptions should be prepared based on the findings from microbial sensitivity and culture tests. Another attribute that must be addressed is the act of patient not completing treatment duration

which, may result in resistance, therefore, more should be done to educate them on the harm this poses to antibiotic effectiveness (Chaudhary, 2016).

Furthermore, if antibiotic misuse is to be discouraged, a more holistic approach which, is patient-centred will guarantee this possibility (McNulty et al., 2007). Patient-centred care can be accomplished by shared decision-making, in conjunction with educational initiatives that may assist in changing attitudes and behaviours and improving access to and completion of appropriate antibiotic therapy. Thus, the community's engagement is of utmost importance in the control of antimicrobial resistance. Also, antibiotic prescribing and resistance need to move beyond the traditional assumptions about patients' demand for antibiotics, the key driver of antibiotic prescribing and resistance (André et al., 2010).

1.3.2 Campaigns to Reduce Inappropriate Antibiotic Use

Educational campaigns are needed to reduce inappropriate use of antibiotics, and this can be done by increasing awareness among patients and healthcare professionals. There is a need for campaigns both at regional and national levels about antibiotic resistance which, results from antibiotic misuse. This will create awareness, change behaviour, improve knowledge and reduce inappropriate prescriptions.

Examples of achievements from the campaign include an awareness campaign called "Antibiotics are not automatic" carried out in France, in 2001. This campaign resulted in a reduction of at least twenty-seven percent in the inappropriate prescription of antibiotics over five years with the most significant decline, thirty-six percent, in children 6 to 15 years of age (Sabuncu et al., 2009).

In 2000, a campaign was done by the Belgian Antibiotics Policy Coordination Committee on reducing antibiotics prescription, which, the success rate was by thirty-six percent over seven years (Goosens et al., 2005). Most high-income countries have focused their antibiotic awareness campaign on reducing antibiotic use related to the treatment of respiratory tract infections (Huttner et al., 2010). These campaigns were done using a multidisciplinary approach by targeting the general public, parents of young children and health authorities.

There was a need to filter awareness indicators as part of an action plan implementation on AMR control. Therefore, future antibiotic awareness campaigns are crucial for providing foundational messages to the public that is more meticulous on scientific evidence, contextual specialities, available in accurate and locally adapted communication and based on current attitudinal and behavioural changes (Huttner et al., 2010). Furthermore, this would encourage narrow-spectrum antibiotic use as the first choice thereby, preserving the broad-spectrum antibiotic classes (Huttner et al., 2010).

The public's knowledge, attitude and behaviour play an essential role in the success of the treatment process and therefore, it is crucial to determine what the community understands about antibiotics and how they use them (Awad and Aboud, 2015). By understanding the magnitude of the issue regarding the antibiotic misuse and the population groups most affected, one can help tailor the efforts to improve the community's knowledge and change their attitudes and behaviour towards rational antibiotic usage which, is the aim of this study (Awad and Aboud, 2015).

1.3.3 Antibiotics in the Community

Community pharmacy, also known as a retail pharmacy, is the most popular type of pharmacy that allows the public access to their medication (self-medication, acute and chronic prescription medication) and advice about their health. In South Africa, community pharmacies have been providing some primary health care services to clients who could afford to pay for them (Malangu, N., 2014). The community pharmacy used in this study is a small, independently owned franchised pharmacy, situated within a relative small but busy shopping mall.

Antibiotics are usually prescribed by means of a prescription that involves an individual consultation between a patient and a prescriber or clinician (Farley et al., 2018). Thus, individual prescriber prescribing behaviour is crucial whereby the prescriber's knowledge and beliefs influence this process. In addition, the perceived patient expectations also influence decision-making at the clinical consultations.

Findings have shown that an eighty percent of all antibiotic use occurs outside the hospital through health posts, clinics and by private physicians at their offices (Kotwani and Holloway, 2011). When antibiotics are used, purchased by or for consumers either directly or indirectly without a clearly written out prescription, this was captured under community use of antibiotics. However, in some high income and LMIC laws and regulations against irrational use of antibiotics exist, and this is known as prescription-only laws even if for only a few antibiotics (Morgan et al., 2011).

Antibiotic use has been noted even in the treatment of infections such as malaria (Means et al., 2014), uncomplicated viral respiratory tract infections (Kotwani et al., 2012), and other viral infections, acute diarrhoea (Kotwani et al., 2012) and influenza (Misurski et al., 2011), not caused by bacteria due to inadequate knowledge about antibiotics and its functions. Often, these all happen and persist due to lack of clinical training, appropriate rules and regulation, clearly stated guidelines on the use of antibiotics in treating infections available to doctors.

Also, an infrastructure issue resulting in antibiotic misuse is the lack of a laboratory, or diagnostic inadequacies in identifying the cause, and susceptibility of infection (Sudarshan et al., 2013). Hence, the older antibiotics are overpassed in favour of the newer generation antibiotics (Kotwani and Holloway, 2011).

Another notable factor determines the generation of antibiotics being used, is patient-specific drug demand. However, there is limited information available about the generations of antibiotics extracted from procurement data, reported antibiotic-resistant infections and the knowledge, perceptions and practices of antibiotic access and use in South Africa, particularly in rural populations (Anstey Watkins et al., 2019).

The knowledge and behavioural patterns related to the burden of antimicrobial resistance in South Africa is inadequate and restricted because of the scarce surveillance data (Yewale, V. N., 2014). A knowledge gap exists on community-based intervention strategies regarding people driven factors that influence antibiotic use and misuse. This further contributes to the growth of antimicrobial resistance. Therefore, the purpose of this study was to assess the knowledge, attitude and behaviour of the people concerning antibiotic use and misuse in South Africa.

1.4 Research Aim

To assess the knowledge, attitude and behaviour of antibiotics use and misuse amongst the general population living in KwaZulu-Natal.

1.5 Research Objectives

- To assess the knowledge, attitude and behaviour amongst retail pharmacy patients towards antibiotic use and misuse.
- To determine what factors, influence antibiotic usage.
- To recommend possible interventions for community pharmacists about antibiotic stewardship for patients.

1.6 Research Questions

- What does the general population understand about antibiotics and their use?
- What factors have an impact on antibiotic use among retail patients?

1.7 The Layout of the Thesis

The dissertation structure is as follows.

Chapter 2: Literature Review

Chapter 3: Submitted Manuscript

Chapter 4: Synthesis

1.8 Chapter Summary

This chapter highlighted the background information, including the study rationale and significance as well as the concerns related to antibiotic misuse and resistance. To provide a foundation for the study, this chapter also described the study aim, objectives, research questions and some strategies to reduce antibiotic misuse.

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CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

2.1.1 Understanding Antibiotics

Antibiotics are powerful medicines used to prevent and treat bacterial infections. An antibiotic is a substance that can eradicate (bactericidal) or inhibit (bacteriostatic) the growth of bacteria (Drexler, M., 2010). Antibiotics do not fight viral infections such as the common colds and flu (Drexler, M., 2010).

In the 1900s, infectious diseases were the leading cause of death worldwide. The discovery of antibiotics was a turning point for human history and has revolutionised medicine in the 20th century. In 1928, Alexander Fleming discovered the first natural product antibiotic, penicillin (Davies, J. and Davies, D., 2010). Following the introduction of penicillin in 1940s, penicillin was used systemically as an antibiotic. During the 20th century, there was an increase in new antibiotic substances for medical use, with new classes of antibiotics launched by pharmaceutical companies. Irrespective of the many benefits of antibiotics, they have also shown harmful effects on human healthy body microbial flora (Russell, 2004).

The global antibiotic use in humans showed an increase by 65% from 21.1 billion defined daily doses (DDDs) in 2000 to 34.8 billion DDDs, in 2015. Also, the rate of antibiotic consumption increased during this period, from 11.3 DDDs per 1,000 inhabitants per day, to 15.7 DDDs per 1,000 inhabitants per day hence, an increase of 39%. The increase in antibiotic consumption was found to be driven by low- and middle-income countries (LMICs), where consumption increased by 114% between 2000 (11.4 billion DDDs) and 2015 (24.5 billion DDDs) (Klein et al., 2018).

The antibiotic consumption rate increased by 77% from 7.6 billion to 13.5 billion DDDs per 1,000 inhabitants per day . Although, the overall antibiotic consumption in high-income countries increased by 6%, from 9.7 billion to 10.3 billion DDDs, the number of DDDs per 1,000 inhabitants per day fell by 4%, from 26.8 to 25.7 billion DDDs. In 2015, the leading high-income country consumers of antibiotics were the United States, France and Italy, while the leading Low-middle income countries (LMIC) consumers were India, China and Pakistan (Klein et al., 2018). However, there is a paucity of consumption data for African countries such as South Africa (Schellack et al., 2017).

It is imperative to understand the various mechanism of actions of these medicines, to ensure that antibiotic misuse does not promote the associated adverse effect of usage. Also, to safeguard antibiotics,

it is essential for proper characterisation and precise understanding of when to use any of the classes of antibiotics, to prevent resistance (Russell, 2004).

The following section will review the classification, mechanism of action, significance, use and misuse of antibiotics.

2.1.2 Classification of Antibiotics and Mechanism of Action

The conventional method of classifying antibiotics seem to be through their molecular structure, the spectrum of activity and mode of action (Calderon and Sabundayo, 2007). Antibiotics are being produced either wholly or partly through synthetic processes. Antibiotics function by killing microorganisms (bactericidal) or by inhibiting the growth or multiplication of microorganisms (bacteriostatic) (Walsh, 2003). At the same time, the body's immune system destroys them (Walsh, 2003).

Several studies indicate that antibiotics have the similar or same structure, whereas the mode of action specifies very close similarity or pattern of effectiveness (Madigan and Martinko, 2006 and Wright, 2010). These characteristics extend to their toxicity and identifiable side effects. Antibiotics act principally by directed action towards bacteria structures or bacterial metabolic processes. The identified mode of action includes (Talaro and Chess, 2008; Madigan and Martinko, 2006 and Wright, 2010):

- Inhibition of cell wall synthesis
- Blockage of vital metabolic pathways
- Inhibition of the structure and function of nucleic acids
- Inhibition of protein synthesis
- Breakdown of cell membrane structure or function

Surprisingly, over 2,000 antibiotics have been discovered so far. However, only a few are in therapeutic use currently. The newer antibiotics have indispensable help in fighting infectious diseases. However, the ongoing antibiotic resistance resulting from antibiotic misuse, if not adequately addressed, will render the newer and older antibiotics ineffective (Schlegel, 2003). Hence, the need to understand the precautionary measures of antibiotic use and the prevention of further misuse through proper characterisation, appropriate behaviour and adequate knowledge on the mode of action of antibiotics.

2.2 Antibiotic Misuse

For as long as they have existed, antibiotics have played a significant role in controlling infectious diseases. However, their increasing widespread misuse and overuse have resulted in the development of resistant microorganisms which, consecutively threatens its efficiency, resulting in more prolonged and severe disease episodes (O' Sullivan et al., 2016 and Spurling et al., 2017). Thereby, causing infectious diseases in the community and hospital settings, increased morbidity, mortality and higher healthcare costs (Laxminarayan et al., 2013 and Avent et al., 2016).

Various studies around Europe revealed that over forty percent of antibiotics were inappropriately used, by self-medication and the unnecessary use of antibiotics (Hawker et al., 2014). The antibiotic dispensing without a prescription is a major contributing factor to its irrational use, leading to the development of AMR (Livermore, 2011). The non-prescription use of antibiotics has been associated with shorter courses, suboptimal medicine and its dose choices (Apisarnthanarak et al., 2008).

In the 1980s, in Cameroon, Africa, particularly in the South West region, antibiotic use and misuse were reported by Sjaak Van der Geest (Ngu et al., 2018). He associated the inappropriate use of antibiotics to the ineptitude of the healthcare facilities run by the state. At that time, it was believed by Cameroonians to be under-staffed because of the "frequent absences of healthcare workers", "characterised by bureaucratisation and poor management" as well as recurrent medication shortage (Ngu et al., 2018).

In 1995, a World Bank report noted that Cameroonians choose to first self-medicate instead of going directly to the formal sector when ill, as per the practice before 1987 (Ngu et al., 2018). The other options included visiting the "quack doctor", street vendor, or one of the many faith or traditional healers and only when very ill would the people visit the hospital (Ngu et al., 2018). Thus, each of these factors has exacerbated inappropriate antibiotic use in Cameroon (Ngu et al., 2018).

Antibiotic misuse might be due to the inadequate knowledge of prescribers and users, the demand of the patients, weak spreading awareness among patients through doctors and negative attitude and practice pattern (Shaikh, 2017 and Sharma et al., 2017). The utilisation of antibiotic control methods is essential factors that involve interactions between healthcare professionals (community doctors and pharmacists) and antibiotic misuse prevention strategies (Roca et al., 2015 and Llor and Bjerrum, 2014).

2.3 Current Knowledge about Antibiotics: Global, African and South African Perspectives

The rapid development of antibiotic resistance is a critical concern in the medical world. The global action plan for antimicrobial resistance aims for the rational use of antimicrobial medicines including antibiotics. Despite the challenges faced, the knowledge on antimicrobial utilization is essential for future research interventions, to provide an understanding of the various measures of antibiotic use and misuse as well as the degree of antibiotic resistance.

In Northern India, a total of 1273 (92.8%) participants admitted to having used an antibiotic at any time in their lifetime, and 78.6% acknowledged their awareness of the rational use of antibiotics (Jain et al., 2016). However, a large portion (68.6%) of respondents were in perspective that antibiotics are effective against both bacterial and viral infections (Jain et al., 2016).

However, another study in Kadapa, India claimed that a more considerable amount of participants (65.55%) stated that antibiotics might be stopped once they feel better after a few doses or when the symptoms of their infections appear to have subsided or stopped (Chandrakanth et al., 2016). Also, in Malaysia, two-thirds of the participants believed that antibiotics could be stopped when symptoms improved, although, the course of antibiotic was not completed as prescribed by the doctor (Lim and Teh, 2012).

The misconception that antibiotics should be stopped when symptoms improved, places these patients at significant risk of infection relapse, the colonisation with antibiotic-resistant organisms and complicated disease outcomes (Liu et al., 2001 and Carey and Cryan, 2003). Thereby, creating sub-inhibitory concentrations of the antibiotic in the body that occurs from incomplete dosage regimen that may result in the evolution of resistance by the pathogen, causing the infection (Sarkar and Gould, 2006).

A high percentage (54%) of Omani study participants claimed to be oblivious of the indications for antibiotic use. The majority (39%) assumed that antibiotics are used for all illnesses including the common colds and cough which, resulted in quick recovery and prevented severe upper respiratory illnesses (Jose et al., 2013). Hence, substandard knowledge about antibiotic use promotes misuse.

A Saudi Arabian study documented that most participants bought antibiotics without prescriptions in addition to their insufficient knowledge regarding the uses, side effects, antibiotic drug interaction, allergy to specific antibiotics and uses of broad-spectrum antibiotics (El Zowalaty et al., 2016). Also, another Saudi Arabian study reported a high level of antibiotic usage per year and the reduced

knowledge (59.6%), which, in turn, resulted in a negative attitude, poor practice pattern and changing the family doctor for not prescribing antibiotics (Awadh et al., 2017).

In a Jordanian study, the confusion around antibiotic effectiveness against bacteria or viruses was raised whereby 70.4% of medical students and 29.9% of non-medical students ($p < 0001$) knew that antibiotics were indicated to treat bacterial infections (Ghadeer et al., 2012). Almost seventy percent (67.2%, CI 70.4 to 64.0%) of non-medical students agreed that antibiotics might be used to treat viral infections and 62.8% believed that they could be used for the common cold (Ghadeer et al., 2012).

These results in Jordan were consistent with a systemic Iranian study carried out using a larger sample size (Jafari et al., 2015). The majority of the study participants (87% compared with 95.8%) perceived that antibiotic resistance is a significant global problem and as a result of patient non-adherence (96% compared with 87.4%) and excessive antibiotic use (99% compared with 97.1%) (Jafari et al., 2015).

However, in Italy, 62% of the study participants believed in utilising antibiotics until the disease symptoms were cured. About half (52.3%) of the participants believed antibiotics are not safe to use, and 52.8% thought that these antibiotics could have possible adverse effects that lead to antibiotic resistance and the adverse effects of antibiotics (Prestinaci et al., 2015).

The study conducted in Cameroon, West central region of Africa showed poor knowledge regarding the role of antibiotics. A total of of the participants were unaware that antibiotics are effective against all microorganisms and 43.7% believed that these medicines induce bacteria death only (Elong Ekambi et al., 2019).

However, only 11.8% of the study participants accounted for the statement that antibiotics could be used in the treatment of viral infections (Elong Ekambi et al., 2019). Just about half (58%) of the participants were able to name one side effect, but, they stated that antibiotics could cause adverse effects (Elong Ekambi et al., 2019). Thus, insufficient knowledge regarding antibiotic use and its effects could perhaps explain their inappropriate use related to self-medication.

A South African study looking at primary care prescribers' knowledge, attitude and perceptions of antibiotic resistance found a lower score (45%) on the knowledge aspects compared to the private practice participants (60%) (Farley et al., 2019). The public sector participants (10%) scored the lowest regarding the closed-ended question; antibiotics are used to treat viruses (Farley et al., 2019). On the other hand, the private practice participants (14% and 28% respectively) accounted for the lowest score related to antibiotic resistance and whether or not the flu was caused by bacteria (Farley et al., 2019). Hence, the prescribers of the private sector in South Africa were aware of the problem concerning

antibiotic misuse and resistance but they felt the pressure from the patients to prescribe antibiotics (Farley et al., 2019).

Thus, there is ample room for improvement on public knowledge regarding appropriate antibiotic use globally. There is a need for the proper and regular lectures, seminars and community meetings for the development of awareness and the growth of knowledge in the community on the rational antibiotic use. This might further assist in defending the menace of the rapid development of antibiotic resistance (Jain et al., 2016).

2.4 Current Attitude and Behaviour Towards Antibiotics: Globally, the African and South African Perspectives

The inappropriate use of antibiotics is additionally associated with other common behaviour patterns, such as failure to complete the recommended treatment or self-medication. Self-medication with antibiotics almost always involves avoidable, inadequate and ill-timed dosing, creating the best environment for microbes to adapt rather than be eradicated. Besides, noncompliance occurs when the patients forget to take their medication, prematurely discontinue the antibiotic as they start to feel better or worse or due to side effects or cannot afford a full course of therapy (Prestinaci et al., 2015).

The Kadapa district in India reported that 76.6% of the participants had administered antibiotics without a doctor's prescription, which, includes 47% of graduates have taken antibiotics as self-medication (Chandrakanth et al., 2016). A total of 79.4% of the study participants kept leftover antibiotics for personal future use, more especially for respiratory-related illnesses (34%) and just over half (55%) of the participants modified their prescription by themselves or by the pharmacists without consulting the doctor (Chandrakanth et al., 2016).

A high percentage (44%) of the participants used antibiotics upon their friends and family member's suggestions, and 31% of the participants share their antibiotics with family members when they are sick (Chandrakanth et al., 2016). These malpractices should be avoided to hinder the spread and emergence of antibiotic resistance. Antibiotic misuse was prominent in Kadapa, India, whereby regardless of their age and educational level, there was no real effect in discouraging antibiotic misuse (Chandrakanth et al., 2016). However, the significant finding regarding the attitude, revealed that most study participants (76.8%) would check the expiry date of their antibiotics before administration (Chandrakanth et al., 2016).

A similar study in Northern India reported that just over half (53.9%) of participants used antibiotics occasionally (Jain et al., 2016). Also, 11.3% used antibiotics most of the times at the slightest illness,

and the most common source of information available to the participants (63.2%) regarding antibiotics and their usage, was in the form of the doctor's prescription or verbal advice (Jain et al., 2016).

Inadequate knowledge and malpractice pattern regarding antibiotic use were reported by the majority in Saudi (Bin et al., 2011). The supercilious attitude of the adult participants (77.6%) was that they could buy antibiotics without a prescription. Also, a high incidence of antibiotic misuse was found among 38.7% of paediatric and 57.8% of an adult in the emergency department at the King Abdullah international medical research centre, Saudi Arabia (Alanazi et al., 2015). Besides, some other study showed that antibiotic misuse was associated with a high rate of infections in a community hospital in Saudi Arabia (Al-Ghamdi et al., 2002).

In Jordan, 65.2% of study participants who have been prescribed an antibiotic in the past year, did not complete their treatment course (Ghadeer et al., 2012). Ironically, 84.6% of those participants agreed that an antibiotic regimen should always be completed. Also, in this study, they observed the inconsistency in antibiotics use, self-medication, purchasing antibiotics without consulting a doctor and the patients requested to be prescribed antibiotics over the phone at various instances which, did not comply with excellent patient care (Ghadeer et al., 2012).

However, if patients are not physically examined, this will deprive the doctors of valuable diagnostic clues and sound evaluation of the patients' conditions. Therefore, educational awareness campaigns should target the need for changing prescribing practices, correcting patients' expectations on antibiotic use and resistance issues (Ghadeer et al., 2012).

A higher prevalence of self-medication with antibiotics was reported in South Europe (19%) compared with northern Europe (3%) and central Europe (6%) (Grigoryan et al., 2006). An Australian based study noted that prescribers of antibiotics were pressurised by patients demand for antibiotics (37.0%), all in an effort of making patients happy and maintaining doctor-patient relationships (Martin-Perez et al., 2015). Also, some countries of Africa, 100% of antimicrobial use is without a prescription, and in Asia, it reaches 58% (Morgan et al., 2011).

In South Africa, large populations are living in poverty and are at high risk of infectious diseases. Also, their medical expenses, days lost from work and transportation costs may account for a substantial economic loss (Awad and Aboud, 2015). Also, poverty interferes with patient compliance on how antibiotics prescribed are to be used, which, aids in the emergence of antibiotic resistance during short-term therapy of acute infections and long-term treatment of chronic diseases (Laxminarayan et al., 2006). Most patients cannot afford to repurchase antibiotics when it is finished; therefore, they either

skip doses during acute infections or do not purchase antibiotics at all during chronic infection thereby, promoting the development of antimicrobial resistance (Awad and Aboud, 2015).

The majority (97.1%) of primary antibiotic prescribers believe that South Africans overuse antibiotics, leading to antibiotic resistance (Farley et al., 2018). A significant portion (95.8%) believe this possesses a great problem exclusively when the prescription of antibiotics is done under patients' pressure (Farley et al., 2018). However, several other factors can contribute to the irrational antibiotic use such as socioeconomic status of the community, residential background and instructions given by the doctor while prescribing the antibiotics (Fernandes et al., 2014).

Besides, it was concluded that there were low levels of confidence regarding antibiotic prescribing among final-year medical students in South Africa (Wasserman et al., 2017). Researchers revealed that most students prefer acquiring further education related to antibiotic resistance and prescribing (Wasserman et al., 2017). Hence, if the awareness of medical students on antibiotic prescribing is inadequate, there seems to be no compelling reason to argue on the limited knowledge of the public on antibiotic usage.

Hence, the majority of antibiotics prescription completed were closely associated with attempting to meet patients' expectations in South Africa (Panda et al., 2016). There is a need to reduce or eliminate these scenarios; however, from an economic point of view, South Africa lacks the financial strength to do so whereby the private sector focuses on a high turnover of patients and not the quality of medical care, to achieve increased revenue. Therefore, more needs to be fulfilled in educating patients and doctors on the need to curb this fast-spreading menace, so that the lesser are the chances of self-medication and inadvertent antibiotic usage, to prevent the ongoing antibiotic resistance crisis (Panda et al., 2016).

2.5 Doctors, Retail Pharmacists and Patients

2.5.1 Doctors, Retail Pharmacists, Antibiotic Use and Misuse

In the developing and developed countries worldwide including South Africa, the free accessibility and availability of antibiotics has been promoted by the inadequate regulation of the unethical distribution and sale of antibiotics (Franco et al., 2009, Davey et al., 2002 and Anstey Watkins et al., 2019). Besides, patients irrationally use antibiotics without prior seeking of medical care and advise in these countries. Also, another compounding concern is the medical consultation and dispensing relatively expensive fees (Jafari et al., 2015; Garofalo et al., 2015 and Shah et al., 2014). These challenges further propagate antibiotic misuse.

The Americans suggests that doctors should always ensure an accurate diagnosis before the issue of a prescription, after determining the need for and the timing of the antibiotic therapy, understanding how dosing affects the antimicrobial activities of different agents, tailoring treatment to host characteristics and adopting a good habit to use the narrowest spectrum and shortest duration of therapy (Leekha et al., 2011).

The informal sector includes the retail pharmacists, street vendors and many more who have been implicated in dispensing antibiotics to patients without a written prescription. This inappropriate antibiotic use accounts for over fifty percent of antibiotics purchased on a private basis in America (Dellit et al., 2007 and Michael et al., 2014).

In Peru, the insufficient knowledge of local resistance rates and profiles lead to inappropriate prescribing and patient or parent demands for antibiotics, which further complicated the problem (Tangcharoensathien et al., 2018). Whereas, the study across seventeen European countries showed that an increase of 1% in the doctor to population density was associated with a rise of 0.52% to 0.86% in the outpatient antibiotic use and that a fee-for-service incentivises much higher usage than the capitation payment method (Holmes et al., 2016).

In South Asian countries, the most common challenges on the supply side in the retail pharmacy sector are the inferior quality dispensing patterns, particularly by unqualified healthcare providers, inadequate labelling and patient counselling (Ahmed et al., 2009). Some of the other difficulties include poor patient-centred care, insufficient clinical history taking and sale of antibiotics that have no proper dosage or are clinically inappropriate. The conventional sources of inadequate counselling are attributable to unqualified drug sellers, patients using old prescriptions and word of mouth from family members and friends (Miller and Goodman, 2016).

The overprescribing and bulk dispensing of antibiotics are associated with a heightened risk of adverse effects, which are propagated by the private doctors and the retail pharmacy sector (Llor and Bjerrum, 2014). To validate these claims, it was concluded that antibiotic misuse is due to limited access to healthcare facilities, inadequate understanding and insufficient knowledge of appropriate antibiotic practices as well as the socioeconomic status of the people (Barker et al., 2017). Hence, for these acts to be curtailed, interventions are necessary.

Besides, these interventions should be precisely drafted to address these concerns and should span across various age groups, educational status, common health problems and people's jobs. These

difficulties can only result in improvement if healthcare services focus on reducing inappropriate antibiotic use (Gebeyehu et al., 2015).

2.5.2 Patient Factors Influencing Antibiotic use and misuse

The leading patient factors associated with antibiotic misuse or overuse consist of psychosocial factors such as behaviours, beliefs and attitudes with regards to self-medication and OTC medication; patient, parents' and guardians' pressure, often documented by doctors and pharmacists; and demographic characteristics namely age, gender, socioeconomic status, education levels and lack of health education (Alumran et al., 2011).

Self-medication is habitually practised worldwide, particularly in developing countries inclusive of South Africa. It is considered an alternative for people who cannot afford the high cost of healthcare services and those that lack access to the healthcare facilities (Chipwaza et al., 2014 and Awad and Aboud, 2015). Hence, antibiotic self-medication can be defined as the use of antibiotics to treat self-recognised disorders or symptoms as well as intermittent or continued use of prescribed antibiotics for chronic or recurrent diseases or symptoms without the doctor's advice (Bennadi, D., 2013).

The determinants of antibiotic self-medication comprise of unregulated importation and sale of OTC antibiotics, the high cost of medical consultation, low satisfaction with the doctors and misunderstanding and misconceptions regarding the efficacy of the antibiotics (Radyowijati and Haak, 2003). The primary risk factor associated with self-medication is the availability of antibiotics at home that encourages use (Grigoryan et al., 2006).

Also, an important association was revealed in a Jordanian study between self-medication, using leftover antibiotics and education level (Shehadeh et al., 2012). Those with a lower education level and those that lacked education were more likely to have incorrect knowledge on leftover antibiotics and its use hence, an increase in antibiotic misuse (Pan et al., 2016). Besides, cultural beliefs and a lack of health insurance or medical aid are other possible determinants of self-medication (Grigoryan et al., 2008).

The majority prefer to receive initial treatment for febrile illnesses at their home using oral antipyretics, herbal medicines and antimalarials or antibiotics purchased at the local shops without a prescription (Chipwaza et al., 2014). These are generally substandard or falsified medications, especially in the case of LMICs, where antimicrobial stewardship is poor (WHO, 1998 cited in Rodrigues, 2019).

The everyday inappropriate antibiotic use without medical guidance by households includes taking insufficient dosages, not completing the antibiotic course, sharing antibiotics and taking antibiotics unnecessarily or for the wrong indications such as viral infection and inflammation (Ocan et al., 2015). Many antibiotics are most commonly misused to treat flu or common cold symptoms (Ocan et al., 2015) due to lack of clinical evaluation of the disease condition, by a healthcare provider.

Thus, misdiagnosis and incorrect choice of antibiotics, delays in seeking the most appropriate treatment, use of excessive or substandard medicines and prolonged duration of use, drug interactions and polypharmacy may occur (Ruiz, 2010). These risks play a pervasive role in the development and increased spread of antibiotic-resistant microbes (Grigoryan et al., 2006). Thus, self-medication is a significant contributing factor to the inappropriate use of antibiotics in patients.

When an antibiotic is being used for a viral infection by self-medication practice, the antibiotic attacks the bacteria in the body (Pavyde et al., 2015). This misdirected treatment approach promotes antibiotic resistant properties in safe bacteria that can be shared with other bacteria, or create a probability for potentially harmful bacteria, to replace the harmless ones. Also, stopping an antibiotic before finishing the course is problematic as a full treatment course is necessary to kill the disease-causing bacteria may result in the need to resume treatment later and promote the spread of antibiotic-resistant properties among harmful bacteria.

Hence, it is important for patients to understand antibiotic use and misuse as they are the key factors that contribute to antibiotic resistance (Awad and Aboud, 2015). The general public, prescribers and healthcare facilities all play a vital role in ensuring the proper use of all antibiotics and in minimising the development of antibiotic resistance.

Transport and associated costs influence the patients ability to access healthcare facilities in South Africa in which case antibiotic access and availability was limited (Anstey Watkins, et al., 2019). In South Africa, structural barriers such as sociocultural and behavioural factors exists, apart from the accessibility, availability and affordability to antibiotics (Anstey Watkins, et al., 2019). Also, vulnerable healthcare systems, poor quality control and unreliable supply chain management hinder antibiotic procurement and distribution to patients in need (Anstey Watkins, et al., 2019). Poor drug discovery due to insufficient government funding on research and development, strain leads to irrational selection and use of antibiotics.

Besides, patients acquire knowledge about antibiotics from previous prescriptions; therefore, doctors must limit superfluous antibiotic prescriptions and follow standard treatment guideline practices (Llor

and Bjerrum, 2014). Also, pharmacists should educate the patients upon dispensing antibiotics on their rational use and stop non-prescription antibiotic sales (Kotwani et al., 2010). Hence, improved knowledge, understanding and practices about antibiotic self-medication may result in the rational use of antibiotics and insubstantial antibiotic resistance concerns.

2.6 South Africa and Antibiotic Misuse

The heightened burden of communicable and noncommunicable diseases generates extensive antibiotic misuse and overuse and subsequently escalating antibiotic resistance with substantial healthcare, financial and social implications, in many countries worldwide, not to mention Africa (Llor and Bjerrum, 2014). It is further exacerbated by the limited access to antibiotic availability and affordability required to treat these diseases (Gelband and Duse, 2011).

South Africa has a comparably functional healthcare system with public surveillance systems frequently producing representative and robust data on antibiotic use in tertiary care but not in primary care, which serves the majority of the South African citizens (Essack et al., 2017). However, the full impact of antibiotic resistance on healthcare in South Africa is not known. Moreover, there is a paucity of consumption data worldwide which, has been incredibly challenging (O'Neill, 2016 and Laxminarayan et al., 2016).

In the public sector, the antibiotic prescribing pattern is regulated by the Standard Treatment Guidelines (STG's). It is directed by the inclusion and availability of medicine on the Essential Medicines List (EML) (Perumal-Pillay and Suleman, 2017). However, in the private sector, the prescribing is greatly unrestricted, with the doctors selecting any antibiotic they feel clinically most appropriate for the medical condition (Chunnilall et al., 2015).

Furthermore, in the private sector, prescribing restrictions may occur on a financial level, when a patient belongs to a private healthcare insurer, the medical aid and the patient are responsible for settling the payment. Sometimes the antibiotics prescribed may not be reimbursed unless the prescribing thereof follows an appropriate medicines formulary or policy, which then needs to be paid by the patient solely (Chunnilall et al., 2015). This results in affordability issues, which, together with the inappropriate dispensing and prescribing practices, influence the increased probability of antibiotic self-medication (Awad and Aboud, 2015).

Antibiotic self-medication is a typical human attitude and practice globally that leads to irrational antibiotic use (inadequate doses, shortened duration of treatment and withdrawal of treatment on symptoms reduction) (Bennadi, D., 2013). Self-medication of antibiotics exposes patients to adverse

effects, drug-drug interactions, antibiotic resistance and difficulties in diagnosing different diseases (Rather et al., 2017). Moreover, this results in increased hospital stays, decreased antibiotic options, the requirement of highly costly medications and even death as the end products (Nepal and Bhatta, 2018).

Public educational activities and awareness-raising programmes are the primary tools of global healthcare policy to change behaviour patterns and address antibiotic misuse and resistance, nonetheless, in the South African context, the factors namely poverty, insecure income and lack of accessibility and availability to healthcare impact on the benefits of these educational interventions. However, if contextualised locally and used in coordination with suitable training for general public and healthcare professionals, the safe use of antibiotics could be promoted through the range of pre-existing materials on antibiotic community education, available from WHO.

2.7 Chapter Summary

The salient findings of the literature review indicate that self-medication is an everyday medical activity, as shown by many studies from various parts of the world. Most participants had an incorrect perspective about antibiotics and its uses. Also, the patients, doctors and pharmacists exhibit destructive conduct and practices. Besides, there is limited communication and understanding related to antibiotic misuse, and the severity of the matter is not dealt with seriously, thereby resulting in an avoidable problem, the fast emerging antibiotic resistance crisis that threatens the extraordinary healthcare benefits.

From the perspective of global studies, there is a great need to protect currently available antibiotics from being rendered ineffective by irrational antibiotic use. The societal and economic impact of self-medication and antibiotic resistance creates tension for patients, doctors, pharmacists, healthcare administrators and the population at large.

Moreover, factors such as poverty, limited healthcare education, free access to antibiotics in retail settings, and inadequate access and affordability of a doctor are the determinants for the public to seek advice from a local pharmacist or indulge in self-medication instead of taking advice from a healthcare professional. These forces necessitate an urgent need to review current awareness programmes for antibiotic monitoring and prevention.

Also, more information to best plan interventions and newer methods are required to curtail the menace and agree on policies to drive the desire, to hinder antibiotic misuse and antibiotic resistance globally and in a different local context. These crucial aspects leave a gap for this research study to fulfil. It focused on gaining an understanding of the evidence around the local patients' and doctors' knowledge,

attitude and behaviour on antibiotic use, especially in the South African context, as there are limited studies related to this topic.

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CHAPTER 3: SUBMITTED MANUSCRIPT

This article has been submitted to [Southern African Journal of Infectious Diseases]. See the submission acknowledgment email as proof (Appendix G).

This chapter presents the submitted paper as per the journal stipulated format [https://sajid.co.za/index.php/sajid] and limitations in terms of graphs, tables and word count.

Written permission to conduct the study was sought from and granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, (BE061/19, Appendix A and B). See also the institutional pharmacy permission letter (Appendix C). See too the data collection sheet and informed consent documents (Appendix D and E).

Sholene Ballaram (SB) was responsible for the proposal development, data collection and analyses (with the assistance of a statistician) and the write up. Professor Fatima Suleman (FS) served as the supervisor.

An evaluation of knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in South Africa.

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ABSTRACT

Background: Antibiotic misuse is a global problem that presents a threat to public health. Antibiotic misuse and overuse are responsible for the increase and spread of antibiotic resistance. The community plays a fundamental role in the appropriate antibiotic use and the increase and spread of antibiotic resistance. Hence, public knowledge and attitude regarding antibiotic use are imperative in treatment success.

Method: A quantitative approach was performed using a descriptive cross-sectional design. The data were collected by a self-administered questionnaire completed by patients accessing the pharmacy. The data was analysed using descriptive statistics, namely Microsoft Excel and the Statistical Package for the Social Sciences (SPSS).

Results: From a total of 135 respondents, the majority (n = 108; 80%) of the respondents were aware that different antibiotics were needed to treat different diseases. However, over two-thirds (n = 98; 73%) of the respondents agreed that antibiotics are effective against viruses. More than half of the respondents (n = 82; 61%) considered that antibiotic resistance is a global problem. The vast majority of the sample population (n = 104; 77%) agreed that the pharmacists often tell them how to use their antibiotics during the dispensing process. However, a high number of respondents (n = 97; 72%) agreed that doctors take time to inform them during the consultation on using the antibiotics that s/he prescribed, but this number is lower (n = 104; 77%) when compared to the pharmacists.

Conclusion: The results demonstrate that the community frequently uses antibiotics. These findings indicate misunderstanding related to the antibiotics' role and their cause of the disease (bacterial or viral). The multifaceted educational interventions and patient-healthcare provider communication tools should focus on the specific socio-demographic factors and misconceptions of antibiotics to promote rational antibiotic use. Community-based interventions will help prevent the development of antibiotic resistance, cross-resistance and anticipated future events of treatment failure.

Keywords: knowledge, attitude, behaviour, antibiotic use, antibiotic misuse, antibiotic resistance, self-medication, South Africa.

Introduction

Among the most commonly purchased medicine worldwide, antibiotics are ranked high.[1] Antibiotics are substances produced to inhibit the growths of microorganisms and are produced solely from other microorganisms, two or of biological origin.[2, 3] Antibiotics can function by killing microorganisms (bactericidal) or being bacteriostatic by inhibiting the growth or multiplication of microorganisms. Meanwhile, the body's immune system also destroys them.[4]

However, their increasing widespread misuse has resulted in the development of resistant microorganisms, reducing antibiotics' effectiveness, resulting in untreatable infectious diseases in the community and hospital settings, increased morbidity and mortality and higher healthcare costs.[5] Antibiotic resistance spread and the uncontrolled irrational use (misuse and overuse) poses a significant global public health problem.[6, 7]

South Africa faces a quadruple disease burden, with the HIV/AIDS epidemic, other infectious diseases, injuries, and non-communicable diseases.[8, 9] The burden of infectious diseases is further exacerbated by limited access, availability and affordability of antimicrobials required to treat infections.[8] However, the full impact of antibiotic resistance on healthcare in South Africa is not known. Therefore, it is essential to know the general patterns of antimicrobial prescribing, patients knowledge and attitude on antibiotic use and misuse, and how these patterns compare to other countries.

Several areas have the potential for reducing antibiotic misuse. In Saudi Arabia, patient factors are one of the leading causes of antibiotic misuse.[10] The patient factors affecting the misuse or overuse of antibiotics include psychosocial factors such as behaviours, beliefs and attitudes regarding self-medication and over-the-counter medication, the pressure put on doctors, demographic characteristics, namely socioeconomic status, education levels and lack of health education.

However, the importance of such factors may vary amongst the public and private healthcare systems. The patient factors that influence antibiotic prescription and consumption in South Africa include symptoms and medical history, socioeconomic factors (access and availability in terms of distance from the healthcare facilities, whether the patient is a one-time or regular patient, cash or medical aid payment method), sociocultural, economic and systems factors.[8, 9]

Additional factors include the inappropriate household use of antibiotics, taking an insufficient dose or not completing the antibiotic course, storage of antibiotics, sharing antibiotics and taking antibiotics for the wrong indications such as viral infection and inflammation. Many antibiotics are erroneously used to treat flu or common cold symptoms.[11]

Self-medication with antibiotics almost always involves avoidable, inadequate and ill-timed dosing, creating the best environment for microbes to adapt rather than be eradicated. Besides, noncompliance occurs when the patients forget to take their medication, prematurely discontinue the medicine as they start to feel better or cannot afford a full course of therapy.[12]

The knowledge individuals have regarding antibiotics, and their use is essential with regards to the misuse. The development of antibiotic resistance has overtaken the speed with which the newer antibiotics are emerging into the pharmaceutical market; thus, there is a necessity to assess the public awareness and attitude towards antibiotic use and misuse.[13]

The economic impact of antimicrobial resistance is a worry to patients, physicians, pharmaceutical producers, healthcare administrators and the population.[14] The socioeconomic impact requires more attention from government agencies, non-governmental organisations, pharmaceutical industries, pharmacists, healthcare professionals and workers, and patients. Also, strategies need to be formulated to manage the current problems associated with antibiotic resistance. Above all, perception, attitude and behaviour change is paramount to preventing antibiotic misuse in communities.[15]

Although many studies, have determined the use of antibiotics and accompanying knowledge, attitude, and behaviour of the population in several parts of the world, there is currently limited research in South Africa. [16, 17, 18 19, 20] Therefore, this study was designed to evaluate the impact of current knowledge, attitude and behaviour of patients regarding antibiotic use and misuse within a community pharmacy setting. It also explored the community's views on perceptions of healthcare professionals and the patient-prescriber relationship when prescribing antibiotics.

Method

Study Location

This study was conducted at a community pharmacy in Durban, KwaZulu-Natal. It is an independently managed retail pharmacy that provides for the healthcare needs of the community, serving a population of 176,989 (Population census, 2011).

Study Population

A convenience sampling method was used to select the sample. The principal investigator drew the sample from the sample population present at the dispensary waiting area during the study period. The questionnaire was administered to those patients that were readily available at the dispensary, willing to participate in the study and met the criteria for participation. The study population included all adult

male and female patients above twenty-one years old and below sixty-five years old who received antibiotics on prescription during the study period. The patients younger than twenty-one years old and greater than sixty-five years old and those who have not been prescribed antibiotics were excluded.

Sample Size

The sample size was determined using the Leslie Fischer's (1998) formula for sample size determination; n = Z2pq/d2, where; n = desired sample size population < 10000; Z = standard normal deviate set at 1, 96 at 95% confidence level and d = 0.05. The minimum sample size of 135 participants was calculated using this formula.

Study Design

This was a quantitative descriptive cross-sectional designed study.

Data Collection

The data was collected by the use of a self-administered semi-structured questionnaire. The survey was conducted over one month after the Biomedical Research Ethics Committee (BREC). A questionnaire from a previous study performed in Kuwait 17 and adapted from the studies in Sweden and the United Kingdom.

The researcher piloted the questionnaire before the commencement of the actual study to ensure the comprehension and applicability of the research items to suit the local study population and determine the duration of the questionnaire completion, as this tool was not used previously in this population. The questionnaire was designed in the English language only, and the necessary amendments were made to suit the local population.

The questionnaire comprised of four sections. Section 1 consisted of ten questions regarding the respondent's demographic information. Section 2 comprised of thirteen questions that aimed to evaluate the respondent's knowledge of antibiotics. Section 3 consisted of seven items that pertained to the respondent's attitude towards antibiotic use. Lastly, Section 4 consisted of five questions that looked at perceptions of doctor/patient relationship regarding antibiotics and their use. A five-point Likert scale ranging from strongly disagree, disagree, neutral, agree, and strongly agree was used to assess the responses.

Data Analysis

All questionnaires were manually sorted. The data were analysed using Microsoft Excel and the Statistical Package for the Social Sciences (SPSS) Version 23, in descriptive statistics, viz. frequencies and percentage proportions. The Cronbach Alpha test, Chi-Square test, and the multivariate analysis of variance and correlation testing were determined in this study.

Ethical Considerations

The ethical approval was sought from the Biomedical Research Ethics Committee at the University of KwaZulu-Natal (BE061/19). The site permission was obtained from the community pharmacy owner/manager/responsible pharmacist. The study respondents written informed consent was obtained before the administration of the questionnaire. All information collected was treated with strict confidentiality.

Results

A total of 135 questionnaires were distributed with a 100% response rate. The Cronbach's Alpha test was used to measure the reliability of the items through internal consistency. The Cronbach Alpha value is 0.752. The results show strong and positive internal consistency results for the scale utilised in the questionnaire with the sample's chosen size.

Table 1 below provides information on the demographic characteristics of respondents.

Table 1: Sociodemographic characteristics of respondents (n = 135)

Characteristics	Category	n (%)
Gender	Male	63 (46.7)
	Female	72 (53.3)
Age	21-29	32 (23.7)
	30-39	52 (38.5)
	40-49	31 (22.9)
	50-59	16 (11.9)
	≥60	4 (3.0)
Antibiotic use in past 6 months	Yes	78 (57.8)
	No	57 (42.2)
Do you work or study in the medical field?	Yes	31 (23)
	No	104 (77)
Educational Qualifications	Matric	54 (40)

	Certificate	23 (17)
	Diploma	15 (11.1)
	Degree	24 (17.8)
	Masters	5 (3.7)
	Doctorate	4 (3.0)
	Other	10 (7.4)
Note: n= frequency (number of respondents) and % = percentage		

Over half of the study respondents (n = 72; 53.3%) were females. The majority of the respondents (n = 52; 38.5%) were between 30 and 39 years old. More than half of the study population (n = 78; 57.8%) used antibiotics in the past six months. A vast majority of the respondents (n = 54; 40%) completed high school as the highest educational qualification, while some had furthered their studies. However, a small portion (n = 31; 23%) worked or studied in the healthcare environment.

Table 2 depicts the results of the respondent's knowledge of antibiotics and their use.

Table 2: Analysis of Respondents Knowledge on Antibiotics use

Statements	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)	Total n (%)
Different antibiotics are needed to cure different diseases	4 (3)	4 (3)	19 (14)	65 (48)	43 (32)	135 (100)
Antibiotics are effective against bacteria	7 (5)	5 (4)	15 (11)	63 (47)	45 (33)	135 (100)
Antibiotics can kill bacteria that normally lives on the skin and gut	2 (2)	7 (5)	17 (13)	67 (50)	42 (30)	135 (100)
Antibiotics speed up the recovery from coughs and colds	14 (10)	17 (13)	17 (13)	57 (42)	30 (22)	135 (100)
Antibiotics work on most coughs and colds	16 (12)	20 (15)	19 (14)	54 (40)	26 (19)	135 (100)
Antibiotics are effective against viruses	15 (11)	8 (6)	14 (10)	60 (45)	38 (28)	135 (100)
If you get side effects during a course of antibiotics, you should stop taking it	9 (6)	7 (5)	6(4)	60 (45)	53 (40)	135 (100)
If you get a skin reaction when using antibiotics, you should not use antibiotics again	2 (2)	12 (9)	13 (10)	59 (44)	49 (36)	135 (100)
Antibiotics can cause an imbalance in the body's own bacterial flora	4 (3)	7 (5)	32 (24)	49 (36)	43 (32)	135 (100)

The unnecessary use of antibiotics can increase the resistance of bacteria to them	6 (4)	7 (5)	23 (18)	54 (40)	45 (33)	135 (100)
Antibiotics resistance is a worldwide problem	9 (6)	11 (8)	33 (25)	46 (34)	36 (27)	135 (100)
Antibiotics use among animals can reduce the effects of antibiotics among humans	21 (16)	34 (25)	31 (23)	29 (21)	20 (15)	135 (100)
Humans can be resistant to antibiotics	6 (4)	12 (9)	20 (15)	49 (37)	48 (35)	135 (100)
Note: n= frequency (number of respondents) and % = percentage						

The majority of the respondents (n = 108; 80%) stated that different antibiotics are needed to "cure" different diseases. Most of the sample (n = 108; 80%) knew that antibiotics are effective against bacteria. Almost two-thirds of the respondents (n = 87; 64% and n = 80; 59%) believed that antibiotics speed up recovery from coughs and colds, and it works on most coughs and colds, respectively. Also, over two-thirds of the respondents (n = 98; 73%) stated that antibiotics are effective against viruses. However, most of the respondents (n = 113; 84%; n = 108; 80%) agreed that antibiotics should be stopped if side effects or a skin reaction were encountered during use, respectively.

Table 3, below presents the results of the respondent's attitude towards antibiotic use.

Table 3: Analysis of Respondents Attitude towards Antibiotic use

Statements	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)	Total n (%)
I always complete the course of treatment with antibiotics even if I feel better	1 (1)	5 (4)	15 (11)	56 (41)	58 (43)	135 (100)
It is good to be able to get antibiotics from relatives or friends without having to see a doctor	64 (49)	37 (27)	6 (4)	22 (16)	6 (4)	135 (100)
I prefer to keep antibiotics at home in case there may be a need for it later	39 (30)	41 (31)	12 (8)	24 (17)	19 (14)	135 (100)
If I feel better, I sometimes stop taking my antibiotics before completing the course of treatment	44 (33)	36 (27)	11 (8)	54 (25)	10 (7)	135 (100)

I prefer to use antibiotics if I have a cough for more than a week	25 (18)	29 (21)	29 (21)	32 (26)	20 (14)	135 (100)
When I have a sore throat, I prefer to use antibiotics	30 (22)	44 (33)	21 (15)	28 (21)	12 (9)	135 (100)
Note: n= frequency (number of respondents) and % = percentage						

A large percentage of the respondents (n = 114; 84%) admitted to always completing the course of treatment with antibiotics, even if they felt better. The majority (n = 101; 74%) disagreed that it is good to get antibiotics from family or friends without having to see a doctor. Just about a quarter of the respondents (n = 31; 23%) agreed that they sometimes stop their treatment course if they feel better.

Table 4 outlines responses concerning the perceptions of healthcare professionals habits and health professional/patient relationships.

Table 4: Analysis of Perception on Doctors Habits and health professional/Patient Relationship

Statements	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)	Total n (%)
Pharmacists often tell you how to use antibiotics	3 (2)	11 (8)	17 (13)	51 (38)	53 (39)	135 (100)
Doctors often take time to inform patients during consult how to use antibiotics	4 (3)	8 (6)	26 (19)	55 (41)	42 (31)	135 (100)
I trust the doctor's decision if they decide not to prescribe antibiotics	5 (4)	8 (6)	15 (11)	65 (48)	42 (31)	135 (100)
Doctors often prescribe antibiotics because the patient expects it	3 (2)	3 (2)	19 (14)	66 (49)	44 (33)	135 (100)
Doctors often take time to carefully consider the need for antibiotics	10 (7)	7 (5)	24 (18)	56 (42)	38 (28)	135 (100)
Note: n= frequency (number of respondents) and % = percentage						

The vast majority of the sample population (n = 104; 77%) agreed that the pharmacists often tell them how to use their antibiotics during the dispensing process. Also, respondents (n = 97; 72%) agreed that the doctors usually take their time to inform them during the consultation on using the antibiotics that s/he prescribed, but this number is lower when compared to the pharmacists. The majority of

respondents (n = 107; 79%) stated that they trusted the doctor's decision not to prescribe antibiotics though many (n = 110; 82%) also believed that doctors often prescribed antibiotics because the patient expects it.

To assess whether the socio-demographic factors have an impact on antibiotic use. Pearson's Chi-Square test of independence was performed to identify the association between two variables: age, gender, education, antibiotic use in the past six months, and job status and antibiotic use. The Phi and Cramer's V depicts the test of the association level between the variables. Overall, based on the Pearson's chi-square test results, apart from gender (p = 0.364), all other socio-demographic variables are associated with using antibiotics as the p-values were less than 0.05.

According to Pearson's chi-square results (p = 0.364), there is no positive relationship between gender and antibiotic use. It can be interpreted that both males and females do not equally favour antibiotic use. However, the association between the two variables is very weak (0.078) based on the Phi and Cramer's V value.

Table 5 presents the results of multivariate analysis of variance.

Table 5: Summary of Multivariate analysis of Variance (MANOVA)

Factor	Category	Knowledge		Attitude		Behavior	
Gender		P-Value					
	Male	0.051		0.118		0.068	
	Female	Reference Group					
	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		3.020	.554	2.355	.671	1.520	.823
Age		P-Value					
	21 - 29	0.000		0.005		0.000	
	30 – 39	0.000		0.003		0.000	
	40 - 49	0.000		0.037		0.000	
	50 – 59	0.000		0.037		0.000	
	> 60	Reference Group					
	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		10.640	.223	7.031	.533	6917.09	.000
Employment status		P-Value					
	Unemployed	0.000		0.037		0.000	
	Employed	Reference Group					

	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		3.067	0.547	4.319	0.365	2.149	0.708
Educational Qualifications		P-Value					
	Matric	Reference Group					
	Certificate	0.565		0.560		0.974	
	Diploma	0.599		0.634		0.978	
	Degree	0.565		0.587		0.327	
	Masters	0.678		0.712		0.097	
	Doctor	0.713		0.761		0.097	
	Other	0.634		0.677		0.097	
	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		18.104	0.947	13.422	0.859	14.104	0.825
Antibiotic usage in past 6 months		P -value					
	Yes	0.288		0.069		0.758	
	No	Reference Group					
	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		1.581	0.812	1.679	0.795	1.147	0.887
Work in medical field		P-Value					
	Yes	0.002		0.005		0.034	
	No	Reference Group					
	Overall	Chi-Square	Sig. Value	Chi-Square	Sig. Value	Chi-Square	Sig. Value
		4.093	0.394	3.713	0.446	1.071	0.899

A multivariate logistics regression was used to determine the relationship between socio-demographic variables and knowledge, attitude, and behaviour of patients regarding antibiotic use. The reference groups were chosen based on the group to which the researcher wanted to compare all other groups within the same category, thus interpretation of the results much easier.

The males were less likely to have good knowledge, attitude, and behaviour on antibiotic usage than the females. It can be seen in Table 5 that neither of the variables (p = 0.051, 0.118 and 0.068 respectively) are statistically significant, as the p = values are greater than the significance value 0.05.

The knowledge and behavioural aspects across all age groups presented p = 0.000 (p - values are less than 0.05), and the association between these variables are statistically significant. When considering the attitude component, age group 21-29 years scored p = 0.005, age group 30-39 years scored p = 0.003, age group 40-49 years and 50-59 years scored p = 0.037. Therefore, the respondents aged 21 –

29, 30 – 39, 40 – 49, and 50 – 59 years old were likely to have good knowledge, attitude, and behaviour of antibiotic usage. The associations were significant, which is different from the reference group.

Based on the survey responses (Table 5), both groups of respondents that used or not used antibiotics in the past six months differed in knowledge, attitude and behaviour regarding antibiotic usage. The results are not statistically significant as the p - values are more than the significance level, 0.05 (knowledge $p = 0.288$, attitude $p = 0.069$ and behaviour $p = 0.758$).

According to Table 5, matric was used as the reference group for educational qualifications. The knowledge did not differ across all educational qualification groups towards antibiotic usage, as the association was not statistically significant, $p > 0.05$. The respondents who have a degree were neutral (39.1%), while those who had completed Masters (50%) or Doctorate (80%) agreed to this statement.

Furthermore, the respondents aged 21-29 years (14.8%), 30-39 years (17.8%), 40-49 years (12.6%) and 50-59 years (8.8%) were in disagreement with the use of antibiotics during a sore throat. However, a minute percentage (2.3%) of those aged 60 years old agreed to use antibiotics during a sore throat. The majority of the respondents in the age group 21-29 years (16.3%), 30-39 years (21.5%), 40-49 years (11.8%) agreed that antibiotic resistance is a global problem.

Whereas, a considerable percentage of respondents within the different age groups were unsure of the above notion 5.2% (20-29 years old), 8.1% (30-39 years old), 8.1% (40-49 years old), 2.2% (50-59 years old) and 0.7% (over 60 years). From these findings, it can be concluded that respondents of various educational backgrounds and all age groups have differing knowledge and opinions about antibiotic resistance as a global issue.

Discussion

The results indicate that antibiotics are frequently used in the community. This study has identified gaps in patient knowledge regarding antibiotic use. The knowledge factor evaluated what the patients know about antibiotics, their use and side effects and antibiotic resistance. The majority of the patients (80%) were aware that different antibiotics treated different diseases. Antibiotics are grouped based on how they function; therefore, it is vitally important to understand that each antibiotic only works against a particular type of bacteria.

The inadequate knowledge of rational antibiotic use is not unique to South Africa but globally. Almost two-thirds of the study population agreed that antibiotics are effective against bacteria (80%) which, is

higher than that reported in Jordan (32.9%), lower than Kuwait (91.8%) and comparable to Malaysia (76.7%).[21,17, 22]

This study revealed that 73% of respondents agreed that antibiotics are effective against viruses, consistent with figures published from studies in Kuwait, Malaysia, and New Jersey.[17, 22, 23] Almost half of the respondents believed that antibiotics speed up the recovery from coughs and colds and work on most coughs and colds, lower than the reported figures in Kuwait and Jordan.[17, 21]Hence, this study demonstrates a correlation between misconception and misunderstanding of viral diseases and antibiotic use.

Antibiotics do not work against infections caused by viruses, for example, the common cold or flu and fungal infections. Hence, most of the community will access antibiotics and self-medicate when they experience a cough, sore throat, flu or the common cold. These results suggest a lack of knowledge that will significantly influence the probability of antibiotic misuse.

A high proportion (61%) of the respondents believed that antibiotic resistance is a global problem. The prevalence of knowledge about antibiotic resistance is considerably lower than the rates in Kuwait and Malaysia.[17, 22] These results build on existing evidence that patients are aware of antibiotic misuse that leads to resistance but still continue to practice self-medication.

The attitude factor evaluated what the patients feel. A large proportion of the respondents (n = 52; 39% and n = 40; 30% respectively) agreed to use antibiotics in cases when a cough persists for more than a week and if they have a sore throat. In this study and Namibia, patients prefer antibiotics for common cold symptoms, including sore throat and cough.[20] The majority (n = 98; 73%) failed to identify that antibiotics have no significant therapeutic effects on viruses.

Hence, these findings indicate apparent misunderstanding and confusion related to the antibiotics' role and their cause of the disease (bacterial or viral). An antibiotic cannot kill viruses because viruses and bacteria have different structure, mechanisms and machinery to survive and replicate. Therefore, the antibiotic has no role in a virus. The patient taking an antibiotic in the presence of a virus will not be cured of the infection or not feel better instead, it will lead to high cost, undesirable side effects, and may contribute to antibiotic-resistant bacteria.

This study reported that patients sometimes stop taking their antibiotics if they feel better (33%), which is similar to Kuwait's findings.[17] However, most (84%) patients agreed that they complete their antibiotics course; this score is higher than in Kuwait.[17] This misconception concerning antibiotic use may put the patient at risk of relapse with resistant bacteria. When the antibiotic does not function, this

results in a more extended infection period, more complicated infection, increased costs (more doctor visits and the use of more potent and more expensive medicines) and eventually possible death.

Furthermore, compared to the proportionality (44.3%) reported in Kuwait, the current study revealed that a smaller portion (31.8%) of the respondents disclosed a negative attitude to keep left-over antibiotics at home for future use.[17] The present study revealed that other sources of obtaining antibiotics include family members and friends. Moreover, 23.3% of Kuwait respondents get antibiotics from family and friends without advice from a prescriber, similarly to this study (20.7%).[17] These findings demonstrated that a portion of the South Africans share used antibiotics with others hence, exposing the local community to antibiotic misuse due to possible self-medication.

Self-medication practices expose the patient to several risks, including incorrect self-diagnosis and choice of therapy, delays in seeking medical attention, possible drug interactions, incorrect dosing, primarily when used in minors or seniors, in some cases incorrect route of administration, masking of severe infections, usage of expired medicines, risk of dependence and antibiotic misuse.

Some of the disadvantages to keeping left-over antibiotics for future use include the antibiotics may be readily accessible to children and if taken may result in death, inappropriate storage conditions may alter the antibiotic making it inactive, poly-pharmacy, drug interactions, misdiagnosis, incorrect choice of treatment, antibiotic misuse or dependence.[17, 21, 22, 20]

The behaviour component evaluated the current practices on antibiotic use. This study has identified gaps in behaviour related to health professionals habits and health professional/patient relationships and antibiotic use. A higher proportion of the respondents affirmed that they obtained information on antibiotic use from pharmacists than doctors. This highlights that doctors and pharmacists play an essential role in patient counselling and public education related to knowledge and attitude towards rational antibiotic use.

In a community such as this one, the inappropriate prescribing and dispensing of antibiotics could be due to patient demands, the healthcare professionals profit interests and their lack of knowledge regarding optimal therapies, which, in turn, may threaten the patient's healthcare and patient safety (Llor and Bjerrum, 2014).[24]

One of the limitations of this study is that the respondents were chosen by the convenience sampling method. The principal investigator recruited participants based on the study's inclusion criteria from the convenient subset of the population at large. This convenience sample did not produce representative

results when needed to extrapolate to a larger target population. To mitigate this problem, the results were treated as a representative.

Another limitation noted in this study which is not reflective of the South African population, is that almost a quarter of the respondents worked in the medical field. Just over half of the respondents had higher than matric qualification.

Despite these limitations, the current findings of this study have important implications for providing additional insights to community knowledge and attitude on antibiotic use, misuse and resistance, and healthcare professionals behavioural patterns.

To better understand the implications of these results, further studies should take into account social practices and cultural environments related to antibiotic use. Further research is needed to establish the relationship between age, gender, employment status and educational qualifications and antibiotic use.

Conclusion

This research aimed to evaluate the impact of current knowledge, attitude and behaviour of patients regarding antibiotic use within a community pharmacy setting in South Africa. Antibiotics are frequently used by the South Africans in the community. Antibiotics are embedded in self-medication practices, whereby individuals are engaged in their own and those of their friends and families therapeutic processes. Also, individuals are using antibiotics to treat viral diseases such as the common cold, flu, sore throat and cough.

Based on the quantitative analysis, it can be concluded that socio-demographic, socioeconomic and sociocultural factors are important patient factors to consider when designing and targeting appropriate educational interventions campaigns and patient-healthcare provider communication tools in addressing rational antibiotic use.

The attention of the local and national healthcare policymakers should be focused on prescribers (the doctors) and dispensers (pharmacists) as the principal information providers upon patient counselling on the proper use of antibiotics, to close the gaps regarding knowledge, attitude and behaviour about antibiotic use and its association to the health and economic risks of antibiotic resistance. Thus, there is a need for a team-based approach (including the patients, prescribers and pharmacists) by building trusting relationships and respect to attain the rational use of antibiotics and quality patient care.

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3.1 Status of Article:

Awaiting approval for publication.

CHAPTER 4: SYNTHESIS

4.1 Discussion

Antibiotic use contributes to the most significant public health crisis of antibiotic resistance globally, mainly when made readily available (Kardas et al., 2005). It is thereby creating an impact on increasing morbidity, mortality, medical care, and related costs (Laxinarayan et al., 2013).

The study results indicate that antibiotics are frequently used in the community. The study revealed the limited knowledge and sub-optimal behaviour within the community regarding the role of antibiotics, their use and their cause of disease. This study highlights that sharing antibiotics is a common practice in the community, exposing them to antibiotic misuse due to possible self-medication.

57.8% of the study population used antibiotics in the last six months, and 100% of the respondents were prescribed antibiotics, as it was one of the inclusion criteria to participate in the study. These results are lower (80.36% over the past twelve months) than the study in Windhoek, Namibia, Southern Africa, but almost comparable (Pereko et al., 2015). Thus, antibiotics are frequently used in communities in South Africa.

This study has identified gaps in patient knowledge regarding antibiotics and their use. The knowledge factor evaluated what the patients know about antibiotics, their use side effects and antibiotic resistance. The majority of the patients (80%) were aware that different antibiotics treated various diseases. Antibiotics are grouped based on how they function. Therefore, it is vitally important to understand that each antibiotic type only works against a particular type of bacteria.

The inadequate knowledge of rational antibiotic use is not unique to South Africa but globally. Almost two-thirds of the study population agreed that antibiotics are effective against bacteria (80%) which, is higher than that reported in Jordan (32.9%), lower than Kuwait (91.8%) and comparable to Malaysia (76.7%) (Shehadeh et al., 2012; Awad and Aboud, 2015; Oh et al., 2011).

This study revealed that 73% of respondents agreed that antibiotics are effective against viruses, consistent with figures published from studies in Kuwait, Malaysia, and New Jersey (Awad and Aboud, 2015; Oh et al., 2011; Vanden et al., 2003). Almost half of the respondents believed that antibiotics speed up the recovery from coughs and colds and work on most coughs and colds, which is lower than the reported figures in Kuwait and Jordan (Awad and Aboud, 2015; Shehadeh et al., 2012). Hence, this study demonstrates a correlation between misconception and misunderstanding of viral diseases and antibiotic use.

Antibiotics do not work against infections caused by viruses, for example, the common cold or flu and fungal infections. Hence, most of the community will access antibiotics and self-medicate when they experience a cough, sore throat, flu or the common cold. These results suggest a lack of knowledge that will significantly influence the probability of antibiotic misuse.

A high proportion (61%) of the respondents believed that antibiotic resistance is a global problem. The prevalence of knowledge about antibiotic resistance is considerably lower than Kuwait and Malaysia rates (Awad and Aboud, 2015; Oh et al., 2011). These results build on existing evidence that patients are aware of the problem of antibiotic misuse that leads to resistance.

The attitude factor evaluated what the patients feel. A large proportion of the respondents (n = 52; 39% and n = 40; 30% respectively) agreed to use antibiotics in cases when a cough persists for more than a week and if they have a sore throat. In this study and Namibia, patients prefer antibiotics for common cold symptoms, including sore throat and cough (Pereko et al., 2015). Besides, the majority (n = 98; 73%) failed to identify that antibiotics have no significant therapeutic effects on viruses.

Hence, these findings indicate apparent misunderstanding and confusion related to antibiotics' role and their cause of the disease (bacterial or viral). An antibiotic cannot kill viruses because viruses and bacteria have different structure, mechanisms and machinery to survive and replicate. Therefore, the antibiotic has no role in a virus. The patient taking an antibiotic in the presence of a virus will not be cured of the infection or feel better. Instead, it will lead to high cost, undesirable side effects, and may contribute to antibiotic-resistant bacteria.

This study reported that patients sometimes stop taking their antibiotics if they feel better (33%), which is similar to Kuwait's findings (Awad and Aboud, 2015). However, most (84%) patients agreed that they complete their antibiotics course; this score is higher than in Kuwait (Awad and Aboud, 2015). This misconception concerning antibiotic use may put the patient at risk of relapse with resistant bacteria. When the antibiotic does not function, this results in a longer infection period, more complicated infection, increased costs (more doctor visits and more potent and more expensive medicines), and eventually possible death.

Furthermore, compared to the proportionality (44.3%) reported in Kuwait, the current study revealed that a smaller portion (31.8%) of the respondents disclosed a negative attitude to keep left-over antibiotics at home for future use (Awad and Aboud, 2015). The present study revealed that other sources of obtaining antibiotics include family members and friends. Moreover, 23.3% of Kuwait respondents get antibiotics from families and friends without advice from a prescriber, similarly to this

study (20.7%) (Awad and Aboud, 2015). These findings demonstrated that a portion of the South African person shares used antibiotics with others hence, exposing the local community to antibiotic misuse due to possible self-medication.

Self-medication practices expose the patient to several risks, including incorrect self-diagnosis and choice of therapy, delays in seeking medical attention, possible drug interactions, incorrect dosing primarily if used in minors or seniors, in some cases incorrect route of administration, masking of severe infections, usage of expired medicines, risk of dependence and antibiotic misuse. Some of the disadvantages to keeping left-over antibiotics for future use include the antibiotics may be readily accessible to children and if taken may result in death, inappropriate storage conditions may alter the antibiotic making it inactive, poly-pharmacy, drug interactions, misdiagnosis, incorrect choice of treatment, antibiotic misuse or dependence.

The behaviour component evaluated the current practices on antibiotic use. This study has identified gaps in behaviour related to health professionals habits and health professional/patient relationships, and antibiotic use. A higher proportion of the respondents affirmed that they obtained information on antibiotic use from pharmacists rather than doctors. This highlights that doctors and pharmacists play an essential role in patient counselling and public education related to knowledge and attitude towards rational antibiotic use.

In a community such as this one, the inappropriate prescribing and dispensing of antibiotics could be due to patient demands, the healthcare professionals profit interests and their lack of knowledge regarding optimal therapies, which, in turn, may threaten the patient's healthcare and patient safety (Llor and Bjerrum, 2014).

Education is associated with good knowledge and attitude on antibiotic use. This study identified gaps in knowledge and specific target groups of patients who were likely to self-medicate and negative attitude towards antibiotic use. Thus, this provides an opportunity for an educational intervention to increase public knowledge of antibiotics and their use. Similar observations were also reported in Kuwait, Jordan, Malaysia and South Africa (Awad and Aboud, 2015; Shehadeh et al., 2012; Oh et al., 2011; Pereko et al., 2015).

4.2 Limitations

This research study has a few limitations. An important limitation of this study is that the respondents were chosen by the convenience sampling method. This convenience sample did not produce representative results; it needs to extrapolate for a larger target population. To mitigate this problem,

the results were treated as representative. Another limitation noted in this study which is not reflective of the South African population, is that almost a quarter of the respondents worked in the medical field. Just over half of the respondents had higher than matric qualification.

This study has potential methodological limitations related to limited access to data and lack of previous research studies on this community's topic. Many conflicts arose from the research participants personal issues, thereby limiting the sample of the study-specific participants, namely: they were in a hurry and could not complete a questionnaire, the research participants that were prescribed antibiotics during the study period was probably not the best time for larger sample size, they did not understand the purpose for the study and did not want to participate, this was a new concept to them and therefore reluctant to participate, and the patients have been using this pharmacy for several years especially the older generation who have a perception that if they say something wrong, the pharmacy may close down.

Due to the various educational levels, each of the research participants would not have had the same understanding but rather their interpretation of each of the questions; hence, the study results can be subjective. The two-page length of the questionnaire may have added as a drawback to unconscientious participant's responses.

Despite these limitations, the current findings of this study have important implications for providing additional insights to community knowledge and attitude on antibiotic use, misuse and resistance, and healthcare professionals behavioural patterns. To better understand the implications of these results, further studies should take into account social practices and cultural environments related to antibiotic use. Further research is needed to establish the relationship between age, gender, employment status and educational qualifications and the patient's knowledge, beliefs and attitude.

4.3 Conclusion

This study results demonstrate that antibiotics are frequently used in the local community. Antibiotics are embedded in self-medication practices, whereby individuals are engaged in their own and those of their friends and family’s therapeutic processes. Also, individuals are using antibiotics on their initiative to treat viral diseases such as the common cold and flu and cough.

The study results suggest that population-based questionnaires are crucial in understanding the community’s attitude and behaviour patterns towards antibiotics and their use, as such knowledge is vital in contributing to patient counselling and community education efforts to minimise irrational antibiotic use. Based on the quantitative analysis, it can be concluded that socio-demographic, socioeconomic and sociocultural factors are important patient factors to consider when designing and

targeting appropriate educational interventions campaigns and patient-healthcare provider communication tools in addressing rational antibiotic use.

The attention of the local and national healthcare policymakers should be focused on prescribers (the doctors) and dispensers (pharmacists) as the principal information providers upon patient counselling on the proper use of antibiotics, to close the gaps regarding knowledge, attitude and behaviour about antibiotic use and its association to the health and economic risks of antibiotic resistance. Thus, there is a need for a team-based approach (including the patients, prescribers and pharmacists) by building trusting relationships and respect to attain the rational use of antibiotics and quality patient care.

These interventions would address the thriving problem associated with antibiotic misuse, the need to prevent further development of microbial resistance, cross-resistance, related health and economic risks, superinfection, and anticipated future treatment failure developments.

4.4 Recommendations

The community pharmacists and prescribers should adhere to current regulations and guidelines on rational antibiotic use. The doctors and pharmacists should keep up-to-date with current knowledge and behavioural patterns related to rational antibiotic use and practices whilst keeping in line with the current national and international guidelines and adapting these to the local setting. Hence, doctors and pharmacists need to engage themselves in continuous professional development following their formal qualifications to enhance their patient counselling skills.

Pharmacists, the frontline, custodians of medication, and the community's pillars should ensure that antibiotics are not dispensed without a valid medicinal prescription from the doctor. Also, the doctors should not feel pressurised by the patients, parents and guardians to prescribe antibiotics if a specific patient case scenario does not warrant it.

The results suggest the need for a team-based approach to patient care to improve the collaboration between the community pharmacists and prescribers, thereby building trusting relationships and respect to encourage the rational use of antibiotics. The community pharmacies are accessible and convenient primary healthcare places with long opening hours and non-appointment based services. The community pharmacists are clinically trained with appropriate pharmaceutical skills and knowledge. They are accessible and available to the patient always; therefore, the community pharmacists must always be positioned as the effective liaison between the prescribers and the patients. This collaborative engagement will help craft a culture of change towards patient safety by prescribing and dispensing habits.

This community healthcare integrated relationships within the patient's pathway will benefit the patients, the community healthcare system and optimal patient care. Thus, when these patients hear consistent information from their prescribers and pharmacists about antibiotic therapy, it will reinforce rational antibiotic use and minimise self-medication.

The multifaceted educational interventions targeting the specific socio-demographic factor related to the study population are required at the doctors' consultation rooms and pharmacies (waiting areas and upon counselling) to promote appropriate antibiotic use. This will help close the gaps regarding knowledge, attitude and behaviour about antibiotic use and its association to antibiotic resistance. Many of the educational interventions by doctors and pharmacists need to focus on the disease and its cause and the antibiotic, its use and side effects profile, at the point of prescribing and dispensing these antibiotics to the patients.

The chosen educational programs could utilise all forms of local media and social to run education campaigns. However, further research on the most effective tools should be conducted, and proven methods should be continued. Also, visual aids in the consultation rooms and pharmacy waiting areas, smartphone apps and messaging, and interactive online platforms, could be proper mediums to use when conducting these intervention programs. The local healthcare policymakers' attention should be focused on prescribers and dispensers, as the principal information providers on the proper use of antibiotics.

These suggestions demonstrate functional pathways that could be used to educate patients, pharmacists and doctors on the endangerment of irrational prescribing, dispensing and utilisation related to the global antibiotic misuse and resistance difficulties. The educational interventions should focus on increasing knowledge about antibiotic misuse, which could then impact the attitudes and behaviours of the patients, pharmacists and doctors.

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APPENDIX A: BREC APPROVAL LETTER

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

05 June 2019

Mrs S Ballaram
School Health Sciences
College of Health Sciences
sholeneh@yahoo.com

Dear Mrs Ballaram

Protocol: An evaluation of knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in South Africa
Degree: Master's in Pharmacy **BREC Ref No: BE061/19**

BREC EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received 01 February 2019.

The conditions have been met and the study is given **full ethics approval** and may begin as from 05 June 2019. Please ensure that site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is valid for one year from **05 June 2019.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **noted** by a full Committee at its next meeting taking place on **11 June 2019.**

Yours sincerely

Prof D Wassenaar
Acting Chair: Biomedical Research Ethics Committee

cc: Postgrad administrator: nenep1@ukzn.ac.za Supervisor: sulemanf@ukzn.ac.za

Biomedical Research Ethics Committee
Professor V Rambiritch (Chair)
Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Telephone: +27 (0) 31 260 2486 **Facsimile:** +27 (0) 31 260 4609 **Email:** brec@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

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APPENDIX B: BREC RECERTIFICATION APPROVAL NOTICE

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

06 May 2020

Mrs S Ballaram
School Health Sciences
College of Health Sciences
sholeneh@yahoo.com

Dear Mrs Ballaram

Protocol: An evaluation of knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in South Africa
Degree: Master's in Pharmacy
BREC Ref No: BE061/19

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved:	**05 June 2020**
Expiration of Ethical Approval:	**04 June 2021**

I wish to advise you that your application for Recertification received on 05 May 2020 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

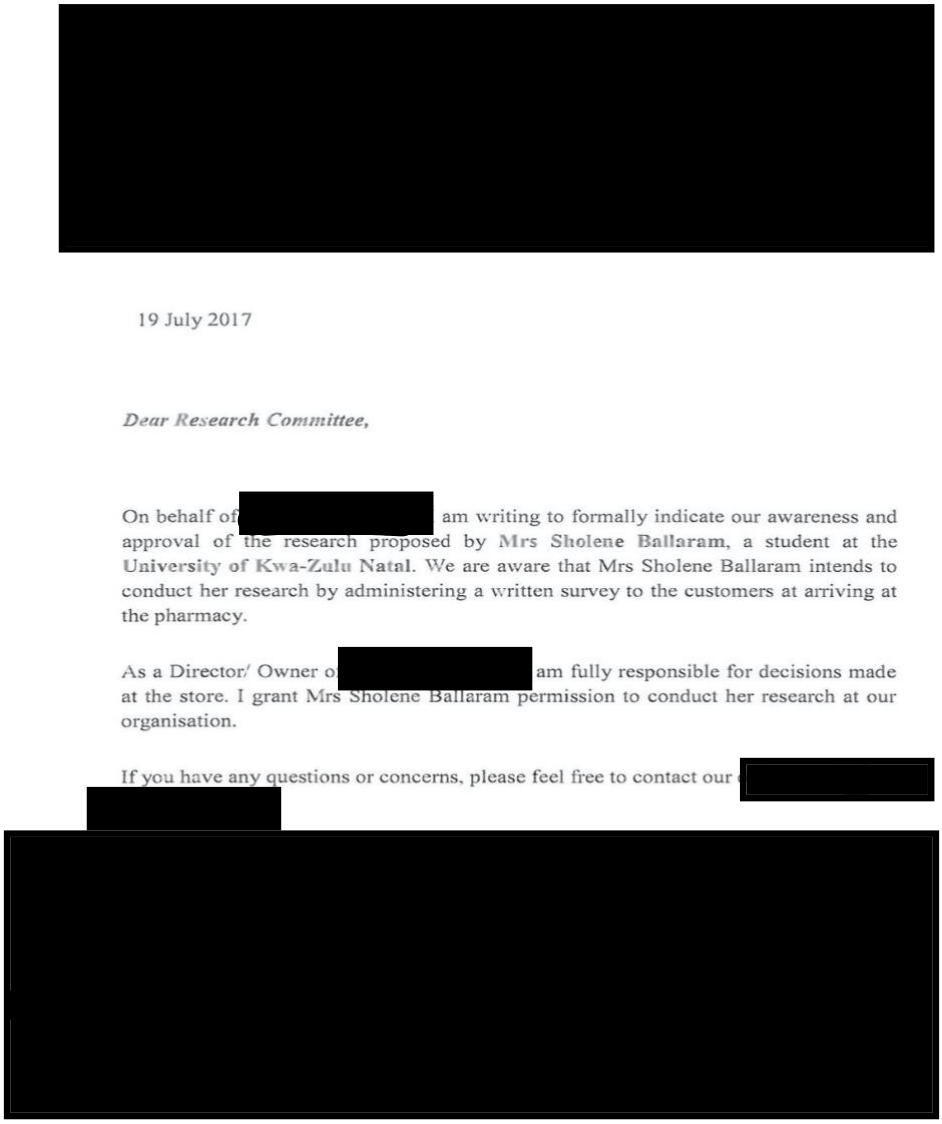
The committee will be notified of the above approval at its next meeting to be held on 09 June 2020.

Yours sincerely

.....
Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

cc: Postgrad administrator: nenep1@ukzn.ac.za Supervisor: sulemanf@ukzn.ac.za

APPENDIX C: RESEARCH PERMISSION LETTER



19 July 2017

Dear Research Committee,

On behalf of [redacted] am writing to formally indicate our awareness and approval of the research proposed by **Mrs Sholene Ballaram**, a student at the **University of Kwa-Zulu Natal**. We are aware that Mrs Sholene Ballaram intends to conduct her research by administering a written survey to the customers at arriving at the pharmacy.

As a Director/ Owner o[redacted] am fully responsible for decisions made at the store. I grant Mrs Sholene Ballaram permission to conduct her research at our organisation.

If you have any questions or concerns, please feel free to contact our [redacted]

[redacted]

APPENDIX D: SURVEY COVER LETTER

DEAR SIR / MADAM:

I am Sholene Ballaram, a post-graduate student at University of KwaZulu-Natal. For the completion of my Master's in Pharmacy Practice degree, I am evaluating the knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in the community pharmacy. I am inviting you to participate in this research study by completing the questionnaire survey.

The following questionnaire survey will require approximately 10-15 minutes of your time to complete. There is no compensation for responding nor is there any known risk. To ensure that all information will remain confidential, please do not include your name. Copies of the project will be provided to my university lecturer. If you choose to participate in this project, please answer all questions as honestly as possible and submit / drop the completed questionnaires in the box provided in the pharmacy.

Participation is strictly voluntary and you may refuse to participate at any time. Thank you for taking the time to assist me in my educational endeavors. The data collected will provide useful information regarding patient care and customer satisfaction level. If you would like a summary copy of this study, kindly email me at the details provided below.

Completion and return of the questionnaire will indicate your willingness to participate in this study. If you require additional information or have questions, kindly contact me at below given contact details or my research supervisor, Professor Fatima Suleman on +27 31 260 7941 (direct) or email: sulemanf@ukzn.ac.za.

In addition, if you are not satisfied with the way this study is being conducted, you may report (anonymously if you so choose) any complaints to the university's Biomedical Research ethics committee on the details below.

RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
University of KwaZulu-Natal
Private Bag X 54001, Durban, 4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2602486 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Kind Regards

Sholene Ballaram
sholeneh@yahoo.com

083 777 2484

APPENDIX E: SURVEY FORM

SURVEY TO PARTICIPANTS

DEAR PARTICIPANT

Thank you for taking time to complete this survey.
Please cross the most appropriate box as shown in the example below

Example 1	Example 2

SECTION 1: DEMOGRAPHIC INFORMATION

1. Gender			Male	Female			
2. Marital status			Single	Married	Other		
3. Age			21 - 29	30 - 39	40 - 49	50 – 59	> 60
4. Race			Indian	White	Colored	Black	Other
5. Employment status			Unemployed	Employed			
6. Did you used antibiotics in the past 6 months?			Yes	No			
7. Do you work or study in the medical field?			Yes	No			
8. Method of payment			Cash	Medical Aid			
9. Personal health			Excellent	Very Good	Good	Poor	
10. Educational qualifications	Metric	Certificate	Diploma	Degree	Masters	Doctor	Other

SECTION 2: RESPONDENTS KNOWLEDGE ON ANTIBIOTICS

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
11. Different antibiotics are needed to cure different diseases					
12. Antibiotics are effective against bacteria					
13. Antibiotics can kill bacteria that normally lives on the skin and gut					
14. Antibiotics speed up the recovery from coughs and colds					
15. Antibiotics work on most coughs and colds					
16. Antibiotics are effective against viruses					
17. If you get side effects during a course of antibiotics, you should stop taking it					
18. If you get a skin reaction when using antibiotics, you should not use antibiotics again					
19. Antibiotics can cause an imbalance in the body's own bacterial flora					
20. The unnecessary use of antibiotics can increase the resistance of bacteria to them					
21. Antibiotics resistance is a worldwide problem					
22. Antibiotics use among animals can reduce the effects of antibiotics among humans					
23. Humans can be resistant to antibiotics					

APPENDIX E: SURVEY FORM

SURVEY TO PARTICIPANTS

SECTION 3: RESPONDENTS ATTITUDE TOWARDS ANTIBIOTICS USE

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
24. I always complete the course of treatment with antibiotics even if I feel better					
25. It is good to be able to get antibiotics from relatives or friends without having to see a doctor					
26. I prefer to be able to buy antibiotics from the pharmacy without a prescription					
27. I prefer to keep antibiotics at home in case there may be a need for it later					
28. If I feel better, I sometimes stop taking my antibiotics before completing the course of treatment					
29. I prefer to use antibiotics if I have a cough for more than a week					
30. When I have a sore throat, I prefer to use antibiotics					

SECTION 4: DOCTORS HABITS AND DOCTOR/PATIENT RELATIONSHIP

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
31. Pharmacists often tell you how to use antibiotics					
32. Doctors often take time to inform patients during consult how to use antibiotics					
33. I trust the doctor's decision if they decide not to prescribe antibiotics					
34. Doctors often prescribe antibiotics because the patient expects it					
35. Doctors often take time to carefully consider the need for antibiotics					

End of Survey

Thank You

APPENDIX F: SAMPLE SIZE CALCULATION

Sample Size Calculation:

The minimum number of subjects required for the study was calculated using the statistical formula for minimum sample size,

Where: N = Z2pq / d2

N = Minimum Sample Size

Z = A Confidence Level Of 95% (1.96 (Constant)

P = Measure of Prevalence = 92% (Abdulrahman et al., 2016)

Q = Opposite of P {1 – p = (1.0 - 0.92)} = 0.08

D = Precision Value at the Level Of 95% Confidence Interval = 0.05

Therefore, N = (1.96 x 1.96 x 0.08 x 0.92) / (0.05 x 0.05)

Minimum Sample Size = 113

18% Non-Respondent Value = 18 x 113 / 100

= 20.34

Therefore, 113 + 20.34 = 133.34 and approximated to 135

Sample Size = 135

APPENDIX G: SAJID SUBMISSION 253 ACKNOWLEDGEMENT EMAIL

****
Ref. No.: 253
Manuscript title: An evaluation of knowledge, attitude and behaviour amongst patients regarding antibiotic use and misuse in South Africa.
Journal: Southern African Journal of Infectious Diseases
****

Dear Sholene Ballaram, Fatima Suleman

The above manuscript, for which you are listed as a contributing author, has been received by the journal. Future communications regarding this manuscript will be sent to the corresponding author only, Sholene Ballaram.

If you need to contact us or the publisher about your manuscript for any reason, please be sure to quote the journal name and manuscript reference number 253.

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