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Exploring oral antibiotic prescription patterns for the management of dental conditions at two public health institutions in Pietermaritzburg, KwaZulu-Natal.

A dissertation submitted in fulfillment of the requirements for the degree of Masters in Medical Science (Dentistry) in the School of Health Sciences, University of KwaZulu-Natal.

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Exploring oral antibiotic prescription patterns for the management of dental conditions at two public health institutions in Pietermaritzburg, KwaZulu-Natal

Dr P. Ramnarain

A dissertation (Masters by research) submitted to the Discipline of Dentistry, School of Health Science, University of KwaZulu-Natal, Westville, for the degree of Masters in Medical Science (Dentistry).

This dissertation is presented in manuscript format. The presentation comprises five chapters, including the Introduction, Literature review, Methodology, Manuscript presentation (two articles) and finally the Conclusion and Recommendations.

This is to certify that the contents of this dissertation are the original work of Dr Prishana Ramnarain, carried out under my supervision.

As the candidate's supervisor, I have approved this dissertation for submission for examination.

_____

Professor Shenuka Singh

Date: 30 November 2020

DECLARATION

I, *Prishana Ramnarain*, hereby declare that:

1. The research reported in this dissertation, except where otherwise indicated, is my original work.

2. This dissertation has not been submitted for any degree or examination at any other university or college.

3. This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledges as a being sourced from other persons.

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Dr P. Ramnarain

DEDICATION

I dedicate this work to my Lord and my wonderful parents, without whom this achievement would never have been possible.

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MANUSCRIPTS ARISING OUT OF THIS STUDY FOR PUBLICATION

Two manuscripts emanated from this study, namely:

1. Public health care practitioners' knowledge, attitudes and practices towards oral antibiotic prescriptions for dental use in the Pietermaritzburg region, KwaZulu-Natal.

Authors: Prishana Ramnarain and Shenuka Singh
Submission: Submission to *South African Dental Journal*

2. Oral antibiotic prescription patterns for dental conditions at two public sector hospitals in Pietermaritzburg, KwaZulu-Natal.

Authors: Prishana Ramnarain and Shenuka Singh
Submission: Submission to *South African Dental Journal*

ABSTRACT

Introduction:

Oral antibiotics are typically prescribed for the management of dental conditions such as acute odontogenic and non-odontogenic infections, and as prophylaxis for patients such as those with infective endocarditis or placement of joint prosthesis. While these measures are intended to limit the spread of possible infection that could occur as a result of oral surgical procedures, very little is known about antibiotic prescription practices and trends for dental purposes, specifically in the public sector in KwaZulu-Natal.

Study Aim and Objectives:

The aim of this study was to determine patterns of oral antibiotic prescription for the management of dental conditions at public health facilities in the Pietermaritzburg complex so as to create practitioner awareness of the need for the judicious use of antibiotics. The study objectives were to determine patterns of oral antibiotic prescription for dental patients at the identified public health institutions; understand dental and medical practitioners' knowledge, attitudes and practices related to antibiotic prescription for dental conditions; and ascertain public health pharmacists' perspectives on these patterns of oral antibiotic prescription.

Method:

This study was divided into 3 phases and a combination of quantitative and qualitative data was collected. The research sites comprised two purposively selected public sector hospitals located in the Pietermaritzburg complex of UMgungundlovu district (Institution A and B respectively). In Phase 1, data collection comprised a retrospective clinical record review to determine oral antibiotic prescription patterns for dental purposes (n=720) at the two identified research sites during the period March 2012- July 2018.

For Phase 2, a cross sectional study design was used. Purposive sampling was used to select the study sample comprising medical and dental practitioners (Group 1, n=123) and pharmacists (Group 2, n=25). A separate self-administered questionnaire was developed for each group.

The questionnaires comprised open and closed ended questions that were designed to assess the identified health care workers' knowledge, attitudes and practices related to oral antibiotic prescriptions or dispensing for dental use; perceptions of therapeutic duplication of antibiotics, availability of laboratory information and recommendations for the improvement of oral antibiotic prescriptions. A Likert scale format was used to elicit responses such as 1 (Strongly agree), 2 (Agree), 3 (Not sure), 4 (Disagree), 5 (Strongly Disagree).

For Phase 3, the qualitative data was derived from focus group discussions held with purposively selected health care practitioners at each institution (Institutions A and B). The study sample included health care practitioners (medical and dental practitioners) and pharmacists, involved in prescribing or dispensing oral antibiotics for dental purposes. Two focus-group discussions (FGDs) comprising six people per group at each research site, were set up.

The quantitative data was analyzed using the Statistical Package for Social Sciences software (SPSS Version 25 ^{R}). Univariate descriptive statistics such as frequency and mean distribution and inferential techniques such as Pearson's Chi-Square test were conducted to determine a possible relationship between the independent and dependent variables. A p-value of 0.05 was established as being significant. The internal consistency of the questionnaire, according to the Cronbach alpha score, was 0.68. Validity of the questionnaire was maintained.

The qualitative data (obtained from the focus group discussions) were analyzed using thematic analysis. All emergent themes were further analyzed to gain a better understanding of participants' perspectives related to oral antibiotic prescriptions for dental conditions. Credibility, conformability, transferability and dependability of the collected data were maintained to enhance rigor and trustworthiness in the qualitative component of the study.

Results:

The results of the retrospective chart review indicated that dental abscesses (n=479; 66%) were the most common dental condition for which oral antibiotic therapy was prescribed. There were inconsistencies in the pattern of oral antibiotic prescription for dental conditions between the two public health care institutions. At Institution A, antibiotic therapy was prescribed for dental

conditions such as trismus (n=13; 6%), soft palate swelling (n=9; 4%), fibrous epulis (n=6; 3%) and acute herpes (n=2; 1%). Interestingly, oral antibiotics were not prescribed at Institution B for the same dental conditions. Antibiotic therapy was prescribed for eruption pain (n=4; 1%) and in cases where patients did not bring their inhaler for asthma treatment (pump) (n=3; 1%) at Institution B.

For the self-administered questionnaire, the response rate for Group 1 (medical and dental practitioners was 77.5% (n=93). The response rate for Group 2 (pharmacists) was 92% (n=23). The majority of participants in this study (n=72, 77.4%) indicated awareness of an Antibiotic Stewardship Programme in their respective institutions yet 42 participants (45%) were not sure on whether the programme was active. More than half of the study participants (n=60, 64.5%) indicated referring to the Standard Treatment Guidelines *'some times'* when prescribing antibiotics. The majority of participants (n=72, 77.4%) indicated that they would prescribe antibiotics for orofacial swellings. Almost 33 participants (35.4%) stated that they would prescribe antibiotics for irreversible pulpitis. Almost 31 participants (88.9%) from Institution A and 40 (75%) from Institution B indicated prescription of antibiotics for pericoronitis. Similarly, 27 participants (76.9%) Institution A and 14 (72.1%) from Institution B would prescribe antibiotics for periodontitis. The majority of participants (n=80, 86%) agreed that there was need to improve antibiotic prescription processes.

With regards to the prescription of oral antibiotics as prophylaxis for the prevention of infections such as infective endocarditis, the following responses were obtained. Almost 13% of respondents from Institution A reported prescribing PEN VK 250mg daily followed by Penicillins, Augmentin, Benzyl Penicillin, Clindamycin and Kefazol while 23% of respondents from Institution B indicated prescribing Amoxicillin 2g stat dose one hour before a dental procedure followed by Pen VK, Penicillin, Clindamycin, Benzyl Penicillin oral and intravenous, Benzatime Penicillin, Penicillin G and Vancomycin.

More than two thirds of study participants in Group 2 (n=18; 78%) perceived a correlation between the dental condition and the antibiotic prescribed thereof. Participants (n=17; 73.9%)

also believed that oral antibiotics were sometimes prescribed without any clinical indication.

The following themes emerged from qualitative data analysis (focus group discussions): inconsistencies in antibiotic coverage for dental-related clinical management between the two sites. There was no consensus among research participants on the need for diagnosis laboratory testing to improve antibiotics prescription. However, all participants agreed that there is a need to improve antibiotic prescription in their various hospitals.

Discussion:

Overall the results of the study indicated inconsistencies in antibiotic prescriptions for dental conditions. This suggests that over and under prescribing may be occurring in the identified clinical settings. The most common dental infection in this study, requiring antibiotic therapy was dental abscesses (66%). While the recommended treatment of choice for the management of periapical abscess, periodontitis abscess and localized dentoalveolar abscess is incision and drainage (Kuriyama *et al.* 2005), Lalloo *et al.* suggested that practitioners might be following some personal or ad-hoc criteria in selecting when to prescribe antibiotics or not (Lalloo *et al.* 2017). Peric *et al.* also reported that antibiotics were prescribed as a precaution because of 'uncertainty concerning the diagnosis, patient's expectations, unavailability of dental services and in short- term cases where there is insufficient time for doing any treatment' (Peric *et al.* 2015:111). Participants in this study also prescribed antibiotics for the treatment of alveolitis (dry socket) (15%). This finding is supported by a previous study done in England, Kuwait and Turkey where almost half of the study population (dentists) reported that they would prescribe antibiotics for dry socket treatment (Dar-odeh *et al*. 2010).

Antibiotics were also prescribed for systemic conditions (10%) in this study. This finding is consistent with previous reviews that concluded patients with low immunity may be at higher risk of infection (Sidana *et al.* 2017). Interestingly, a pattern of antibiotic prescription emerged based on the clinical site where the respondent was located. According to Standard Treatment Guidelines 2018, the prescribed regimen should be as follows: Amoxil, oral, 2g one hour before

the procedure. Respondents from Institution B appeared to adhere to the Standard Treatment Guidelines. This difference in prescription pattern for the same health condition, which was dependent on the clinical site, was an interesting observation. Additionally, only 65% of respondents referred to the Standard Treatment Guidelines. In contrast, a previous study reported that only 45% of practitioners adhered to the Standard Treatment Guidelines and Essential Medicines List in Primary Health Care settings in South Africa (Gasson 2018). In a recent South African study, it was also reported that dentists were aware of the treatment guidelines but few followed the recommendations for antibiotic prophylaxis (Mthethwa *et al.* 2018). More research is thus required to further understand these differences across clinical settings.

On the other hand 78% of pharmacists perceived a correlation between the dental condition and the antibiotic prescribed for the dental condition. This is a significant finding as a previous study has shown that when the treatment guidelines are adhered to, the resistant micro-organisms reduce in numbers (Ntsekhe *et al.* 2011).

Gutierrez *et al.* therefore, highlight the need for professional agreement and consensus building with regards to the conditions for antibiotic prescriptions (Gutierrez *et al.* 2006). Such efforts are also needed in a South African context to facilitate practitioner consensus building and ensure consistency in antibiotic prescription. Antimicrobial Stewardship and infection and prevention control teams could provide opportunities to augment prescribing practices and streamline this process (South African National Department of Health 2015). Additionally, there is need for continuing professional development so as to better equip health practitioners with updated knowledge on antibiotic prescription for dental conditions (Rocha-Periera, Lafferty, Nathwani 2015; Lee *et al.* 2015).

Conclusion:

The results indicated that health care practitioners reported inconsistent knowledge, attitudes and practices related to antibiotic prescription patterns. The study showed that there was inconsistency in antibiotic therapy prescription for dental conditions at the two public health institutions. There is a need for consensus building among health professionals and better guidance for antibiotic prescription in the management of dental conditions.

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LIST OF ABBREVIATIONS

ABR	Antibiotic resistance
AMR	Antimicrobial resistance
AMRRU	Antimicrobial Resistance Reference Unit
AMU	Antimicrobial usage
DDD	Usual dose of an antimicrobial treatment for on patient for one day.
DID	DDD for every 100 patients per day for the total population.
EDRU	Enteric Disease Reference Unit
ES	Electronic Surveillance
ESKAPE	Enteroccocus Faecium, Staphylococcus Aureus, Klebsiella Pneumoniae, Actinetobacter Baumanni, Pseudomonas Aeruginosa,Enterobacter species
FAO	Food and Agriculture Association
GAP	Global Action Plan
GERMS-SA	Group for Enteric, Respiratory and Meningeal Disease Surveillance
GLASS	Global Antimicrobial Surveillance System
LARS	Laboratory-based Antimicrobial Resistance Surveillance
LMIC	Lower- and- Middle- income- countries
HAI	Hospital acquired infection
HAST	HIV, AIDS, STIs and TB
HPTC	Hospital Pharmaco-therapeutics committee
NAFDAC	National Agency for Food and Drug Administration and Control

NASF	National Antibiotic Surveillance Forum
NICD	National Institute for Communicable Diseases
NHLS	National Health Laboratory Service
SAASP	South African Antimicrobial Stewardship Programme
SASCM	South African Society for Clinical Microbiology

CHAPTER 1: INTRODUCTION

1.1. Introduction

The World Health Organization outlined that antibiotic resistance occurs when the micro-organisms change in ways that may render antimicrobial agents ineffective against infections (National Institute for Health and Clinical Excellence 2016). Antibacterial resistance emanates when the consumption of antibiotics expands the selective pressure on the bacterial growth (Torres 2019). This will result in the elimination of the most susceptible bacteria while the majority of resistant bacteria will proceed to grow into an antibiotic resistant colony (Torres 2019). The effects of antibiotic resistance on the clinical outcomes due to unsuccessful treatment or through the development of severe infections, needs to be explored in South Africa (Crowther-Gibson *et al.* 2011). The HIV /AIDS epidemic, injuries from trauma and violence and non-communicable diseases, such as tuberculosis and maternal, newborn and child health creates a fourfold burden of diseases in South Africa (Schellack *et al.* 2017; Crowther-Gibson *et al.* 2011). HIV /AIDS accounts for 26% of the deaths amongst South Africans from all age groups followed by 7% of Ischemic heart disease, strokes, and then Tuberculosis and domestic violence of which each account for 6 % of deaths in South Africa (Crowther- Gibson *et al.* 2011). Given the associated oral manifestations of HIV infections, it is important to recognize the impact of systemic health conditions on oral health status and overall well-being (Boyles *et al.* 2017). Bacterial resistance is due to the misuse of antibiotics and this has caused bacterial resistance to the extent that it has now led us into a post antibiotic-era (Boyles *et al.* 2017). Almost 80% of human antibiotic consumption is involved with the management of diseases at primary health care level (Gasson 2018).

Globally, there is also an annual increase in the prescription of antibiotics for dental care (Haliti *et al.* 2017). It is thus important to examine current trends in antibiotic prescriptions so as to address the growing concerns around associated bacterial resistance linked to over-prescription. It is necessary to assess dental conditions for which antibiotics are indicated, including the types of medications prescribed by dental professionals so that antibiotic prescription strategies and preventive programs could be developed to address antibiotics resistance (Huang and Owen 2012; Peric *et al.* 2015). Likewise, it is important to also determine the frequency at which medications are prescribed and compliance with set appropriate prescribing protocols (Huang and Owen 2012).

Antibiotic prescription by dentists for the treatment and prevention of the dental infections has limited indications because majority of dental and periodontal diseases could be effectively managed by prevention techniques or operative interventions (Dar-Odeh *et al.* 2010). Interestingly, dentists still prescribe antibiotics for the most common dental infections such as pulpitis and periapical periodontitis (Dar-odeh *et al*. 2010). Apical periodontitis is a polymicrobial infection in which the bacteria implicated could become resistant to the available antibiotics (Agnihotry *et al*. 2016). If the host response system is poor, systemic antibiotics are the only adjunct to endodontic treatment (Agnihotry *et al*. 2016).

Similarly, the appropriate management for "irreversible pulpitis" is the urgent removal of the pulp tissue from the infected tooth. Despite this general consensus on the management of irreversible pulpitis, antibiotic therapy is still prescribed for this condition (Agnihotry *et al.* 2016). These are some examples of the use or abuse of antibiotics for dental conditions despite the availability of information indicating other optimal methods of clinical intervention. From a dental perspective in South Africa, antibiotics are commonly prescribed for orofacial and dental infections (Huang and Owen 2012).

To address antibiotic prescription trends in general, several strategic directions were adopted in South Africa. 'In May 2014, South Africa pledged its commitment to The World Health Organization to combat antibiotic resistance and adopted to construct the National Action Plan (NAP) for Antimicrobial Resistance' (South African Department of Health 2017:6 ;Food and Agriculture Organization 2016). In order to support interventions that would combat antibiotic resistance in South Africa, the Antimicrobial Resistance National Strategic Framework, 2014-

2024 was developed and launched in October 2014 to the relevant sectors that are involved in human and animal health, agriculture, science and technology (Food and Agriculture Organization 2016). The National Strategic Framework 'comprises five interlinked strategic objectives that include rational use of antimicrobials and improved patient outcomes, appropriate diagnosis through diagnostic stewardship to enhance antibiotic surveillance, ensure appropriate application of antibiotics through Antimicrobial Stewardship Program and lastly to intensify infection prevention and control' (Matsoso 2015:18). This framework thus highlights South Africa's approach to control antimicrobial resistance. Such efforts reiterate the need for careful deliberations and the judicious prescription of antibiotics by health-care practitioners (Aslam *et al*. 2018). Other available guidance documents include the Standard Treatment Guidelines and the Essential Medicines List (Mthethwa *et al*. 2018).

A recent report further suggested that 'only 45% of health care practitioners adhered to the Standard Treatment Guidelines and the Essential Medicines List for primary health care in South Africa in 2014 and that adherence is significantly comparable between different facilities and for the management of various infections' (Gasson 2018:307). 'The lack of adherence was evident through findings such 'unknown diagnosis, inappropriate choice of antibiotic, incorrect dosage, incorrect indication for the antibiotic prescription and the incorrect duration of antibiotic therapy' (Gasson 2018). The implications are that there could be poor adherence to these identified guidelines (Gasson 2018).

From a global perspective, the COVID-19 pandemic has added another dimension to challenges in antibiotic prescriptions given the limited access to in-person dental treatment (that is, limited physical access) during the outbreak (Shah *et al*. 2020). The extent to which the pandemic has impacted on antibiotic prescription rates and possibly contributed to antibiotic resistance, needs to be further explored (Shah *et al*. 2020).

1.2. Problem Statement

From a South African perspective, there is limited published evidence in understanding prescription trends and practitioner attitudes towards oral antibiotic prescription, specifically in KwaZulu-Natal. Despite the availability of the Standard Treatment Guidelines and the Essential Medicines List for South African Health practitioners and the fact that dental schools have been

teaching according to the British or American guidelines, there is insufficient available information on clinical protocols developed for guiding prescription of antibiotics for dental conditions. There is also insufficient information available on clinical protocols that have been developed for guiding antibiotic prescription for the management of dental conditions. There are limited available statistical records on antibiotic prescription patterns in the public oral health sector. There is also paucity of data on the availability of antibiotics for dental use and access to these services. The extent to which clinical guidance support is available for health practitioners that manage dental conditions, remains unclear.

Overall there is an unclear picture of prescription trends on antibiotics for dental conditions in KwaZulu-Natal. The possible impact of the current trends in dental management on perpetuating antimicrobial resistance is largely unknown and the implications are that oral health policy and planning are occurring in the absence of sound epidemiological data.

1.3. The significance of the study

This study will attempt to contribute to the existing body of knowledge through better understanding of prescription trends and practitioner attitudes towards antibiotic prescription in the identified geographic region of the province. The study will attempt to provide much needed data to construct a clearer picture of antibiotic prescription patterns in the identified research sites. The oral health sector is largely overlooked in terms of the development of appropriate antibiotic prescribing protocols. Such data could contribute to practical guidelines to aid in appropriate antibiotic prescriptions for dental conditions (Chetty *et al.* 2019). Additionally, the study findings could guide oral health policy and planning in the province related to the judicious use of oral antibiotics for dental use.

Although the results of the study are limited to the research sites, the study could nevertheless create awareness on the value of monitoring antibiotic prescription trends in the province. Such awareness could strengthen efforts such as programmes related to Antimicrobial Resistance National Strategic Framework. There are also opportunities for the early identification of at-risk populations for antibiotic resistance.

Overall, this study could contribute towards strengthening the health care system and the need for proper guideline adherence through audits. The goal of the Antimicrobial Resistance National

Strategic Framework is to ensure that there is continuity in the ability to prevent infectious diseases with the consumption of safe and effective antibiotics that are of good quality, that are recommended in a safe and appropriate manner and are available to people who require them. Continued effort is required by all oral health care practitioners to evaluate their antibiotic prescribing behavior for the appropriateness and effectiveness in order to combat antibiotic resistance (Fluent 2017). Dentists should aspire to reduce antibiotic prescriptions, to improve the way they prescribe antibiotics and all the prescriptions should be done with the correct indications and not under the influence of patients (Sanderson 2019). Strong knowledge through surveillance and research are significant. In addition, qualitative study approaches can be used to explore reasons for practitioners' non-compliance or poor adherence to guidelines on antibiotic prescriptions (Ncube *et al.* 2017).

Educating patients on the spread of antibiotic resistance and its consequences should form an integral part of the dental practitioner's responsibility towards combating antibiotic resistance (Sanderson 2019).

There are also opportunities to work in multidisciplinary teams in respect of creating antibiotic awareness education programmes so that there is a multi-pronged approach to addressing antibiotic resistance. Simultaneously, there should be consensus, consistency and standardization among health practitioners for the indications of oral antibiotic prescriptions for dental prescriptions.

1.4. Research questions

1. What are the trends in oral antibiotic prescription among dental and medical practitioners in the public sector in the Pietermaritzburg complex?

2. What prescription protocols do health care practitioners use for the management of dental conditions?

3. Are practitioners aware of the National Strategic Framework on Antimicrobial Resistance and the Essential Medicines List or the Standard Treatment Guidelines? To what extent are these guidance documents used for the prescription of oral antibiotics for dental conditions?

1.5. Aim

The aim of this study was to determine the patterns of oral antibiotic prescriptions for the management of dental conditions at two public health institutions in the Pietermaritzburg complex so as to create practitioner awareness of the need for the judicious use of oral antibiotics.

1.6. Objectives

The study objectives were:

1. To determine the patterns of oral antibiotic prescriptions for dental patients in the identified public health institutions by means of a retrospective chart review.

2. To determine dental and medical practitioners' knowledge, attitudes and antibiotic prescription practices for the management of dental conditions by means of a self-administered questionnaire.

3. To ascertain pharmacists' perspectives on the patterns of oral antibiotic prescription rates for dental use by means of a self- administered questionnaire.

4. To explore health practitioners' perspectives (medical and dental practitioners, and pharmacists) on oral antibiotic prescription patterns for dental patients by means of a focus-group discussion.

1.7. Chapter Outline (Format for the dissertation)

The study is presented in five chapters as outlined below:

Chapter 1: Introduction

The first chapter outlines the trends in the practice and patterns of antibiotics prescription rates for dental conditions involving health care practitioners in the public sector. The existent shortfalls which need to be addressed are framed explicitly in the study problem statements. The

purpose and research questions are also included in this chapter. The study's aim and objectives are outlined.

Chapter 2: Literature Review

This chapter outlines possible reasons for the increased antibiotic prescription patterns and antimicrobial resistance among South Africans and at a global level. It also describes the perceptions of health care practitioners and their response to antibiotic prescriptions for dental conditions. This chapter focuses on global challenges as well those within South Africa. The different levels of care are explored to identify their contribution to the increase of antimicrobial resistance. The chapter also outlines the various systemic conditions and dental conditions requiring antibiotic prophylaxis as well as the treatment options. The Antimicrobial Resistance Strategic Framework is reviewed together with the South African Antibiotic Stewardship Programme and the surveillance methods that are available in South Africa and worldwide to measure antibiotic resistance. Practitioner adherence to the Standard Treatment Guidelines is explored and differentiation is made between the guidelines from the Standard Treatment Guidelines and the National Institute for Health Care and Excellence. The scope of oral health care in the public sector is identified. The microbiology of odontogenic infections, the inflammatory process and the host response system to respond to the mechanism of action of the antibiotics prescribed are highlighted.

Chapter 3: Methodology

This chapter describes the steps involved in designing the study and highlights the research site, study population, sample size, sampling process, including the selection criteria. The data-collection methods together with the research instruments and data analytical processes are described. All ethical considerations for the study are identified and described.

Chapter 4: Manuscript presentations

The fourth chapter highlights the manuscripts developed. These two articles are intended for submission to a peer-reviewed journal.

Chapter 5: Conclusion and Recommendations

The last chapter summarizes the quantitative and qualitative results obtained from this study according to the study aim, objectives and the research questions. Recommendations are made for the prescriptions of antibiotics for dental conditions.

1.8. Summary

This chapter highlighted the trends of antibiotic prescription and patterns for dental conditions amidst the rise in antimicrobial resistance. The purpose of the study and the research questions, together with the aim and objectives, were outlined. The next chapter will explore the challenges associated with antibiotic resistance, the development and implementation of the National Strategic Framework on Antimicrobial Resistance, surveillance methods for antibiotic resistance worldwide, the status of the Antibiotic Stewardship Programmes as well as adherence to the Standard Treatment Guidelines and Essential Medicines list for the various systemic conditions and dental conditions that may require antibiotic treatment.

CHAPTER 2: LITERATURE REVIEW

Preamble

The literature review focused on identifying possible reasons for antimicrobial resistance and prescription trends among health care practitioners in South Africa and internationally. An overview of the challenges facing the health care system in terms of antimicrobial resistance and antibiotics prescription trends was highlighted by the World Health Organization as a public health concern. A comprehensive and thorough search was conducted through several dental, medical and pharmaceutical journals and search engines online so as to have a sound background on the content of the matter related to antimicrobial resistance and antibiotic trends in prescription patterns and practices among health care practitioners in South Africa.

2.1. Introduction

Antimicrobial resistance threatens the safety of South Africans as it is a multi-faceted and public health concern (South African National Department of Health 2015). The burden of infectious diseases in developing countries is heightened by the insufficient and expensive supply of antibiotics to treat infectious diseases (Watkins *et al.* 2019).

In South Africa, surveillance on antimicrobial resistance is vital due to the vast number of people that are vulnerable to HIV/AIDS and tuberculosis (Torres 2019). The English Surveillance Program on Antimicrobial Utilization and Resistance (ESPAUR) in 2004 reported that antibiotic prescription increased in England on a yearly basis and the resistance varied across England (Thornhill *et al*. 2016). The overall rate of antibiotic prescription declined in British Columbia and Canada but there was an increase in the prescription rates by dentists (Marra *et al.* 2016). A study conducted indicated that during the period 2011-2016, the prescriptions for dental infections accounted for 6-8 percent of the total prescription in Primary care in England, Scotland, Norway and Sweden (Smith *et al*. 2020). Medical physicians are accountable for 80 percent of the antibiotics prescribed in the United Kingdom (Sancho-Puchades *et al.* 2009). Dental practitioners are accountable for 10 percent of the antibiotics prescriptions in the UK public health pharmacies (Elaouafkaoui *et al.* 2016). Resistance among oral commensals in the oral cavity that are associated with dental infections is identified as an international problem according to studies done in Germany, Taiwan and Brazil as these countries found that resistance

exists in specific oral flora that are frequently related to distinct dental infections (Sancho-Puchades *et al*. 2009). However, another study further revealed that most dentists in Kuwait prescribed antibiotics when appropriate as opposed to the previous study that showed that many dental practitioners prescribed antibiotics for pain control and for reversible pulpitis (Maslamani and Faraj 2018). Most dental practitioners used empirical treatment by utilizing broad spectrum antibiotics without culture testing to help correctly diagnose diseases and rationally prescribe antibiotics (Sancho-Puchades *et al.* 2009). Consequently, antibiotic prescriptions are issued for a variety of dental infections, even when these not required (Sancho-Puchades *et al.* 2009).

With restricted access to oral health care during the COVID-19 pandemic, there was a 60% increase in prescriptions by dentists in London between April 2020 and July 2020 compared to the same three-month period a year earlier (Shah *et al*. 2020) while the lowest increase was in South West England with an increase of 10% in the same period (Shah *et al*. 2020).

A study done in Australia showed that even though dentists had adequate knowledge about antibiotic prescriptions, over-prescription still occurred and, in a study conducted in Switzerland, dental practitioners were wary about antibiotic prescriptions, however, there was inconsistency on when to prescribe antibiotics (Sweeney *et al.* 2004). English and Scottish dental practitioners avoided antibiotic prescriptions for non-clinical factors such as convenience and demand that may be warranted by the patient's social status because they considered these as unscientific reasons for antibiotic prescription (Dar-Odeh *et al*. 2010).

In a study done in Zagreb, the reasons for prescribing antibiotics were *"just in case",* because of uncertainty concerning the diagnosis, the patient's expectations, the unavailability of dental services and in short- term cases where there is insufficient time for performing any treatment (Peric *et al.* 2015). Dental patients sometime exerted coercion on dentists to get antibiotic prescription and there are also reports that patients could self-medicate (Dar-odeh *et al.* 2010). This is a common practice in some developing countries (Dar-odeh *et al.* 2010). In Europe, it was discovered that patient's self-prescription was high in the eastern and southern parts of the continent (Dar-odeh *et al.* 2010). Patients frequently self-medicate therefore, pharmacists are also well placed to influence the practice of antibiotic prescription with symptomatic treatment and to offer advice on the self-limiting nature of the treatment (Brink 2014). Pharmacists can also reinforce a delayed prescription for antibiotics where applicable (Brink 2014), therefore,

when providing advice to a patient, it is important to provide information that will attach significance to a patient (Dar-odeh *et al.* 2010).

A study done in Spain in 2008, showed that the prescriptions for antibiotic prophylaxis for the prevention of local odontogenic infection were not correctly implemented (Sancho-Puchades *et al.* 2009). A survey done in Kosovo evaluated the prescription of antibiotics in the primary dental care of the health system (Haliti *et al.* 2017). Six individual antibiotics were identified in this survey (Haliti *et al.* 2017). Co-Amoxiclav followed by Amoxicillin was found to be the most frequently used antibiotic (Haliti *et al.* 2017). It was found that a high prescription rate was not rational in primary health care in Kosovo because there was no prior sensitivity testing done to obtain a diagnosis and antibiotic therapy was used empirically (Haliti *et al.* 2017). This may have a negative impact on the bacterial resistance profiles (Haliti *et al.* 2017). This could result in a generation of new bacterial resistances and facilitate adverse drug reactions that could contribute to an increase in the number of opportunistic infections (Sanchos-Puchades *et al.* 2009). Inappropriate prescribing and inappropriate dispensing leads to the misuse and over use of antibiotics if health care professionals fail to update information and cannot diagnose infections correctly or yield to patient pressure to prescribe antibiotics and benefit financially from the supply of medicines (World Health Organization 2015).

The challenges highlighted at the 68th World Health Organization Assembly, Global Action Plan on Antimicrobial Resistance in 2015, were concerns that the medical practitioners in third world countries were likely to prescribe “last resort” and expensive remedies that were not readily available and could have adverse effects (World Health Organization 2015). The overuse of antibiotics is contributing to antimicrobial resistance internationally and a paradigm shift towards the appropriately selected antibiotic for humans, animals and the environment are considered essential to preserve the efficacy of available antimicrobials (South African National Department of Health 2015). The potential effects of antibiotic resistance on the environment may be of concern through the misuse and overuse of antimicrobials (World Health Organization 2015). Antimicrobial resistance can affect all patients and their families (World Health Organization 2015). International alliances should be reinforced as a collaborative action that shows responsibility from all sectors such as health care sector, human, animal and agriculture sectors (South African National Department of Health 2015).

A review commissioned by the United Kingdom Government in 2014 predicts the death of ten million people from infectious diseases by 2050 if a solution to the antimicrobial resistance is not found (Fleck and Humphrey 2016). This global threat requires a collaborative approach from all countries to prevent, detect, and respond to threats of antimicrobial resistance. Managing antibiotic resistance is prioritized by the World Health Organization, thus the Global Action Plan on Antimicrobial Resistance was endorsed by the organization in 2015 (World Health Organization 2015). The establishment of the Global Action Plan was to ensure prevention and that infectious diseases were treated with more suitable antibiotics (World Health Organization 2015). The Antimicrobial resistance Challenge at the United Nations General Assembly includes a five-year commitment to monitor antibiotic prescription and consumption, environmental and personal hygiene, vaccinations, the implementation of Infection Prevention Control, therapeutics and diagnostics. This worldwide effort requires effort from the public sector, private sector and non-governmental organizations to implement policies that enhance strategies against antibiotic resistance. Antimicrobial resistance needs to be highlighted in the Agenda for Sustainable Development Goals in order for the Sustainable goals to be achieved by 2030.

A study showed a decline in antibiotic prescriptions since 2011-2016. This suggests that antibiotic stewardship initiatives are having a positive effect on decreasing antibiotic prescription trends in countries such as Sweden, England, Norway and England (Smith *et al*. 2020).

Global Antimicrobial Surveillance

The Global Action Plan on Antimicrobial Resistance requires the reinforcement of four essential areas such as Infection and Prevention Control, awareness and understanding, monitoring and surveillance and sustainable research and development towards the post–antibiotic era (Sanderson 2019). World Health Organization stated that the Global Action Plan (GAP) for Antimicrobial Resistance (AMR) in combating antimicrobial resistance involves the “One Health” initiative because it is a unifying effort for multi- disciplinary sectors from all levels of organizations to obtain the ideal care to all sectors of human health, veterinary health and environmental health to make up the “One Health” triad (South African National Department of Health 2017). This applies to multi-faceted teams to answer complex issues faced by the public health care sector (South African National Department of Health 2017).

The Global Antimicrobial Surveillance System (GLASS), established by World Health Organization in 2015 reveals an extensive degree of antibacterial resistance to a vast majority of progressive bacterial infections in indigent countries (World Health Organization 2018). GLASS will prioritize information that is derived from each country in order to sanction a comprehensive description in the shift of antibacterial resistance profiles (WHO 2018). In June 2017, The World Health Organization developed the AWaRE Tool to contain rising resistance and to make antibiotic use safe and more effective when following the Essential Medicines List (WHO 2019). The Access group includes 1st and 2nd line treatments for common infections. For instance, Amoxicillin for Pneumonia (South African National Department of Health 2017). The Watch group highlights the list of antibiotics that should be minimized to prevent the onset of resistant strains. Such efforts include the use of Ciprofloxacin to treat upper respiratory infections such as bacterial sinusitis or bacterial bronchitis (South African National Department of Health 2017). The Reserve group comprises of last resort antibiotics such as Cephalosporins, which are used in life-threatening infections due to multi-drug resistant bacteria (South African National Department of Health 2017). The various methods of surveillance are outlined in Table 2.

The National Surveillance on Antimicrobial Resistance is expected to report on the outcomes of sensitivity test and the course of shift in the resistance to antibiotics for specific bacteria that cause life-threatening infections across every level of the health care sector (South African National Department of Health 2015). The surveillance methods (Table 2) are limited to a minority of specific health facilities and do not reflect Antimicrobial Resistance throughout South Africa (Bamford *et al.* 2011). It is unfeasible to differentiate and evaluate the course of Antimicrobial Resistance because of the widespread approaches that are involved in the monitoring of Antimicrobial Resistance (Bamford *et al.* 2011).

2.2. COVID-19 Pandemic and Antimicrobial resistance

The COVID-19 pandemic has shown that dental practitioners are at the highest risk of transmitting and contracting the Corona virus due to various routine dental procedures that have the potential to generate aerosols (Dar-odeh *et al.* 2020). It should be noted that dental practice has a role to play ‘in tackling antibiotic resistance by reducing unnecessary antibiotic prescriptions’ (Shah *et al*. 2020: 602). Likewise, published evidence suggests that over-

prescription of antibiotics for dental use occurred prior to the onset of the COVID-19 pandemic (Shah *et al.* 2020). Almost 80 percent of prescriptions in the United Kingdom and United States were deemed unnecessary and not in accordance with the guidelines (Shah *et al*. 2020).

During the pandemic, there was restricted access to oral health care dental practitioners in Jordan resorted to social media professional groups that discussed oral infections and antibiotic prescribing (Dar-odeh 2020). The main goal was to provide treatment of the infection by prescribing an appropriate antibiotic (Dar-odeh *et al.* 2020).

In England, in 2011, a trend in antibiotic prescription was reported but with restricted face to face consultations during the COVID-19 pandemic, dental practitioners were instructed to approach oral health care through advice, prescribe analgesics and antibiotics appropriately for the remote management of dental conditions (Shah *et al.* 2020).

From a South African perspective, there are no specific guidelines, to our knowledge, that South African dental practitioners could refer to during the COVID-19 pandemic (Koutras *et al*. 2020).

2.3. South African challenges

There were four noted national level records of outbreaks in antimicrobial resistance (Ekwanzala *et al.* 2018). The following was identified by the National Institute for Communicable diseases: Methicillin-resistant Staphylococcus aureus in 2010, Klebsiella pneumonia (2010-2012), Vancomycin-resistant Enterococci in 2012 and Carbapenemase producing bacteriaceae (Ekwanzala *et al.* 2018). Antimicrobial infections were previously sufficiently managed with first line antibiotics with preference of a narrow spectrum antibiotic but it is becoming difficult to manage now and such is evident in the case of drug resistant Tuberculosis (South African National Department of Health 2015). The antimicrobial resistant bacteria are increasing in and this is contributing to more infections that are complicated and costly to manage (Matsoso 2015).

With regards to the development of new antibiotics, those that target ‘gram positive bacterial infections’ are licensed for consumption in South Africa, however, ‘there will be no advanced antibiotics anticipated for treatment against gram negative bacterial infections for the foreseeable future’ (Wasserman 2014:5). The data obtained from the South African laboratory surveillance for the period of 2012-2014 reveal that *Escherichia Coli* resistant to Fluoroquinolone is at 27%

over during this period (Matsoso 2015). It was stated that antimicrobial surveillance data should be collected by all laboratories by province and facility (Matsoso 2015). Each provincial department has been tasked to implement plans against the National Antimicrobial resistance framework strategy (Matsoso 2015). In a study done by Boyles *et al. 2017*, over a five-year period from 2012-2015 at the Groote Schuur Hospital, it was found that although the laboratory costs increased by 8, 6%, the consumption of antibiotics reduced by 19, 6% through awareness, education and opting for Intravenous antibiotics with better patient compliance (Boyles *et al.* 2017). Revenue should be invested in Infection Prevention Control and Quality Improvement to improve the safety of patients in relation to the management of bacterial infections by reducing the duration of hospital admissions which is currently jeopardizing many health care facilities in South Africa (Boyles *et al* .2017).

There is a demand for precise and clinically evident guidelines for the prescription of antibiotics to decrease the likelihood of antibiotic resistance as it is evident that antibiotic prescription patterns do not seem to apply to a cogent set of criteria for antibiotic prescription (Lalloo 2016).

2.4. Situational analysis: Pietermaritzburg

Pietermaritzburg is the second largest city in the province of KwaZulu-Natal. It falls within the boundaries of the Msunduzi Municipality. It was founded in 1838. The current population is estimated to be 618, 536 from the statistics done in 2011 (Statistics SA 2011). There is a population growth of 1, 12 percent each year (Statistics SA 2011). There are three levels of health care services provided at each of the public health institutions, Northdale Hospital, Edendale Hospital and Greys Hospital that comprise the Pietermaritzburg complex while dental services are also provided at Bruntville clinic, Umgeni clinic as well as three mobile clinics that travels further on as far up to Mooi River (KwaZulu-Natal Department of Health 2018). The estimate number of patients managed for dental treatment in the Pietermaritzburg complex over a five-year period from March 2012 till July 2018 is 181,097 dental patients (KwaZulu-Natal Department of Health 2018).

The majority of dental conditions that are managed at Northdale Hospital and Edendale Hospital are related to dental caries, dental impactions, periodontal disease, trauma and various types of pathology. At Greys hospital, which is a tertiary hospital, the majority of the maxillofacial

injuries that are sustained during motor vehicle accidents, assaults, sports injuries, and pathology and gunshot wounds are managed with specialist care (KwaZulu-Natal Department of Health 2014). However, as indicated earlier, the extent to which antibiotics is prescribed for dental related conditions remains unclear.

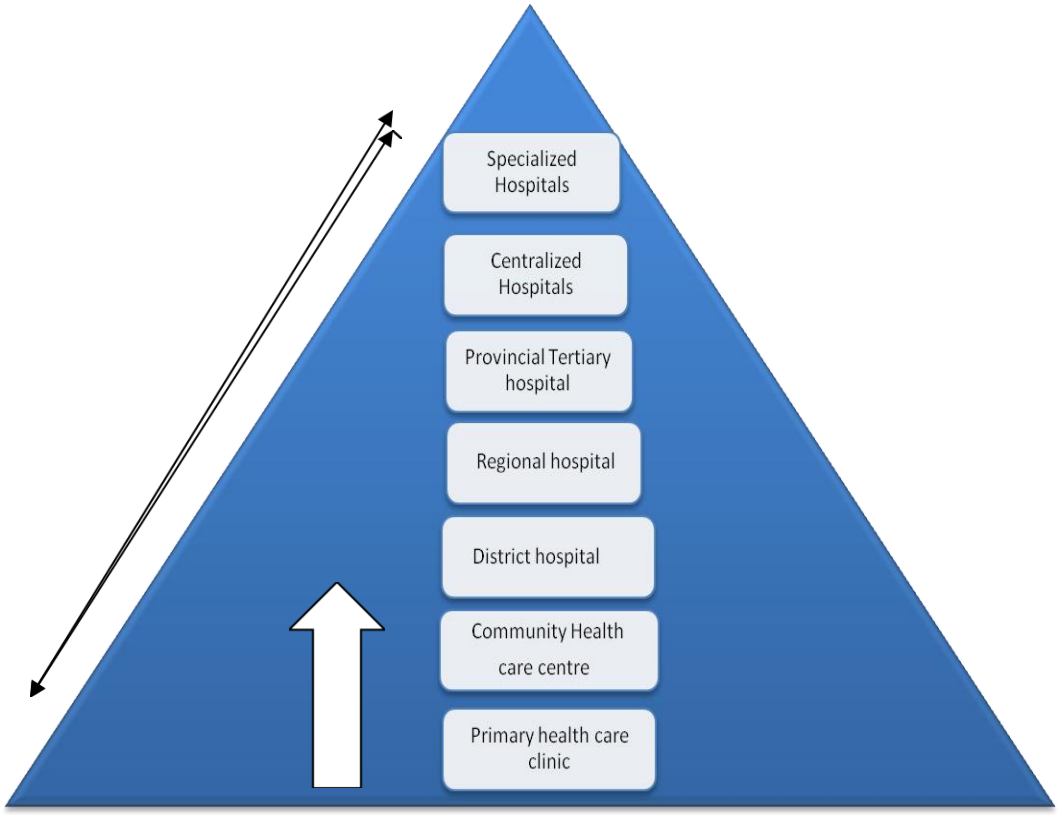
In order to develop antibiotic prescription strategies and preventive programs that are effective against antibiotic resistance, it is necessary to assess the dental conditions for which antibiotics are prescribed (Huang and Owen 2012; Peric *et al*. 2015). The frequency, efficacy, efficiency of the antibiotic of choice, the appropriate prescribing protocols and review of the success of the antibiotic prescribed in treating a dental condition must also be considered when developing antibiotic prescription strategies and preventive programmes (Huang and Owen 2012; Peric *et al*. 2015).

2.5. Referral systems levels of care

Poor access to the right care for the right people at the right time has been previously identified as a factor which influences dental prescribing decisions. The access to Primary Health care and Secondary Health care dental services influences the dental practitioners and the patients in the decision making process when it comes to Out-of-Hours and General dental practices but this lies beyond the scope of conventional practice-based antibiotic prescribing intervention and strategic considerations should be made to address access to dental care by those responsible for delivering the National Action Plans for combating antibiotic resistance (Thomson *et al.* 2020).

The following diagram and table (Table 1) highlights the structure and package of care offered at the different levels of the South African health system.

Figure 1: Levels of Health care



Source: Department of Health 2014

Table 1: Levels of Health care in the public sector

Provision of Health care
The first step in the provision of health care is ● Services offered: ✔ Immunization ✔ Family planning ✔ Antenatal care ✔ Treatment of common diseases, treatment and management of Tuberculosis, HIV/AIDS counselling. ✔ **If the Primary Health care clinic cannot assist, they will refer the patient to a Community Health Centre.** The primary health care level indicates preventive services and offers basic services such as oral examinations, radiographs, dental extractions, restorations and antibiotic prescriptions which are at no cost to the patient. Most of the services can be provided by an oral hygienist or dental therapist except for antibiotic prescriptions, for which they refer patients to a medical officer within the institution.

This is the second step in the provision of health care but can also be used for first contact care

- Services offered are similar to Primary health care clinic in addition of :
- ✔ 24 hours maternity service
- ✔ Emergency care and
- ✔ Casualty
- ✔ Short stay ward
- ✔ Will refer a patient to a District Hospital when necessary.

The third step in the provision of health care

- Receive referral from the Community Health care center and clinics
- Provide generalist support such as:
  - ✔ Diagnostic treatment
  - ✔ Care, counselling and rehabilitation services.
- Clinical services include:
  - ✔ Surgery
  - ✔ Obstetrics & Gynecology
  - ✔ Out-Patients Department
  - ✔ Medicine
  - ✔ Pediatrics
  - ✔ Mental Health
  - ✔ Geriatrics
  - ✔ Casualty
  - ✔ Clinical Forensic Medical Services amongst other services.

If the District Hospital cannot help a patient they will be referred to the local Regional Hospital for treatment. The secondary level of health care is provided at District health care institutions. The dentists and therapists usually provide curative care of prevalent diseases, removable dentures, removable orthodontic appliances and the extraction of impacted teeth.

This is the second level of health care

- These hospitals will normally receive referral from and provide specialist support to a number of district hospitals.
- If the Regional Hospital cannot help they will refer to the Provincial Tertiary Hospital.

These hospitals will receive referral from and provide sub-specialist support to a number of regional hospitals and is the third level of health care.

- These hospitals are staffed by specialists and generalists
- Services offered such as:

- ✔ Neurosurgery
- ✔ Neurology
- ✔ Plastic & reconstructive surgery
- ✔ Cardiology
- ✔ Urology
- ✔ Pediatric surgery
- ✔ Maxillo-facial surgery
- ✔ Psychiatry
- ✔ Occupational health an
- ✔ Orthopedics

If a Provincial Tertiary Hospital cannot help they will refer to a National Central Hospital. The tertiary level of oral health service delivery is provided at academic hospitals and provides highly specialized dental services and rehabilitative therapy. The services include orthodontics, prosthodontics and rendered mainly by dentists, dental specialists and registrars.

Source: National Department of Health 2014; Bhayat and Chikte 2019

From an antibiotic stewardship perspective, the National surveillance on monitoring Antimicrobial Resistance is required to produce a review on the antimicrobial test results and the shift in the antibiotic resistance patterns for antibiotic prescriptions for specific bacteria that are managed at every tier of the health care organization (Brunce and Hellyer 2018). A comprehensive scrutiny on antibacterial consumption at all levels of the health care system is deficient because the consolidated information structure that connects pharmacy with laboratory clinical information is out of order (South African National Department of Health 2015). To obtain accurate information on antimicrobial usage in South Africa's bilateral healthcare organization is demanding in recent times (Shellack *et al.* 2017). South Africa has a comparatively efficient health care organization (Watkins *et al.* 2019). It comprises of the National Surveillance Systems that frequently produces data on antibacterial consumption at tertiary level health care facilities as opposed to primary level care facilities that provide greater accessibility to antibiotic treatment for the greater population (Watkins *et al.* 2019).

The link between the levels of healthcare, antibiotic prescription and resultant resistance was seen in various public sector hospitals in KwaZulu-Natal (Essack *et al.* 2005). There was a trend among 1270 isolates of the highest susceptibility was discovered in the district hospitals followed by regional and tertiary hospitals (Essack *et al.* 2005). It was found that 3% of the total number of isolates was sensitive to all the antibiotics that were tested and 6% of the total number of isolates was resistant to a single antibiotic only (Essack *et al.* 2005). About 91% of the isolates showed acquired resistance to more than one antibiotic (Essack *et al.* 2005). The results of this investigation formed the basis on which antibiotic prescription and administration should be investigated to prevent antibiotic resistance in South Africa (Essack *et al.* 2005). The extent of oral diseases in South Africa is considerably low than other countries, however, dental caries remains a huge global health concern (Thema and Singh 2013). The early detection of oral diseases, collaboration, prevention and promotion of oral health care programs will contribute towards depleting the strain on the health care system as a result of oral diseases (Thema and Singh 2013). Oral hygienists should be employed at the Primary Health care facilities to assist with oral screening and to receive the children from the PHC Nurses, doctors and immunization clinics so that they can offer fissure sealants, preventive resin restorations, scaling and polishing

and brushing programs to prevent the onset of dental caries (Monajem 2006). It is recommended that oral hygienists should be employed at ante-natal clinics to provide information and oral health care support and management to pregnant women and that oral health examination be included in the "Road to Health chart" (Bhayat and Chikte 2019:3)

The management of health care should be merged with nursing management at a primary level of health care to provide a comprehensive policy that will involve holistic clinical care (Thema and Singh 2013). The potential contribution of nurses in an outpatient setting could impact significantly on reducing the rate of development on antimicrobial resistance (Brink 2014). There is no specific data that has been published defining the role of primary health care nurses in clinics or in the doctors' rooms (Brink 2014). Patients who were consulted by nurses were more satisfied because their consultations were significantly longer and the patients were provided with more information (Brink 2014). Nurses would therefore be ideally suited to decrease antibiotic consumption in primary health care facilities (Brink 2014).

At the National level, the South African Antibiotic Stewardship Programme (SAASP) co-ordinates proposals and recommendations from the public and private sector to encourage National institutional change (South African National Department of Health 2015) and (South African National Department of Health 2016). The provincial team is responsible for co-ordination of antimicrobial stewardship activities at the various provincial hospitals (South African National Department of Health 2016). A situational analysis to determine laboratory and dispensing data is followed by an assessment of the Antimicrobial Stewardship and Infection prevention control practices (South African National Department of Health 2016). At the government institutions, Antimicrobial Stewardship activities are driven from central hospitals with support from secondary and district institutions (South African National Department of Health 2016). A few district level health care facilities have implemented antimicrobial prescription forms that require substantial clinical and diagnostic information to enhance antimicrobial prescription while private health care institutions focus on pharmacist observing and administering a shift through a particular approach with the health care practitioners that prescribe antibiotics because there is a lack of prescriber-led antibiotic stewardship participation (South African National Department of Health 2015). Antibiotic Stewardship Committees and

Infection Prevention Control teams in tertiary public health hospitals provide an opportunity to augment and improve prescribing patterns (South African National Department of Health 2015).

Monitoring and controlling the prescribing practices in the private sector remains a challenge (South African National Department of Health 2015). This calls for clear plan that can serve both, the public and private sectors (South African National Department of Health 2015).

2.6. The South African Antimicrobial Resistance Strategic Framework

The Antimicrobial Resistance Summit held in October 2014, spearheaded efforts for the South African Antimicrobial Resistance National Strategy Framework (2014-2024) (Schellack *et al.* 2017). This framework is a nationwide public health collaborative approach that provides data for antimicrobial resistance for all the main regions within South Africa and it highlights the similarities and differences between the different areas in the country (Bamford *et al.* 2011). It has been in existence for ten years and trends in prescription patterns have been observed (Bamford *et al.* 2011). The clinically invasive pathogens causing infections and the antibiotics that are available for the management of infections in the public sector are highlighted in the initiative by the South African Antibiotic Resistance Framework (Bamford *et al.* 2011).

The South African Antimicrobial Resistance Strategy Framework was developed to manage antibacterial resistance by limiting diseases that are associated with antibacterial resistance and for improving clinical results of the patient (South African National Department of Health 2018). The South African Antimicrobial Resistance Strategy Framework represents an integration of One-Health to highlight the monitoring of antibacterial resistance in humans, animals and the environment at every level of the health care system (South African National Department of Health 2018). The South African Antimicrobial Resistance Strategic Framework is implemented and antibiotic stewardship is in action and all institutions are recommended to complete the amended prescription forms that include diagnosis and laboratory testing (South African National Department of Health 2015).

The strengths of the South African Antimicrobial Resistance Strategic Framework lies in the National Health Laboratory Services (NHLS) and networks of the private sector laboratories and for the public sector, in the sentinel active surveillance through the Group of Enteric, Respiratory and Meningeal Disease Surveillance (GERMS) and the National Institute of Communicable

Disease (South African National Department of Health 2015). This complements institutional as well as provincial data from a Central Data Warehouse (South African National Department of Health 2015).

The limitation of the South African Strategic framework is that it is solely based on laboratory diagnosis but there is a gap in tallying the patient's clinical outcomes (Bamford *et al.* 2011). It is further postulated that 'the community versus hospital acquired infections are not precisely differentiated' (Bamford *et al.* 2011:580). There is thus a need to monitor and evaluate information that links laboratory services for human and veterinary health care both from a public and private sector perspective (South African National Department of Health 2015). There is lack of standardization of data in the different health care facilities which contributes greatly to inadequate data recording nationally (South African National Department of Health 2015). There are insufficient antimicrobials to treat resistant microorganisms such as antibiotics for Multi-drug resistant tuberculosis and Extreme Drug Resistant Tuberculosis (South African National Department of Health 2015). The outbreaks involving multidrug resistant–bacteria that could cause closure of hospital wards and high morbidity and mortality rates have largely influenced the implementation of the Antimicrobial Resistance Strategy Framework as an initial measure to counteract the global problem of Antimicrobial Resistance (South African National Department of Health 2015).

2.7. The South African Antimicrobial Stewardship Programme

A strong antimicrobial stewardship which is defined as the appropriate administration of antibiotic therapy, aligned to optimal clinical outcomes for the patient, while avoiding possible toxicity or resistance (Doron and Davidson 2011). The antimicrobial stewardship programme focuses on the HAST (Human Immunodeficiency virus, acquired immunodeficiency syndrome, sexually transmitted infections and Tuberculosis) monitoring system. The Essential Medicines List and Standard Treatment Guidelines appropriately guide antimicrobial prescribing practices but there is a lack of non-pharmaceutical issues of Antimicrobial Stewardship Programme such as hand washing etc. (South African National Department of Health 2015). The aim is shifting the trend in health care that is provided by health care practitioner towards the focus on Infection Control practices and vaccination programmes (South African National Department of Health 2015).

Data is summarized from the National Antibiotic Surveillance activities and the records that are produced by the individual health care facilities. The cause of illness and death are inadequately tallied in South Africa which is common in lower-income countries (Crowther- Gibson *et al.* 2011). For most antimicrobial infections in South Africa, surveillance data are laboratory- based and this restricts the potential to distinguish between the colonization of the bacteria and the infection (Bramford *et al.* 2011).

The data sources vary between the private and public sectors (Schellack *et al.* 2017). The data is mainly report-specific in the public sector and is acquired from information that is provided by tenders which is produced by wholesalers while in the private sector the data is electronic –based and is obtained from IMS Health (Schellack *et al.* 2017). The DDD (usual adult dose of an antimicrobial for treating one patient for one day) estimates the antibacterial prescription practices in the health care facility and it includes hospital participation such as patient's admissions and the discharging of patients. There are alternative methods to comparatively evaluate information on antibiotic consumption to the global standards of the defined daily doses DDD and DID. The DDD is the mean of the indicated prescription dosage per day. For the data on antimicrobials, the (DID) is calculated by utilizing the DDD per 1000 patients per day for the total population including all age groups and gender groups (WHO 2018; Schellack *et al.* 2017). The Defined Daily Dose is recommended for comparative analysis of various antimicrobials in the diverse health care domains (Schellack *et al.* 2017). South Africa does not have this type of surveillance available (Schellack *et al*. 2017). Three extensive groups for antimicrobial consumption were identified by the World Health Organization: Antimicrobials for systemic indication that is classified as ATC group J01; Antiretroviral for systemic indication that is classified as ATC group J05and Anti-tuberculosis group for systemic indication that is classified as ATC group J01GB and J04 (Schellack *et al.* 2017). In order to comparatively enhance the standard of antibiotics that are consumed and to compare the antibiotic usage at the different levels of health care provision, the Anatomical Therapeutic Chemical classification (ATC) is utilized (Schellack *et al.* 2017; South African National Department of Health 2017: 29).

In South Africa, when the monitoring systems for antibiotic usage are deficient or inadequate, the IMS Health and the tender information could provide a sufficiently reliable source for data collection (Schellack *et al*. 2017). Data is documented through software that is formulated for the

laboratory data analysis or from the assessment of previously reported documentation (Bamford *et al.* 2011). Data is collected by the microbiologist or technologist, checked by the pathologist and then submitted to a national co-coordinator who then collates the annual report which is disseminated through publications in local journals, organizations, websites or scientific presentations at meetings and conferences (Bamford *et al.* 2011). One of the noted challenges are to determine 'data on antimicrobial consumption in low-resource countries' (Schellack *et al.* 2017: 105). Over a period of six years, there have been crucial trends in the policies aimed towards combating Antimicrobial Resistance at a national level (Schellack *et al.* 2017).

2.8. National Antimicrobial Surveillance

The National Institute for Communicable Diseases (NICD) is the national coordinating center that participates in the WHO Global system on Antimicrobial Resistance (South African National Department of Health 2018). The NICD observes and manages the surveillance for infectious diseases that are a concern to the public health sector (South African National Department of Health 2015). The NICD monitors infectious diseases and since it is a platform for a prospective sentinel surveillance programme, it expands to also integrate Tuberculosis and HIV surveillance (South African National Department of Health 2015).

Table 2: Surveillance methods

World Health Organization Action Plan	**South African Action Plan**
● Global antimicrobial surveillance system (GLASS) (WHO 2018) ● Access, Watch, Reserve (AWaRE)	● National Institute for Communicable Diseases (NICD) ● National Health Laboratory Service (NHLS) ● National Antibiotic Surveillance Forum (NASF) ● South African Society for Clinical Microbiology (SASCM) ● Centralized data and Sentinel reporting ● Antimicrobial Resistance Reference Unit (AMRRU) ● Laboratory-based Antimicrobial Resistance Surveillance (LARS) ● Electronic Surveillance (ES) ● HAST screening tool ● Enteroccocus Faecium, Staphylococcus Aureus, Klebsiella Pneumoniae, Actinetobacter Baumanni, Pseudomonas Aeruginosa,Enterobacter species (ESKAPE) ● Group for Enteric, Respiratory and Meningeal Disease Surveillance (GERMS-SA) ● Enteric Disease Reference Unit (EDRU) ● Sexually Transmitted Reference Unit

Source: WHO 2018; WHO 2019; Department of Health 2018; Bamford *et al.* 2011

The monitoring of Antimicrobial Resistance was implemented by the Antimicrobial Resistance Reference Unit (AMRRU) which is a division of the NICD for HAI-Associated Staphylococcus Aureus and Klebsiella Pneumoniae specimens that are obtained from patients for specific regions in South Africa (Bamford *et al.* 2011). The implementation of forewarning systems is important to monitor drug resistance (Bamford *et al*. 2011). The information on Antibiotic Resistance from South African public and private institutions is collected by the Centralized Data Warehouse (South African National Department of Health 2015). The specific drug resistance patterns will become statutorily notifiable and a notification of resistance patterns from antibiotic resistant specimens with familiar pathogenesis will be identified, for example, a notification of Multi-Drug Resistant bacteria that is currently at a low prevalence such as Cabapenemase-producing gram negative bacteria (South African National Department of Health 2015). The sentinel reporting provides an alert for an Antimicrobial Resistance outbreak (South African National Department of Health 2015). The Centralized Data Warehouse provides oversight for drug-resistant Tuberculosis surveillance systems (South African National Department of Health 2015).

The Antimicrobial Surveillance system has two levels. The laboratory–based antimicrobial resistance surveillance (LARS) collects data from the recognized public sector sites (South African National Department of Health 2018). The Electronic surveillance (ES) makes use of data from the National Health Laboratory Services (NHLS) as well as the Private Laboratory Services (South African National Department of Health 2018). A retrospective laboratory-based method for observing specific virulent agents that are obtained from blood and fluid samples forms the Antimicrobial Surveillance in the public health care sector and it is reliant on the information that is submitted from the Nation Health Laboratory Services, however, the clinical effects of Antibacterial Resistance are impossible to determine (Bamford *et al.* 2011). Improvements in the preventive strategies focus mainly on Infection and prevention control and enhanced vaccination programmes which is encouraged as well as fundamental standards for Antimicrobial Resistance, patient championing and understanding of campaigns against Antimicrobial Resistance to eliminate the misuse of antibiotics in the health care of humans and animals (South African National Department of Health 2015).

The National Institute for Health and Care Excellence advocated e-prescribing in 2016 to support monitoring of antibiotic prescribing practices (Shah *et al*. 2020).

2.9. Standard Treatment Guidelines and the Essential Medicines List

The South African public health care sector adopted the Essential Medicines List with the Standard Treatment Guideline in 1996 for Primary Health Care (Perumal-Pillay and Suleman 2017). The guideline-adherent empirical antimicrobial therapy is derived either from the Standard Treatment Guidelines and Essential Medicines List or South African Antimicrobial Stewardship Programme (South African National Department of Health 2017).

The World Health Organization highlighted that inadequate antibiotic prescribing practices as well as the misuse of antibiotics are linked to treatment failures that give rise to the evolution of Antibiotic Resistance (Adorka *et al*. 2014; Ntsekhe *et al.* 2011). It was found that dental practitioners were aware of the treatment guidelines although only a fraction of dental practitioners followed the recommendations correctly (Mthethwa *et al.* 2018).

South African medical practitioners use the South African Antibiotic Stewardship program for guidelines and protocols (Brink 2014).

Table 3: Availability of guidelines for prescription of antibiotics

Available Guidelines	
South African Antibiotic Stewardship Programme	National Institute of Health care and Excellence
Essential Medicines List	American Heart Association
Standard treatment Guidelines	British Society of Antimicrobial Chemotherapy
South African Medicines Formulary	European Society of Cardiology
	American Association of Endodontic

Source: Brink 2014, Bamford *et al*. 2011, Chidgey *et al.* 2007, Mthethwa *et al.* 2018, Lalloo *et al.*2017

The guidelines for antibiotic prescription attempt to narrow the gap between the recommendations and the actual practice of antibiotic prescription by acknowledging the diagnostic complexity and uncertainty that clinicians are faced with (Brink 2014). The hospital pharmaco-therapeutic committees (HPTCs) should provide guidance for health care workers involved in antibiotic prescriptions (Ntsekhe *et al*. 2011). There should be in line with monitoring and adherence to the Standard Treatment Guidelines (Ntsekhe *et al*. 2011).

The National Essential Medicines List (EML) for South Africans was developed to manage deficiencies in the pharmaceutical sector such as the increased financial implications that are associated with the unjustifiable consumption of antibiotics (Perumal-Pillay and Suleman

2017).The Essential Medicines List was developed to reduce the cost of antibiotics and enhance the cogent consumption of antibiotics by securing only a restricted amount of antimicrobials that can be regarded as crucial for the management of infections and will be listed and procured (Perumal-Pillay and Suleman 2017). The World Health Organization supports the Essential Medicines List on the provided that infections are widespread and that safety, feasibility and effectiveness of the medications are evident for disease management of diseases (Perumal-Pillay and Suleman 2017). The Essential Medicines List does meet health care requirements for the public but the pharmaco-economic aspect still requires some strengthening in South Africa (Perumal-Pillay and Suleman 2017). The Essential Medicines list is flexible and can be responsive to local settings. With the Essential Medicines List, the patient outcomes are not monitored and there could be challenges associated with the availability of appropriate antibiotics (Perumal-Pillay and Suleman 2017).

In middle income countries like South Africa and in times of economic crisis, controls need to be implemented to make certain that funds are available for antibiotics while refining the cogent indication of antibiotics without compromising the standard health care delivery (Perumal-Pillay and Suleman 2017). The Standard treatment guidelines ensures the availability and the accessibility of antibiotics for the treatment of every patient while keeping in mind the patient's safety, the efficacy of the medicines, the quality of drugs and appropriate prescribing and dispensing practices (Gopalakrishnan *et al*. 2014). The Standard Treatment Guidelines encourage the idea of independent management for health care, prevention of diseases and resolutions that are appropriate for the prescription of antibiotics by health care practitioners and for the patients by providing adequate training and education (Gopalakrishnan *et al.* 2014). To achieve oral health goals for the management of dental conditions in South Africa, attention is required to the adherence to pharmacotherapy and the organization of dental management incorporates the availability of antibiotics and the prevention of oral diseases. Misused medical funds are consequences of poor adherence to the Standard Treatment Guidelines that can lead to less optimal management and control of pathogens infections (Gopalakrishnan *et al*. 2014).

The twelve editions of the Standard Treatment Guidelines and Essential Medicines List were published for two levels of health care. The Primary health care Standard Treatment Guidelines and distinct books for the management of hospital health care for adults and pediatric patients are

available while tertiary or quaternary level health care focuses on the use of the Essential Medicines List to guide treatment regiments (Perumal-Pillay and Suleman 2017).

The National Institute for Health and Care Excellence Guidelines are clinically verified guidance for medical provision in England (Chidgey *et al.* 2007). It was accepted in April 1999 to implement a high quality of health care and the fruitful consumption of funds that belong to the National Health System (Chidgey *et al.* 2007). It was established on the basis of the foremost obtainable confirmation that is aimed at improving the standards of medical management by adapting the course of medical provision and boosting the patient's chance of recovery (Chidgey *et al.* 2007). The National Institute for Health and Care Excellence is an independent organization that is accountable for maintaining public advice for the advancement of health care, the counteraction of disease, improved quality of health care services modify and supply medical assistance and finally to adapt and provide health and social care services (Chidgey *et al.* 2007). The National Institute for Health and Care Excellence Guidelines recommend the establishment of guidelines that are required to evaluate the clinical application on independent health care practitioners in teaching and training in order to assist the patient in making a well-informed conclusion and to enhance understanding between the medical practitioner and the dental practitioners (Chidgey *et al.* 2007). The National Institute for Health and Care Excellence Guidelines was used to develop standards to support individual care level clinical decision-making (Chidgey *et al.* 2007).

Table 4: The differences between the Standard Treatment Guidelines and The National Institute for Health and Care Excellence

Standard treatment guidelines and Essential medicines list	**The National Institute for Health and Care Excellence**
Established mainly for Primary Health Care	Established for: ✔ self-care, ✔ Primary health care and ✔ specialized services ● Decisions are made on an individual basis ● Measures cost quality adjusted life (QAL) ● Requires practitioners to keep in touch with updated medical knowledge and skills
Recommendations:	
Not indicated for uncomplicated acute bronchitis except in the case of co-infections with HIV	Non- antibiotic or delayed prescribing strategy. Antibiotic prescription should be consideration when a patient has high potential complicating, that is: ● Acute bronchitis (chronically ill patients),

	● Above 65 years of age with confirmed co-morbidities ● Confirmed bacterial infections
The consumption of antibiotics in the management of acute bronchitis: restricted to patients with longstanding illnesses	No antibiotic prescription for: ● Uncomplicated bacterial bronchitis ● Viral bronchitis ● Causative agent is unspecified

Source: Chidgey *et al*.2007; Ncube *et al.* 2017

Compromised oral health can negatively influence one's potential to eat, speak and socialize and the most common dental conditions that are managed are stated in the Standard Treatment Guidelines and Essential Medicines List such as dental abscess, dental caries, oral candidiasis, gingivitis, periodontitis, necrotizing periodontitis, herpes simplex virus of the mouth and lips, aphthous ulcers and teething infants.

Tooth decay and gingivitis are the most common dental conditions in the United Kingdom but is largely preventable (National Institute for Health and Care Excellence 2016). Poor dental health leading to pain or infection can precipitate a crisis in people with dementia such as oral cancer which is rapidly increasing in people aged 65 years and over.

The National Institute for Health and Care Excellence developed the programme caring for smiles for the elderly in 2005 to improve the oral health and to implement a modern approach to the National Health System dental services for the elderly in care homes (National Institute for Health and Care Excellence 2017). The aim came about to increase the cognizance of optimal dental hygiene of the elderly patients living in care settings and to raise awareness, educate and train health care workers on the importance of good oral hygiene (National Institute for Health and Care Excellence 2017). Poor dental health care for the elderly patients affects their overall health, nutrition, communication, appearance and the standard of well-being (National Institute for Health and Care Excellence 2017). Many elderly people retain their teeth and often enter into assisted-living facilities with unmet oral health need (National Institute for Health and Care Excellence 2017).

A recent study showed that dental practitioners that manage a high volume of pediatric patients displayed poor adherence of 26,1% to 44,2%, to the professional guidelines for the antibiotic prescription patterns for the management of dental infection (Ahsan *et al*. 2020).

A survey conducted in 2012, showed that a very low response rate was established for the health practitioners' knowledge of treatment guidelines and the prescribing patterns for antibiotic prophylaxis for the management of dental conditions (Mthethwa *et al.* 2018). Dentists were aware of the treatment guidelines but few followed the recommendations for antibiotic prophylaxis and for patients allergic to penicillin (Mthethwa *et al.* 2018). The dental practitioners in South Africa do not have a familiar knowledge of when to precisely prescribe antibiotics; therefore, widespread precise clinically sound recommendations should be considered as a requirement when prescribing antibiotics for the management of dental conditions (Lalloo *et al* 2017).

2.10. The scope of oral health care

South Africa has been observing antibiotic resistant infections especially as a result of the susceptibility of individuals infected with HIV/AIDS and Tuberculosis (Torres and Chibi 2019). Practices such as self-medication, sharing of antibiotics and non-compliance could be contributing to antibiotic resistance (Torres and Chibi 2019).

The indications for systemic antibiotics in dentistry is limited since most dental infections appear as pulpitis or periapical periodontitis which may need operative interventions like extractions, restorations or endodontic therapy (Mthethwa *et al.* 2018). Dental practitioners have the responsibility to reduce and improve the way they prescribe antibiotics and should prescribe antibiotics with the correct indications, not under the pressure of patients requesting prescriptions for antibiotics (Sanderson *et al.* 2019). Dental practitioners are also liable for educating patients about the importance and the development of antibiotic resistance (Sanderson *et al.* 2019).

During the COVID-19 pandemic dental practitioners were instructed to follow an AAA approach that comprised of advice, analgesics and appropriate antibiotic prescription for the remote management of dental infections (Shah *et al*. 2020). Dental practitioners are advised to contemplate the indications for antibiotic prescription and patients need to be cautioned about self-medicating with antibiotics to obtain relief from dental pain (Dar-odeh *et al.* 2020).

2.10.1. Antibiotic prophylaxis for systemic conditions

It should be noted that 'antibiotic prophylaxis requires that an agent is directed at the most likely organism causing an infection, should be administered for a brief period, starting one hour before the procedure and is warranted when the post-operative infections are common or unusually severe' (Sweeney *et al.* 2004: 571). Mono-microbial systemic infection occurs in patients that have an infection-susceptible focal point such as Infective Endocarditis, bone or joint prosthesis, that are susceptible to extensive infections as a result of specific pathogens such as diseases caused from encapsulated bacteria like Streptococcus mutans or in patients that have a compromised immune system (Gutierrez *et al.* 2006). In a study done by Mthetwa *et al.* in 2018, it was found that HIV infected patients constituted the second largest category of patients who were prescribed oral antibiotics and South Africa's national average is 12, 6 % (Mthethwa *et al.* 2018).

Antibiotic prophylaxis acts by killing bacteria and by inhibiting bacterial adherence (Maestre-Vera *et al.* 2007). Previous studies indicate that resistant micro-organisms are frequently present in patients that have congenital heart disease and this may contribute to failure of prophylactic treatment if the inappropriate antibiotic is utilized (Maestre-Vera *et al.* 2007).

The National Institute for Health and Care Excellence changed the routine prescription of antibiotics for the prevention of Infective Endocarditis in 2008 but the American and European cardiologists still recommend its use (Brunce and Hellyer *et al.* 2018). Antibiotic prophylactic treatment in oral surgery is aimed at the prevention of the possible emergence of a surgical wound (Gutierrez *et al.* 2006). The scientific societies in Spain have established policies and a plan of action on the professional basis of extensive curative and preventive strategies for antibiotic prescription (Gutierrez *et al.* 2006). Similarly 'prophylaxis guidelines recommended by American Heart Association, European Society of Cardiology and British Society of Antimicrobial Chemotherapy are applied in South Africa' (Mthethwa *et al.* 2018:4).

For prophylaxis against other disease such as rheumatic fever, tetanus, patients with surgical prostheses and compromised immunity where the bacteria may cause septic arthritis and osteomyelitis, the patient's physician or specialist treating the specific condition must be consulted (Sweeney *et al.* 2004). Antibiotic changes the normal flora of the gut; therefore a

patient may suffer from concomitant gastrointestinal tract disorders such as diarrhea (Sweeney *et al.* 2004).

The first step of infection is generally bacteremia, which is produced after an invasive procedure (Gutierrez *et al.* 2006). Bacteremia that is prevalent in periodontal disease occurs as a result of an increased concentration of prostaglandins in the blood stream that cause an increase in the concentration of leukocytes and fibrinogen, thereby reducing the flow of blood circulation through the porous epithelium that encapsulates the periodontium and consequently favors the passage of bacteria to the blood (Gutierrez *et al*. 2006). Approximately, 51%- 55% of bacteremia in humans occurs following extensive dental procedures (Gutierrez *et al* 2006). Standard Amoxicillin and Clindamycin regimens may not cover dental pathogenic bacteria and this is partly due to the production of B-lactamase by anaerobic bacteria (Maestre-Vera *et al.* 2007). A study done in Alfonso X el Sabio University in Madrid, indicated that the 'vulnerability to virulent pathogens may influence a patient's overall well-being as a result of oral pathogens being present in the artheromatous plaques found in the blood vessels' (Maestre-Vera *et al.* 2007:44). This finding is significant as it suggested that this may potentially lead to the development of vascular arteriosclerotic wounds as well as the progression cardiovascular or cerebrovascular accidents (Maestre-Vera *et al.* 2007). Antibiotic prophylaxis to prevent Infective Endocarditis should be given in advance for biopsies of the oral cavity (Mthethwa *et al.* 2018). Dental and endoscopic procedures may cause transient bacteremia and is sometimes preceded by an interventional procedure and the antibiotics administered before such procedures can reduce the frequency of positive blood cultures (Parrish and Maharaj 2012). Prophylactic antibiotic cover was indicated to prevent infective endocarditis and this is widely accepted by the dental fraternity (Mthethwa *et al.* 2018). The dental practitioner's choice of antibiotic should be made on the basis of health care coverage and financial implications compared to the value of the dental treatment (Gutierrez *et al.* 2006). The advantage of antibiotic prescriptions is to prevent complex post-operative infections that arise from surgical procedures (Gutierrez *et al.* 2006).

2.10.2 Antibiotic prophylaxis in dental surgery

Antibiotic coverage in dental surgery is distinguished by empirical antibiotic therapy involving a restricted array of wide spectrum antibiotics for a brief duration (Mthethwa *et al* 2018). Inappropriate antibiotic prescriptions include those for the management of dry socket, acute

periapical infection and pulpitis, and non-clinical reasons such as patient expectations, convenience. Other inappropriate prescriptions include antibiotic cover for infections linked to viral conditions such as Herpes Simplex Virus-1 infections (Mthethwa *et al* 2018). Antibiotic prophylactic therapy related to surgical procedures should be prescribed to prevent further infection or scar formation (Gutierrez *et al.* 2006).

A review by Soodan *et al*. highlighted the principles of antibiotic prophylaxis with the aim to reduce possible risk of infection; therefore, the recommendation provided was that there should be increased antibiotic levels, a correct duration of administration that is efficacious and has a short half-life (Soodan *et al.* 2014).

The type of maxillofacial procedure and the extent of contamination of the wound will advocate the need for the appropriate consumption of antibiotics (Salmeron- Escobar *et al.* 2006). The saliva, skin, teeth and tumour are sources of microorganisms in the disease state; therefore, the antibiotic of choice should attain an antimicrobial blood-serum concentration which will prevent the duplication and dissemination of pathogens through the surgical site (Salmeron-Escobar *et al.* 2006). Good prophylaxis will happen when there are effective serum concentrations of the antibiotic since the opening of the skin of the mucosa, until the closure of the skin is done (Salmeron-Escobar *et al*. 2006). Therefore, antibiotics should be used an hour previous to incision (Salmeron-Escobar *et al*. 2006). In certain cases, such as prolonged surgery, a repeat dose of the antibiotic prescribed may be done so to prevent further infection (Salmeron-Escobar *et al.* 2006).

Antibiotic therapy is suggested for cases that have a high potential for contamination (Gutierrez *et al*. 2006). Surgical interventions are classified into two large groups. (Gutierrez *et al*. 2006). Firstly, dental procedures with the existence of bacteria such as unerrupted teeth, benign outgrowth from bone, odontogenic cysts and tumours, uncontaminated epulis as well as prior prosthetic surgery or orthodontic surgery, closed-jaw fractures, infections of the glands, osteotomes, grafts and surgical flaps (Gutierrez *et al.* 2006). Secondly, surgery in the existence of bacteria of the wisdom teeth, inflamed cysts, radicular cysts, granulomas, jaw fractures, trauma, injuries with contusions, re-infections, to tumors and radio necrosis (Gutierrez *et al.* 2006).

When surgical injury involves skin wound, the main physical barrier that prevents the entrance of microorganisms into the body will break down (Salmeron- Escobar *et al.* 2006). The microorganisms penetrate and colonize and may cause infection of the deep tissues (Salmeron-Escobar *et al*. 2006). The quantity of bacteria will determine the possibility of infection as well as taking into consideration if the wound and the surgical site is clean, clean-contaminated or soiled because the main source of infection occurs as a result of saliva which carries a great amount of bacteria (Escobar *et al* 2006). If the contamination is great, the risk of post-surgical infection is more (Salmeron- Escobar *et al.* 2006). The risk of contamination will reduce if the appropriate surgical technique is used; the good health state of the patient and antibiotic prophylaxis is prescribed (Salmeron-Escobar *et al.* 2006).

In a published study by the American Dental Journal Medications supplement in 2005, it was indicated that it is possible for a patient to experience inflammation and trismus following dentoalveolar surgery (Lawler *et al*. 2005). Likewise, 'fluctuation and purulent discharge from the surgical wound site of the third molars is the most visible sign and symptom for more than 72 hours after surgery while pain and edema may worsen with persistent hyperpyrexia at 48 hours or more post-surgery' (Lawler *et al*. 2005: 55).

Dentists are more likely to prescribe antibiotics for individuals who are undergoing extraction of impacted teeth and all the HIV infected patients who received medication from the pharmacy were for dental extractions (Mthethwa *et al.* 2018).

The extraction of impacted third molars and dental implant surgery has the highest potential for infection with significant detrimental consequences (Lawler *et al.* 2005). As outlined previously those with a greater risk of infection could possibly benefit from antibiotic prophylaxis (Mthethwa *et al.* 2018). Such risks include; the type of dental extraction, difficulty of a dental extraction and the patient's compliance with the post-operative management that tend to determine the occurrence of post-operative complications (Mthethwa *et al.* 2018). A study conducted by Soodan *et al.* in India suggested that prophylactic antibiotics could be useful to prevent complications occurring after the surgical removal of a third molar. There is decreased pain, decreased swelling, reduced trismus and the quality of life is better with antibiotic therapy (Soodan *et al*. 2014). The study done by Lawler *et al*. 2005, showed that based on prescribing patterns, prophylactic antibiotics were used for the extraction of 19% of asymptomatic impacted

third molars as well as 75% of third molars with recurrent pericoronitis (Lawler *et al*. 2005). According to Lawler *et al.* about '70-90% of patients were prescribed a five-day course of Amoxicillin' and only '22% of practitioners knew the correct history for penicillin allergy' (Lawler *et al.* 2005: 54).

It is a general consensus that systemic antimicrobials are contraindicated for the management of acute osteitis because there is no additional advantage when compared to the local measures that are aimed to manage the dental alveolus of a healthy individual but the findings by Mthethwa *et al.* 2018 revealed 'that two-thirds of the cases that presented with acute osteitis had an immunodeficiency, flu or diabetes and both conditions for which are indicated for antibiotic therapy according to the current evidence' (Mthethwa *et al* 2018). There are instances where dry socket or acute osteitis occurs as a result of poor wound healing and not as a result of a bacterial infection (Lawler *et al*. 2005) because there is a greater dissolution of fibrin and the removal of small blood clots that takes place in the initial healing of a socket in a healthy individual (Lawler *et al*. 2005).

Surgical antibiotic prophylaxis is one component of a broader strategy to prevent surgical site infection (Jocum 2018). In cases of oral surgery where the infection rate is low, prophylactic antibiotic treatment will be indicated for any active infection, for patients with co-morbidity and the immunocompromised patients (Gutierrez *et al*. 2006; Salmeron-Escobar *et al*. 2006). Additionally, 'systemic antibiotics given before the oral surgical procedure will potentially reduce the frequency of dry socket and wound infection after third molar extraction' (Mthethwa *et al* 2018:10). The factors that contribute to an increased risk of infection are poor state of health of the patient, immuno-suppression, preoperative radiotherapy or chemotherapy, reconstructive flaps or the exposure of tissues to ischemia or necrosis that can occur during dental clinical management (Salmeron– Escobar *et al*. 2006). Antibiotic prophylaxis may be administered in a procedure that does not typically require prophylaxis if there are other patient–related factors that predispose a patient to a higher risk of surgical site infection, such as poor nutritional status, obesity, diabetes, smoking, extremes of age, immune system compromised for instance, corticosteroid therapy, HIV/AIDS, chemotherapy and other systemic illnesses (Jocum 2018).

In traumatology, prophylaxis is recommended for those cases with active infection and middle and upper third fractures of the face, communicating with the paranasal sinuses that may be

considered complex or compound (Salmeron-Escobar *et al*. 2006). Orthognathic and pre-prosthetic surgery are considered clean contaminated surgeries therefore, short term antibiotic prophylactic treatment is preferred (Salmeron-Escobar *et al*. 2006). In oncological surgery, the need for prophylactic antibiotics decreases when there are no complications in the oral cavity (Salmeron-Escobar *et al.* 2006). In South Africa, from 1997-2001, oral cancers made up 5% of all cancers presenting in males while 0, 6 % of females were affected (Botha *et al.* 2018). The early identification of these lesions could result in less invasive treatment options and an increased survival rate (Botha *et al.* 2018).

Ten percent of antibiotic prescriptions in Spain are required for odontogenic infections and a significant part is mainly prescribed as a preventive measure for certain clinical interventions (Gutierrez *et al*. 2006). Local infections following dental procedures are multi- microbial as most species are isolated in pairs, such as Bacteroides species and Fusobacterium species, Peptostreptococcus species and Prevotella species and Eubacterium species and those 'that present with a strong aerobic and anaerobic portion as well as a microaerophilic component that may be link to a potential infection or contamination during a surgical procedure by normal microbiotes that are present in the oral cavity and saliva' (Gutierrez *et al*. 2006:71). Patients that receive antibiotic treatment for odontogenic infections should be consulted daily (Maslamani *et al.* 2018).

Oral surgery could contribute to 'cutaneous-mucosa, dental or bone infections which will consequently result in multi-microbial local infections' (Gutierrez *et al*. 2006:70). The complications of invasive dental procedures result in edentulism, edemas, dental abscesses, implants or prostheses (Gutierrez *et al*. 2006). The use of antibiotic-impregnated bone cement has become common during arthroplasty procedure and although the evidence largely favors it, the use of the cement has not been endorsed by the South African guidelines (Jocum 2018). Osteotomy and prolonged surgical durations increased the rate of infectious complications (Gutierrez *et al*. 2006). Likewise, 'the infecting inoculants increases as the surgical time increases, therefore, the chances of a surgical infection around dental implants is dependent on the severity of trauma and the duration of the surgical procedure as well as the loss of the implant which is usually due to contamination during the insertion phase' (Gutierrez *et al*. 2006:70).

In England, the levels of prophylactic antibiotic prescription were low as the guidelines do not recommend the routine use of antibiotic prophylaxis however this situation could have changed during the COVID-19 pandemic, as explained earlier (Shah *et al*. 2020).

2.10.3 Antibiotic prophylaxis for Endodontic treatment

The widely accepted standard for the management of "irreversible pulpitis" is the removal of the pulp from the infected tooth, however, in various regions across the world antibiotic prescription is still recommended (Agnihotry *et al*. 2016). A study done in Spain in 2008 showed incorrectly implemented antibiotic regime for preventing local odontogenic infections (Sancho-Puchades *et al.* 2009). This could result in a 'generation of new bacterial resistances, the facilitation of adverse drug reactions and it can contribute to the increased number of opportunistic infections' (Sancho-Puchades *et al*. 2009; 573). There is no clear evidence on whether South African health care practitioners are over-prescribing antibiotics for the management of root canal treatment (Lalloo *et al.* 2017).

When the host response is reduced, systemic antibiotics are considered an adjunct to endodontic treatment (Brunce and Hellyer *et al*. 2018). A survey done in Canada found that antibiotic use was prescribed over an average duration of 6,92 days (Dar-Odeh *et al*. 2010). In the United States of America, a survey revealed that endodontic specialist prescribe antibiotic for an average duration of 7,58 days (Dar-Odeh *et al.* 2010).

If the cause of the root canal infection is adequately treated through the debridement of the pulp, obturation and the restoration of the pulp cavity then most of the endodontic infections will not require a prescription for systemic antibiotics (Morrow 2012). Endodontic therapy is sufficient for the resolution and healing of asymptomatic apical periodontitis that originates from the pulp, therefore, there is no need to routinely prescribe systemic antibiotics (Morrow 2012). Chronic apical abscesses generally commence with mild symptoms and possibly presenting with a sinus tract (Morrow 2012). Systemic antibiotics are not required for the optimal healing in most of the chronic apical abscesses that originate from the pulp (Morrow 2012). Acute apical abscesses have a rapid onset with accompanying pain and inflammation that could progress to cellulitis (Morrow 2012).

If the abscess is a wide spread, the clinical management could include surgical incision, pulp removal and possible oral or systemic antibiotic cover, depending on the severity of the condition and symptoms presented by the patient (Morrow 2012). Apical periodontitis is a polymicrobial infection where the causative bacteria become resistant to the available antibiotics (Brunce and Hellyer *et al*. 2018). Narrow spectrum antibiotics, with low toxicity and low cost are recommended for endodontic treatment (Lalloo *et al* 2017). Metronidazole is uniquely effectual against anaerobic bacteria but is not recommended to be solely prescribed in the management of root canal treatment (Morrow 2012). Oral infections should not recur if the infection is eradicated properly (Morrow 2012).

South African dental practitioners adhered to the American Association of Endodontics by prescribing narrow spectrum antibiotics as a first line of choice for dental conditions (Lalloo *et al* 2017).

2.11. The Inflammatory process

South African health care facilities share common grounds for bacterial infections that are caused by bacteria that are resistant to multiple antibiotics (Albert 2018). Patients who are immune-compromised may have a higher potential for complications as a result of wide spread bacterial infections and distant site infections that may follow invasive dental procedures (Sweeney *et al.* 2004).

The presence of a particular bacterial population that is prone to occur in different areas of an infection will require antibiotic coverage (Gutierrez *et al.* 2006). Additionally, 'the mechanism of spread of infection spreads in five paths; through local spread, natural paths, lymphatics, blood stream and nerves' (Sweeney *et al*. 2004:569).

The body's response to infection or injury is inflammation (Hasturk *et al*. 2012). The factors that contribute to infection are the 'virulence of the organism, which are the ability of the organism to spread and the ability to cause tissue damage, the number of organisms and the local and systemic defenses of the host' (Gutierrez *et al*. 2006:73). The agents of acute orofacial inflammation are agents of acute inflammation and chronic inflammation (Hasturk *et al.* 2012). Acute inflammation may occur as a result of trauma, chemical agents, infarction, antigen-antibody reaction and living organisms such as bacteria, fungi, viruses and parasites (Sweeney *et*

al. 2004). If the host immune system cannot neutralize pathogens that arise from the acute inflammation, then the inflammation will become chronic resulting in consequences such as destruction of the bone, scarring and fibrosis (Hasturk *et al*. 2012). If the bacteria cause infection of the bone it may result in chronic osteomyelitis (Hasturk *et al*. 2012).

The inflammatory process is initially directed against microorganisms and their virulence factors, the production of cytokines and the release of neuropeptides that result in the vasodilation of local blood vessels (Hasturk *et al*. 2012) In the first line defense, the neutrophils leave the blood vessels and migrate to the site of microbial invasion, followed by the production and release of macrophages (Hasturk *et al.* 2012). The cardinal signs of inflammation following the first line of defense such as bleeding, swelling and redness of the gingival, (Hasturk *et al.* 2012). When the macrophages are released, they eliminate the bacteria, clear the excessive neutrophils, produce cytokines and chemokines and activate the lymphocyte mediated adaptive immune response (Hasturk *et al.* 2012). The infection may resolve however a chronic inflammation will be established if the inflammation is not resolved (Hasturk *et al.* 2012).

The 'innate immunity and adaptive immunity make up the two lines of defense for the human immune system' (Warrington *et al*. 2011:1). The innate human system is evolved under selective pressure because it is the first line defense against invading pathogens (Reddick and Alto 2014). The 'innate immune system is an antigen-dependent and non-specific type of defense that is instantly utilized by the host defense upon encountering an antigen and has no immunologic memory' (Warrington *et al*. 2011:1). Similarly, 'adaptive immunity is an antigen-dependent and antigen-specific defense mechanism that has a volume for memory and rapidly prompts the host immune response following exposure of pathogens' (Warrington *et al*. 2011:1). A mismatch in the innate and adaptive immunity could increase host susceptibility for disease onset (Warrington *et al*. 2011). Such pathogens could inhibit the immunity by creating barriers in the 'secretion of cytokines and trafficking of cell surface receptors' (Reddick and Alto 2014). It is recommended that antibiotics be used on an intensive basis with a high dosage at a short duration of 3-7 days to control the infection and a consult should be done within 3 days to determine whether the antibiotic treatment should be continued or stopped as the only guide to determine the effectiveness of the antibiotic treatment is the clinical improvement of the patient (Maslamani and Faraj 2018). Therefore, when there is sufficient clinical evidence that the patient's host

defenses have regained control over the infection and the infection is resolving, the antibiotic treatment can be stopped (Maslamani *and* Faraj 2018).

2.12. The pathogenesis of odontogenic infections

It is important to note that 'the oral cavity is a complex ecosystem that changes constantly throughout life' (Sweeney *et al*. 2004:568). It comprises of almost 300-500 species of various micro-organisms (Sweeney *et al*. 2004). An estimated '700 species may colonize the oral cavity, 400 species colonize the subgingival area' (Lopez-Piriz *et al*. 2007:154). Supragingival biofilm is mainly gram positive facultative and saprophytic (Lopez-Piriz *et al*. 2007). Almost '12%of antibiotics are prescribed for odontogenic infections with the most common odontogenic infections being 25% of periapical abscess, 11% of pericoronitis and 7% of periodontal abscess (Lopez-Piriz *et al*. 2007:154). Approximately '7% of common odontogenic infections such as alveolar abscess, periodontal abscess, dental pulp infection, chronic periodontitis and acute necrotizing gingivitis consist of anaerobic bacteria' (Jain. and Oswal 2013:21). When the bacteria invade the tooth's internal tissues, the biofilms evolve and the root canal becomes infected with gram negative anaerobic proteolytic bacteria (Lopez-Piriz *et al.* 2007). In the initial stage of odontogenic infections the predominant microorganisms are gram positive cocci and facultative anaerobes that comprise of 85% of the infection (Peric *et al*. 2015). In the advanced stages of odontogenic infection, where abscess formation is present, strict anaerobes such as gram negative and gram positive cocci are greatly involved (Peric *et al*. 2015). These microorganisms could 'comprise 30%-50% of the infection' (Peric *et al.* 2015:112), therefore, the antibiotic of choice must cover gram positive and gram negative anaerobic bacteria (Salmeron-Escobar *et al.* 2006).

Since the 1930's, a majority (75%) of blood samples showed the presence of streptococcus mutans in patients that were diagnosed with caries, gingivitis and periodontitis while only 30% of blood samples of healthy individuals were positive for streptoccocus mutans (Maestre Vera *et al*. 2007). It was reported that '4% -7% of the cases presented with odontopathogens are gram negative bacilli of HACEK group (Haemophilus, Actinbacillus, Cardiobacterium, Eikenella, and Kingella)' (Maestre Vera et al 2007:E44). Other periodontal pathogenic anaerobic bacteria were found in 64% of blood cultures, these included mixed bacteria or only anaerobic bacteria (Maestre-Vera *et al.* 2007). Anaerobic bacteria are mainly present in well-circumscribed,

chronic, non- advancing abscesses. If the infection is severing, it may present with mixed flora, aerobic and anaerobic bacteria (Maestre-Vera *et al.* 2007; Lopez-Piriz *et al.* 2007). If the infection becomes chronic, contained and controlled the likelihood that only anaerobic bacteria will be present, is high (Jain and Oswal 2013).

In 1986, 'streptococci that produce B-lactamase were extracted from the subgingival plaque of adult patients that were diagnosed with periodontitis' (Maestre- Vera *et al*. 2007:E48) The isolated samples showed bacterial resistance that was uniquely mediated and altered to the Penicillin-binding proteins because the production of the B-lactamase was uncommon for most streptococci (Maestre- Vera *et al*. 2007). A study done in Spain found that strains of 'P.gingivalis that produce B-lactamase were less frequently isolated from periodontal pockets' (Sanchu-Puchades *et al*. 2009; E536). In a study done at the Alfonso X el Sabio University in Madrid, it was found that streptococcus viridans was the most commonly isolated bacteria among the post-operative bacteraemia (Maestre- Vera *et al*. 2007).

According to Gutierrez *et al*. saprophytes are the bacteria that are generally involved in odontogenic infections. The opportunistic anaerobic bacteria that penetrate the dentinal tubules such as streptococcus, staphylococcus and lactobacilli species are involved in the evolution of dental caries (Gutierrez *et al*. 2006). The bacteria diffuse along the root canal when the pulp is necrotized and the process results in a periapical inflammation which is predominantly composed of 'Prevotella species, Porphyromonas species, Fusobacterium species and Peptostreptococci species in the inflammatory phase' (Gutierrez *et al*. 2006:78).

Bacterial plaque is formed by the presence of streptococcus mutans and the lactobacillus genus could lead to dental caries (Gutierrez *et al*. 2006). Bacterial penetration through the tooth results in pulpal invasion and a possible inflammatory response (Gutierrez *et al*. 2006).

A chronic non-advancing abscess consists mainly of anaerobic bacteria (Jain and Oswal 2013). Aerobic bacteria present in wide spread cellulitis type of infections will lack abscess formation (Jain and Oswal 2013). If the infections are severe, it may present with mixed flora, aerobic and anaerobic bacteria (Jain and Oswal 2013). If the infection becomes chronic, contained and controlled, it will contain aerobic bacteria only (Jain and Oswal 2013).

Certain bacteria are genetically antibiotic resistant while some bacteria require alteration and destruction via the evolution process so that bacterial resistance is transmitted from one bacteria to another by the process of moving genetic products by direct contact between the cells, or by the process of absorption of raw DNA from the local environment (Brunce and Hellyer 2018).

Table 5: The mechanism of action of antibiotics and its contribution to antibiotic resistance

Antibiotic Class	**Mechanism of action**	**Contribution to antibiotic resistance**
Beta- Lactam antibiotics (Penicillins) *Target:* Treat infection caused by Enterobacteria	● Inhibits the last stage of peptidoglycan biosynthesis where transpeptidation occurs. ● Deactivation of enzymes ● Prevent formation of cross-links on the bacterial cell wall ● Lysis	● Mechanism of resistance against Beta-lactam antibiotics. ● Gram negative bacteria ● Ezymes act in the periplasmatic space through enzymatic hydrolysis of the antibiotic. ● Slow process ● Allows for bacterial multiplication. ● Antibiotic resistance will emerge locally ● Increased use of one antibiotic
Nitroimidazoles (Metronidazole) *Target:* Anaerobic bacteria for aggressive periodontitis	● Form of a prodrug: penetrates bacterial cells by passive diffusion (It is then activated by Ferrodoxin ● Activated Metronidazole would induce the denaturation of the double stranded DNA and an extensive, irreparable single strand break in facultative anaerobic bacteria ● Periodontal pathogens are sensitive to Metronidazole	● Resistance results from alteration of the enzymes involved in the drugs intracellular activation ● Health care practitioners must provide education to the patients to abstain from alcoholic beverages to reduce the disulfiram reaction symptoms.
Macrolides (Clindamycin) *Target:* It is active against gram positive aerobic bacteria and gram negative anaerobes. They are mainly bacteriostatic and their bactericidal activity depends on the concentration of bacteria	● Has great absorption capacity and reaches high concentrations in the phagocytic cells of abscess so that very high levels of the antibiotics can be obtained in the inflammatory tissues ● Inhibits protein synthesis through disrupting the bacterial ribosome function by bonding to the ribosome subunit 50s ● This drug is mainly recommended when allergy to Beta-lactam exists. ● A combination of Clindamycin and aminoglycoside is the therapy of choice for mixed anaerobic-aerobic infections	● Bacterial resistance to Clindamycin results from methylation of the ribosome subunit ● When this happens, the Clindamycin cannot interact with the subunit

Source: Blanc *et al*. 2015: 2-3

2.13. Managing antibiotic resistance

Antimicrobial resistance can be grouped such as intrinsic, mutational and acquired (Soares *et al.* 2012). Resistance occurs in bacterial populations as a result of selective pressure that is applied by antibiotic therapy to the oral bacteria that are exposed to a lower concentration of the antibiotic such as Minocycline resistance that has resulted from the emergent bacterial strains that indicate a lower sensitivity to the antibiotic (Sweeney *et al.* 2004). Selective resistant bacteria present in the oral flora require a critical concentration of antibiotic to be achieved in the oral cavity (Sweeney *et al.* 2004).

The choice of antibiotic for the treatment of bacterial infections could determine if resistance could set in (Sweeney *et al*. 2004). Narrow spectrum antibiotics such as Penicillins are preferred to broad spectrum drugs such as Cephalosporins and Sulfonamides and a more restrictive pattern should be implemented in a policy (Sweeney *et al.* 2004) and (Jain and Oswal 2013). Patient compliance is seen as a critical factor (Sweeney *et al.* 2004; Dar-Odeh *et al.* 2010; Jain *et al*. 2013). It is recommended that narrow spectrum antibiotics with low toxicity and low cost be used for endodontic treatment (Morrow 2012). Dental practitioners should strive to achieve compliance with the recommendations for antibiotic prescriptions and understanding the proper indications for antibiotics used for the management of dental conditions (Peric *et al.* 2015).

In a study done in Alfonso X el Sabio University in Madrid it revealed that the indication for Amoxicillin and Clavulanic acid is the ideal prophylaxis for most infections that involve bacteria from dental origin (Maestre-vera *et al*. 2007). The antimicrobial drugs have a broader cover over dental bacteria (Maestre-Vera *et al.* 2007). In the United Kingdom, the Faculty of General Dental Practice (FGDP) and the Scottish Dental Clinical Effectiveness Program (SDCEP) recommend the first choice of Amoxicilin in the management of acute dento -alveolar infections (Smith *et al.* 2020)

In 2013, the most commonly used agents in dentistry were Amoxicillin and Clindamycin (Marra *et al*. 2016). Although the use of Amoxicillin and Clindamycin has increased, the use of Penicillin V has declined. (Marra *et al* 2016). In Sweden, 70 percent of the total prescriptions in the country are comprised of prescriptions of Phenoxymethyl Penicillin for adults as recommended by the Swedish Medical Products Agency (Smith *et al.* 2020).

Prolonged antibiotic therapy can progress to the evolution of bacterial resistance that is at first susceptible to antibiotics therapy and then completely resistant to antibiotic therapy (Giedratiene et al. 2011). Antibiotics could 'establish a detectable concentration through their chemical structure in the salivary component at the intracellular level of the oral tissues' (Soriano and Rodriguez-Cerrato 2002; 51). The lack of resistant bacteria and the ability of an antibiotic to achieve an optimal concentration in the upper respiratory tract contribute to a lower potential for antibiotic resistance in the upper respiratory tract (Soriano and Rodriguez-Cerrato 2002).

Azithromycin used in the management of COVID-19 showed some success and could be applied to dental practice (Dar–odeh *et al.* 2020). It is a macrolide and is recommended for treating odontogenic infections in patients that have allergies to penicillin (Darodeh *et al.* 2020). As a result of the COVID-19 pandemic, the trend in oral health care has moved towards the provision of emergency management only, the expansion of antibiotic prescription for the management of severe dental conditions could thus include the use of Azithromycin (Dar-odeh *et al.* 2020).

Table 6: Antibiotic concentration in Saliva and Serum

Antibiotic class	**Action**
Penicillin	Many B-lactam antibiotic concentrations are achieved in the serum, however, the extent of sensitivity for the oral Streptococci in low salivary concentrations does not cause any problems (Soriano and Rodriguez-
Erythromycin	Erythromycin reaches a higher concentration in serum than in saliva
Azithromycin	Azithromycin is significantly higher in the saliva but in the treatment of oral infections, Azithromycin depresses the concentration of Non-steroidal anti-inflammatory drug present s in the periodontium

Source: Soriano and Rodriguez-Cerrato 2002:52

Broad spectrum antibiotic are recommended as empirical therapy against majority of the bacteria (Jain and Oswal 2013).

Table 7: Mechanism of action of Bactericidal Antibiotics and Bacteriostatic Antibiotics

Bacteriostatic Antibiotics	Bactericidal Antibiotics
● Bactericidal antibiotics are preferred over bacteriostatic antibiotics ● Antibiotic therapy is indicated to reduce the bacterial problems	● The bacteriostatic drugs decelerate the growth of bacteria in order for the immune system to abolish the static bacterial population and restore healing
● If the host defenses system is immune-compromised at some stage, the use of bactericidal drugs becomes critical ● Bactericidal drugs exert prolonged post antibiotic effect after consumption so that the serum drug level is maintained	● With bacteriostatic drugs, if the drug level is decreased, the bacteria will multiply and there will be a relapse of infection
● Bactericidal drugs incorporate into the bacterial cell, exert their influence and then cause the cell to die	● Bacteriostatic antibiotics can only exert their effect only when they exert their presence in the patient's tissues

Source: Jain and Oswal 2013:21 -22

It is recommended that the least toxic antibiotic be used because sometimes the drug and living pathogens can harm or destroy the human cells (Jain and Oswal 2013; 22).

Table 8: Broad spectrum antibacterial mouthwash

Broad spectrum Antibacterial Mouthrinse	Target	Mechanism of Action	Contribution to Antibiotic Resistance
Bis-biguanide biocide (Chlorhexidine Gluconate-containing mouthrinse)	● Cationic with broad spectrum antibacterial activity. ● Membrane disruption causes concentration dependent growth inhibition and cell death	● Membrane disruption ● Concentration-dependent growth inhibition and cell death ● Interactions cause obstruction of the proteolytic and glycosidic enzymes. ● The cationic nature of the Chlorhexidine Gluconate has a cationic profile that improves substantivity to the tooth surface and the oral mucosa ● This will reduce the formation of pellicle through a controlled release of antimicrobial agents thereby greatly reducing plaque formation and preventing gingivitis	● Received little research attention.

Source: Mc Bain *et al.* 2003:4770

Tests such as the microbial-enzymatic N-benzoyl-DL-arginine-2-napthylamide (BANA) could be used to identify bacteria in subgingival plaque such as *Porphyromonas gingivalis*, *Treponema denticola* and *Tannerella forsythia* (Dhalla *et al.* 2015).

The opportunity to design new evidence –based theory-informed contextually fit approach to combat antibiotic resistance through by tackling unnecessary antibiotic prescribing practices and to improve the quality of care for patients with acute dental infections does exist (Thompson *et al*. 2020). Dental practitioners are involved in almost ten percent of all antibiotic prescriptions; therefore, it is essential for dental practitioners to be involved in the development, strategic planning and implementation of the Nation Action Plan against Antimicrobial Resistance when managing dental conditions (Sanderson 2019).

2.14 Summary

This chapter outlined the global and local context of antibiotic prescriptions. The chapter also focused on the various systemic conditions and dental conditions requiring antibiotic prophylaxis including the treatment options. The microbiology of odontogenic infections, the inflammatory process and the host response system to respond to the mechanism of action of the antibiotics prescribed were highlighted, so as to establish possible contributing factors to antimicrobial resistance among South Africans. The different levels of care were explored to identify their possible contribution to the increase of antimicrobial resistance. The Antimicrobial Resistance Strategic Framework was reviewed together with the South African Antibiotic Stewardship programme and the available the surveillance methods to measure antibiotic resistance. The next chapter highlights the study design and methodology.

CHAPTER 3: STUDY DESIGN AND METHODOLOGY

3.1. Introduction

This was an exploratory study, using a combination of qualitative and quantitative data which examined the trends in the practice and patterns of antibiotic prescription rates for dental conditions among health care workers in Pietermaritzburg, KwaZulu-Natal.

Three phases were used in this study (Table 9). The first phase comprised of a retrospective patient clinical record review. The second phase was a cross-sectional design and required participation from a purposive sampled group of health care practitioners in the public health sector who prescribed antibiotics, such as dental and medical practitioners who prescribe antibiotics and pharmacists who dispensed antibiotics. This phase utilized two questionnaires to get a perception on the knowledge, practices and patterns of antibiotic prescription in the public health sector. The third phase was an exploratory study to gain a better understanding on the trends in antibiotic prescription patterns and practices among health care practitioners. This aspect comprised of a semi-structured focus group discussion.

Table 9: Phases of data collection

Phase 1		
Objectives	**Activity**	**Sample population**
To determine the patterns of antibiotic prescription for dental patients in the identified public health institutions by means of a retrospective chart review.	Retrospective chart review	Patient clinical records
Phase 2		
To determine dental and medical practitioners' knowledge, attitudes and antibiotic prescription practices for the management of dental conditions by means of a self-administered questionnaire.	Self-administered questionnaire	Medical and dental practitioners
To ascertain pharmacists' perspectives on the patterns of antibiotic prescription rates for dental use by means of a self- administered questionnaire.	Self-administered questionnaire	Pharmacists
Phase 3		
To explore health practitioners' perspectives (medical and dental practitioners, and pharmacists) on antibiotic prescription rates for dental patients by means of a focus group discussion.	Focus group discussion	Dental and medical practitioners. Pharmacists

3.2. Phase 1

3.2.1. Study design

This was a retrospective, quantitative based clinical record review.

3.2.2. Study site

The research site was the Pietermaritzburg complex in KwaZulu-Natal. Two public health facilities were purposively selected for this study (Institution A) and (Institution B).

3.2.3. Sample population

This comprised clinical record for patients that received antibiotics cover for dental conditions during the period: March 2012 to July 2018. A total of 720 patient clinical records were reviewed as part of the retrospective chart review. The required information from each clinical chart was captured on a clinical record evaluation sheet and antibiotic therapy worksheet. (Annexure 6)

3.2.4. Selection Criteria for patient clinical record

Inclusion- Clinical records for patients aged 6 to 80 years were eligible for the study. Evidence of documented antibiotic prescription for dental conditions, antibiotic prophylaxis for systemic conditions such as infective endocarditis and other instances such as antibiotic cover prior to dental surgery or after dental treatment was considered for this study.

Exclusion- The clinical records for the patients below the age of 6 and above the age of 80 years. The clinical record that did not have any prescription for antibiotics for dental conditions but had information that showed management through other dental interventions was excluded from the study. The clinical record that had no prescription for antibiotics was excluded from the study.

3.2.5. Sample framework

3.2.5.1. Sample technique

Purposive sampling was implemented, where only clinical records of patients that received antibiotics for dental management was selected. The dental registers at each hospital, indicated

patients who had antibiotic prescriptions for dental conditions. The sampling was done for each year at each of the public health hospitals and a final total was obtained for the period March 2012 till July 2018. The manager at the admissions department of the respective research sites was responsible to assist with selecting and retrieving the patient clinical records based on the criteria set by the researcher. From this every file that had the information that was required for this study, was selected based on the sample size per year and per hospital to give a total of 720 files. This was done to enhance the study's credibility.

3.2.5.2. Sample size

The sample size was obtained after consultation with the statistician. The sample size was calculated taking into consideration the sample proportional to the size of the hospital. The sample of patient clinical records was proportional to the population size of each hospital in the past five years (March 2012 until July 2018). The initial sample size was set at approximately 1000 patient clinical records; however, Hospital C withdrew from the research. The sample size was then re-calculated and set at 354, 8 from Hospital A and 529, 9 from Hospital B. The final sample was set at 884, 7 patient clinical records. Due to shortcomings and challenges faced by the administrative departments at the two public health hospitals, in archiving patient medical records, the total sample number was 720 clinical records that were assessed for this study (n=720).

3.2.6. Procedure

Ethical clearance was obtained from the Biomedical Research Ethics Committee, University of KwaZulu-Natal (Reference number. BE026/190) and permission to conduct the study was obtained from the KwaZulu-Natal Department of Health (Reference Number. KZ_201902_018). Gatekeeper permission was obtained from the Chief Executive Officers of the public health care hospitals chosen to participate in this study. The managers of the administrative departments of the public health care hospitals were also informed of the nature of the study so that they had a clear understanding of the criteria selection for the patient clinical records that was required for the purpose of the research. A schedule was drawn up to view the patient clinical records at each hospital once the clinical records were made available by the managers of the administrative departments. The information from the clinical records was captured on a data collection sheet

that comprised of a clinical record sheet and clinical assessment sheet. (Annexure 6).The data was then transcribed on a Microsoft excel sheet and Microsoft word sheet which was analyzed using Nvivo version 11.

3.2.7. Data collection tools

An antibiotic worksheet (developed by Huang and Owen 2012 and Ntsekhe 2011) was used to document information on the research site, gender, age of the patient, history of the dental infection, symptoms, whether the patient experienced similar symptoms before, provisional diagnosis, laboratory information, treatment prescribed, number of medication prescribed, dose, frequency and route of administration. The treatment outcomes were also noted. The prescriptions of antibiotics for the common dental infections were compared to the recommendations made in the Standard Treatment Guidelines 2018. The antibiotic therapy worksheet (Annexure 6) was used to gather information related to the appropriateness of the antibiotic regimen, compared with the Standard Treatment Guidelines 2018 and the therapeutic duplication and adverse reactions were noted. This worksheet for data capturing was validated in previous studies (Huang and Owen 2012; Ntsekhe 2011).

3.3. Phase 2

3.3.1. Study Design

This is a cross-sectional study design that used purposive sampling to determine health care practitioners' perspectives in a single point in time. The quantitative approach was to elicit health care practitioners' knowledge, attitudes and trends in antibiotic prescription practices for dental use. The data was obtained from closed and open-ended questions as well as a Likert scale in the form of a questionnaire for healthcare practitioners who prescribe antibiotics for dental conditions and pharmacists who dispense antibiotics for dental conditions.

3.3.2. Study site

The research site was the Pietermaritzburg complex in KwaZulu-Natal. Two public health facilities were purposively selected for this study (Institution A) and (Institution B). This phase of the study was conducted in the actual departments where dental practitioners, medical practitioners and public pharmacists worked.

3.3.3. Sample Population

Purposive sampling technique was used as it is concerned with a particular characteristic of a population for participant selection (Tobias *et al*. 2018), as this study is concerned with practitioners who prescribed antibiotics for dental conditions. The health care practitioners who prescribed antibiotics for dental conditions such as dental practitioners, and medical practitioners in the public sector and public health pharmacists, who dispense antibiotics at the hospitals that participated in the study, were selected. Sampling was done so that confounding variables are distributed evenly and bias is eliminated on the part of the researcher (Shenton 2004).

3.3.4. Sample size

The sample size for the quantitative phase was obtained after consultation with the statistician. The sample size was calculated taking into consideration the sample proportional to the size of the hospital. It was established that all health care practitioners who prescribe and dispense antibiotics was included in the study. There were 79 medical practitioners, 14 dental practitioners (Group 1) and 23 pharmacists (Group 2) that participated in the study. Although 123 participants were approached the total number of participants that responded for this study was 116 public health care practitioners.

3.3.5. Selection Criteria

Inclusion- All dental and medical practitioners and pharmacists employed in the public health sector. The health care practitioners selected must be eligible to prescribe antibiotics for dental conditions. The public health pharmacists who dispense antibiotics were included in this study.

Exclusion- The dental and medical managers who were not clinically involved in the management of patients. The practitioners who do not treat patients or prescribe antibiotics for patients were excluded from the study. Dental, medical and pharmacy students were excluded. Oral hygienists and dental assistants as well as pharmacy assistants did not participate in this study.

3.3.6. Sample Framework

3.3.6.1. Sample technique

The Human resources recruitment officers were contacted regarding the staff establishment at the participating public health care institutions. A purposive sampling of the public health care practitioners such as medical practitioners, dental practitioners and pharmacists was conducted and they were approached to participate in the study. The nature of the study was explained and then informed consent was obtained. The medical and dental practitioners and the pharmacists that consented to participate in the study were thereafter given survey questionnaires to complete (Annexure 4) and that group formed the sample for the research.

3.3.7. Procedure

Ethical clearance was obtained from the Biomedical Research Ethics Committee, University of KwaZulu-Natal (Reference number. BE026/190) and permission to conduct the study was obtained from the KwaZulu-Natal Department of Health (Reference Number. KZ_201902_018). Gatekeeper permission was obtained from the Chief Executive Officers of the public health care hospitals chosen to participate in this study. A register of all employed health care practitioners and pharmacists from the participating hospitals was obtained from each of the heads of department at each hospital. Disclosure, understanding and voluntariness are essential for informed consent to be valid; therefore participants were given informed consent forms to sign prior to their participation in the study. Information about the nature of the study was fully disclosed to the participants in an understandable language and manner explaining the potential risks and benefits of the study. The participants were also informed about the time commitments and had the right to withdraw from the study. To prevent any undue influence or coercions, the participation in the study was entirely voluntary.

The written informed consent was obtained from each participant willing to participate in the study. The signature on the consent forms indicated that he/ she was fully willing to form a part of the study without being subjected to compulsion from a second party, therefore, avoiding undue influence and coercion. Once the consent forms were received the participants were issued with the survey questionnaire. The researcher was responsible for administering the questionnaires to the participants. For privacy purposes, each participant was issued a questionnaire personally and privately.

3.3.8. Data collection tool

1. Self-administered semi-structured questionnaire for the medical and dental practitioners (Annexure 7)

The questionnaires were distributed to 123 medical and dental practitioners (Group 1. n=123). The questionnaires comprised of fifteen open-ended and closed-ended questions that were designed to assess the health care workers' knowledge, attitudes and practices related to antibiotic prescriptions for dental use. The first part of the questionnaire included socio-demographic data such as age, gender and year of study, the National Strategic Framework on antimicrobial resistance, the Antibiotic Stewardship Committee and the adherence to the Standard Treatment guidelines. The second part of the questionnaire focused on the participants' awareness of the guidelines developed by the National Institute of Health Care and Excellence and the guideline by the American Heart Association, the South African National Strategic Framework on Antimicrobial Resistance and Antibiotic Stewardship. The last part of the questionnaire comprised of questions in the form of a Likert Scale to analyze perception of the outcome of the antibiotics often prescribed. This focus was mainly on the perceived impact or influence on public health and on practitioner perceptions regarding the effectiveness and the efficacy of antibiotic therapy of choice, and the recommendations, thereof, for the improvement in antibiotic prescription for dental use in the public sector. The last part of the questionnaire focused mainly on the perceptions and barriers that health care practitioners' experienced. The questionnaire was designed to assess the trends in antibiotic prescription patterns and perceptions health care workers have on antibiotic resistance. Information on the knowledge, the attitudes towards antibiotic prescription practices and the adherence to the standard treatment guidelines was also gathered from the questionnaire. The data was captured on a excel spread sheet.

2. **Self-administered semi-structured questionnaire for the pharmacists (Annexure 8)**

A second questionnaire was utilized for the 25 public health pharmacists (Group 2: n=25). The questionnaire comprised of 10 questions that were designed to elicit the pharmacists' perspectives on antibiotic prescription trends. The first part of the questionnaire comprised of questions examining the pharmacists' perceived correlation between the antibiotics prescribed and the dental condition, the indications for the antibiotic therapy for dental conditions and the perceptions on the health care practitioners' adherence to the Standard Treatment Guidelines. The questions posed also included perceptions on the identified drug's mechanisms of action and

possible adverse effects. The Likert Scale format required responses such as 1 (Strongly agree); 2 (Agree); 3 (Not sure); 4 (Disagree); 5 (Strongly Disagree). The questionnaire also comprised of open and closed-ended responses. The second part of the questionnaire focused on perceptions of therapeutic duplication of antibiotics, the availability of laboratory information and the recommendations for the improvement in antibiotic prescriptions. The data was captured on a Microsoft excel spread sheet.

3.3.9. Data Collection Process

When the survey questionnaire was completed it was returned to the researcher. The participants completed the questionnaire within a day or over a period of a week. Once it was completed the researcher retrieved the completed questionnaire from the participants' respective departments. In some instances, follow up visits had to be made to collect the outstanding questionnaires as some practitioners required more time to complete the questionnaire. All the participants were acknowledged verbally and appreciated for their participation. The data was captured on a Microsoft excel spread sheet.

3.3.10. Quantitative Data Analysis

Quantitative data analysis was used for Phases 1 and 2 of this study. The data was first cleaned and coded. A code book was prepared to ensure that codes were exclusive. The data was counted numerically and used to identify patterns. The data was then captured on Microsoft Excel spread sheet and was analyzed using SPSS (version 25^{R}). Univariate descriptive statistics such as frequency and mean distribution was conducted for all variables. The data was organized and coded to give meaning to the data using univariate descriptive statistics such as frequency which will account for the number of times a particular score or value has been found on the data sheet. Percentages were used to express the scores or values as a percentage of the population. Mean is a numerical average of the scores or values for a particular variable. A median is a numerical midpoint of the scores or values that is the centre of the distribution of the scores. The minimum or maximum range will indicate the highest or lowest value or score for any variable.

Bivariate statistics was also be used to assess the outcome and the outcome was analyzed by the explanatory variable (Betani *et al*. 2018). Bivariate statistics and p-values are required for the data collection process. P-value is the probability of obtaining a result that is equal to or more

extreme than what was actually observed (Dahiru 2008). P represents probability and its value closest to 0 indicates significant difference while 1 suggests no difference between the groups tested (Dahiru 2008).

Bivariate statistical inference will display a general impression of the effectiveness of the treatment (Zhang 2016). When there is an association between two variables such as the practices and patterns of prescription, the one variable defines the outcome and the different values are defined by the other variable which is known as the explanatory variable (Bertani *et al.* 2016). Therefore, bivariate analysis allows for the assessment of the outcome variable which depends on the values displayed by the explanatory variable (Bertani *et al.* 2016).

The responses to open-ended questions were grouped and emergent themes were examined and compared for possible associations. Inferential techniques included Pearson's Chi-Square tests to assess a possible relationship between the independent variable (age, gender, etc.) and dependent variable (frequency of antibiotic prescription and guidelines). The p-value of 0, 05 level was established as being significant.

3.4. Phase 3

3.4.1. Study Design

This was an exploratory design comprising of qualitative data obtained from focus group discussion using a semi-structured scheduled questionnaire.

3.4.2. Study Site

The research site was the Pietermaritzburg complex in KwaZulu-Natal. Two public health facilities were purposively selected for this study (Institution A) and (Institution B). This phase of the study was conducted in the hospital board room at the participating hospitals.

3.4.3. Sample Population

This phase comprised of health care practitioners (medical and dental practitioners) and pharmacists, involved in prescribing and dispensing of antibiotics for dental purposes at the identified research sites. Purposive sampling was used to set up two focus group-discussions (FGDs) comprising of six people per group at each research site.

3.4.4. Selection Criteria

Inclusion- All dentists, dental therapists, medical doctors and pharmacists employed in the public sector and are eligible to prescribe antibiotics for dental conditions or dispense antibiotics for dental use and those who are registered with the Health Professionals Council of South Africa or the Pharmacy Council of South Africa (in the case of pharmacists).

Exclusion- The managers who are not clinically involved in the management of patients and those practitioners who do not treat or prescribe medication for patients. Dental, medical and pharmacy students were excluded. Oral hygienists and dental assistants as well as pharmacy assistants did not participate in this study.

3.4.5. Sample Framework

3.4.5.1 Sample technique

After consultation with statistician to minimize bias and increase significance of the study, Purposive Sampling Technique (which is a non-probability sampling technique) was used as it is concerned with a particular characteristic of a population for participant selection as this study is concerned with health care practitioners who prescribe antibiotics for dental conditions and pharmacists who dispense antibiotics for dental conditions in the public sector. Sampling was done so that confounding variables would be distributed evenly and bias on the part of the researcher is eliminated. Theoretical saturation occurs when the focus-group sessions continue until a clear pattern emerges and the subsequent groups produce no new information (Tobias *et al*. 2018).

3.4.5.2. Sample size

The sample size for the qualitative phase was obtained after consultation with the statistician. The sample size was calculated taking into consideration the sample proportional to the size of the hospital. It was estimated that six practitioners will comprise a group. One group per hospital was finally established for the purpose of this research.

3.4.6. Procedure

A meeting was set up with health care practitioners in the hospital board room at each of the participating hospitals to outline the purpose of the study. Each focus group discussion was scheduled based on the participants' availability and convenience. The date, time and venue for each appointment were determined through consultations with the interested participants and when a general consensus was obtained. All the discussions were audio recorded and transcribed verbatim. The participants were thanked for their participation and time for the research and were informed that their participation will be acknowledged in the upcoming manuscripts that will arise from the focus group discussions.

3.4.7. Data collection tool

The focus group schedule comprised of open-ended questions that explored the participants' perspective on the National Strategic framework, Essential Medicines List, Standard Treatment Guidelines, The South African Antibiotic Stewardship Programme, prescription patterns of antibiotic prescriptions practices for the management of dental conditions, adverse events related to antibiotic prescription and the trends and perceptions of antibiotic prescription practices from a multi-disciplinary approach. The second part of the questions include perceived barriers, challenge and opportunities to access oral health care, patient compliance, and the value of a multi-disciplinary team approach in combating antibiotic resistance. The questions in the discussion included fifteen questions designed to assess the trends in antibiotic prescription patterns and practices among health care practitioners. The last part of the open -ended questions included existent support for promotional activities and combating antimicrobial resistance like risk factor intervention programs and antibiotic stewardships to reduce antibiotic resistance and to improve the access to oral health services in Pietermaritzburg.

3.4.8. Data collection Process

The interviews for the focus group discussion were audio recorded and the recordings were transcribed verbatim and then cleaned. The information was then transcribed onto a Microsoft word document. Each research consultant was engaged to assist with the data analysis process. Data coding was done independently by the researcher and the research consultant in order to identify significant features of the data and to sort the data, thereby allowing the emergence of

sub-themes and themes from the participants' response as part of the thematic analysis (Thomas and Harden 2008; Bazeley 2009; Dookie *et al*. 2017). The data was then compared to develop common themes.

3.4.9. Qualitative data analysis

Qualitative data was used to measure the quality of the pattern and to determine the reasoning behind the identified prescribing patterns and trends. This refers to the processes and procedures that were used to analyze the data to provide a level of explanation, of understanding, or of interpretation. As the research progressed, the meaning and understanding would increase in a non- linear fashion. The Nvivo version 11 program was used for the synthesis of the focus group discussions but the data analysis was conducted by the researcher. The focus group discussions were first transcribed verbatim and the data clean-up process was applied. The data-coding was done independently by the researcher and the research consultant to identify significant features of the data and to sort the data, thereby, allowing the emergence of sub-themes and themes from the participants' responses as part of the thematic analysis (Thomas and Harden 2008; Bazeley 2009; Dookie *et al.* 2017).

A code guide was developed to guide and support the coding process. This added significance to the data and allowed for inductive reasoning on the emergent themes. The grouping of the data and dividing it in respect to its relevance or irrelevance to the study was important (Thomas and Harden 2008; Bazeley 2009; Dookie *et al.* 2017). The data was then compared to develop common themes. Data analysis for the qualitative study required mainly content analysis and thematic synthesis. The content analysis was used to analyze and interpret verbal data. Thematic synthesis identified themes or patterns that may consist of ideas, patterns, interactions and phrases (Thomas and Harden 2008). It connected and linked relative importance in the responses that were received (Thomas and Harden 2008). It was used to 'identify relationships between the themes or data sets in an attempt to find explanations from the data' (Thomas and Harden 2008:4). Themes and valid points were connected to form significant findings in the report of the results. The availability of the Standard Treatment Guidelines and the Essential Medicines List in the dental departments and the rate of adherence to the guidelines were explored in the focus-group discussion.

3.5. Scientific validity and Reliability in the Quantitative Data

3.5.1. Scientific Validity

Scientific validity is applicable in quantitative research. It is concerned with the degree to what an assessment tool measures what it is intended to measure. The questionnaires used in the study were adapted from previous studies. The study also used research methods that were supported by published literature. A pilot test was done by non-participants of this study to refine the questionnaires to add to the validity. The responses were anticipated and checked for coherence. The questionnaires were formulated due to the objectives and other literature. The questions were aligned to the aims and objectives of the study which would add to the internal validity of the study. The findings were limited to the Pietermaritzburg Complex and if the overall shortcomings that were identified were consistent with other districts and provinces. This would enhance and add credibility to the external validity of the study.

3.5.2. Reliability

Reliability in a quantitative study is the ability to reproduce the results of the study if a particular instrument is used at different times by different researchers. This study instrument was not used by other researchers previously. It was self-structured based on the objectives of this study. Reliability was maintained by double-checking the data during the data entry and all outliers were eliminated. The data from the semi-structured focus-group discussion were relatively reliable. The responses were from the practitioners who are engaged in the prescription or dispensary of the antibiotics and are responsible for oral health service delivery. The Cronbach alpha test had a statistical number of 0, 68 for internal consistency.

3.6. Rigor and trustworthiness of the qualitative data

Credibility, conformability, transferability and dependability were maintained to guarantee rigor and trustworthiness in the qualitative component of the study.

3.6.1. Credibility

Credibility, through ‘internal validity in qualitative research establishes whether the findings of the study are genuine and a true reflection of the participants’ original view’ (Braun and Clarke

2006:88). In this study, peer debriefing was conducted by another member of the research team who reviewed the data collection methods and processes, transcripts and data analysis procedures.

Maintaining credibility is important to guarantee trustworthiness. In order to maintain credibility, previous well-established literature was reviewed. Sampling was used so that confounding variables are distributed evenly within the sample and bias on the part of the researcher was eliminated. Purposive sampling was used to focus only on the participants possessing characteristic pertinent to the study, about the trends in perceptions and practices of prescription of antibiotics in the management of dental conditions among health care workers in the Pietermaritzburg complex.

Voluntary participation of participants was implemented and, in this case the health care professionals had a right to withdraw on their own free will without being compelled to give clarification. This was a fundamental requirement in maintaining credibility. It was also emphasized in the consent forms that were issued to the participants. The participants were encouraged to be honest about the way they feel as there is no right or wrong answers.

3.6.2. Confirmability

Confirmability was concerned with the extent to which the results would be confirmed by others and was present when there was dependability, credibility and transferability in the study. This was maintained by doing an "audit trail" which took into account the consideration of the pathway from the data collection process to the data analysis process where the readers could track the course of the research via the description of the methodologies involved in the study. Conformability was achieved through the use of quotations of actual dialogues expressed by the study participants (Mandal 2018).

3.6.3. Transferability

Transferability refers to the external validity of the qualitative research. This is usually facilitated by providing a concise description of the context of the enquiry and comparing the research findings with findings in previous and current literature (Creswell 2017).

This was concerned with the degree to which the results of the study could be applied or generalized to other situations. This was maintained by providing a description of: the data collection process, the selection and characteristics of the participants, of the study site and the data analysis process.

3.6.4. Dependability

It was concerned with the ability to reproduce the same results if a study would be repeated with the same participants. It refers to the reliability in the quantitative study design. Dependability was maintained by reporting the process involved in the study so that there was understanding of the subject and can be used as a guide to repeat the research. Maintaining credibility ensures dependability (Shenton 2004).

The interviews for the focus group discussion were audio recorded and the recordings were transcribed verbatim and then cleaned. The information was then transcribed onto a Microsoft word document. A research consultant was engaged to assist with the data analysis process. Data coding was done independently by the researcher and the research consultant to identify significant features of the data and to sort the data thereby allowing the emergence of sub-themes and themes from the participants' responses as part of the thematic analysis (Thomas and Harden 2008, Bazeley 2009, Dookie *et al* 2017). The data was then compared to develop common themes.

Summarizing and respondent validation are useful measures to ensure validity, authenticity and credibility, especially for focus group discussions. On-going communication with the supervisor throughout the research refined the study process.

Dependability was established by getting a few participants to evaluate the analyzed data which comprised their interpretations that were made by the researcher (Creswell 2017). The quotations of actual dialogues of the participants ensured conformability of the research (Mandal 2018). The participants' confidentiality and anonymity were maintained.

3.7. Ethical Considerations

3.7.1. Ethical clearance and permission to conduct the study

After ethical approval was granted and the necessary gatekeeper permissions were secured, written consent was first obtained from all the participants in this study. The signature of the participant on the consent form indicated that he/she is fully willing to form a part of the study voluntarily without being subjected to compulsion from a second party; therefore it was important to minimize undue influence and coercion.

For the privacy concerns each clinical record examined and participant interviewed and assessed through the survey was in done in confidence. All the participants were informed that they had the right to withdraw from the study at any stage should they wish to do so. The study did not include any clinical examination or intervention. Therefore, there was minimal risk of clinical adverse effects. The study did not carry any social or economic risks for the patient or the Department of Health.

3.7.2. Confidentiality and raw data storage

The study did not include any clinical examination or intervention. Therefore, there was minimal risk of clinical adverse effects.

No names or personal particulars were requested upon filling the clinical evaluation or survey questionnaires. The questionnaires only required the profession of the participants. The questionnaires for the survey and the focus group discussion as well as the consent forms were placed in an envelope and then placed in boxes that were sealed. The completed questionnaires, voice recorder and transcripts are kept safely secured in a location where access to external parties is restricted. In order to intensify discretion of the data obtained, the raw data in the form of the clinical evaluation forms and survey questionnaires were quarantined in a location at the University of KwaZulu-Natal, Discipline of Dentistry, where access to the external parties is restricted. A locked cabinet was used for this purpose. The data will only be accessed by the supervisor and the researcher. The data derived from the study was entered onto a Microsoft Excel sheet and was thereafter, electronically stored in a secured or password-protected database and used for the sole purpose of this study. All the data is stored according to the rules and

regulations specified by the University of KwaZulu-Natal, Discipline of Dentistry, which states that the data will be stored for a period of five years and, thereafter, it will be destroyed.

3.8. Dissemination of the results

The results will be made available to the KwaZulu-Natal Department of Health. The head of the discipline of Dentistry at the University of KwaZulu-Natal, the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and the medical managers in charge of the hospitals where the data collection process will be undertaken. The results will also be disseminated via conference presentations and journal publications.

The results of the research will be published in the KwaZulu-Natal, public hospital newsletters and journals. The results will also be presented at Continuing Professional Development presentations for health practitioners. The relevant stakeholders could include educators at training institutions, future researchers and dental and health practitioners in the public and private sectors. Students will also benefit from this study. Participants will be given the results personally and a feedback survey based on anonymity online or in person can be conducted.

3.9 Summary

The study used various methods in three different phases and both qualitative and quantitative data was analyzed accordingly. A retrospective chart review, a self-administered questionnaire and a focus group interview formed the instrument tools for this study. All three phases were used to highlight the dental conditions for which antibiotics are prescribed and the trends in antibiotic prescription patterns among health care practitioners for dental conditions. The knowledge, attitudes and practices of health care practitioners in prescribing antibiotics for dental conditions highlights the perception of their role in combating antimicrobial resistance and the awareness of such a public health concern.

CHAPTER 4

First Manuscript: Preface

The purpose of the first manuscript entitled *Public Health Care Practitioners' knowledge, attitudes and practices towards antibiotic prescriptions for dental use in the Pietermaritzburg region, KwaZulu-Natal,* was to have an insight into the health care practitioners' perspectives on antibiotic prescription trends for the management of dental conditions in Pietermaritzburg, KwaZulu-Natal.

This manuscript focused on two of the study objectives, namely to ascertain dental and medical practitioners' knowledge attitudes and antibiotic prescription practices for the management of dental conditions attitude towards antibiotic prescription and to ascertain pharmacists' perspectives on the patterns of antibiotic prescription rates for dental use. The manuscript explicitly outlined perspectives on antibiotic prescription trends and the need for clear evidence-based guidelines for antibiotic prescription for the management of dental conditions to reduce antimicrobial resistance.

Manuscript 1: Public Health Care Practitioners' knowledge, attitudes and practices towards oral antibiotic prescriptions for dental use in the Pietermaritzburg region, KwaZulu-Natal. P. Ramnarain[1], BDS; S. Singh[2], PhD

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Abstract

Background: There is limited published evidence on health workers' perspectives on antibiotic prescription trends for dental purposes in KwaZulu-Natal. The aim and objectives of this study was to determine health care practitioners' knowledge, attitudes and practices towards antibiotic prescription for dental use in public hospital settings in the Pietermaritzburg area.

Methods: This was a cross-sectional study using quantitative data. Purposive sampling was used to select medical and dental practitioners' (Group 1, n=123) and pharmacists' (Group 2, n=25) from two purposively selected public sector hospital sites in Pietermaritzburg (Institution A and B). A separate questionnaire was developed for each group, using open and close-ended questions. Data was collected and analyzed using the Statistical Package for Social Sciences (SPSS Version 25 ^{R}). Univariate descriptive statistics such as frequency and mean distribution and inferential techniques such as Pearson's Chi-Square test was conducted on the collected data. A p-value of 0.05 was established as being significant.

Results: The response rate for Group 1 was (n=93; 77.5%). The response rate for Group 2 was (n=23; 92%). The majority of participants in this study (n=72, 77.4%) indicated existence of an Antibiotic Stewardship Programme in their respective institutions yet 42 participants (45%) were not sure if the programme was active. More than half of the participants (n=60, 64.5%) indicated referring to the Standard Treatment guidelines *'some times'* when prescribing antibiotics. The majority of participants (n=72, 77.4%) indicated that they would prescribe antibiotics for orofacial swellings. Almost 33 participants (35.4%) also indicated that they would prescribe antibiotic cover for irreversible pulpitis. Almost 31 participants (88.9%) from Institution A and 40 (75%) from Institution B indicated they would prescribe antibiotics for pericoronitis.

Similarly, 27 participants (76.9%) Institution A and 14 (72.1%) from Institution B suggested they would prescribe antibiotics for periodontitis. The majority of participants (n=80, 86%) indicated that there is a need to improve antibiotic prescription trends.

More than two-thirds of study participants in Group 2 (n=18; 78%) perceived a correlation between the dental condition and the antibiotic prescribed thereof. Participants (n=17; 73.9%), however, also indicated that antibiotics were sometimes prescribed without any indication.

Conclusion: The results indicated that health care practitioners reported inconsistent knowledge, attitudes and practices related to antibiotic prescription patterns. The study highlighted the need for clear evidence-based guidelines for antibiotic prescription for dental conditions.

Introduction

The burden of infectious diseases in the developing world is compounded through limited access in both the availability and affordability of antibiotics to treat infections (Watkins 2019). Despite this, there is a global increase in the rate of prescriptions for antibiotics in dental care (Haliti *et al.* 2017). This misuse of antibiotics has contributed to increased bacterial resistance to such an extent that a post-antibiotic era has emerged (Boyles *et al.* 2017; Matsoso 2015). This post-antibiotic era is characterized by efforts to address antimicrobial resistance and includes the need to understand trends and patterns in antibiotic prescriptions (Carter *et al.* 2016; Truter 2015; Crowther-Gibson *et al.* 2011). From a South African perspective, surveillance on antimicrobial resistance is important given the quadruple burden of disease (HIV/AIDS, TB; maternal and child mortality; non-communicable diseases such as hypertension and cardiovascular diseases, diabetes, cancer, mental illnesses and chronic lung diseases, as well as injury and trauma) (Torres 2019:1). This ever-increasing burden of disease places a huge strain on the public health system and the over-use of antibiotics further compounds these challenges in the face of depleting resources. There is need for sustained antibiotic stewardship programmes to be directed at health care practitioners, as one possible public health strategy, to ease the burden on the health system. Similarly, there should be awareness among dental health care workers in South Africa of the possible impact of antimicrobial resistance and how this affects clinical management of dental conditions requiring dental prescriptions (Mthethwa *et al.* 2018). From a

dental perspective, antibiotics are commonly prescribed for orofacial and dental infections in South Africa (Huang and Owen 2012).

Trends in antibiotic prescriptions

There is limited published evidence on antibiotic prescription trends for dental use in South Africa; however, studies conclude that antibiotic resistance can occur through its indiscriminate use. A study conducted in Spain iterated that antibiotic prophylactic prescriptions for the prevention of local odontogenic infections were not aligned to recommended guidelines (Sancho-Puchades *et al*. 2009). The implications of these findings are that such disregard for set guidelines could result in 'novel bacterial strains' or 'increased opportunistic infections' Additionally, there could be increase in adverse drug reactions (Sancho-Puchades *et al.* 2009:537). On the other hand, a study conducted in Australia showed that over-prescription still occurred even though dentists had adequate knowledge about antibiotic prescriptions. Conversely, Swiss dentists expressed uncertainty with regard to when to prescribe antibiotics (Sweeney *et al.* 2004). This uncertainty is not unique. Dental practitioners in South Africa also did not indicate consensus on the need for antibiotic prescription (Lalloo *et al.* 2017). The author further postulated that South Africans 'did not appear to be over prescribing antibiotics for dental use', but that there is a need to review the indications for the use of antibiotics in dentistry (Lalloo *et al.* 2017:6). Ncube *et al.,* on the other hand, cautioned that there are concerns regarding the contribution of and inappropriate use of antibiotic (Ncube *et al.* 2017).

This study arose owing to the limited available data and research regarding the trends and practitioners' attitudes towards antibiotic prescription in South Africa, specifically in KwaZulu-Natal. There is limited available data on the patterns of prescription and the treatment outcomes in terms of statistical records in the public oral health sector. There is a nebulous picture of prescription trends on antibiotics for dental conditions in KwaZulu-Natal. Hence, the possible impact of current dental management on perpetuating antimicrobial resistance is largely unknown. Consequently, the implications are that oral health policy and planning are occurring in the absence of sound epidemiological data. As a result, the aim and objectives of this study was to determine health care practitioners' knowledge, attitudes and practices towards antibiotic prescription for dental purposes in the Pietermaritzburg region of KwaZulu-Natal.

The Pietermaritzburg Complex

Pietermaritzburg is the second largest city in KwaZulu-Natal with a population estimate of 11 527 96 in the UMgungundlovu district which increases annually by 1.12% (Statistics SA 2013-2018). According to Statistics South Africa 2013-2018, there is a projected uninsured population estimate of 925 695 for health in the UMgungundlovu district (KwaZulu-Natal Department of Health 2015), thus creating a huge dependence on the public health system for service delivery (World Health Organization 2018). Likewise, the public oral health sector is largely responsible for the delivery of oral health services (Singh, Myburgh and Lalloo 2010; Singh 2011; Thema and Singh 2017). The estimate number of clients managed for dental treatment in the Pietermaritzburg Complex over a five-year period from March 2012- July 2018 was 181,097 (KwaZulu-Natal Department of Health 2018). The majority of oral health problems such as dental caries, dental impactions, periodontal disease, trauma and various types of pathology are managed at the District Level and Regional Level hospitals while the Provincial Tertiary Level hospital provides specialized maxillo-facial services. The majority of the maxillofacial injuries that are sustained during motor vehicle accidents, assaults, sports injuries, and pathology and gunshot wounds are managed with specialist care (KwaZulu-Natal Department of Health 2018).

Methods

This was a cross-sectional study using a quantitative approach to elicit health care practitioners' knowledge, attitudes and trends in antibiotic prescription practices for dental use. The research site was the Pietermaritzburg Complex in KwaZulu-Natal. Two public oral health facilities were purposively selected for the study (Institution A and Institution B). Ethical clearance was obtained from the University of KwaZulu-Natal (BREC Reference number: BE026/190). Gatekeeper permission and approval was obtained from the KwaZulu-Natal Department of Health (Reference number: NHRD Ref: KZ_201902_018).

The study sample comprised ninety-three medical and dental practitioners (n=93) in Group 1 and twenty-three pharmacists (n=23) in Group 2. Purposive sampling was used to select the study sample (Table 1). For Group 1, the selection criteria included all health care professionals who prescribed and dispensed antibiotics for dental use. The study excluded all dental and medical managers and practitioners not involved in the clinical management and prescription of

antibiotics for dental use. For Group 2, all pharmacists who dispensed antibiotics for dental use were included in the study. The study excluded pharmacy assistants.

Table 1: Study participants

Group 1				
Medical staff	No of participants	Dental staff	No of participants	
Surgeons	6	Dentists	8	
Medical officers	37	Dental therapist	6	
Emergency medical specialists	2			
Emergency medical officers	8			
Interns	39			
Specialists	4			
Registrars	4			
Clinical managers	4			
Anaesthesiologists	4			
Total number of respondents	109		14	N=123
Group 2				
Total number of pharmacists that responded			23	N=25

A self-administered questionnaire with open and closed-ended questions was developed for each group respectively. Questions were also formulated by using a Likert scale format that required responses such as: 1 (Strongly agree), 2 (Agree), 3 (Not sure), 4 (Disagree), 5 (Strongly Disagree).

For Group 1 (medical and dental practitioners, n=123), the questionnaire comprised fifteen questions that were designed to assess the identified health care workers' knowledge, attitudes and practices related to antibiotic prescriptions for dental use. The first part of the questionnaire included a socio-demographic data such as age, gender, year of study, the National Strategic Framework and adherence to the Standard Treatment Guidelines. The second part of the questionnaire focused on participants' awareness of guidelines developed by National Institute

for Health care and Excellence and the guideline by the American Heart Association, the South African National Strategic Framework on Antimicrobial Resistance, and antibiotic stewardship. The final part of the questionnaire comprised of questions on practitioner perceptions on the effectiveness and efficacy of the antibiotic therapy of choice, and recommendations for improvement in antibiotic prescription for dental use in the public sector.

For Group 2 (pharmacists, n=25), the questionnaire comprised of 10 questions that were designed to elicit pharmacists' perspectives on antibiotic prescription trends. The first part comprised of questions examining pharmacists' perceived correlation between the antibiotics prescribed and the dental condition, the indications for the antibiotic therapy for dental conditions, and the perceptions of health practitioners' adherence to the Standard Treatment guidelines. Furthermore, the questions posed included perceptions on the identified drugs' mechanism of action and possible adverse effects. The second part of the questionnaire focused on perceptions of therapeutic duplication of antibiotics, availability of laboratory information and recommendations for improvement in antibiotic prescriptions.

Data was first cleaned and coded. It should be noted that participants did not respond to all questions posed. A code book was prepared to ensure that codes were exclusive. Data was then captured on an Excel spread sheet and analyzed using SPSS (Version 25^{R}). Univariate descriptive statistics such as frequency and mean distribution was conducted for all variables. Bivariate statistics was also be used to assess the outcome and the outcome was analyzed by the explanatory variable (Betani *et al*. 2018). The responses to open ended questions were grouped and emergent themes were examined and compared for possible associations. Inferential techniques included Pearsons Chi-Square test to assess a possible relationship between the independent variable (age, gender etc) and dependent variable (frequency of antibiotic prescription). A p-value of 0.05 was established as being significant.

Results

The response rate for Group 1 was (n=93; 77.5%). The response rate for Group 2 was (n=23; 92%). The male participants comprised (n=29; 31, 2%) and the female participants comprised (n=59; 63, 4%).

Group 1 (medical and dental practitioners' perspectives)

The majority of participants in this study (n=72, 77.4%) indicated that an Antibiotic Stewardship Programme existed in their respective institutions. Only a minority of participants (n=18; 19.3%) indicated awareness that the Antibiotic Stewardship Programme was active. Alarmingly a significant number of participants (n=42; 45%) were not sure on whether the Antibiotic Stewardship Programme was active. Conversely an overwhelming majority of participants (n=85; 91.3%) were aware of the Standard Treatment Guidelines and the Essential Medicines List. More than half of the participants (n=60; 64.5%) indicated referring to the Standard Treatment guidelines *'some times'* when prescribing antibiotics.

A greater number of participants (n=73; 78.4%) were aware of the American Heart Association Guidelines. Similarly, more than half of the study participants (n=53; 57%) were aware of the National Institute of Health Care and Excellence Guidelines. Less than half of the participants in this study (n=44; 47.3%) followed the American Heart Association Guidelines when prescribing antibiotics for the prevention of Infective Endocarditis while a smaller number of participants (n=26; 28%) followed the National Institute for Health Care and Excellence guidelines for antibiotic prescription for the prevention of Infective Endocarditis.

Differences were noted in the two research sites in terms of the reported dosage with regards to the prescribed antibiotics. At Institution A, a small number of participants (n=12; 13%) indicated that they would prescribe Pen VK, 250mg daily for the prevention of infective endocarditis in dental patients presenting with such cardiac conditions. Other health care practitioners (n=9:8, 4%) preferred to prescribe Amoxicillin, 2g stat dose one hour before treatment while a low number of health care practitioners preferred antibiotics in other forms of Penicillin such as Augmentin Benzylpenicillin and Lincosamides such as Clindamycin, and Cephalosporin such as Kefazol, respectively.

At institution B, participants (n=21; 22.6%) preferred to prescribe an Amoxil 2g Stat dose one hour before the procedure. A low number of health care practitioners (n=1;2.1%) preferred to prescribe other Penicillins such as Pen VK, Benzylpeniclillin, Benzatime Penicillin, Benzyl Penicillin, Penicillin G, Lincosamide such as Clindamycin and Vancomycin, respectively.

Table 2: Preferred prophylactic antibiotic cover for the prevention of Infective Endocarditis

Preferred antibiotic cover	Number of respondents (%)	
	Institution A	**Institution B**
Amoxil	9(30)	21(44.7)
Augmentin	2(6.7)	2(4.3)
Benzylpenicillin	1(3.3)	1(2.1)
Clindamycin	1(3.3)	4(8.5)
Penicillin	3 (10)	5 (10.6)
Pen VK	12 (40)	6 (12.8)
Unsure	1 (3.3)	2 (4.3)
Augmentin	2 (6.7)	
Kefzol	1(3.3)	
Benzatime Penicillin		1 (2.1)
Benzyl Penicillin IV		1 (2.1)
Penicillin G		1 (2.1)
Vancomycin		1 (2.1)
None		3 (6.4)

Surprisingly a limited number of participants (n=3; 2, 97%) across both the institutions would not prescribe any prophylaxis for the prevention of Infective Endocarditis while 2 participants (1, 86%) were unsure of which antibiotic prophylaxis to prescribe for this cardiac condition.

Less than half of the participants (n=36; 38.7%) across the two institutions preferred to prescribe Azithromycin (Macrolide) 500mg for clients that are allergic to Penicillin. About 29 participants (27.9%) preferred to prescribe Erythromycin (Macrolide) 400mg while 21 participants (19.6%) preferred Clindamycin (Lincosamide) 600mg for clients that are allergic to Penicillin.

An overwhelming number of participants (n=90, 96.7%) indicated that they would prescribe antibiotics prophylaxis for cardiac transplantation recipients who could develop cardiac valvulopathy. The majority of participants (n=75, 84%) would prescribe antibiotic prophylaxis for HIV positive clients with CD4 cell count <200. A small percentage of participants (n=9, 8.4%) also indicated that they would prescribe antibiotics for immunocompromised clients undergoing chemotherapy.

The dental conditions for which antibiotics were prescribed were additionally explored. The majority of participants (n=72; 77.4%) indicated that they would prescribe antibiotics for

orofacial swellings. Almost 33 participants (35.4%) also indicated that they would prescribe antibiotic cover for irreversible pulpitis.

Differences were noted in the responses obtained from the two research sites. There was a variety of dental conditions for which those health care practitioners in each institution would prescribe antibiotics for. A large group of participants (n=26; 75%) from Institution A would prescribe antibiotics for orofacial swellings while a greater number of participants (n=46; 86.5%) from Institution B would prescribe antibiotics. The majority of participants from both institutions would prescribe antibiotics for pericoronitis. Almost 31 participants (88.9%) from Institution A and 40 (75%) from Institution B would prescribe antibiotics for pericoronitis. Similarly, 27 participants (76.9%) Institution A and 14 (72.1%) from Institution B would prescribe antibiotics for periodontitis. More than half of the participants (n=19; 53.8%) from Institution A indicated they would prescribe antibiotics for acute alveolar osteitis/ dry socket. Likewise, 37 participants (70.3%) from Institution B indicated the same. Participants in both institutions generally supported prescription of antibiotic prophylaxis pre and post-dental surgery (Table 4).

Table 3: Dental conditions requiring antibiotics from an institutional perspective

Dental condition	Hospital		P-values
	Institution A (n=35)	Institution B (n=53)	
Orofacial swelling	75%	86.5%	0.675
Dental pain related to irreversible pulpitis	57.1%	31%	0.029
Dental pain related to reversible pulpitis	51.9%	46.3%	0.656
Dental pain related to dental fillings	17.9%	23.3%	0.586
Pericoronitis	88.9%	75%	0.159
Periodontitis	76.9%	72.1%	0.658
Impacted teeth	25%	30%	0.651
Acute alveolar osteitis/ Dry socket	53.8%	70.3%	0.183
Mandibular fractures/ Maxillary fractures	70.4%	68.3%	0.856
Trismus	46.7%	44.7%	0.874
Prophylaxis before dental surgery	86.7%	67.4%	0.061

Post –operative treatment for dental surgery	50%	68.4%	0.130
Aphthous ulcers	31%	19.4%	0.281

*P<0.05

Less than half of the study participants (n=43, 40%) indicated that sometimes they would review their clients in a follow-up visit after antibiotic prescription and a minority of participants (n=34, 31.6%) responded that they believed that the antibiotic prescribed would have worked effectively.

The majority of participants (n=80, 86%) indicated that there was need to improve antibiotic prescription trends as indicated in Table 3.

Table 4: Recommendations: Improvement in antibiotic prescriptions

Wrong and irresponsible prescription (n=8)	Limited drug availability (n=4)	Use of prescription guidelines (n=5)	Awareness of drug dosage (n=2)	Monitoring and control of drug dosage (n=4)
1.To avoid resistance and wrong prescription 2. Unnecessary prescription of antibiotics when not indicated. 3.Antibiotics are being irresponsibly prescribed 4. Antibiotics are sometimes prescribed for viral illness. 5.Consider weight and age when prescribing antibiotics 6.Over-prescribing is a problem 7. Over-prescription of antibiotics with insufficient diagnosis. 8. Unnecessary prescription of antibiotics when not indicated.	1. Limited spectrum of medication or antibiotics available after hours when the pharmacy is closed. 2. Mostly administer prophylaxis. 3. Prescribe prophylaxis in theatre only.	1. Standardize in-service training across disciplines. 2. Improvement in prescription patterns is required to reduce resistance. 3. Need appropriate antibiotics. 4. Better use of new antibiotic prescribing sheets. 5. Ward round with antibiotic stewardship committee present.	1. All managers should be informed if dosages have changed to avoid resistance. Essential Medicines List does not provide enough information about dental prescriptions and the last update is 2007. 2. More awareness.	1. Need collaboration from Multidisciplinary team as there is no control over the amount and type of antibiotics prescribed. 2. Noticed that there is antibiotic stewardship committee but still different antibiotic charts are filled out by different doctors and different departments. 3. Regular check of dosages in each department that is prescribing so that in subsequent years there is no under-dosing. 4. Local guidelines are required.

Participants indicated the need to increase awareness of prescribed drug dosages and to monitor and control drug dosage, given the limited availability of antibiotics in some health institutions (Table 4). Other recommendations included proper use of prescription guidelines when prescribing antibiotics (n=5; 4, 7%) and proper monitoring and control of drug dosage.

Group 2 (Pharmacists' perspectives)

More than two thirds of the study participants in Group 2 (n=18; 78%) perceived a correlation between the dental condition and the antibiotic prescribed thereof. Participants (n=17; 73.9%), however, also indicated that antibiotics were sometimes prescribed without any indication. The majority of participants (n=18; 78.2%) perceived that antibiotic prescriptions complied with the Standard Treatment Guidelines and Essential Medicines List. The majority of participants (n=19; 82.6%) indicated that the length of course of antibiotic therapy was appropriate. More than half of participants (n=12; 52%) agreed that sometimes there was duplication and a combination of the antibiotics prescribed. Less than half of the study participants (n=8; 34.7%) strongly agreed on diagnostic laboratory testing for antibiotic treatment.

Discussion

The results of this study suggest inconsistencies in practitioner trends in antibiotic prescriptions for dental use. One such inconsistency was noted for the management of patients with allergy to Penicillin. According to the Standard Treatment guidelines, patients with allergy to Penicillin should consume Clindamycin 600mg orally, an hour before the dental procedure. However, 39% of respondents indicated that they would prescribe Azithromycin 500mg orally for Penicillin allergy clients. Azithromycin is a macrolide that allows for less frequent dosage (Hajheydari *et al.* 2011). Azithromycin has as a half-life of three days and a large volume of distribution, and though the serum concentration is low, the concentrates are readily within the tissues (Whitman *et al.*1992). This finding is consistent with Marra *et al.* in that differences were also noted in the antibiotic prescription trends in their study (Marra *et al.* 2016). Similarly, Mthethwa reported a low response rate for a study that investigated practitioner knowledge of treatment guidelines and prescribing patterns for antibiotic prophylaxis (Mthethwa *et al.* 2018).

Alarmingly, antibiotics were prescribed for dental conditions that did not require such cover. Some participants in this study indicated that they would prescribe antibiotics for pain related to reversible and irreversible pulpitis, dental fillings, pericoronitis, periodontitis, impacted teeth, trismus and aphthous ulcers (Table 4), This study findings are consistent with Peric *et al.* who reported that antibiotics were prescribed as a precaution because of 'uncertainty concerning the diagnosis, patient's expectations, unavailability of dental services and in short- term cases where there is insufficient time for doing any treatment' (Peric *et al.* 2015:111). The inappropriate prescription or the excessive use of antibiotics in dental practice occur when antibiotics are prescribed for conditions that are not indicated for antibiotic prophylaxis such as dry socket, irreversible pulpitis, acute periapical infection and pulpitis, non-clinical factors such as patient expectations, convenience or for viral infections like herpes simplex virus-1 infections (Mthethwa *et al.* 2018; Agnihotry *et al*. 2016; Sancho-Puchades *et al.* 2009). Gutierrez *et al.*, therefore, highlighted the need for professional agreement and consensus-building with regards to the conditions for antibiotic prescriptions (Gutierrez *et al.* 2006). Such efforts are also needed in a South African context to facilitate practitioner consensus-building to ensure consistency in antibiotic prescription.

Almost all respondents (97% of health practitioners) in this study reported that they would prescribe antibiotic prophylaxis for clients with cardiac transplantation; cardiac valvulopathy, immunosuppression, chemotherapy, respiratory infections (such as pneumonia), meningitis, abscess, septic shock and cellulitis. Despite this, inconsistencies were still observed in the selection of antibiotics for the management of the same clinical condition (in this case being: prevention of Infective Endocarditis). Interestingly, a pattern of antibiotic prescription emerged based on the clinical site where the respondent was located. Almost 13% of respondents from Institution A reported prescribing PEN VK 250mg daily. Other participants opted for various Penicillins, Augmentin, Benzyl Penicillin, Clindamycin and Kefazol while 23% of respondents from Institution B indicated prescribing Amoxicillin 2g stat dose one hour before a dental procedure. According to Standard Treatment Guidelines 2018, the prescribed regimen should be as follows: Amoxil, oral, 2g one hour before the procedure. Respondents from Institution B appeared to adhere to the Standard Treatment Guidelines. This difference in prescription pattern for the same health condition is surprising. Additionally, only 65% of respondents referred to the Standard Treatment Guidelines. In contrast, a previous study reported that only 45% of

practitioners adhered to the Standard Treatment Guidelines and Essential Medicines List in the Primary Health Care in South Africa (Gasson 2018).

Seventy-four percent (74%) of health care practitioners were aware of the American Heart Association guidelines while 57% were aware of the National Institute of health care and excellence guidelines. Conversely, less than half of the respondents in this study (48% of health care practitioners) followed the American Heart Association guidelines while only 26% reported following the National Institute of Health Care and Excellence guidelines. This finding is supported by Lalloo who postulated that antibiotic prescription patterns do not appear to follow a coherent set of guidelines or sound indications for antibiotic use (Lalloo 2016). Mthethwa *et al.* also reported in their study that dentists were aware of the treatment guidelines but few followed the recommendations for antibiotic prophylaxis (Mthethwa *et al.* 2018). More research is thus required to further understand these differences across clinical settings. One possible reason for the reported difference in prescription patterns in this study could be as a result of professional tribalism where practitioners at one institution tend to follow a particular trend in prescribing antibiotics. This could also be related to the fact that more than half of the study populations (56, 8% of health care practitioners) were unsure of the status of the antibiotic stewardship committee at the respective research site. It is essential to ensure that there is consistent monitoring and adherence to the available guidelines as this could harmonize antibiotic prescription patterns (Ntsekhe *et al*. 2011).

Inconsistencies in the recognized guidelines for antibiotic prescriptions have added to this confusion. The National Institute for Health Care and Excellence changed the routine prescription of antibiotics for the prevention of Infective Endocarditis in 2008 but the American and European cardiologists still recommend the use of antibiotic prophylaxis for the prevention of Infective Endocarditis (Brunce and Hellyer 2018). According to the Standard Treatment Guidelines, the National Institute of Health Care and Excellence Review, these institutions noted a lack of consistent association between the clinical procedures and the onset of infective endocarditis (South African National Department of Health 2018). These observations suggest that clarity and guidance are required at an antibiotic stewardship level. It is concerning to note that while 78% of respondents reported the existence of a hospital based antibiotic stewardship programme, yet only 41% were aware of the activities related to this initiative. This suggests an

urgent need to strengthen antibiotic stewardship at an institutional level. Antimicrobial stewardship and infection and prevention control teams could provide opportunities to augment prescribing practices and streamline this process (South African National Department of Health 2015).

Additionally, the prophylaxis guidelines recommended by American Heart Association, European Society of Cardiology and British Society of Antimicrobial Chemotherapy are applied in South Africa (Mthethwa *et al.* 2108). The guidelines should attempt to narrow the gap between recommendations and the actual practice by acknowledging the diagnostic complexity and uncertainty faced by clinicians (Brink 2014). This highlights the need for more practitioner support through the use of developed guidelines on antibiotic prescriptions (Lalloo 2016). There is need for collaboration at a multidisciplinary team level.

Only 40% of respondents indicated to sometimes review their clients' health status after antibiotic prescription, while 32% of the respondents reported that they assumed the antibiotics would have worked effectively. It is unclear how antimicrobial resistance would impact on clinical outcomes (Bamford *et al.* 2011).

On the other hand, 78% of pharmacists perceived a correlation between the dental condition and the antibiotic prescribed for the dental condition. This is a very important finding as studies have shown that when the treatment guidelines are adhered to, the resistant micro-organisms reduce in numbers (Ntsekhe *et al.* 2011). More than half of the respondents (52% of pharmacists) agreed that sometimes there was duplication and a combination of the antibiotics prescribed. This is an important finding because it suggests wastage in scarce resources. From a South African perspective, it is important to optimize the prudent use of antibiotics to maximize positive clinical outcomes (Perumal-Pillay and Suleman 2017). This study finding is supported by Darj *et al.* in 2019 who concede that 'pharmacists hesitated to provide multiple antibiotics even when prescribed by health care practitioners' (Darj *et al.* 2019).

The hospital pharmaco-therapeutic committees (HPTCs) should be able to provide support and mentorship to the prescribing health care practitioner (Ntsekhe *et al.* 2011). The laboratory testing for dental conditions for definitive treatment is imperative in the post-antibiotic era

(Ntsekhe *et al*. 2011). Preventive oral health programmes, including antimicrobial resistance information to the public, should be planned and implemented (Ntsekhe *et al.* 2011).

Surprisingly, almost 74% of pharmacists indicated that antibiotics were sometimes prescribed without indication. This is consistent with the study done by Darj *et al*. in 2019 where pharmacists expressed the view that medicines lacked proper indication because health care practitioners were prescribing different antibiotics in response to the ever-increasing resistant bacterial strains (Darj *et al.* 2019). According to a study done by Gajdacs *et al*., health care practitioners (including pharmacists) had a proper level of knowledge about antibiotic therapy but were less familiar with the pathomechanisms of infectious diseases and bacterial resistance. Thus, adequate practitioner knowledge does not guarantee proper prescription practices since many reports have suggested that practices are mainly influenced by the attitudes of the health care practitioners (Gajdacs *et al.* 2020).

Clearly, the study findings indicated serious shortcomings in the antibiotic prescription patterns for dental conditions and further suggested obvious gaps to support medical and dental practitioners' decision-making in this regard. It is, therefore, incumbent upon the National Department of Health to review its National Strategic Framework on Antimicrobial Resistance to include the oral health sector in the planning and implementation of guidelines for antibiotic prescription for dental conditions, as well as in the other activities associated with the importance of the awareness of reducing antimicrobial resistance. It is the responsibility of oral health care practitioners to review strategies from a curative oral health care perspective to a more preventive approach. Oral health promotion and the awareness of antimicrobial resistance should be an important part of the health care service provision in the public and private health care facilities. National and international recommendations as well as facility-specific recommendations should be required to combat antimicrobial resistance (Ellas *et al*.2017). Antibiotic resistance data and trends in antibiotic prescribing practices are required when considering recommendations for antibiotic prescriptions (Ellas *et al*.2017).

Limitations of the study

This study provided valuable insight into the knowledge, practices and attitudes of health care practitioners regarding the trend of antibiotic prescription patterns for dental conditions. The

generalizability of the study findings are limited to the study sites. There could have been over-reporting. More research is required to unpack the complexities associated with prescription trends and patterns. The findings clearly emphasize the urgent need for clear evidence-based guidelines for health care practitioners that prescribe antibiotics for dental conditions.

Conclusion

The results indicate that health care practitioners reported inconsistent knowledge, attitudes and practices related to antibiotic prescription patterns. The study highlights the need for clear evidence-based guidelines for antibiotic prescription for dental conditions.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Second Manuscript: Preface

The second manuscript titled, *Antibiotic prescription patterns for dental conditions at two public sector hospitals in Pietermaritzburg*, made use of quantitative and qualitative data obtained from the retrospective clinical chart reviews of patients that were prescribed antibiotics for dental conditions for the period March 2012 till July 2018 and a focus group discussion with health care practitioners (n=12) that were prescribing or dispensing antibiotics for dental conditions in the public sector.

The purpose of the second manuscript was to identify the dental conditions for which antibiotics were prescribed mainly in the two public health care institutions in Pietermaritzburg, KwaZulu-Natal. The second manuscript focused on two objectives. Firstly, it aimed to determine the patterns of antibiotic prescription for dental patients in the identified public health institutions by means of a retrospective chart review and secondly it explored the medical and dental practitioners' as well as pharmacists' perspectives on antibiotic prescription rates for dental patients by means of a focus group discussion.

Manuscript 2: Oral antibiotic prescription patterns for dental conditions at two public sector hospitals in Pietermaritzburg

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Both authors consent to publication and declare that there are no conflicting interests.

Abstract

Antibiotic resistance is a growing public health concern yet there is a paucity of published data in KwaZulu-Natal on antibiotic prescription trends and patterns related to dental use.

Objectives

The objectives of this study were to identify the range of dental conditions for which antibiotics are prescribed at two public health settings (Institution A and B) in the Pietermaritzburg Complex.

Methods

The study used a two-phased approach and collected a combination of qualitative and quantitative data in order to determine the patterns of antibiotic prescription for dental use. Phase 1 comprised a retrospective clinical chart review (n=720). Phase 2 comprised of a focus-group discussion with purposively selected health care practitioners at each institution. The quantitative data was analyzed using SSPS version 25^{R}. The qualitative data was analyzed using thematic analysis.

Results

The results of the retrospective chart review indicated that dental abscesses (n=479; 66%) were the most common dental condition for which antibiotic therapy was prescribed. There were inconsistencies in the pattern of antibiotic prescription for dental conditions between the two public health care institutions. At Institution A, antibiotic therapy was prescribed for conditions such as trismus (n=13; 6%), soft palate swelling (n=9; 4%), fibrous epulis (n=6; 3%), acute herpes (n=2; 1%). Interestingly, antibiotics were not prescribed at Institution B for the same dental conditions. Antibiotic therapy was prescribed for eruption pain (n=4; 1%) and for cases

when patients did not bring their inhaler for asthma treatment (pump) (n=3; 1%) at Institution B. The findings from the focus-group discussion indicate that there is a need to improve antibiotic prescription by health care practitioners for dental conditions.

Conclusion

This study showed that there was an inconsistency in antibiotic therapy for dental conditions at the two public health institutions. There is a need for consensus-building among health professionals and the provision for more dedicated guidance for antibiotic prescription in the management of dental conditions.

Introduction

Antimicrobial resistance is a global threat and it is estimated that 700 000 people die annually as a result of antimicrobial resistance (Farley *et al*. 2018). By 2050, this figure is set to escalate to 10 million (O'Neill 2016). The indiscriminate or inappropriate use of antibiotics for dental conditions requires a review, specifically in light of the proliferation of resistant bacterial strains that could lead to antibiotic resistance (Lalloo *et al.* 2017). Additionally, there is an unclear picture of antimicrobial consumption rates in the country (Schellack *et al. 2*017). Similarly, discrepancies in antibiotic prescriptions also exist in other countries. Jaunay *et al.* (2000) reported that 'health care practitioners in Australia had adequate knowledge of antibiotic prescription yet over-prescription still occurred' (Juanay *et al.* 2000:183). Similarly, dentists in Switzerland were cautious about prescribing antibiotics and there were uncertainties on when to prescribe antibiotics (Mainjot *et al. 2*009).

From a South African perspective, Mthethwa *et al.* reported that oral health care practitioners lacked knowledge of the available treatment guidelines and prescribing practices for antibiotic prophylaxis (Mthethwa *et al.* 2018). A more recent study reported that antibiotic prescribing patterns by dentists following tooth extraction did not appear to follow a consistent or coherent set of guidelines for antibiotic use (Lalloo *et al.* 2017). Despite the availability of several clinical practice guidelines on the use of systemic antibiotics to treat pulpal and peri-apical infections (Matthews *et al.* 2003), there was very little is knowledge on antibiotic- prescribing practices of dentists in South Africa (Lalloo *et al.* 2016).

The South African Antibiotic Stewardship Programme was formed in 2012 in response to this identified gap and its purpose was to implement antibiotic stewardship programmes in hospitals and primary health care facilities (South African Department of Health 2017). The aim of this programme is to 'strengthen the antimicrobial surveillance, ensure uninterrupted access to quality essential medicines, to enhance infection prevention and control and to stimulate further research innovations' (Schellack *et al. 2*017:101). Antimicrobial prescribing practices in the public sector in South Africa are also guided by the Standard Treatment Guidelines and the Essential Medicines List. These documents are available electronically and could be a valuable resource to guide practitioners on antibiotic use (Perumal-Pillay and Suleman 2017; Schellack *et al.* 2017; Owen and Huang 2012). The judicious use of antibiotics could delay the emergence of resistant bacteria (Farley *et al.* 2018). Adherence to the Standard Treatment Guidelines and the South African Antibiotic Stewardship Programme could contribute to the reduction of inappropriate antibiotic prescribing and improved prescribing practices in dentistry. While these documents are available and accessible, little is known about the extent to which health practitioners use these guidelines for the prescription of antibiotics for dental clinical conditions.

Given this unclear picture of antibiotic prescription patterns for dental conditions, this study aimed to determine antibiotic prescription rates for dental use in the public health care sector in Pietermaritzburg, in order to have a better and deeper understanding of the rationale for these patterns and trends.

Methodology

This was an exploratory study, using a combination of qualitative and quantitative data. The research sites comprised two purposively selected hospitals (Institution A and Institution B) in the Pietermaritzburg Complex. Two phases were used in this study. The first phase comprised of a retrospective clinical chart review for the period March 2012 to July 2018 (n=720). The second phase comprised two focus-group discussions (FDGs) with purposively selected health practitioners (one FGD at Institution A and Institution B respectively) to gain a better understanding of the trends in antibiotic prescription patterns and practices for dental purposes. Ethical clearance was obtained from the Biomedical Research Ethics Committee, University of KwaZulu-Natal (Reference number. BE026/190) while permission to conduct the study was

obtained from the KwaZulu-Natal Department of Health (Reference number. NHRD Ref: KZ_201902_018).

For the retrospective clinical record review, managers for each admissions department in the respective research site were responsible for selecting and retrieving the clinical records based on the criteria set by the researcher. The inclusion-criteria incorporated patients aged 6 to 80 years; evidence of documented antibiotic prescription for dental conditions; antibiotic prophylaxis for systemic conditions such as Infective Endocarditis; and in other instances, such as antibiotic cover prior to dental surgery or after dental treatment. The clinical records were retrieved by the administrator at the institutions. A data capturing sheet was used to document information related to the patients' age, gender, dental history, main complaint, symptoms, differential diagnosis, laboratory reports, prescribed treatment, and number of prescribed medications, drug dosage, frequency and route of administration. The prescriptions of antibiotics for the common dental infections were compared to recommendations made in the Standard Treatment Guidelines 2018. An antibiotic therapy worksheet (developed by Huang and Owen 2012 and Ntšekhe 2011) was used to gather information related to the appropriateness of the antibiotic regimen, comparisons with the Standard Treatment Guidelines, therapeutic duplication and adverse reactions. This worksheet was validated in previous studies (Huang and Owen 2012 and Ntšekhe 2011).

Phase 2 comprised of health care practitioners (dental practitioners and medical practitioners) and pharmacists, involved in the prescribing and dispensing of antibiotics for dental purposes at the identified research sites. Purposive sampling was used to set up two focus-group discussions (FGDs) comprising six people per group at each research site. The inclusion criteria encompassed practitioner eligibility to prescribe or dispense antibiotics for dental use; and registration with the Health Professionals Council of South Africa or the Pharmacy Council of South Africa (in the case of pharmacists). A semi-structured schedule was used to collect data.

The FGD schedule comprised of open-ended questions that explored participants' perspectives on the National Strategic Framework, Essential Medicines Lists, Standard Treatment Guidelines, the South African Antibiotic Stewardship Program, prescription patterns of antibiotic prescriptions practices and dental conditions, adverse events related to antibiotic prescription and trends and perceptions of antibiotic prescription practices from a multi-disciplinary approach. Other questions include perceived barriers, challenges and opportunities to access oral health

care, patient compliance, and the value of a multi-disciplinary team approach in combating antibiotic resistance. A meeting was set up with health care practitioners in the hospital board room at each participating hospitals to outline the purpose of the study. Each focus-group discussion was scheduled based on the participants' availability and convenience. The date, time and venue for each appointment were determined through consultations with interested participants after general consensus was obtained.

The interviews for the focus group discussion were audio recorded and the recordings were transcribed verbatim and then cleaned. The information was then transcribed onto a Microsoft word document. A research consultant was engaged to assist with the data analysis process. Data coding was done independently by the researcher and the research consultant to identify significant features of the data and to sort the data thereby allowing the emergence of sub-themes and themes from the participants' responses as part of the thematic analysis (Thomas and Harden 2008, Bazeley 2009, Dookie *et al*. 2017). The data was then compared in order to develop common themes. The qualitative data was analyzed using Nvivo version 11. The credibility of the study was achieved by establishing that the findings of the study were a true reflection of the participants' original view (Braun and Clarke 2006). Transferability was achieved by comparing the study findings with previous and current literature (Creswell 2017). Conformability was achieved through the use of quotations of actual dialogues expressed by study participants (Mandal 2018). To satisfy privacy concerns, each clinical record, was examined and participants interviewed in the focus group discussion was in done in confidence. All the participants were informed that they had the right to withdraw from the study at any stage if they wished to do so. The patient's and health care professional's anonymity and data confidentiality was the fundamental rule governing ethics. The study did not include any clinical examination or intervention. Therefore, there was minimal risk of clinical adverse effects. The study did not carry any social or economic risks for the patient or the Department of Health.

The quantitative data (derived from the clinical charts) was analyzed using SPSS (version 25^{R}). Univariate descriptive statistics such as frequency and mean distribution was conducted for all variables. Bivariate statistics was also be used to assess the outcome and, thereafter, the outcome was analyzed by the explanatory variable (Bertani *et al*. 2018).

Results

Phase 1

The response rate for the retrospective clinical chart review was 72% (n=720). A total number of 220 clinical charts (n=22%) were reviewed at Institution A and 500 clinical charts (50%) were reviewed at Institution B.

In total, the study sample across the two institutions comprised 490 females (65.3 %). Almost half of the study sample (n= 357; 49.7 %) were in the age group 40-60 years. Only 86 patients (12%) recorded were in the 6-year-old age group.

The main reasons for antibiotic prescription for identified dental conditions are indicated in Table 1. The most common dental infection requiring antibiotic therapy was dental abscesses (n= 479; 66%). Antibiotics were also prescribed for acute alveolar osteitis (dry socket) (n=110; 15%) and dental impactions (n=78; 11%). However, some differences were noted in the prescription patterns between the two health institutions. At Institution A, antibiotic therapy was prescribed conditions such as trismus (n=13; 6%), soft palate swelling (n=9; 4%), fibrous epulis (n=6; 3%), acute herpes (n=2; 1%). Interestingly, antibiotics were not prescribed at Institution B for the same dental conditions. Antibiotic therapy was prescribed for eruption pain (n=4; 1%) and for cases when patients did not bring their inhaler for asthma treatment (pump) (n=3; 1%) at Institution B.

Table 1: Antibiotic prescriptions for dental and health related conditions

Health conditions for which antibiotics are prescribed	**Institution A (n=220 files)**	**Institution B (n=500 files)**	**Total (n=720 files)**
1. Dental conditions			
Dental Abscess	204 (93%)	275 (55%)	479 (66%)
Dry socket	46 (21%)	64 (13%)	110 (15%)
Impaction	58 (26%)	20 (4%)	78 (11%)
Dental Extractions	39 (18%)	23 (5%)	62 (9%)
Surgical Extractions	13 (6%)	9 (2%)	22 (3%)
Necrotizing ulcerative gingivitis	8 (4%)	12 (2.4%)	20 (3%)
Facial Cellulitis	10 (5%)	21 (4%)	31(4%)
Pericoronitis	8 (4%)	5 (1%)	13 (2%)
Trismus	13 (6%)		13 (2%)
Fractured Maxilla/Mandible	6 (3%)	5 (1%)	11 (2%)
Soft palate swelling	9 (4%)		9 (1%)
Gingivitis	8 (4%)	1 (0.2%)	9 (1%)

Acute Herpes	2 (1%)		2 (0.3%)
Aphthous Ulcers	3 (1%)	4 (0.8%)	7 (1%)
Fibrous Epulis	6 (3%)		6 (1%)
2. Trauma			
Motor vehicle accidents	2 (1%)	3 (1%)	5 (1%)
Facial trauma	4 (2%)		4(1%)
Assault	16 (7%)	9 (2%)	25 (3%)
Bony spiclues	3 (1%)		3 (0.4%)
3. Systemic Conditions			
Uncontrolled Hypertension	19 (9%)	39 (8%)	48 (7%)
Uncontrolled Diabetes	3 (1%)	10 (2%)	13 (2%)
Infective endocarditis	5 (2%)	2 (0.4%)	7 (1%)
Valve replacements	1(0.4%)		1 (0.1%)
Uncontrolled Asthma		3 (1%)	3 (0.4%)
3. Miscellaneous			
Fillings	3(1%)	5 (1%)	8 (1%)
Biopsy	1(0.4%)	2 (0.4%)	3 (0.4%)
Root canal therapy	7 (3%)	2 (0.4%)	9 (1%)
Eruption Pain		4 (1%)	4 (0.5%)
Referrals to regional and tertiary hospitals for further management	5 (2%)	6 (1%)	11 (2%)
Patients undergoing dental treatment under General Anaesthesia	13 (6%)	2 (0.4%)	15 (2%)
Patient request	2 (1%)		2 (0.2%)
Uncooperative Patients	20 (9%)	4 (1%)	24 (3%)
Treatment deferred	2 (1%)	16 (3%)	18 (3%)

Antibiotic therapy was prescribed for 16 patients treated for assault (7%) at Institution A while only 9 cases were prescribed antibiotics for assault at Institution B (2%). Less than half of the cases with uncontrolled blood pressure (n=48; 7%) required antibiotic therapy across both the institutions. Alarmingly, unco-operative clients from Institution A (n=20; 9%) required antibiotic therapy in comparison to Institution B (n=4; 1%). Patients undergoing treatment under general anaesthesia were prescribed antibiotics (n=13; 2%) at Institution A compared to Institution B (n=2; 0. 4%).

Allergies were recorded and alternate antibiotics were prescribed in a small number of clinical files (n=5; 3% in Institution A and n=7; 1% in Institution B). Participants in Institution A prescribed both Clindamycin and Azithromycin for patients allergic to Penicillin (n=5; 0.7%) while those in Institution B prescribed Erythomycin (n=2; 0.3%). There were discrepancies in the availability of laboratory tests, that comprised mainly of biopsies, in the clinical notes (n=50; 23% in Institution A and n=30; 6% in Institution B).

Phase 2

The following themes emerged from data analysis: Inconsistency in antibiotic coverage for dental-related clinical management, the prescription of antibiotics and the adherence to the standard treatment guidelines as well as the strategies to combat antibiotic resistance.

Theme 1: Inconsistency in antibiotic cover for dental-related clinical management

Medical practitioners indicated that they were not specifically involved in the prescription of antibiotics for common dental conditions. Patients presenting for the management of dental conditions are instead referred to the dental department. The results also indicated that antibiotics prescription patterns differed between Institution A and Institution B.

"Antibiotics were prescribed for dental abscesses, patients with multiple carious teeth presenting for general anesthesia, prophylaxis for rheumatic heart fever and cases of open wound fractures and trauma" (Institution A).

On the other hand, antibiotic coverage was prescribed for dental abscess and open wound fractures cellulitis, dry socket, pericoronitis, and periodontitis, and antibiotic prophylaxis after tooth extraction, necrotizing ulcerative gingivitis, rheumatic fever and infective endocarditis at Institution B.

Theme 2: Antibiotic prescription and the adherence to the Standard Treatment Guidelines

All participants (medical and dental practitioners) affirmed prescription of antibiotics based on the Standard Treatment Guideline, as reflected in the following quotation.

"Yes, the standard treatment guidelines are followed when prescribing antibiotics." (Institution A)

"The medical and dental practitioners seem to be prescribing the correct regimen according to the Standard treatment guidelines." (Pharmacists from Institution A)

Theme 3: Strategies to combat antibiotic resistance

There was no consensus among research participants on the need for diagnosis laboratory testing to improve antibiotics prescription. However, all participants agreed that there was a need to improve antibiotic prescription in their various hospitals.

"Prescribers use empirical treatment which may result in antibiotic resistance." (Institution B).

Some recommendations to improve antibiotics prescription trends and reduce possible resistance are listed in Table 2.

Table 2: Recommendations for improved antibiotic prescriptions

Recommendations	**Quotations**
Improvement of antibiotics prescription	"Strategies are implemented to combat antimicrobial resistance." (Institution A) "The last line of antibiotics prescribed now requires authorization from the consultant." (Institution B) "Diagnostic tests are recommended before prescribing antibiotics for clients." (Institution B) "Start first line antibiotics based on differential diagnosis and prescribe the definitive treatment based on confirmed diagnosis test results." (Dental practitioners from Institution A) "Antibiotic prescription was changed according to weight as instructed by the Standard Treatment Guidelines as opposed to assuming the dosage as per the age of the pediatric patient." (Institution A)
2. Reduce the adverse effect from incorrect antibiotic prescription	"Yes, there has been one incident of an adverse effect from the incorrect antibiotic prescribed which was due to insufficient history taking and patient transparency." (Dental Practitioner from Institution A)
3. Multi-disciplinary team approach	"The pharmacists always check and approve the prescriptions recommended by medical and dental practitioners" (Institution A). "If there is an adverse effect related to antibiotic allergy, the medical practitioners always work together with the dentists to stabilize the patient." (Institution B).

Discussion

This study aimed to identify antibiotic prescription patterns for dental management. The results of the study indicated inconsistencies in antibiotic prescriptions for dental conditions. This suggests that over and under-prescribing may be occurring in the identified dental clinical settings. The most common dental infection in this study requiring antibiotic therapy was dental abscesses (66%). This finding is consistent with other studies. Long postulated that dental abscesses larger than 5 cm, cellulitis or conditions with mixed abscess-cellulitis required antibiotics coverage (Long 2016). Likewise sepsis could progress to cellulitis, and possibly

leading to Ludwig's angina which could be life-threatening. This thus justifies the prescription of antibiotics (Olsen and van Winkelhof 2014). Antibiotic therapy and drainage are recommended for infections such as facial cellulitis, pericoronitis, lateral periodontal abscess and necrotizing ulcerative gingivitis (Dar-Odeh *et al.* 2010). The recommended treatment of choice for periapical abscess, periodontitis abscess and localized dentoalveolar abscess is incision and drainage (Kuriyama *et al.* 2005). However, Lalloo *et al* suggested that practitioners might be using subjective measures or even personal preferences when deciding whether to prescribe antibiotics or not (Lalloo *et al.* 2017).

Participants in this study also prescribed antibiotics for the treatment of alveolitis (dry socket) (15%). This finding is supported by a previous study done in England, Kuwait and Turkey. Almost half the dentists surveyed would prescribe antibiotics for dry socket (Dar-odeh *et al*. 2010). This study further indicated that antibiotic prophylaxis was prescribed for impacted third molar (11%). Prescription for the prophylaxis antibiotic therapy in third molar surgery in healthy patients is highly controversial and conflicting results have been reported (Lodi *et al*. 2012). A Cochrane review indicated that prophylactic antibiotics reduced the risk of infection, dry socket and pain following third molar extraction (Mthetwa *et al.* 2018). These indications are, however, not highlighted in the Standard Treatment Guidelines in South Africa (2018). Lalloo *et al.* further observed a possible mismatch between prescribing patterns in relation to patients' health status and dental extractions (Lalloo *et al.* 2017).

The indications for systemic antibiotics in dentistry is limited since most dental infections present in the form of pulpitis and periapical periodontitis require only operative procedures such as extractions, fillings or root canal therapy (Mthethwa *et al.* 2018).

Antibiotics were also prescribed for systemic conditions (10%) in this study. This finding is consistent with previous reviews which concluded that patients with low immunity may be at higher risk of infection (Sidana *et al.* 2017). In such cases this could be beneficial to patients (Sidana *et al.* 2017). The results of this study showed that antibiotics prescribed for the prevention of Infective Endocarditis constituted 1% of the study sample. This observation is consistent with the findings reported by Mthethwa *et al*. 2018, in that 2, 2% of the antibiotic prescriptions were indicated for the prevention of infective endocarditis. Bacterial endocarditis remains a risk following dental treatment (Pallasch 2003). This is supported by the British

Society for Antimicrobial Chemotherapy and the American Heart Association which recommend that only high-risk patients require cover (Gould *et al.* 2006; Wilson *et al.* 2007). Although antibiotic prophylaxis to prevent infective endocarditis is widely accepted by the dental profession (Mthethwa *et al*. 2018), the effectiveness of such antibiotic prophylaxis in humans, however, remains unproven (Jankelow *et al.* 2017; Chambers *et al.* 2011).

There is no clear evidence that pre-operative antibiotic prophylaxis for routine third molar surgery is necessary for patients with no underlying medical complications (Dar-Odeh *et al*. 2010). A single dose of Metronidazole was not found to be effective in preventing the onset of dry socket. Similarly, most dentoalveolar surgical procedures in healthy individuals did not require antibiotic prophylaxis (Dar-Odeh *et al.*2010). Clinicians thus need to be aware of the ongoing evidence base for antibiotic prescription practices (Lallo *et al.* 2017). More research is required for appropriate antibiotic prescription in the field of clinical dentistry (Peric *et al.* 2015).

The study, therefore, suggests that some over-prescription of antibiotics does exist. This needs to be reviewed for clinical and financial reasons because an increase in bacterial resistance to antibiotics and the associated costs becomes a concern for the health care sector and the health care funding sector (Lalloo *et al.* 2017). Dental practitioners have a responsibility to reduce and improve the way they prescribe antibiotics and should prescribe with the correct indications and not under pressure of patients (Sanderson *et al.* 2019). Dental practitioners also have a responsibility to educate patients on the spread and consequences of antimicrobial resistance (Sanderson *et al.* 2019). There should be greater community awareness on the appropriate use of antibiotic (Lalloo *et al.* 2017) and the injudicious prescription of antibiotics for the treatment of ‘toothache’ should be avoided (Lewis 2008).

Study strengths and Limitations

This study provided much needed data on antibiotic prescription patterns for dental conditions in the public health sector in Pietermaritzburg. While the value of such timely data cannot be overstated, several limitations were noted. The study findings are limited to the two participating health institutions. The study findings are also limited to the reporting period (March 2012- July 2018). Poor record keeping and insufficient diagnostic data could have also skewed the study findings. From a data analytical process, inferential statistics were a challenge given the nature of

the data collected in the retrospective clinical chart review. Further research can be done in the future to determine other statistical relationships in collected data. A further research question for future studies could focus on practitioners' source of knowledge for antibiotic prescriptions (e.g. is it university education, continuing professional development?). This could perhaps identify the gaps that seem to contribute to practitioners' decision-making. Despite these limitations, a clear picture has emerged on antibiotic prescription patterns at the identified health institutions.

Conclusion

This study showed that there was an inconsistency in antibiotic therapy for dental conditions at the two public health institutions. The dental conditions for which health care practitioners prescribed antibiotics at each institution differed and empirical treatment was prescribed as opposed to definitive treatment after laboratory diagnosis. There is a need for consensus building among health professionals and for better guidance in respect of antibiotic prescription in the management of dental conditions.

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Conflict of interest

None

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CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1 Introduction

The purpose of this study was to contribute towards the strengthening of the health care systems and the need for proper guideline adherence through audits. The goal is to ensure that there is a continuity in the ability to prevent infectious diseases with the use of effective and safe medicines that are high quality, that are used in a safe and responsible manner and are accessible to all those who need them.

Therefore, this study was conducted owing to the paucity of information on the patterns of antibiotic prescription practices and the lack of information on dental conditions for which health care practitioners prescribe antibiotics in the public health sector, in the Pietermaritzburg Complex, KwaZulu-Natal

This chapter will focus on the extent to which the study aim, objectives and research questions were addressed. The study objectives were to determine the patterns of oral antibiotic prescription for dental patients in the identified public health institutions by means of a retrospective chart review. The results of the retrospective clinical chart review (n=720; 72% indicated dental abscesses were the most common dental infection requiring antibiotic therapy was dental abscesses (n= 479; 66%). Antibiotics were also prescribed for acute alveolar osteitis (dry socket) (n=110; 15%) and dental impactions (n=78; 11%). However, some differences were noted in the prescription patterns between the two identified health institutions. At Institution A, antibiotic therapy was prescribed conditions such as trismus (n=13; 6%), soft palate swelling (n=9; 4%), fibrous epulis (n=6; 3%), acute herpes (n=2; 1%). Interestingly, antibiotics were not prescribed at Institution B for the same dental conditions.

The second objective was to ascertain dental and medical practitioners' knowledge, attitudes and antibiotic prescription practices by means of a self- administered questionnaire. The majority of participants (n=72, 77.4%) indicated that they would prescribe antibiotics for orofacial swellings. Almost 33 participants (35.4%) also indicated that they would prescribe antibiotic cover for irreversible pulpitis. Almost 31 participants (88.9%) from Institution A and 40 (75%) from Institution B would prescribe antibiotics for pericoronitis. Similarly, 27 participants (76.9%).

The results of the study indicated that health care practitioners reported inconsistent knowledge, attitudes and practices related to antibiotic prescription patterns. The majority of the participants in this study (n=72, 77.4%) indicated awareness of an Antibiotic Stewardship Programme in their respective institutions yet 42 participants (45%) were not sure on whether the programme was active.

The third objective was to determine public health pharmacists' perspectives on the patterns of antibiotic prescription rates for dental use by means of a self- administered questionnaire. More than two thirds of study participants in Group 2 (n=18; 78%) perceived a correlation between the dental condition and the antibiotic prescribed thereof. Participants (n=17; 73.9%) however also indicated that antibiotics were sometimes prescribed without any indication. A clearer evidence-based guideline is required for oral health care practitioners.

The fourth objective was to explore medical and dental practitioners' as well as pharmacists' perspectives on antibiotic prescription rates for dental patients by means of a focus group discussion. There was a variation of themes that were identified such as inconsistency in antibiotic therapy for dental-related clinical management between the two public health care institutions, the adherence to the Standard Treatment Guidelines when prescribing antibiotics and strategies to combat antimicrobial resistance. Participants indicated the need to improve antimicrobial prescription patterns to reduce the adverse effects from incorrect antibiotic prescription and to consider working towards a multi-disciplinary team approach when prescribing antibiotics.

The three research questions were structured with respect to the aims and objectives of the study.
1. What are the trends in antibiotic prescription among dental and medical practitioners in the public health sector in the Pietermaritzburg Complex, KwaZulu-Natal?
This was established with the use of a retrospective clinical chart review. The results indicated that there were inconsistencies in antibiotic prescription for the management of dental conditions at the two public health care institutions. The dental conditions that were managed at the two institutions varied. The type of empirical treatment chosen for the management of the dental condition differed between each institution.

2. What antibiotic prescription protocols are health care practitioners following in the management of dental conditions?

The second research question was established with the use of a focus group discussion and a self-administered questionnaire to dental and medical practitioners and public health care pharmacists. The findings indicated serious inconsistencies in the antibiotic prescription patterns for dental conditions. This suggested that more support could be required for medical and dental practitioners in the decision-making processes for the appropriate antibiotic prescription for the management of dental conditions.

3. Are the health care practitioners aware of the National Strategic Framework on Antimicrobial Resistance, the Essential Medicines List and the Standard Treatment Guidelines? To what extent are these guidance documents used for the prescription of antibiotics for dental conditions? The study found, via the focus-group discussions and the self-administered questionnaire that health care practitioners were generally aware of the National Strategic Framework on Antimicrobial resistance and the Standard treatment Guidelines/ Essential Medicines List. More than half of participants (n=60, 64.5%) indicated referring to the Standard Treatment guidelines *'some times'* when prescribing antibiotics. The findings of this study indicate that more awareness is required for the existence of the Antibiotic Stewardship Programme for health care practitioners and the adherence to the Standard Treatment Guidelines needs to be reinforced.

The aim of the study was thus achieved, namely, that a clear picture emerged on health and dental practitioners' knowledge, attitudes and prescription patterns related to oral antibiotics for dental use in the public sector in Pietermaritzburg.

5.2 Significance of the study findings

The findings of this study indicated that oral antibiotic prescription policies and protocols require review for clinical and financial reasons because an increase in antimicrobial resistance to antibiotics and the associated costs becomes a concern for the health care sector and the health care funding sector. The shortcomings in the oral antibiotic prescription patterns for the management of dental conditions were identified and this suggests obvious gaps to support health care practitioners in the decision-making for antibiotic prescription for the management if

dental conditions. The study emphasized the urgent need for clear-evidence based guidelines for health care practitioners that prescribe oral antibiotics for the management of dental conditions. Health care practitioners reported inconsistent knowledge, attitudes and practices related to antibiotic prescription patterns. There is a need for consensus building among health professionals and better guidance for antibiotic prescription in the management of dental conditions.

More research is required to unpack the complexities associated with the trends in the prescription of oral antibiotics for the management of dental-related conditions. Further research is required to identify further mechanisms to improve antibiotic prescription practices and reduce antimicrobial resistance. The choice of oral antibiotics and its dosing regimen are dependent upon the severity of the dental infection and the predominant type of causative bacteria that is associated with the dental condition (Dar-Odeh *et al.* 2010). From a clinical perspective, the availability of tests such as the microbial-enzymatic N-benzoyl-DL-arginine-2-napthylamide (BANA) test could be used to detect oral pathogens in subgingival plaque (*Porphyromonas gingivalis*, *Treponema denticola* and *Tannerella forsythia*). This could assist the practitioner in determining the need for antibiotic prescription for the patient (Dhalla *et al* 2015).

There is an urgent need to develop and implement oral disease prevention and antimicrobial resistance intervention programmes that could be aimed at educating and supporting at-risk populations.

Community awareness of the appropriate use of oral antibiotics and curbing antimicrobial resistance is important. It is equally important for health care practitioners to make an informed decision on the appropriate prescription of oral antibiotics (Lalloo *et al.* 2017). Together with the proper dosing regimens and responsible prescribing practices, the general public needs to be educated about the importance of restricting the use of antibiotics confining only to cases of severe infection as clients have become accustomed to being given an antibiotic for a range of medical complaints. It is the responsibility of the health care practitioner to review strategies from a curative oral health care to a more preventive approach. Oral health promotion and the awareness of antimicrobial resistance should be an important part of the health care service provision in the public and private health care institutions.

5.3 Study limitations

The study findings were limited to two public health care institutions in Pietermaritzburg, KwaZulu-Natal. The generalizability of the two study sites is limited. The study findings were limited to the reporting period of March 2012-July 2018. Poor record keeping and insufficient diagnostic data could have skewed the study findings in the retrospective clinical chart review.

From the data analytical process inferential statistics were a challenge given the nature of the data collected in the retrospective clinical chart reviews.

There could have been possible over-reporting by respondents to ensure social desirability. Despite these limitations, a clear picture emerged on oral antibiotic prescription patterns for the management of dental-related conditions in the identified public health care institutions.

5.4 Recommendations

The following recommendations are made for this study:

- There is urgent need for review and clearer oversight in oral antibiotic prescription patterns for dental use in the identified health institutions.
- Similarly, there should be a process to facilitate consensus building among health and dental practitioners to develop a list on dental conditions that could require oral antibiotic coverage, so as to provide guidance to practitioners.
- There is need to for better facilitation within the KZN Department of Health to ensure practitioner compliance with the Standard Treatment Guidelines for the prescription of oral antibiotics for dental conditions.

5.5 Conclusion

In summary, the study indicated inconsistencies in the management of dental-related infections requiring oral antibiotic therapy, at the two public health institutions. The dental conditions for which antibiotics were prescribed at each institution varied and the empirical treatment of choice between the two institutions differed. The results indicated inconsistency in health practitioners' knowledge, attitudes and practices related to oral antibiotic prescription patterns. There is need

for more evidence-based guidelines for antibiotic prescription in the management of dental-related conditions so as to better equip practitioners to engage with antibiotic stewardship.

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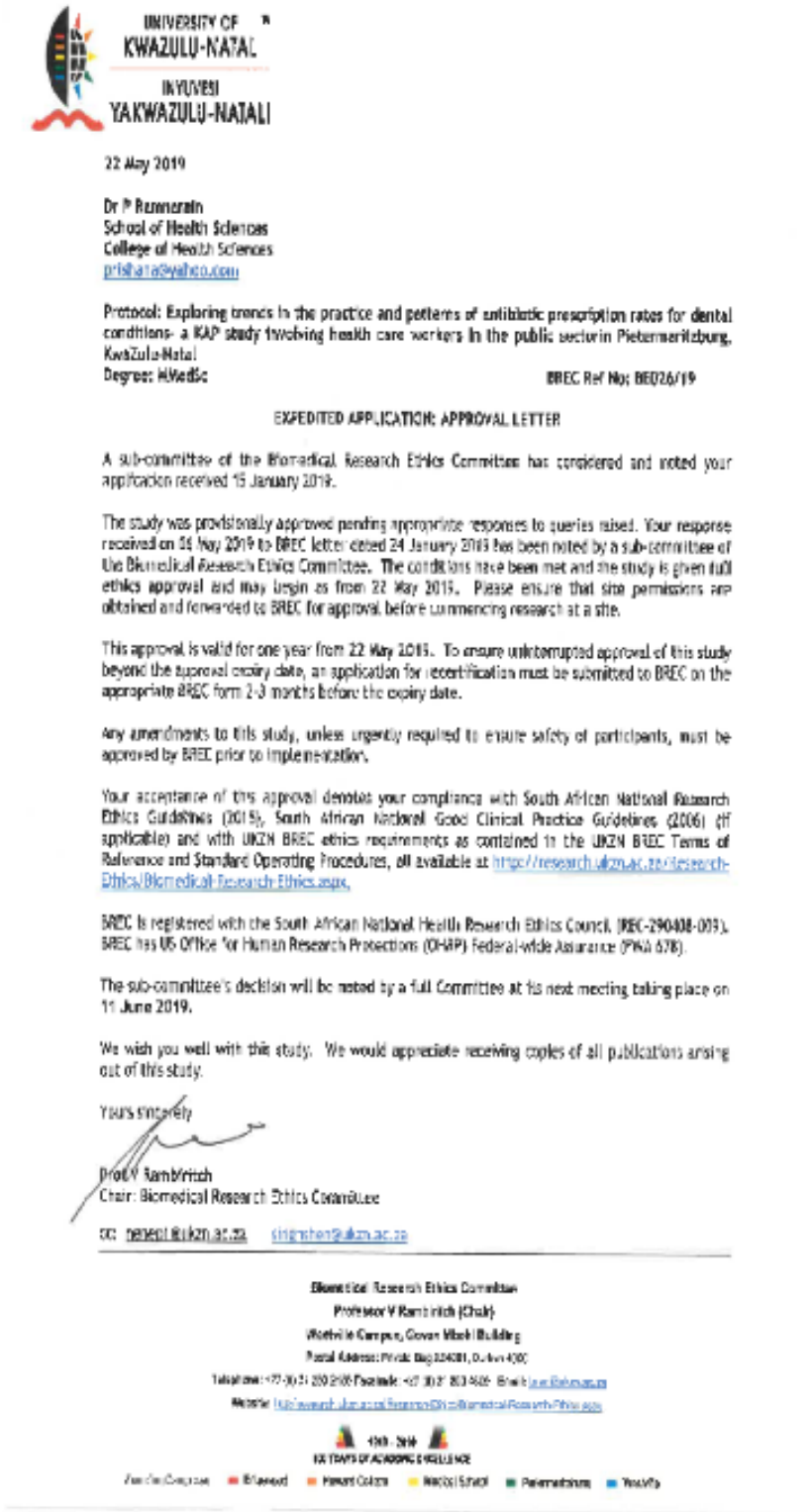
ANNEXURE 1: BREC ETHICAL CLEARANCE LETTER



UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

22 May 2019

Dr P Ramnarain
School of Health Sciences
College of Health Sciences
prishata@yahoo.com

Protocol: Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions- a KAP study involving health care workers in the public sector in Pietermaritzburg, KwaZulu-Natal
Degree: MMedSc

BREC Ref No: BE026/19

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received 15 January 2019.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 16 May 2019 to BREC letter dated 24 January 2019 has been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have been met and the study is given full ethics approval and may begin as from 22 May 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 22 May 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-290408-019). 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.

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

cc: penyel@ukzn.ac.za singhsh@ukzn.ac.za

Biomedical Research Ethics Committee
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ANNEXURE 2: BREC ETHICAL CLEARNCE LETTER FROM DEPARTMENT OF HEALTH

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
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DIRECTORATE:
Health Research & Knowledge Management

NHRD Ref: KZ_201902_018

Dear Dr P. Ramnarain

Approval of research

1. The research proposal titled **'Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions - a KAP study involving health care workers in the public health sector in Pietermaritzburg'** was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at Edendale and Northdale Hospital.

2. You are requested to take note of the following:
   a. Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.
   b. Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.
   c. Provide an interim progress report and final report (electronic and hard copies) when your research is complete to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge

Chairperson, Health Research Committee

Date: 06/05/2019

Fighting Disease, Fighting Poverty, Giving Hope

ANNEXURE 3: SUPPORT LETTER FROM THE CEOS OF THE HOSPITALS ALLOWING GATEKEEPER PERMISSION

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

NORTHDALE HOSPITAL

1389 Chota Motala Road, Pietermaritzburg,3201
Private Bag X 9006,Pietermaritzburg,3200
Tel: 033 - 3879009Fax: 033 - 3871990 Email: karen.naidoo@kznhealth.gov.za
www.kznhealth.gov.za

MEDICAL

Date: 09. March 2019
Enquiries: Dr MAG Molla

Dr P Ramnarain
School Of Health Science
College Of Health science
BREC Ref No : BE 026/19

RE: EXPLORING TRENDS IN THE PRACTICE AND PATTERNS OF ANTIBIOTIC PRESCRIPTION RATED FOR DENTAL CONDITIONS-A KAP STUDY INVOLVING HEALTH CARE WORKERS IN THE PUBLIC HEALTH SECTOR IN PIETERMARITZBURG, KZN

Your request regarding "to conduct a research on the above is acknowledged and refers.
I have pleasure in informing you that permission has been granted to you by Northdale Hospital to conduct research.

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Please ensure this office is informed before you commence your research.
4. The Hospital will not provide any resources for this research.
5. You should not disrupt service delivery and patient waiting times
6. Study to be conducted in own time
7. Access to patient files during working hours only
8. Patient records are not to be taken out of the institution
9. You are expected to provide an interim progress report and final report when the research is completed

Thanking you.

Sincerely

Dr MAG Molla
Medical Manager
Northdale Hospital

Fighting Disease. Fighting Poverty. Giving Hope

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE: CHIEF EXECUTIVE OFFICER

Physical Address: No.89 Selby Msimang Road, Pietermaritzburg, 3216
Postal Address: P/Bag X 509, PLESSISLAER, 3216
Tel: 033 395 4040 Fax: 033 395 4087 Email: Fortunate.Mbele@kznhealth.gov.za

EDENDALE HOSPITAL

Enquiries: Ms.N.F Mbele
Ext: 4042
Date: 04 April 2019

Dr P Ramnarain
School of Health Science
Collage of Health Science

Dear Dr Ramnarain

RE: EXPLORING TRENDS IN THE PRACTICE AND PATTERNS FOR DENTAL CONDITIONS – A KAP STUDY INVOLVING HEALTH CARE WORKERS IN THE PUBLIC SECTOR IN PIETEMARITZBURG, KWAZULULU- NATAL

Your request dated 10 February 2019 is acknowledged and refers.

I have pleasure in informing you that permission has been granted by Edendale Hospital to conduct research.

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. The Hospital will not provide any resources for this research.
3. You will be expected to provide feedback on your findings to Edendale Hospital.
4. You will also be expected to notify the Medical Manager's office prior start date of the research.

Yours Sincerely

Dr EK Mthembu
Senior Manager- Medical Services
Edendale Hospital

ANNEXURE 4: INFORMED CONSENT FOR THE PARTICIPANTS OF THE SURVEY

Information Leaflet and Informed consent to participate in the research

Study title: Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions – a KAP study involving health care workers in Pietermaritzburg, KwaZulu-Natal.

Investigator: Dr P. Ramnarain and Professor Shenuka Singh

Institution: School of oral health sciences at the University of KwaZulu-Natal

Email: prishanar@yahoo.com / singhshen@ukzn.ac.za

Contact number: 0737191958 / 0738417384

This consent form describes the study and requests you to participate by answering the questionnaires. If you have any queries, please contact the investigator.

Introduction:

As a student studying towards a master's degree in Medical science-dentistry and a full time dentist at the Northdale hospital, I would like to invite you to consider participating in a research study. Your participation in this study is entirely voluntary. You have an option of refusing to participate and this will not involve any penalty or loss of benefit to the participant.

The information leaflet will provide understanding to what is actually involved in the study. This should help you to decide if you would like to participate before you agree to take part in the study. If you have any questions, please contact the investigator. Unless you are satisfied with the procedures involved you should agree to participate in the study. If you decide to participate in the study, the completion of the questionnaire will be confirmation that you understand and agree to the study

Purpose of the study:

The purpose of this study is to investigate the patterns and practices of antibiotic prescription trends for the management of dental conditions, among health care workers in the Pietermaritzburg complex. It is also to investigate whether health care workers are following the standard treatment guidelines and essential medicines list when prescribing antibiotics. It is important to establish the current practices, knowledge and awareness about antibiotic prophylaxis and antimicrobial resistance among South Africans. Guidelines have been published over the years in the USA and UK but not in South Africa concerning antibiotic prophylaxis for dental procedures. This study will highlight the need for local guidelines so that recommendations can be made to antibiotic stewardship committees on the suitable mechanisms for determining and disseminating guidelines created for South Africa.

Methodology:

Your participation would require that you complete the questionnaire. Answer the questions on your current knowledge regarding antibiotic prophylaxis and your current practice in this regard. Dental conditions that patients present with and the antibiotics that are prescribed for those

conditions will be recorded in the data collection sheet. The antibiotics prescribed are checked to see if they are according to the standard treatment guidelines.

Your right as a participant in this study:

Your participation in this study is entirely voluntary and you can decline to participate, without stating any reason.

Financial arrangements:

There are no financial implications for you, other than your time taken to read about the study and to complete the questionnaire.

Ethics approval:

This study protocol has been submitted to the University of KwaZulu-Natal Biomedical research ethics committee and written approval has been granted by that committee.

Confidentiality:

All the information obtained during the course of this study, including patient and professional data as well as research data will be kept strictly confidential in a locked up cupboard at the University of KwaZulu-Natal, discipline of dentistry. Only the researcher will have access to the study data and information. The study will not require any use of the participants' names. All the responses to the questionnaires will remain anonymous and only the investigator will know you as a respondent. Data recorded in the scientific journals will not include any information that will identify any of the participants in this study.

Informed consent:

Before agreeing to this study, it is important that the purpose of this study has been clearly explained to you and that you have understood. This agreement states that you have understood all the information that has been explained to you and that you agree to participate in this study. You may voluntarily withdraw at any time should you not wish to participate in this study.

By completing the questionnaire and / or signing and returning the document, I _____ (Name of participant) have been informed about the study entitled , Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions – a KAP study involving health care workers in Pietermaritzburg, KwaZulu-Natal by Dr Prishana Ramnarain and Professor Shenuka Singh.

- I hereby confirm that I have been informed about the nature, conduct, benefits and risks of this study.
- I have received, read and understood the above written information (Participant Information Leaflet) regarding this study.
- I understand the purpose and procedures of the study
- I am aware that the results of this study will be anonymously processed into a study report.
- In view of the requirements of the research, I agree that the data collected during the study can be processed in a computerized system.

- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will), declare myself prepared to participate in the study when I complete the questionnaire.
- I declare that my participation in this study is entirely voluntary and that I may withdraw at any time.
- If I have any further questions/ concerns related to the study I understand that I may contact the researcher at 0737191958/ prishanar@yahoo.com and 0738417384/ singhshen@ukzn.ac.za.
- If I have any questions or concerns about my rights as a study participant, or if I am concerned about the aspect of the study or the research then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research office, Westville Campus
Govan Mbeki Building
Private Bag X54001
Durban
4000
KwaZulu Natal, South Africa
Tel: 27 31 2604769 – Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Participant

DATE	PRINT NAME	SIGNATURE

Study Doctor

I, Dr P. Ramnarain, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____

Signature Date

ANNEXURE 5: INFORMED CONSENT FOR THE PARTICIPANTS OF THE FOCUS-GROUP DISCUSSION

Information Leaflet and Informed consent to participate in the research

Study title: Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions – a KAP study involving health care workers in Pietermaritzburg, KwaZulu-Natal.

Investigator: Dr P. Ramnarain and Professor Shenuka Singh

Institution: School of oral health sciences at the University of KwaZulu-Natal

Email: prishanar@yahoo.com / singhshen@ukzn.ac.za

Contact number: 0737191958 / 0738417384

This consent form describes the study and requests you to participate in the focus group discussion. If you have any queries, please contact the investigator.

Introduction:

As a student studying towards a master's degree in Medical science-dentistry and a full time dentist at the Northdale hospital, I would like to invite you to consider participating in a research study. Your participation in this study is entirely voluntary. You have an option of refusing to participate and this will not involve any penalty or loss of benefit to the participant.

The information leaflet will provide understanding to what is actually involved in the study. This should help you to decide if you would like to participate before you agree to take part in the study. If you have any questions, please contact the investigator. Unless you are satisfied with the procedures involved you should agree to participate in the study. If you decide to participate in the study, the completion of the consent will be confirmation that you understand and agree to the study

Purpose of the study:

The purpose of this study is to investigate the patterns and practices of antibiotic prescription trends for the management of dental conditions, among health care workers in the Pietermaritzburg complex. It is also to investigate whether health care workers are following the standard treatment guidelines and essential medicines list when prescribing antibiotics. It is important to establish the current practices, knowledge and awareness about antibiotic prophylaxis and antimicrobial resistance among South Africans. Guidelines have been published over the years in the USA and UK but not in South Africa concerning antibiotic prophylaxis for dental procedures. This study will highlight the need for local guidelines so that recommendations can be made to antibiotic stewardship committees on the suitable mechanisms for determining and disseminating guidelines created for South Africa.

Methodology:

Your participation would require that you participate in a focus group discussion with multidisciplinary team members. The discussions may be audio recorded. Answer the questions

on your current knowledge regarding antibiotic prophylaxis and your current practice in this regard. Dental conditions that patients present with and the antibiotics that are prescribed for those conditions will be discussed. The antibiotics prescribed are checked to see if they are according to the standard treatment guidelines.

Your right as a participant in this study:

Your participation in this study is entirely voluntary and you can decline to participate, without stating any reason.

Financial arrangements:

There is no financial implications for you, other that your time taken to read about the study and to complete the questionnaire.

Ethics approval:

This study protocol has been submitted to the University of KwaZulu-Natal Biomedical research ethics committee and written approval has been granted by that committee.

Confidentiality:

All the information obtained during the course of this study, including patient and professional data as well as research data will be kept strictly confidential in a locked up cupboard at the University of KwaZulu-Natal, discipline of dentistry. Only the researcher will have access to the study data and information. The study will not require any use of the participant's names .All the responses to the questions in the focus group discussion will remain anonymous and only the investigator will know you as a respondent. Data recorded in the scientific journals will not include any information that will identify any of the participants in this study.

Informed consent:

Before agreeing to this study, it is important that the purpose of this study has been clearly explained to you and that you have understood. This agreement states that you have understood all the information that has been explained to you and that you agree to participate in this study. You may voluntarily withdraw at any time should you not wish to participate in this study.

By completing the questionnaire and / or signing and returning the document, I _____ (Name of participant) have been informed about the study entitled , Exploring trends in the practice and patterns of antibiotic prescription rates for dental conditions – a KAP study involving health care workers in Pietermaritzburg, KwaZulu-Natal by Dr Prishana Ramnarain and Professor Shenuka Singh.

- I hereby confirm that I have been informed about the nature, conduct, benefits and risks of this study.
- I have received, read and understood the above written information (Participant Information Leaflet) regarding this study.
- I understand the purpose and procedures of the study
- I am aware that the results of this study will be anonymously processed into a study report.

- In view of the requirements of the research, I agree that the data collected during the study can be processed in a computerized system.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will), declare myself prepared to participate in the study when I complete the questionnaire.
- I declare that my participation in this study is entirely voluntary and that I may withdraw at any time.
- If I have any further questions/ concerns related to the study I understand that I may contact the researcher at 0737191958/ prishanar@yahoo.com and 0738417384/ singhshen@ukzn.ac.za.
- If I have any questions or concerns about my rights as a study participant, or if I am concerned about the aspect of the study or the research then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research office, Westville Campus
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Private Bag X54001
Durban
4000
KwaZulu-Natal, South Africa
Tel: 27 31 2604769 – Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Participant

DATE	PRINT NAME	SIGNATURE

Study Doctor

I, Dr P. Ramnarain, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____

Signature Date

ANNEXURE 6: CLINICAL RECORD EVALUATION SHEET

1.1. Data Collection sheet for review of the patient files

1. Name of hospital: _____

2. Patient number: _____

3. History of the dental infection:

_____

4. Presenting symptoms:

_____

5. Has the patient presented with the same dental condition previously?

a. YES

b. NO

If YES, what medication was prescribed previously? (Include route, dosage, and frequency)

_____

_____

_____

_____

6. Are there any diagnostic tests available relating to the dental condition?

_____

7. What is the provisional diagnosis?

_____

8. What is the number of medicines prescribed by generic name? _____

9. What was the number of medicines dispensed? _____

10. Have specimens been sent to the laboratory for microbiological test?

a. YES

b. NO

11. Which professional prescribed the medicines?

a. Dentist

b. Dental therapist

c. Medical doctor

d. Pharmacist

12. Is there any evidence of patient outcomes after treatment?

a. YES

b. NO

1.2. Antibiotic therapy worksheet

Type of Problem		Assessment
1. Correlation between dental therapy provided and the dental condition	1. Are there antibiotics without dental indication 2. Are there any untreated dental conditions? 3. If "YES" do they require dental treatment	
2. Medicine Regimen	1. Has the antibiotic regimen been prescribed according to the standard treatment guidelines? 2 Are the prescribed doses and dosing frequency appropriate considering the patient and the patient factors? (Age etc.) 3. Are the doses scheduled to maximize the therapeutic effects and minimize the adverse effects? 4. Is the length or course of antibiotic therapy appropriate? 5. How many antibiotics were prescribed for this patient?	
3. Therapeutic duplication	1. Is there antibiotic duplication or combinations? 2. Are there antibiotics that have the same mechanism of action and are not to be used together?	
4. Interactions	1. Are there medicine-medicine interactions that are clinically significant? 2. Are there any antibiotics contraindicated given the patient	

	characteristics of the dental or medical conditions?	
5. Laboratory Information	1.Has the specimen been sent to the laboratory 2. Is the antibiotic indicated for the condition or microorganism	

ANNEXURE 7: QUESTIONNAIRE FOR MEDICAL AND DENTAL PRACTITIONERS

Hospital: _____

Occupation: _____

1. DEMOGRAPHICS

1.1. Age

- 20-29
- 30-39
- 40-49
- 50-59
- 60+

1.2. Gender

- MALE
- FEMALE
- OTHER

1.3. Years since graduation _____

1.4. Are you currently a:

- Dentist
- Community service dentist
- Maxillofacial and Oral surgeon
- Medical practitioner
- Dental Therapist
- Pharmacist

2. ADHERENCE TO GUIDELINES

2.1. Is there a hospital stewardship committee?

- YES
- NO

If "YES", on a scale of 1-5, how active is the committee in your opinion?

1	2	3	4	5
Very Active	Active	Not sure	Not Active	Not Active at all

2.2. Are you aware of the Standard treatment guidelines and the essential drug list?

- YES
- NO

2.3. Do you have a copy of the Standard treatment guidelines and Essential drugs list in your consultation room?

- YES
- NO

a. If "NO", why not_____

_____

b. Have you tried to get copy of the standard treatment guidelines and essential medicines list?

- YES
- NO

2.4. How often do you ever refer to the Standard treatment guidelines when you prescribe antibiotics? Please indicate on a scale 1-5, with 1 being always and 5 being you never refer to them.

1	2	3	4	5
Always		Sometimes		Never

2.5. Do you think that there is a need to improve the prescribing of antibiotics in the hospital?

- YES
- NO

2.6. Any other comments:

_____

_____

3. ANTIBIOTIC PROPHYLAXIS FOR ENDOCARDITIS

3.1. Are you aware of the guidelines for antibiotic prophylaxis to prevent endocarditis published by the American Heart Association?

- YES
- NO

3.2. Are you aware of the guidelines by the (UK NHS) National institute for health and clinical excellence (NICE)

- YES
- NO

3.3 Which guidelines do you follow?

- The American Heart association
- NICE
- NONE

4. WHAT DO YOU PRESCRIBE WHEN AN ADULT REQUIRES ANTBIOTIC FOR THE FOLLOWING SITUATIONS

4.1. Patients who are allergic to Penicillin or Ampicillin

- NONE
- Name of antibiotic : _____
  Dosage and duration: _____

4.2. Patients who require antibiotic prophylaxis for Infective Endocarditis

- NONE
- Name of antibiotic :_____
- Dosage and duration:_____

4.3. If you are unsure about the dosage and means of administration, where would you look for this information?

_____

4.4. If there are other systemic conditions that may require antibiotic coverage, which of the following would you prescribe antibiotic prophylaxis for? Please tick YES or NO

SYSTEMIC CONDITIONS	YES	NO
1. History of Rheumatic fever		
2. Hereditary haemorrhagic telangiectasia		
3. Diabetes Mellitus		
4. Hip replacement therapy (Within 6 months)		
5. HIV positive with no antiretrovirals		
6. HIV positive and on antiretrovirals		
7. Rheumatoid arthritis		
8. Systemic Lupus Erythematosus		
9. Tuberculosis		
10. Prosthetic cardiac valve repair		

11. Previous endocarditis		
12. Congenital heart disease		
13. Cardiac transplantation recipients who can develop cardiac valvulopathy		

4.5. Are there any other systemic conditions for which you would prescribe antibiotics?

- YES
- NO

If "YES", please state: _____

4.6. Tick the conditions for which antibiotics should be prescribed for.

DENTAL CONDITION	YES	NO
1. Orofacial swelling		
2. Dental pain related to irreversible pulpitis		
3. Dental pain related to reversible pulpitis		
4. Dental pain related to dental fillings		
5. Pericoronitis		
6. Periodontitis		
7. Impacted teeth		
8. Acute alveolar osteitis/ Dry socket		
9. Mandibular fractures/ Maxillary fractures		
10. Trismus		
11. Prophylaxis before dental surgery		
12.Post –operative treatment for dental surgery		
13. Aphthous ulcers		

4.7. What is the antibiotic regimen in your dental surgery for adult patients? Please circle the correct choice/s.

- 500 mg Amoxil
- 400mg Flagyl
- 600mg Clindamycin
- 250mg Tetracycline

- Other (Please list) : 1._____
  2. _____

4.8. How would you prescribe the antibiotic of choice for your selected regimen at your hospital?

ANTIBIOTIC	ROUTE OF ADMINISTRATION	FREQUENCY	DOSAGE

5. OUTCOME OF THE TREATMENT PRESCRIBED

5.1. Do you review your patient after antibiotic prescription? Please indicate on a scale 1-5, with 1 being always and 5 being you never review your patient after antibiotic prescription.

1	2	3	4	5
Always		Sometimes		Never

5.2. Do you think the antibiotic would have worked effectively? Please indicate on a scale 1-5, with 1 being strongly agreed and 5 being you disagree that the antibiotics would have worked effectively.

1	2	3	4	5
Strongly Agree	Agree	Sometimes	Disagree	Strongly Disagree

6. ANY OTHER COMMENTS:

ANNEXURE 8: QUESTIONNAIRE FOR THE PHARMACISTS

Hospital: _____

1. From you observation, is there correlation between the antibiotics prescribed for the dental condition and the dental condition? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

2. Are the antibiotics prescribed without dental indication? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

3. Are the antibiotic regimens been prescribed to the Standard treatment guidelines and essential drug list? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

4. Are the doses scheduled to maximize the therapeutic effects and minimize the adverse effects? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

5. Is the length / course of antibiotic therapy appropriate? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5

Always		Sometimes		Never

6. How many antibiotics are usually prescribed per patient? _____

7. Are the duplication and combinations? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

8. Are there antibiotics that have the same mechanism of action and are not to be used together? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

9. Are there medicine-medicine interactions that are clinically significant? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

10. Are there any antibiotics contraindicated given the patient characteristics of the dental or medical condition that have been prescribed? Please indicate on a scale 1-5, with 1 being always and 5 being never.

1	2	3	4	5
Always		Sometimes		Never

11. Do you recommend diagnostic laboratory testing? Please indicate on a scale 1-5, with 1 being strongly agreed and 5 being strongly disagree.

1	2	3	4	5
Strongly agree	Agree	Uncertain	Disagree	Strongly Disagree

12. ANY OTHER COMMENTS

ANNEXURE 9: SEMI-STRUCTURED FOCUS-GROUP QUESTIONNAIRE

Hospital _____

Date: _____ Time: _____

1. Do you know why the Antimicrobial resistance strategic framework 2014-2024 was implemented?

2. What standard treatment guidelines are used at you hospital?

3. Do all the departments in your hospital have a copy of the Standard treatment guidelines and essential drug list?

4. What is the latest version that you have in your hospital?

5. Do you refer to the standard treatment guidelines when you prescribe antibiotics?

6. Do you prescribe antibiotic regimen according to the standard treatment guidelines?

7. Does your hospital have an antibiotic stewardship committee?

8. How often does the committee meet?

9. Who comprises the committee?

10. Have you implemented any changes in your hospital to combat antibiotic resistance?

11. Have there been adverse events related to antibiotic prescription in your hospital. If yes, approximately how many cases per month?

12. Did you work together as a multi-disciplinary team to manage the adverse event?

13. Is there a need for diagnostic laboratory testing for correct diagnosis prior to prescription?

14. Do you think there is a need to improve the prescription of antibiotics in you hospital?

15. What are the most common dental conditions for which antibiotics are prescribed?

ANNEXURE 10: RESEARCH ETHICS CERTIFICATES

TRREE

Clinical Trials Centre
The University of Hong Kong

Zertifikat Certificado

Certificat Certificate

Promouvoir les plus hauts standards éthiques dans la protection des participants à la recherche biomédicale

Promoting the highest ethical standards in the protection of biomedical research participants

Certificat de formation - Training Certificate

Ce document atteste que - this document certifies that

Prishana Ramnarain

a complété avec succès - has successfully completed

Introduction to Research Ethics

du programme de formation TRREE en évaluation éthique de la recherche

of the TRREE training programme in research ethics evaluation

Release Date: 2018/01/07

Professeur Dominique Sprumont
Coordinateur TRREE Coordinator

FMH

FPH

Ce programme est soutenu par - This program is supported by :

Zertifikat
Certificat
Certificado
Certificate

Promouvoir les plus hauts standards éthiques dans la protection des participants à la recherche biomédicale
Promoting the highest ethical standards in the protection of biomedical research participants

Clinical Trials Centre
The University of Hong Kong

Certificat de formation - Training Certificate

Ce document atteste que - this document certifies that

Prishana Ramnarain

a complété avec succès - has successfully completed

Informed Consent

du programme de formation TRREE en évaluation éthique de la recherche
of the TRREE training programme in research ethics evaluation

Release Date: 2019/01/07

Professeur Dominique Sprumont
Coordinateur TRREE Coordinator

FMH

FPH

Ce programme est soutenu par - This program is supported by