Prescribing Practices of Antibiotic Prophylaxis used for Surgical Procedures in Paediatric Patients at Dr. George Mukhari Academic Hospital (DGMAH) and a Private Hospital

A mini-dissertation submitted by

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DECLARATION

I, N van der Sandt, declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University (SMU) for the degree of Master of Pharmacy, in the Faculty of Health Sciences, School of Health Care Sciences, has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

_________________________________________  _______________________

N van der Sandt (Mrs)  Date
DEDICATION

To my parents, Charmain and Marius, my sister, Michelle van der Sandt, and Jaco Schoeman. I owe this accomplishment to you. Thank you for giving me the opportunity to chase my dreams, for wholeheartedly believing in me and for your never ending support.
ACKNOWLEDGEMENTS

I am sincerely thankful for the following individuals who assisted me during the course of this study. Thank you all for your support and guidance. Without you this study would not have been possible.

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The Department of Pharmacy for the opportunity to conduct this research, their logistical support and for the arrangements of funds for this study.

Dr. George Mukhari Academic Hospital and the private hospital used for the opportunity to conduct my study in their wards.
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**Introduction:** Little is known about the practice patterns for the use of surgical antimicrobial prophylaxis (SAP) in the current paediatric surgical population and whether trends are in line with the recommended guidelines. In paediatrics undergoing surgery at the teaching and private hospital used, SAP is not being monitored. The aim of this study was to evaluate compliance to SAP guidelines for paediatrics requiring surgery in four specialised areas; urology, ear, nose and throat (ENT), general and maxillofacial surgery. Furthermore, the study sought to assess medical practitioners’ knowledge and perception of SAP use in paediatrics.

**Methods:** Both aspects of the study was conducted via a multi-centre and health care system approach in South-Africa. A retrospective chart review was used to assess the compliance of SAP prescriptions to current SAP Guidelines on appropriate antimicrobial selection, dosing, timing of administration, redosing and duration of treatment. To assess the knowledge and perceptions of medical practitioners, regarding SAP use in paediatrics, a prospective survey was conducted. Knowledge on pre- and post-operative SAP use in paediatrics in four surgical disciplines specified (urology, ear, nose and throat, general and maxillofaical surgery) was compared to current SAP guidelines.

**Results:** The retrospective aspect utilised charts dated between February and August 2015. A total of 224 charts we reviewed, 112 each from the teaching and private hospitals respectively. The majority (p=1.000) of paediatrics from both hospitals received SAP when indicated (77.27% and 100% respectively). The minority of paediatrics from both hospitals received antimicrobials without an indication (21.11% and 45.88% respectively). Compliance to all five of the criteria was not met by either hospital. Overall, the teaching hospital met the most criteria (three out of five) in 58.82% of paediatrics. In the prospective aspect of the study, 33 surveys were completed, 18 from the teaching and 15 from the private hospital. Comparative results were seen in both study populations regarding the consideration of potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR due to the use of antimicrobials (55.55%, 66.67%, 77.77% and 66.67% for the teaching hospital respectively, compared to 66.67%, 73.34%, 80% and 53.34% for the private hospital respectively). However, a statistically significant difference (p=0.0363) between the two study populations, in terms of SAP costs consideration when prescribing SAP was noted. Variations in ready knowledge of the medical practitioners, for pre- and post-operative SAP, was noted for the four surgical sub-categories in both hospitals.
Conclusion: Current SAP practices in South Africa’s teaching and private hospitals diverge from current SAP Guidelines. Inappropriate overuse of SAP occurs in both hospitals, whilst underuse is limited to the teaching hospital. Full compliance to the five criteria was not met by either hospital. Non-compliance was largely attributed to inappropriate selection and dosing. Areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing in paediatrics has been identified. The areas in most need of improvement include; pre- and post-operative SAP administration. Standardisation of education on SAP in paediatrics should receive attention from statutory bodies in South Africa as medical practitioners require further education to enhance ready knowledge pertaining to SAP use in paediatrics. Quality improvement interventions, continued surveillance and local standardised evidence-based SAP guidelines are also needed.
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<tr>
<td>ACOG</td>
<td>American College of Obstetricians and Gynecologists</td>
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<tr>
<td>AMR</td>
<td>Antimicrobial resistance</td>
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<td>AMS</td>
<td>Antimicrobial stewardship</td>
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<tr>
<td>ASHP</td>
<td>American Society of Health-System Pharmacists</td>
<td></td>
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<tr>
<td>AAPD</td>
<td>American Academy of Paediatric Dentistry</td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>Choc Children’s</td>
<td></td>
</tr>
<tr>
<td>CDC</td>
<td>Centre for Disease Control</td>
<td></td>
</tr>
<tr>
<td>CMS</td>
<td>Centres for Medicare and Medicaid Services</td>
<td></td>
</tr>
<tr>
<td>CI/s</td>
<td>Confident interval/s</td>
<td></td>
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<tr>
<td>CONS</td>
<td>Coagulase-negative Staphylococci</td>
<td></td>
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<tr>
<td>DGMAH</td>
<td>Dr. George Mukhari Academic Hospital</td>
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<tr>
<td>EML</td>
<td>Essential Medicines List</td>
<td></td>
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<tr>
<td>EMSA</td>
<td>Emergency Medical Services Authority</td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>Ear, nose and throat</td>
<td></td>
</tr>
<tr>
<td>GDP</td>
<td>Gross domestic product</td>
<td></td>
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<tr>
<td>HAI</td>
<td>Hospital acquired infections</td>
<td></td>
</tr>
<tr>
<td>HCP/s</td>
<td>Health care practitioner/s</td>
<td></td>
</tr>
<tr>
<td>Hr/s</td>
<td>Hour/s</td>
<td></td>
</tr>
<tr>
<td>ICD</td>
<td>International list of Cause of Death</td>
<td></td>
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<tr>
<td>ICU</td>
<td>Intensive care unit</td>
<td></td>
</tr>
<tr>
<td>IDSA</td>
<td>Infectious Diseases Society of America</td>
<td></td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
<td></td>
</tr>
<tr>
<td>kg</td>
<td>Kilogram</td>
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<tr>
<td>MSSA</td>
<td>Methicillin-susceptible Staphylococci</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>MEDUNSA</td>
<td>Medical University of South Africa</td>
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<tr>
<td>min</td>
<td>Minutes</td>
<td></td>
</tr>
<tr>
<td>mg</td>
<td>Milligram</td>
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<tr>
<td>mg/kg</td>
<td>Milligram per kilogram</td>
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<tr>
<td>NCS</td>
<td>National core standards</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>NDoH</td>
<td>National Department of Health</td>
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<tr>
<td>NHLS</td>
<td>National Health Laboratory Service</td>
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<tr>
<td>NHS</td>
<td>National Health Service</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<tr>
<td>NICHD</td>
<td>National Institute of Child Health and Human Development</td>
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<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
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<td>NHSN</td>
<td>National Healthcare Safety Network</td>
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<tr>
<td>PIDS</td>
<td>Paediatric Infectious Disease Society</td>
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<tr>
<td>RHSC</td>
<td>Reproductive Health Supplies Coalition</td>
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<tr>
<td>SADC</td>
<td>Southern African Development Community</td>
<td></td>
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<tr>
<td>SAP</td>
<td>Surgical antimicrobial prophylaxis</td>
<td></td>
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<tr>
<td>SAP®</td>
<td>Systems, Applications and Products</td>
<td></td>
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<tr>
<td>SAS®</td>
<td>Statistical Analysis System®</td>
<td></td>
</tr>
<tr>
<td>SCIP</td>
<td>Surgical Care Improvement Project</td>
<td></td>
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<tr>
<td>SHEA</td>
<td>Society for Healthcare Epidemiology of America</td>
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<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
<td></td>
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<tr>
<td>SIS</td>
<td>Surgical Infection Society</td>
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<tr>
<td>SMU</td>
<td>Sefako Makgatho Health Sciences University</td>
<td></td>
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<tr>
<td>SMUREC</td>
<td>Sefako Makgatho Health Sciences University research ethics committee</td>
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<tr>
<td>SSIs</td>
<td>Surgical site infections</td>
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STGs  Standard Treatment Guidelines
UNGA  United Nations General Assembly
USA  United States of America
WHO  World Health Organisation
Chapter 1: Introduction

CHAPTER 1
INTRODUCTION

1.1 INTRODUCTION

This introductory chapter describes the background to and rationale for the study. The primary and secondary research questions are provided, followed by the aims and objectives of the study. Additionally, the significance of the study is discussed and lastly an outline of the dissertation concludes the chapter. For the purposes of the study Dr. George Mukhari Academic Hospital (DGMAH) will henceforth be referred to as a teaching hospital. A teaching hospital is a hospital that is affiliated with a medical school, where health care professionals receive practical training.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Globally, antimicrobial resistance (AMR) is an increasingly serious threat to public health that requires action across all government sectors and society (O’Neill, 2016). Importantly, factors contributing to the growing resistance includes: the incorrect selection, incorrect timing of administration and incorrect duration of use of antimicrobials (Mohamoud & Akilu, 2016).

Antimicrobials are the most commonly prescribed medicine in both the community and hospital health care setting, alarmingly, especially among paediatric patients (De Luca, Donà, Montagnani, Lo Vecchio, Romanengo, Tagliabue, Centenary et al, 2016). Surgical antimicrobial prophylaxis (SAP), also referred to as primary peri-operative prophylaxis, is defined as the pre-operative administration of SAP, and accounts for 30-50% of all antimicrobial use (Chandrasekaran, Saeed, Gandhiraj, Prasad Mohanta & Rajasekaran, 2016). The overall goal for SAP is to prevent surgical site infections (SSIs) by using an antimicrobial that is safe and cost-effective, with a spectrum of activity that covers the most common pathogens for the specific surgical procedures (Anderson & Sexton, 2016).

In order to define the use of SAP as appropriate the following five criteria has to be met: an appropriate SAP selection for the surgical procedure performed, used in an appropriate dose based on participant’s body weight (in kg). It should be administered within 60 minutes prior to incision (except during the use of fluoroquinolones and vancomycin, where administration over one to two hours was recommended), if redosing is required it should be done at one to two times the half-life of the drug and lastly the SAP use should be discontinued.
within 24 hours post-surgery. If, however the SAP use does not comply to all five of the criteria, it is deemed as inappropriate. Hence, this same five criteria is used to determine compliance to the latest evidence based guidelines (National Department of Health, 2015; Choc Children’s, 2010; American Society of Health-system Pharmacists, 2013; Reproductive Health Supply Coalition, 2016; Scottish Intercollegiate Guidelines Network, 2014).

A recent study found substantial variability in the overall and appropriate use of SAP in paediatrics at hospital level compared to the the used SAP guidelines. They concluded that a large percentage of SAP use does not comply to guidelines, as the use in paediatrics is inappropriate, potentially exposing them to avoidable adverse events (Sandora, Fung, Melvin, Graham & Rangel, 2016).

In the face of a post-antibiotic era, with declining efficacy in SAP and increased multi-drug resistance organisms, an urgent need for the implementation of antimicrobial stewardship (AMS) has been identified. AMS is shortly defined as specific interventions and measures to encourage optimal selection and use of antimicrobials (Barlam, Cosgrove, Abbo, MacDougall, Schuetz, Septimus, Srinivasan et al, 2016).

The inappropriate use and misuse of antimicrobials by medical practitioners is not only a global concern but a significant contributor to AMR (Bai, Wang, Yin, Bai, Gong & Lu, 2016). A contributor to this inappropriate use by medical practitioners is their antimicrobial prescribing behaviour (Quet, Vlieghe, Leyer, Buisson, Newton, Naphayvong, Keoluangkhot et al, 2015). A key factors that affects individual prescribing behaviour and provides a reason for the inappropriate use of antimicrobials is the medical practitioner’s knowledge, perception and experience of antimicrobials and AMR (Bai et al, 2016; Awad & Aboud, 2015). Seeing as this individual behaviour poses a particular challenge in reducing antimicrobial use, which could possibly cause a disconnection between individual behaviour and population level AMR, an integration of behavioural modification into AMS would provide a powerful weapon (Gould & Lawes, 2016). Although studies have been performed on the medical practitioner’s knowledge and belief of antimicrobial use and AMR in higher income countries, the results are not necessarily applicable to the lower-income countries. Additionally, limited data involving this topic targeted towards paediatrics exist (Abera, Kibret & Mulu, 2014).

Additionally, the majority of literature and recommendations on SAP are for adult patients (Galinkin, 2015). As it is often seen, because of the inherent challenges in paediatric re-
search, the paediatric population tends to follow the adult population (Romano, 2016). Unfortunately however, little is known about the subspecialties and indications for the use of SAP in the paediatric population (Lewis, 2016). Although paediatrics are commonly prescribed antimicrobials, little is known about the extent of their use and whether trends are in line with the current recommended guidelines, as very few clinical experiences with SAP have been published involving paediatrics (Gadzhanova, Roughead & Pont, 2015; Rangel, Fung, Graham, Ma, Nelson & Sandora, 2010; Groselj, Grenc, Derganc, Trsinar & Cizman, 2006).

In paediatrics undergoing surgery at a teaching and a private hospital, SAP used was not being monitored nor recorded as part of a formal process. Urgent attention should thus be directed to the use of SAP in paediatrics. Additionally, the need to fully understand the medical practitioners’ knowledge and perception on antimicrobials and what factors influence their prescribing patterns, was identified. Therefore a study was initiated to investigate both the prescribing practices of SAP as well as the knowledge and perception of medical practitioners thereof.

1.3 RESEARCH QUESTION

The study posed two questions:

The primary research question was whether or not medical practitioners from both a teaching and a private hospital, whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ear, nose and throat (ENT), general surgery and maxillofacial, in the paediatric surgical wards complied to the following parameters during the administration of SAP: the correct indication, correct choice of antimicrobial/s, correct timing of administration, correct dose, correct duration of use and dosing interval.

Secondly, what knowledge and perception of the use of SAP did the medical practitioners from the same teaching and a private hospital used, whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial, in the paediatric surgical wards have?

1.4 AIM OF THE STUDY

The study posed two aims:
Chapter 1: Introduction

The primary aim of the study was to evaluate compliance to SAP guidelines by medical practitioners treating paediatrics in a paediatric surgical ward, requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial in the paediatric surgical ward at a teaching and a private hospital.

Additionally, the knowledge and perception, regarding SAP used in paediatrics, of the medical practitioners whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial, in the paediatric surgical wards at the same teaching and private hospital, were assessed.

1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To describe the practice of SAP used in paediatrics at a teaching and a private hospital by medical practitioners whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial, in the paediatric surgical wards.

- To determine if the SAP prescribed in paediatric surgery at the same teaching and a private hospital used by medical practitioners whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial, in the paediatric surgical wards was appropriate compared to the latest literature.

- To perform a knowledge and perception survey of the use of SAP amongst medical practitioners whom treated paediatrics requiring surgical procedures in four different specialised areas, including; urology; ENT, general surgery and maxillofacial, in the paediatric surgical wards at the same teaching and a private hospital used.

1.6. SIGNIFICANCE OF THE STUDY

AMR threatens not only the fundamentals of modern medicine, but also the sustainability of an effective global health response to infectious disease threats (O’Neill, 2016).

An international global action plan, which reflected the global consensus that AMR poses a significant challenge to public health, was therefore initiated by the World Health Organization (WHO) to curb the increasingly serious threat towards a post-antimicrobial era and to
ensure a sustainable investment in defying AMR. This study, though retrospectively, supported the objective to limit AMR by monitoring the use of SAP (WHO, 2015).

In line with the global action plan’s aim to conserve effective antimicrobials through stewardship, this study set out the objectives outlined, specifically by improving awareness and understanding of AMR, via the monitoring of SAP prescribing practices in paediatrics. The importance and understanding of AMR was further enhanced by effectively presenting and communicating the topic to all medical practitioners taking part in the survey, and stressing the importance of staying up-to-date with the latest guidelines. Secondly, this study in itself strengthened knowledge by researching and surveying SAP use and the appropriateness thereof grounded on evidence-based guidelines. By performing this study in a teaching hospital, where surveillance and reporting of SAP use is limited, it contributed to the collection and analysis of data. It further highlighted the importance of optimal use of SAP along with the importance of evidence-based prescribing and dispensing. Lastly, the global action plan highlights the imperative role that health care practitioners (HCPs) have in the protection of antimicrobials.

Recently, a high-level meeting on AMR was held by the United Nations’ General Assembly (UNGA). The primary objective of this meeting was to summon and maintain strong national, regional and international political commitment in addressing AMR both comprehensively and multi-sectorally, and additionally to increase and improve awareness of AMR. This meeting emphasised the vital role and the responsibilities of governments and intergovernmental organisations (e.g. the WHO) to respond to the challenges facing AMR. This meeting also recalled the “Global Action Plan on AMR” and emphasised the paramount significance of achieving the five strategic objectives outlined (UNGA, 2016).

In order to compliment the international response to AMR, a national response to AMR was required. The National Department of Health (NDoH) therefore constructed an AMR National Strategy Framework for 2014-2024 (NDoH, 2014). Although the AMR strategy’s framework is focused on a national level, this study nonetheless obliged to some of the strategic objectives; namely surveillance of SAP use, prescribing and administering errors as well as SAP quality. The research study utilised both a retrospective- and a prospective approach. SAP stewardship was retrospectively performed by assessing the appropriateness of the SAP choice, dose, timing and duration. A survey was used as part of the prospective approach for a targeted campaign towards medical practitioners to not only scrutinise their practices, but to also increase awareness of SAP recommendations and the risks of AMR linked to inappropriate use (NDoH, 2014).
Prior to the AMR Strategy Framework, a domain of patient safety, clinical governance and clinical care was established in 2011 by the NDoH known as the National Core Standards (NCS) for Health Establishments. This domain provided guidelines on how to ensure quality nursing, clinical care and ethical practice. As SSIs are a major cause of post-operative morbidity and mortality, patient safety, one of the cross-cutting domains addressed by the standards, is at possible risk. Patient safety was a major concern of this study. This concern was addressed by retrospectively assessing, and thereby in future, contributing to quality clinical care and ethical practice to reduce unintended harm. Another domain addressed was public health. Collateral damage was restricted highlighting the importance of appropriate use of SAP according to the latest literature (NDoH, 2011).

The significance of this study therefore lay in addressing specific needs highlighted both internationally and nationally, using a multi-centre approach. This approach ensured an increased study population, exposure to different geographic locations, demographic information and the possibility of a wider range of population groups.

Finally, to the researcher’s knowledge, this study was the first to, not only specifically focus on the appropriateness of SAP used in paediatric surgery, but additionally to assess medical practitioners’ knowledge and perception of SAP via a multi-centre approach. This study consequently opened the opportunity to establish whether equitable and evidence-based care was provided as it should be in both teaching and private hospitals. Thus, the importance of optimised use of SAP to limit antimicrobial resistance was highlighted.

1.6 OUTLINE OF THE DISSERTATION

Chapter 1 introduces the reader to the study and highlights the rationale therefore. The research questions with subsequent aim and objectives are provided. Chapter 2 describes the literature review on the study topic and outlines previous research conducted in this particular field of practice. Chapter 3 provides a detailed description of the methodology of the study. Chapter 4 presents the results of the study with a relevant discussion of the findings. Chapter 5 provides a summary of the results, overall conclusions, and recommendations made, based on the results of the study and the limitations of the study. Figure 1.1 provides a short illustration of the outline of this dissertation.
SAP accounts for one of the most common reasons for prescribing antimicrobials, primarily to prevent hospital acquired SSIs. However, data on SAP used in the current paediatric population is limited, as the majority of literature is based on adults. At the teaching and a private hospital, SAP used in paediatrics is not being monitored.

In line with the global threat towards public health as a result of AMR, this study aimed to assess not only whether paediatric medical practitioners were adhering to the latest guidelines’ recommendations on SAP use, but also to assess their knowledge and perception of SAP.

The significance of this study lay in addressing both international and national aims in the fight against AMR. This first study of its kind, incorporated the Global Action Plan on AMR, and three South African NDoH documents via a multi-centre approach. This study not only provided the opportunity to monitor SAP use, but also strengthened the knowledge on SAP, improved awareness and understanding of AMR and highlighted the importance of evidence-based SAP prescribing. In conclusion this study prioritised patient safety and contributed to quality clinical care and ethical practice.

1.7 SUMMARY

Chapter 1 discussed the background and rationale for this study, which allowed for the identification of the two separate research questions. The aim and objectives followed which
led to the discussion of the significance and a brief outline of this study. Finally an all-encompassing conclusion was provided. In the next chapter, the emphasis will be on a literature review pertaining to the study.
CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter an overview of published literature on the study topic and previous research done in this particular field is provided. The chapter begins with defining SSIs, followed by SAP use in paediatrics, its goals, indications and overall approach. Thereafter, a definition and classification of paediatrics is provided, followed by a discussion on SSIs, SSIs in paediatrics and the classification of surgical wounds. A comprehensive discussion on SAP administration, including the choice, recommendations, dosages, timing and inappropriate use thereof is provided. Defining types of surgeries follows, along with the international list of cause of death (ICD) codes, challenges in SAP use, behavioural changes and knowledge and perception of medical practitioners. Furthermore, health care in South Africa is explored as well as AMS. Finally, the conclusion and a summary are provided.

2.2 DEFINING SURGICAL ANTIMICROBIAL PROPHYLAXIS

In the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, the American Society of Health-System Pharmacists (ASHP) defines prophylaxis as a method of preventing an infection (ASHP, 2013). Prophylaxis is further classified as primary, secondary prophylaxis or eradication. The term ‘primary prophylaxis’ refers to the prevention of an initial infection, ‘secondary prophylaxis’ refers to the prevention of a recurrent infection or the reactivation of a pre-existing infection, while ‘eradication’ refers to the elimination of a colonised organism to prevent the development of an infection. With reference to the aforementioned definition, primary peri-operative prophylaxis, referred to as surgical antimicrobial prophylaxis in this study, can be defined as the pre-operative administration of antimicrobials to patients to reduce the risk of post-operative wound infection (NDoH, 2013).

2.2.1 Surgical antimicrobial prophylaxis in paediatrics

The ASHP’s therapeutic guidelines refer to paediatric patients as a special patient population. As is often seen, due to the inherent challenges in paediatric research, the paediatric population tends to follow the adult population (Romano, 2016). Unfortunately, however, little is known about the sub-specialties and indications for the use of SAP in the paediatric population (Lewis, 2016). Although paediatrics are commonly prescribed antimicrobials, little is known about the extent of their use (Gadzhanova et al, 2015). Fortunately, although
specific paediatric SAP data are scarce, paediatric patients do undergo numerous procedures similar to adults. Thus the selection of SAP agents have been extrapolated from adult data and is based on expert opinion. Mirroring adult guidelines, first- and second-generation cephalosporins are the agents of choice, as well as reserving the use of vancomycin for β-lactam allergic patients. In paediatric patients the use of a penicillin with a β-lactamase inhibitor in combination with cefazolin or vancomycin and gentamicin has been studied. However the study populations remain limited. Generally all recommendations, unless otherwise explicitly specified for adults, are the same for paediatrics, except the dosage. An important exception is the routine use of fluoroquinolones as SAP in paediatrics, due to the possibility of toxicity (ASHP, 2013).

Khoshbin & colleagues (2015) agree that although there is abundant studies in adults, the benefit of SAP in the prevention of SSIs in paediatrics is uncertain (Khoshbin, So, Aleem, Stephens, Matlow & Wright, 2015). They therefore performed a prospective cohort study on 5309 patients aged 0 to 21 years, who underwent surgical procedures. SAP indication and administration were recorded. Of the 5309 patients, 73.5% of patients received SAP when indicated, within 60 minutes before incision and had an infection rate of 3.0%, while 26.5% of patients did not receive SAP when indicated and had an infection rate of 4.3%. Of 4156 patients, for whom antimicrobials were not indicated, 21.5% of the patients who received SAP had an infection rate of 1.7% compared to 0.7% of the 78.5% of patients who did not receive antimicrobials. It was concluded that in paediatric surgery, complete compliance with evidence-based SAP use was associated with a decreased risk for SSIs of 30% (Khoshbin et al., 2015).

### 2.2.2 Surgical antimicrobial prophylaxis goals and indications

Anderson et al (2016) stated that the aim of SAP is to prevent a SSI during an operative procedure by decreasing the load of organisms at the surgical site and to decrease the associated morbidity and mortality, hospital length of stay and the accompanied cost.

In order to accomplish these goals SAP should cover the most common pathogens associated with the type of surgery, be administered in an appropriate dose, at an appropriate time, to ensure sufficient serum and tissue concentrations throughout the period of potential infection risk and lastly, be administered for the shortest effective period of time to minimise adverse effects, emergence of resistance and cost (Anderson et al., 2016).

SAP efficacy in reducing SSIs has been recognised and is necessary in surgeries with a high infectious risk or harmful outcomes should an infection develop (Anderson et al., 2016).
Additionally, appropriate use of SAP enables the reduction in incidence of a significant and preventable source of morbidity and mortality in hospitalised patients (Chandrasekaran et al, 2016).

2.2.3 Surgical antimicrobial prophylaxis overall approach

General factors to consider for SAP selection in the prevention of SSIs include cost, safety, pharmacokinetic profile and bactericidal activity. Furthermore, the need for SAP should be based on the risk of wound contamination. The medication chosen should be active against the pathogens most likely to be associated with the type of surgical procedure. Finally, prophylaxis must be given within 60 minutes after the first incision, normally at the indication of anaesthesia. However, studies have shown that, should the 60-minute window elapse, efficacy seemed better with administration within 30-60 minutes prior to incision compared to immediately before the surgical incision (Anderson et al, 2016). Evidence on key recommendations for SAP practices are highlighted in Table 2.1.

Table 2.1: Key recommendations for practice

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Evidence rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP should be infused within one hour prior to incision to prevent SSI</td>
<td>A</td>
</tr>
<tr>
<td>SAP use should be consistent with published guidelines</td>
<td>C</td>
</tr>
<tr>
<td>Discontinuation of SAP should generally be within 24 hour after surgery</td>
<td>C</td>
</tr>
</tbody>
</table>

A = Consistent, good-quality patient-oriented evidence; C = Consensus, disease-oriented evidence, usual practice, expert opinion or case series. As adapted (Salkind and Kavitha, 2011).

In support of the above-mentioned principles, the Surgical Care Improvement Project’s (SCIP) performance measures, further discuss three core infection prevention measures, namely, the importance of administering an antimicrobial, appropriate for the specific surgical procedure, within one hour prior to surgical incision and two hours in the case of vancomycin or fluoroquinolones use, along with the discontinuation within 24 hours of surgery completion (48 hours in cardio-thoracic surgery). Other measures include controlled postoperative 6 a.m. blood glucose levels in cardiac surgery (11.10 mmol per L or less) and the removal of hair at the site of incision. In contradiction, the guidelines of the National Institute for Health and Care Excellence (NICE) (2008) states that hair removal should not be done routinely to reduce the risk of a SSI. If it is however required, the use of a single-head electric clipper is recommended on the day of surgery. Razors are contraindicated and may
increase the risk of a SSI. Lastly, colorectal surgical patients should be normothermic (36°C or greater) within the first 15 minutes after discharge from theatre. Ideally, SAP should not cause adverse drug effects to the patient, the patient’s microbial flora or the hospital (Anderson et al, 2016).

Lastly, recommendations for SAP are limited to class II, which entails clean procedures with limited contamination and exposure to microorganisms colonising the epithelial surfaces and/or lumen of the respiratory, gastrointestinal and urinary or genital tract, with no evidence of infection (NDoH, 2013).

2.2.4 Surgical antimicrobial prophylaxis overall approach in paediatrics

The same main principles of SAP apply in paediatrics: a single dose of SAP is sufficient, pre-operative dosing should be within 60 minutes prior to incision and intra-operative dosing is required if the surgical procedure exceeds two half-lives of the SAP or if there is extreme blood loss. Discontinuation of SAP should be within 24 hours of the procedure, regardless of the presence of intravascular catheters or indwelling drains (Makino & Oropello, 2016; ASHP, 2013).

The recommendations of the Reproductive Health Supplies Coalition (RHSC) (RHSC, 2016) for SAP in paediatric surgery state that four-hourly repeat dosing is required for cefuroxime, ceftazidime, clindamycin, amoxicillin-clavulanic acid and flucloxacillin. Eight-hourly redosing is necessary for clarithromycin and metronidazole. Teicoplanin should not be redosed. In the case of severe blood loss redosing must be done with a full prophylactic dose for cefuroxime, flucloxacillin, clarithromycin, amoxicillin-clavulanic acid, metronidazole and a half prophylaxis dose for gentamicin.

The paediatric dose is a single dose equal to the standard therapeutic dose and a second dose is only given if surgery is prolonged, i.e. > four hours for cefazolin or eight hours for metronidazole (NDoH, 2013).

A former study evaluated compliance to current paediatric SAP guidelines in different surgical procedures, which included 150 paediatric surgical procedures. In this study 97.3% of patient cases reflected compliance to the local guidelines, with 83.8% compliant on the choice of antimicrobial, 66% compliant regarding timing, 92% compliant with the dose, 40.7% compliant with duration, and finally 94.1% compliant to the dosing interval. However, compliance to all of the parameters was achieved in only 25.3% of cases (Groselj et al, 2006).
1.3. THE DEFINITION AND CLASSIFICATION OF PAEDIATRICS

According to the WHO, paediatric patients are defined as those younger than 18 years of age (WHO, 2014). The Health and Human Services Guidelines of the Emergency Medical Services Authority (EMSA) in California state that paediatric patients can be classified into different categories based on their age. This paediatric classification is done according to the National Institute of Child Health and Human Development (NICHD) (NICHD, 2015). The paediatric terminology was developed by Eunice Kennedy Shriver in the United States of America (USA) (see Figure 2.1).

<table>
<thead>
<tr>
<th>Classification</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>0-27 days</td>
</tr>
<tr>
<td>Infant</td>
<td>birth to 12 months</td>
</tr>
<tr>
<td>Toddler</td>
<td>13 months to 2 years</td>
</tr>
<tr>
<td>Early childhood</td>
<td>2-5 years</td>
</tr>
<tr>
<td>Middle childhood</td>
<td>6-11 years</td>
</tr>
<tr>
<td>Early adolescent</td>
<td>12-18 years</td>
</tr>
<tr>
<td>Late adolescent</td>
<td>19-21 years</td>
</tr>
</tbody>
</table>

Adapted from the NICHD (2015)

**Figure 2.1:** Paediatric life stage classification

1.4. SURGICAL SITE INFECTION

A SSI is classified as a hospital-acquired infection (HAI), when a wound infection occurs after an invasive surgical procedure. SSIs are rated as not only the most common complication of surgery, but also as the third most common cause of HAI (15%) (Chandrasekaran et al, 2016). The Centre for Disease Control (CDC) and the National Healthcare Safety
Network (NHSN) further define a SSI as a superficial, deep, or organ space infection occurring within 30 days of a surgical procedure. However, in the case of patients with surgical implants, a time period of one year is used (Khoshbin et al, 2015).

Additionally, one or more of the following clinical criteria is required to define a SSI (CDC, 2016):

- A purulent exudate draining from the surgical site;
- A positive fluid culture obtained from the surgical site that was closed primarily;
- A surgical site that is reopened in the setting of at least one clinical sign of infection (pain, swelling, erythema or warmth) and is culture-positive or not cultured;
- Diagnosis of infection by the surgeon.

SSIs are classified as either incisional or organ/space, as explained in Figure 2.1. Incisional SSIs are divided into either a superficial or deep incision. An organ/space SSI involves any part of the anatomy (other than the incision) that was opened or manipulated throughout the operative procedure. One-third of all SSIs are attributed to organ/space SSIs, but account for more than 90% of SSI-related deaths (Anderson et al, 2016).

Additionally, compared to surgical patients without an SSI occurring during the first eight weeks after hospitalisation, a SSI results in an estimated three-fold higher cost of care, decreased quality of life and increased hospital length of stay. Furthermore, these patients have a five-fold increase for readmission, are 60% more likely to spend time in the intensive care unit (ICU), and twice as likely to die (Anderson et al, 2016).

Table 2.2: Classification of SSIs

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incisional</td>
<td>Only involving the skin or subcutaneous tissue</td>
</tr>
<tr>
<td></td>
<td>Involving deep soft tissues</td>
</tr>
<tr>
<td>Organ/space</td>
<td>Any part of the anatomy (other than the incision) opened or manipulated during surgery</td>
</tr>
<tr>
<td></td>
<td>E.g. meningitis following an elective neurologic procedure or mediastinitis following coronary artery bypass surgery</td>
</tr>
</tbody>
</table>
2.2.5 Paediatric mortality rate

Paediatric mortality is largely recognised as a surrogate marker for the quality of care within health services and a crude reflection of the true health status of a society. Not only does the paediatric mortality rate serve as an indicator for monitoring trends of paediatric survival, but also as an indicator of the quality of health care delivered at different stages in a paediatric patient’s life (McKerrow & Mulaudzi, 2010).

Globally, 5.9 million paediatrics below the age of five demised in 2015, resulting in a total of 16,000 paediatric deaths per day. Africa still has the highest mortality rate, at 81 paediatric deaths per 1,000 live births under the age of five, estimated to be more than seven-fold that of WHO European Region (11 per 1,000 live births). Not only is Africa home to six of the seven countries with an under-five mortality rate above 100 deaths per 1000 live births, but also to large inequities in paediatric mortalities compared to high-income countries. The 2015 results motivate this statement, stating that lower-income countries when compared to higher-income countries, had an estimated 11-fold higher under-five mortality rate at 76 deaths per 1,000 live births. It is thus of utmost importance to save paediatric lives by reducing the disproportions and terminating preventable paediatric deaths (WHO, 2015).

A substantial proportion of the South African population consists of paediatric patients, 30% of the population being below the age of 15 years (Torborg & Coté, 2015). This is a noteworthy point, as the burden of surgical diseases in the paediatric population is a vital concern in developing countries. Although epidemiological data is limited, the pattern of paediatric surgical diseases in Sub-Saharan Africa provides an insight into this, as it embodies numerous challenges inherent in attempting to provide surgical care. Data show that 6-12% of all paediatric admissions are for surgery, while the proportion may be higher in urban areas (Jarnheimer, Kantor, Bickler, Farmer & Hagander, 2015).

2.2.6 Surgical site infections in paediatrics

SSIs are essentially preventable HAI. However, along with the shortage of published experience-defining risk factors and preventative strategies in paediatric SSIs, few quality improvement programmes have been initiated to reduce SSIs in this population (Toltzis, O’Riordan, Cunningham, Ryckman, Bracke, Olivea & Lyren, 2014).
1.5. SURGICAL WOUND CLASSIFICATION

Wounds are classified as clean, clean-contaminated, contaminated or dirty. Closed uninfected wounds, without entering the viscera or the presence of pus, are termed clean wounds. In clean-contaminated wounds, the viscus is entered under controlled conditions, without unusual contamination during the operation. A contaminated wound may be an open accidental wound, with pus present during the surgical procedure, a wound resulting from a major break in sterile technique, or from an operation with gross viscous spillage (ASHP, 2013).

Dirty wounds entail prior traumatic wounds with retained devitalised tissue, foreign bodies, faecal contamination or wounds that involve existing clinical infection or a perforated viscus (ASHP, 2013).

SSIs resulting from clean procedures are normally due to skin flora organism; streptococcal species, Staphylococcus aureus and coagulase-negative staphylococci (CONS). Gram-negative bacilli and enterococci, in addition to skin flora, are the most predominant organism identified in clean-contaminated procedures. During surgical procedures, in which the viscus is involved, the organisms identified normally represent the endogenous flora of the viscus or neighbouring mucosal surface (Anderson et al., 2016).

The aim of SAP is thus to prevent a SSI during an operative procedure, by decreasing the load of organisms at the surgical site (Anderson et al., 2016).

2.3 SURGICAL ANTIMICROBIAL PROPHYLAXIS ADMINISTRATION

2.3.1 Choice of surgical antimicrobial prophylaxis

The SCIP Guidelines state that SAP should be appropriate for the specific surgical procedure, and provide adequate coverage against the most common organisms associated with the procedure, without eliminating every possible pathogen. It is recommended that the choice of SAP is based on the local antibiogram. Furthermore, SAP is recommended for all clean-contaminated procedures or in cases in which a SSI may have devastating consequences for the patient. Generally, SAP is not recommended for dirty or contaminated procedures, as the patient is possibly already on antimicrobial for the established infection (Anderson et al., 2016). There is limited comparative studies on SAP, however, compared to narrower spectrum antimicrobials, there is little evidence to suggest that broad-spectrum
antimicrobials result in lower rates of postoperative SSIs (Anderson et al, 2016). It is, however, clear that cephalosporins are recommended for most surgical procedures due to their activity against the most common skin pathogens, Staphylococcus aureus and Streptococcal species (Anderson et al, 2016). Besides being the drug of choice for numerous surgical procedures, cefazolin is also the most extensively studied SAP with proven efficacy. This is a cost-effective agent that has the required duration of action, a spectrum of activity against organisms frequently encountered during surgery, including streptococci, methicillin-susceptible staphylococci (MSSA), some gram-negative organisms and sensible safety (Anderson et al, 2016). In gynaecological or gastrointestinal surgical procedures combination SAP is often recommended (Anderson et al, 2016).

### 2.3.2 Recommended paediatric surgical antimicrobial prophylaxis

The ASHP therapeutic guidelines provide paediatric dosages, which are largely extrapolated from adult pharmacokinetic data. Since limited clinical trials have been conducted in the paediatric surgical population, strength of evidence criteria have not been applied to those recommendations. The ASHP therapeutic guidelines are recommendations for paediatrics aged 1-18 years. These guidelines do not specifically address new-borns, premature/full-term neonates or infants (ASHP, 2013).

In order to define in which surgical procedures SAP is indicated, a comprehensive literature search was conducted, using the following search engines; Scopus®, Science Direct®, Ebsco Host®, PubMed®, Medline® and Google Scholar®.

The SAP Guidelines, used for the purposes of this study, were defined from prior evidence-based guidelines. A comprehensive literature search was conducted by studying SAP recommendations of several guidelines. The principal guidelines included:

- The Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, which were developed jointly by the ASHP, the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS), and the Society for Healthcare Epidemiology of America (SHEA) (ASHP, 2013);
- RHSC recommendations (2014).

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• Standard Treatment Guidelines and Essential Medicines List (STGs/EML) for South Africa, Hospital level, Paediatrics (NDoH, 2013).

The following articles were used to provide more information on surgical antimicrobial use in tympanostomy, hernia repair, circumcision and dental extractions, as the recommendations regarding these surgical procedures were not addressed by any of the five guidelines: Clinical Practice Guidelines: Tonsillectomy in children (Baugh, Archer, Mitchell, Rosenfeld, Amin, Burns, Darrow et al., 2011); Current evidence regarding prophylactic antimicrobials in head, neck and maxillofacial surgery (Kreutzer, Storck & Weitz, 2014); and the Cochrane collaboration review of antimicrobial prophylaxis for hernia repair (Sanchez-Manuel, Lozano-García & Seco-Gil, 2012). Kreutzer & colleagues (2014) stated that, although studies showed beneficial use of SAP in tooth extractions, recommendations for tooth extractions cannot be made because of the adverse effects and the fact that no differences in the rate of SSIs were seen, whether antimicrobials were administered pre-, peri- or post-operatively. However, SAP use in tympanovstomy has shown beneficial results. Lastly, Sanchez-Manuel et al (2012) concluded that the universal use of SAP for elective inguinal hernia repair cannot be recommended.

It is important to note that recommendations from the ASHP therapeutic guidelines and Choc Children’s guidelines received priority. The ASHP therapeutic guidelines received priority because they were developed by members from the ASHP, IDSA, SIS and SHEA, who served on an expert panel using primary literature from the previous ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery, together with literature published between 1999 and 2010. All of the recommendations listed are graded based on the strength of evidence available. Randomised, controlled, double-blind studies received the highest credence.

Furthermore, the following published guidelines were also used to compile the ASHP therapeutic guidelines:

• American College of Obstetricians and Gynecologists (ACOG);
• Centers for Disease Control and Prevention (CDC);
• Scottish Intercollegiate Guidelines Network (SIGN);
• Medical Letter;
• Surgical Infection Society (SIS);
The Society for Healthcare Epidemiology of America/Infectious Disease Society of America (SHEA/IDSA).

The Choc Children’s guidelines also received priority as evidence-based care guidelines, based on the best available evidence and expert opinion and were developed to help paediatricians provide the best possible care to patients. These guidelines were overseen by the multidisciplinary evidence-based medicine committee. Table 2.3 summarises a clinical approach to SAP in the four areas of surgery specified in this study.
### Table 2.3: SAP recommendations

<table>
<thead>
<tr>
<th>TYPE OF SURGERY</th>
<th>ASHP</th>
<th>CC</th>
<th>SIGN</th>
<th>STG</th>
<th>RHSC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EAR, NOSE AND THROAT (ENT) SURGERY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tympanostomy (Grommets)</td>
<td>-</td>
<td>-</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
</tr>
<tr>
<td>Adenoidectomy</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
</tr>
<tr>
<td><strong>GENERAL SURGERY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Colorectal surgery</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Hernia-repair groin (inguinal/femoral with or without mesh)</td>
<td>-</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hernia-repair groin (laparoscopic with or without mesh)</td>
<td>-</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hernia repair (incisional with or without mesh)</td>
<td>-</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Obstructed hernia repair (hernioplasty and herniorrhaphy)</td>
<td>✔️</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>UROLOGY SURGERY</strong></td>
<td></td>
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<tr>
<td>Circumcision</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>MAXILLOFACIAL</strong></td>
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<td></td>
</tr>
<tr>
<td>Extractions</td>
<td>✗</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

- Not addressed in the guideline. ✔️ Recommended, ✗ - Not recommended, ASHP = ASHP Therapeutic Guidelines, CC = Choc Children’s, SIGN = SIGN document, STGs/EML = Standard Treatment Guidelines and Essential Medicines List for South Africa, Hospital Level, Paediatrics, RHSC = RHSC recommendations.
Table 2.4 describes the SAP agents recommended for specific surgical procedures, based on the results from Table 2.3.

**Table 2.4: Recommended SAP agents for specific procedures**

<table>
<thead>
<tr>
<th>ASHP</th>
<th>CC</th>
<th>SIGN</th>
<th>STG</th>
<th>RHSC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EAR, NOSE AND THROAT (ENT) SURGERY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tympanostomy (Grommets)</td>
<td>-</td>
<td>-</td>
<td>Single dose of topical antimicrobial</td>
<td>-</td>
</tr>
<tr>
<td><strong>GENERAL SURGERY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>Cefazolin + metronidazole</td>
<td>Cefoxitin/ Amoxicillin/sulbactam/ Cefazolin + Metronidazole</td>
<td>Cefazolin + metronidazole</td>
<td>-</td>
</tr>
<tr>
<td>Colorectal surgery</td>
<td>Cefazolin + metronidazole</td>
<td>Cefoxitin/ Amoxicillin/sulbactam/ Cefazolin + Metronidazole</td>
<td>Cefazolin + metronidazole</td>
<td>-</td>
</tr>
<tr>
<td>Hernia-repair groin (Inguinal/femoral with or without mesh)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Obstructed hernia repair (hernioplasty and herniorrhaphy)</td>
<td>Cefazolin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 2.5 shows the SAP and doses recommended if indicated for dental procedures.

**Table 2.5: Regimens for dental procedures according to the American Heart Association recommendations**

<table>
<thead>
<tr>
<th>FOR PATIENTS WHO CAN TAKE ORAL MEDICATION</th>
<th>For Not allergic to penicillin</th>
<th>For Allergic to penicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>50mg/kg</td>
<td>Cephalexin* 50 mg/kg</td>
</tr>
<tr>
<td>Or clindamycin</td>
<td></td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>Or azithromycin or clarithromycin</td>
<td></td>
<td>15 mg/kg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FOR PATIENTS WHO CANNOT TAKE ORAL MEDICATION</th>
<th>For Not allergic to penicillin</th>
<th>For Allergic to penicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin OR</td>
<td>50 mg/kg IM/IV</td>
<td>Cefazolin or ceftriaxone** 50 mg/kg IM/IV</td>
</tr>
<tr>
<td>Cefazolin or ceftriaxone</td>
<td>50 mg/kg IM/IV</td>
<td>Or clindamycin 20 mg/kg IM/IV</td>
</tr>
</tbody>
</table>

As adapted from the American Academy of Paediatric Dentistry (AAPD) (2014) and Huang (2014). Single dose 30-60 min prior to procedures, *or other first- or second-generation oral cephalosporin in equivalent paediatric dosage, **Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema or urticarial with penicillin’s or ampicillin.

According to Kreutzer & colleagues (2014) the timing of SAP administration, whether pre-, peri- or post-operative, had no influence on the rate of SSIs during tooth extractions and osteotomies.

Table 2.6 provides an overview on the specific SAP dosing used in paediatrics based on several guidelines.
Table 2.6: Paediatric SAP guidelines

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>CCs</th>
<th>ASHP</th>
<th>RHSC</th>
<th>STG/EML 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IV dose (mg/kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>-</td>
<td>-</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>Ampicillin/sulbactam</td>
<td>50</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>-</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>-</td>
<td>30</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>25</td>
<td>30</td>
<td>-</td>
<td>25</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>-</td>
<td>50</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>-</td>
<td>50</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>40</td>
<td>40</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>-</td>
<td>40</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>-</td>
<td>-</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>-</td>
<td>50-75</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefepime</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ciproflaxacin</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>10</td>
<td>10</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>-</td>
<td>15</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>2.5</td>
<td>2.5</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>10</td>
<td>15 ; Neonates weighing &lt;1200 g = 7.5</td>
<td>7.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>Adult Dose</td>
<td>Children 2–9 mo</td>
<td>Children &gt;9 mo and ≤ 40 kg</td>
<td>-</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------</td>
<td>-----------------</td>
<td>---------------------------</td>
<td>---</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>-</td>
<td>80 mg/kg of the piperacillin component</td>
<td>100 mg/kg of the piperacillin component</td>
<td>-</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>-</td>
</tr>
</tbody>
</table>

Adapted from Choc Children’s (2015) and the ASHP’s Therapeutic Guidelines.

- = Not addressed in the guideline, a= for normal renal function. b= Begin within that amount of minutes prior to incision. c= based on typical case length; *The SIGN document (2014) does not provide any dosages. **for unusually long procedures, redosing may be needed.

Table 2.7 indicates the administration time, infusion time and inter-operative reducing time for specific SAP agents based on a comprehensive literature review of the previously mentioned five guidelines.
<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>CHOC CHILDREN’S</th>
<th>ASHP</th>
<th>STG/EML 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intra-operative re-dosing (hrs)</td>
<td>Timing of first dose (b)</td>
<td>Infusion time (min)</td>
</tr>
<tr>
<td>Ampicillin/ sulbactam</td>
<td>3</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>4</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ciproflaxacin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>3</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Cefepime</td>
<td>4</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>6</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>8</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Levoflaxapin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>6</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Piperacillin-tazo-bactam</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Vancomycin

12

60-120

60

N/A

- 

-  

Recommended redosing intervals marked as "not applicable" (NA) are based on typical case length; for unusually long procedures, redosing may be needed. *The RHSC recommendations and SIGN document does not provide any recommendations on specific interoperate redosing time, infusion time or timing of first dose per specific agent.

Table 2.8 indicates the recommended intravenous antimicrobials for specific surgical procedures in paediatrics.

Table 2.8:  Recommended Intravenous antimicrobials for surgical procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Common Pathogens</th>
<th>Recommended Antimicrobial Prophylaxis</th>
<th>Post-Operative Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary, including lap cholecystectomy</td>
<td>Enteric gram negative bacilli, gram positive cocci, Clostridia</td>
<td>For high risk: Cefazolin Beta-lactam allergy: Clindamycin + Gentamycin</td>
<td>Discontinue within 24 hours of surgical end time.</td>
</tr>
<tr>
<td>Colorectal, Appendectomy or ruptured viscus</td>
<td>Enteric gram negative bacilli, anaerobes, enterococci</td>
<td>Cefoxitin or ampicillin/sulbactam or Cefazolin = metronidazole. Beta-lactam allergy: Clindamycin + Gentamycin</td>
<td>Discontinue within 24 hours of surgical end time.</td>
</tr>
<tr>
<td>Genitourinary Bladder augmentation, peyloplasty</td>
<td>Enteric gram negative bacilli, anaerobes, enterococci</td>
<td>For high risk: only Cefazolin or cefoxitin or ampicillin+ metronidazole+ gentamicin Beta-lactam allergy: Clindamycin + Gentamycin</td>
<td>Discontinue within 24 hours of surgical end time.</td>
</tr>
</tbody>
</table>

Adapted from Choc Children’s Guidelines (2015).

2.3.3  Dosing of surgical antimicrobial prophylaxis

SAP should be administered in an appropriate dose to achieve adequate serum and tissue concentration for the time interval during which the surgical site is open. There is sufficient pharmacokinetic studies of most SAP agents to demonstrate that the recommendations for
paediatrics provide effective exposure and efficacy compared to that of adults (Anderson et al, 2016).

Generally, since milligram per kilogram (mg/kg) is used to calculated paediatric dosages, paediatrics weighing more than 40kg will surpass the maximum recommended dosage for adults and thus adult dosages should be used (Anderson et al, 2016).

2.3.4 Timing of surgical antimicrobial prophylaxis

SAP should be administered 60 minutes prior to surgical incision to optimise adequate drug tissue concentrations at the time of initial incision. Limited studies found a decreased infection risk with initiation of SAP administration within 30 minutes prior to surgical incision. However, data is inadequate to motivate this method as a routine practice. It is important to note that, if the 60-minute SAP window elapses, SAP administration 30-60 minutes prior to incision seems to be more effective than administration immediately prior to incision (Anderson et al, 2016).

Contrary to the above mentioned, the NICE guidelines (2008) recommend consideration of a single-dose of SAP during induction of anaesthesia, unless a tourniquet is used in which case SAP should be administered earlier.

According to Anderson et al (2016) errors in the choice of SAP or dosages are common. A study, performed in centres around the USA, evaluated 34,133 patients, who underwent surgical procedures. Results found that only 56% of patients received SAP within one hour before incision and in only 41% SAP was discontinued within 24 hours.

A prospective study, performed on 4472 patients, who underwent either cardiac surgery, a hysterectomy, hip or knee arthroplasty, evaluated the problems related to the timing, duration, and intra-operative redosing of SAP and the risk of SSIs. Patients were assigned to one of four groups for analysis. Group 1 received SAP with a short infusion time within 30 minutes prior to incision or vancomycin or a fluoroquinolone within 60 minutes prior to incision. Group 2 received SAP with a short infusion time 31-60 minutes prior to incision or vancomycin or a fluoroquinolone 61-120 prior to incision. Group 3 received SAP earlier than recommended, and Group 4 received initial SAP after incision. The risk of SSIs were 1.6, 2.4, and 5.3% respectively, with a non-statistically significant difference between Group 1 and 2.
Additionally, a study involving total hip arthroplasty reported the lowest risk of a SSI in case, where SAP was administered within one hour prior to incision. This finding was supported by a recent multi-centre study in the USA involving 29 hospitals, which also indicated a possible reduced risk of SSIs during administration within 30 minutes prior to incision. Significantly lower SSI rates with the administration of SAP just before or at the time of anaesthesia in spinal surgery patients was reported in a meta-analysis of randomised controlled trials (Salkind et al, 2011).

However, the ASHP therapeutic guidelines (2013) that were jointly developed by the ASHP, the IDSA, the SIS, and the SHEA, counter the NICE guidelines’ recommendation by confirming that the optimal time for SAP administration is within 60 minutes prior to surgical incision, stating that it is a more-specific timeframe than the previously “at induction of anaesthesia” recommendation, except for the fluoroquinolones and vancomycin, where there is consensus on the administration over one to two hours.

As seen in Table 2.9, SAP administered within zero to two hours before the initial incision has shown lower rates of SSIs compared to administration outside of this window.

<table>
<thead>
<tr>
<th>TIME OF ADMINISTRATION</th>
<th>DEFINITION</th>
<th>% WITH SSI</th>
<th>ODDS RATIO</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>2-24 hours prior to incision</td>
<td>3.8</td>
<td>4.3</td>
<td>1.8-10.4</td>
</tr>
<tr>
<td>Preoperative</td>
<td>0-2 hours prior to incision</td>
<td>0.6</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Perioperative</td>
<td>Within 3 hours after incision</td>
<td>1.4</td>
<td>2.1</td>
<td>0.6-7.4</td>
</tr>
<tr>
<td>Postoperative</td>
<td>More than 3 hours after incision</td>
<td>3.3</td>
<td>5.8</td>
<td>2.4-13.8</td>
</tr>
</tbody>
</table>

% = percentage, Adapted from (Anderson & Sexton, 2015).

### 2.3.5 Redosing of surgical antimicrobial prophylaxis

During either surgical procedures surpassing two half-lives of the drug or excessive blood loss (more than 1500ml), intra-operative redosing is necessary to ensure adequate serum and tissue concentrations. Redosing may also be necessary in patients with a shortened antimicrobial half-life, such as extensive burn patients. On the contrary, in patients with a prolonged half-life, such as renal failure patients, redosing is not required. The SAP dosing interval is measured from the time of the pre-operative dose (Anderson et al, 2016).
Most study results support a single dose of SAP within one hour prior to incision. SAP should be redosed at one to two times the half-life of the drug. A retrospective study of cardiac surgical patients, undergoing surgeries lasting more than four hours, found a decreased SSI risk from 16 to 7.7% with intra-operative cefazolin redosing. Another study found an increased risk of SSI in colorectal surgical patients with low gentamycin levels at wound closure (Salkind et al, 2011).

### 2.3.6 Duration of surgical antimicrobial prophylaxis

The results of a systematic review of randomised trials found no difference in the rate of a SSI with single-dose regimens compared to multiple-dose regimens given for less than or more than 24 hours. Generally, if SAP is necessary past the period of surgery, the duration should be less than 24 hours (Anderson et al, 2016). According to present guideline recommendations, SAP should be discontinued within 24 hours of the completion of surgery (Salkind et al, 2011). Repeat antimicrobial dosing following wound closure is generally not warranted, due to the possible increased risk for antimicrobial resistance development (Anderson et al, 2016). Furthermore, there is no supporting evidence that SAP reduces the risk of SSIs after 48 hours after completion of surgery (Salkind et al, 2011).

However, the society of thoracic surgeons recommend SAP continuation up to 48 hours after the completion of cardiothoracic surgery. This recommendation is motivated by the effects of a cardiopulmonary bypass on the immune system and antimicrobial pharmacokinetics (Salkind et al, 2011). In the case of the implantation of a pacemaker or defibrillator, the recommendation is discontinuation within 24 hours of surgery.

### 2.4 INAPPROPRIATE USE OF SURGICAL ANTIMICROBIAL PROPHYLAXIS

In 2003 the CDC, Centres for Medicare and Medicaid Services (CMS) and 10 additional national organisations developed SCIP incorporating the surgical infection prevention project measures. These measures were created to ensure evidence-based SAP selection, administration and discontinuation for patients, who underwent clean-contaminated surgeries. Decreased SSI incidences, following the execution of the SCIP measures, were reported. However, a recent survey in the USA established that the recommendations were not routinely followed. Only 55.7% of surgical patients received SAP within one hour of incision, while in only 40.7% of patients SAP was terminated within 24 hours after surgery.
Further studies have indicated that in approximately 80-90% of surgical patients, who received SAP, 25-50% received an inappropriate regimen, untimely administration of SAP, or incorrect duration thereof (Salkind et al, 2011).

Another study performed in the orthopaedic paediatric surgical population, found that in 62% of patients, antimicrobials without a documented infection were continued. A survey executed on paediatric cardiothoracic surgeons in the USA, reported that 68% of the surgeons continued SAP for longer than 48 hours, despite adult literature indicating comparable worth within 24 hours of coverage (Rangel, Graham, Nelson & Sandora, 2011).

The significance of the consequences of both overuse and underuse of SAP cannot be disregarded. Augmented incidence rates of SSIs and increased HAI-related hospital costs can be attributed to the underuse of SAP. As major infection-related complications may increase hospital length of stay by up to 20 times and hospitalisation costs by up to five times, overuse again contributes to the growing emergence of the resistant organisms, which may also increase diagnosis and treatment costs (Rangel et al, 2011).

Additionally, there is increasing evidence suggesting a potential harmful practice is the administration of unwarranted antimicrobials. This practice facilitates the emergence of resistant organisms and exposes patients to avoidable risk of side-effects and antimicrobial-associated complications, e.g. Clostridium difficile infection (Rangel et al, 2011).

South African hospitals are battling with the growing emergence of resistant organisms and are facing several challenges. Moreover, 49% of South African surgical patients receive SAP, but 19% of these patients receive an inappropriate drug (Mendelson, 2015). This highlights the importance of monitoring the consumption of antimicrobials in order to ensure appropriate use (Meyer & Sibanda, 2016).

A retrospective study, performed in 22 paediatric hospitals, which focused on procedures within the scope of paediatric general and urologic surgical practice, identified 246,316 procedures. Only 25% of the paediatric surgical population met the criteria for SAP. More than 80% received SAP when indicated and 40% received SAP in the absence of an indication. Furthermore, increased adverse events were identified in paediatrics receiving SAP compared to those who did not. This study concluded, and was in agreement with results published in former studies, that major discrepancies exist in the use of SAP in the paediatric surgical population. Profound consequences to the paediatric surgical population’s health...
in teaching hospitals is implicated, as SAP administered in the lack of an indication out-
weighs the significant extent of SAP not being given when indicated (Rangel et al, 2011).

### 2.5 AN OVERVIEW OF THE TYPES OF SURGERY REVIEWED

Table 2.10 provides a definition of each surgical procedure evaluated in this study, under its specific division. The table was compiled using the following references.

**Table 2.10: Definitions of the types of surgeries**

<table>
<thead>
<tr>
<th><strong>EAR, NOSE AND THROAT SURGERY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoidectomy</td>
</tr>
<tr>
<td>Adenotonsillectomy</td>
</tr>
<tr>
<td>Myringotomy</td>
</tr>
<tr>
<td>Nasopharyngoscopy</td>
</tr>
<tr>
<td>Tonsillectomy</td>
</tr>
<tr>
<td>Tympanostomy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>MAXILLOFACIAL SURGERY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental fillings</td>
</tr>
<tr>
<td>Extractions</td>
</tr>
<tr>
<td>Impactions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>UROLOGY SURGERY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumcision</td>
</tr>
<tr>
<td>Orchiolysis</td>
</tr>
<tr>
<td>Pixie dorsal slit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>GENERAL SURGERY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendectomy</td>
</tr>
</tbody>
</table>
2.6 INTERNATIONAL LIST OF CAUSE OF DEATH (ICD) CODES

During 1893, the international statistical institute adopted the first ICD classification. Years later, the WHO was entrusted with the ICD classification and in 1948, the first version (the ICD-6), which included mortality, was published by them. In 1967, the WHO nomenclature regulations, demanded that member states use the most up-to-date ICD version for mortality and morbidity statistics (WHO, 2015).

As advances have been made in medical sciences and health over time, the ICD classification has been revised and published in a series of editions. As the ICD classification serves as an international standard, it provides a global foundation for both the identification of statistics and health trends. Additionally, it is the diagnostic classification standard for all clinical and research performed. The ICD classification has several uses, namely to keep book of safety and quality guidelines, to monitor incidence and prevalence of diseases and to observe reimbursements and resource allocation trends. Furthermore, it not only provides a platform for injury-, disease-, symptoms- and morbidity-counts, but it also allows for the identification of external causes of disease and factors that influence health status (WHO, 2015). Table 2.11 provides the ICD-10 codes of all the surgical procedures identified in this study.
Table 2.11: ICD-10 codes identified during data collection

<table>
<thead>
<tr>
<th>ICD-10 Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H60-H95: DISEASES OF THE EAR AND MASTOID PROCESS</td>
<td></td>
</tr>
<tr>
<td>H65.0</td>
<td>Acute supplicative otitis media</td>
</tr>
<tr>
<td>H65.3</td>
<td>Chronic mucoid otitis media Glue ear OR Otitis media, chronic: Mucinous, Secretory, Transudative</td>
</tr>
<tr>
<td>H66.0</td>
<td>Acute supplicative otitis media</td>
</tr>
<tr>
<td>J00-J99: DISEASES OF THE RESPIRATORY SYSTEM</td>
<td></td>
</tr>
<tr>
<td>J30-J39: Other diseases of upper respiratory tract</td>
<td></td>
</tr>
<tr>
<td>J35.0</td>
<td>Chronic tonsillitis</td>
</tr>
<tr>
<td>J35.1</td>
<td>Hypertrophy of tonsils/ Enlargement of tonsils</td>
</tr>
<tr>
<td>J35.2</td>
<td>Hypertrophy of adenoids/ Enlargement of adenoids</td>
</tr>
<tr>
<td>J35.3</td>
<td>Hypertrophy of tonsils with hypertrophy of adenoids</td>
</tr>
<tr>
<td>J35.9</td>
<td>Chronic disease of tonsils and adenoids/ unspecific Disease (chronic) of tonsils and adenoids NOS</td>
</tr>
<tr>
<td>J40-J47: Chronic lower respiratory diseases</td>
<td></td>
</tr>
<tr>
<td>J45.0</td>
<td>Predominantly allergic asthma/ Allergic: Bronchitis NOS, Rhinitis with asthma/Atopic asthma/ Extrinsic allergic asthma/ Hay fever with asthma</td>
</tr>
<tr>
<td>K00-K93: Diseases of the digestive system</td>
<td></td>
</tr>
<tr>
<td>K00-K14: Diseases of oral cavity, salivary glands and jaws</td>
<td></td>
</tr>
<tr>
<td>K00.6</td>
<td>Disturbances in tooth eruption/ Dentia praecox/ Natal tooth/ Neonatal tooth/ Premature: Eruption of tooth, Shedding of primary (deciduous) tooth/ Retained (persistent) primary tooth</td>
</tr>
<tr>
<td>K01.1</td>
<td>Impacted teeth (An impacted tooth is a tooth that has failed to erupt because of obstruction by another tooth).</td>
</tr>
<tr>
<td>K02.0</td>
<td>Caries limited to enamel/ White spot lesions (initial caries)</td>
</tr>
<tr>
<td>K35-K38: Diseases of appendix</td>
<td></td>
</tr>
<tr>
<td>K35.2</td>
<td>Acute appendicitis with generalised peritonitis/ Appendicitis (acute) with generalised (diffuse) peritonitis following rupture or perforation</td>
</tr>
<tr>
<td>K35.3</td>
<td>Acute appendicitis with localised peritonitis/ Acute appendicitis with localised peritonitis with or without rupture or perforation/ Acute appendicitis with peritoneal abscess</td>
</tr>
</tbody>
</table>
2.7 CHALLENGES IN SURGICAL ANTIMICROBIAL PROPHYLAXIS

Although clear principles of SAP exist and despite several published guidelines, the implementation of these guidelines by medical practitioners remain both troublesome and controversial. Significant contributors to the malpractice is over-prescribing, inappropriate timing and duration of the SAP. This poor compliance to the SAP guidelines further contributes to increased incidences of SSIs and new resistant bacteria. Despite the afore-mentioned challenges having been widely addressed in several developed countries, very little regard has been shown by developing countries (Al-Abri & Elsheikh, 2016).

2.8 BEHAVIOURAL CHANGE

AMR is an “urgent” worldwide dilemma. Unfortunately, the pipeline for new antimicrobials has run dry (Gould & Lawes, 2016), and thus AMS is the only weapon left in the arms race against antimicrobial resistance (Gould et al, 2016). In order to contain this global emergence of AMR, change is needed in antimicrobial prescribing behaviour, which necessitates a change in the medical practitioner’s behaviour towards the magnitude of AMR (Abera et al, 2014). The integration of behavioural modification into AMS thus provides a powerful weapon (Gould et al, 2016). However, the conversion of awareness into successful AMS is a worldwide challenge, which is worsened by the “disconnect between individual behaviour and population level resistance” (Gould et al, 2016). Inappropriate use is one the major contributors to antimicrobial resistance, hence the paramount importance of addressing and managing the prescribing behaviour of the outlier medical practitioner (Charani, Edwards, Sevdalis, Alexandrou, Sibley, Mullett, Franklin et al, 2011; Goldstein, Goff, Reeve, Naumovski, Epson, Zenilman, Kaye et al, 2016). An outlier medical practitioner is defined as one that behaves completely different from his peers, deviating from set norms.
By performing key research into the prescribing intention and practices of medical practitioners, outlier behaviour and the current barriers might be identified. Through understanding the behaviour and the associated barriers, interventions may be developed, carries can be overcome and a sustainable powerful end result may be achieved (Charani et al, 2011).

Henceforth, the crucial elements to modify current outlier antimicrobial behaviour encompass the implementation of specific AMS programmes, identifying the causative reasons, ensuring effective communication and support, and lastly, the application of evidence-based recommendations (Goldstein et al, 2016).

The major intervention to address inappropriate prescribing would involve studies, which would focus on the current literature to assess prescribing effectiveness and intervention possibilities. It was stated in a study performed by Charani & colleagues (2011) that the application and importance of behavioural change in antimicrobial prescribing has not yet been considered. Internationally published studies have only recently come to light in identifying that the main intervention to improve antimicrobial prescribing was behavioural change of the outlier medical practitioner (Charani et al, 2011).

Behavioural change is neglected as a key aspect in the evolution of antimicrobial prescribing interventions (Charani et al, 2011). Motivated by the current international movement, the need to investigate the behaviour of medical practitioners with a targeted multidisciplinary study was stressed.

### 2.9 KNOWLEDGE AND PERCEPTION

Since antimicrobials are mainly prescribed by medical practitioners, any action aimed at improving the use of antimicrobials necessitates targeting them. Yet the optimal methods for addressing this problem remains obscure. However, because such reform would require fundamental changes in the medical practitioners’ behaviour (as discussed in the previous section), it is important to understand that the process of bringing about these changes is affected by their knowledge and awareness (Awad et al, 2015; Kheder, 2012).

The reason behind this observation is that one of the key factors affecting individual prescribing behaviour of antimicrobial entails the extent of a medical practitioner’s knowledge on antimicrobial use, their perception and experiences of antimicrobials and AMR (Navarro-San Francisco, Del Toro, Cobo, De Gea-García, Vañó-Galván, Moreno-Ramo, Rodríguez-Baño et al, 2013; Awad et al, 2015; Bai et al, 2016).
Therefore, interventions are required to identify and change antimicrobial-use behaviour of medical practitioners, to rationalise the further use thereof and to contain the growing emergence of resistance (Quet et al, 2015). Information to design such interventions may be obtained through knowledge, attitude and practice surveys of the prescribers (Quet et al, 2015). Furthermore, considering that knowledge is the first step in modifying antimicrobial use, a more sustainable approached would be to influence knowledge and attitude (Bai et al, 2016).

In a cross-sectional survey completed by 761 medical practitioners, Bai et al (2016) found that sub-optimal knowledge regarding antimicrobials exists amongst medical practitioners in China, and even poorer knowledge on antimicrobial use amongst medical practitioners in primary healthcare institutions.

A study by Gonzalez et al (2015) targeted 2100 primary healthcare medical practitioners over a three year follow-up cohort study to establish the attitudes and knowledge that influence prescribing behaviour. The researchers found that patient satisfaction, the fear of complications and insufficient knowledge are factors that influence prescribing behaviour. In order to maintain a good medical practitioner-patient relationship, misprescriptions of antimicrobials occurs. Fear, the primary attitude linked to quality of prescriptions, results in marked use of broad-spectrum antimicrobials or increased use of antimicrobials for incorrect indications. Insufficient knowledge leads to inappropriate such as attitudes that amoxicillin is convenient to resolve most respiratory infections. In conclusion the study found that medical practitioners’ attitudes and knowledge does dictate the quality of antimicrobial prescriptions and thus interventions to combat AMR should address inappropriate attitudes, false believes and gaps in knowledge. Kheder et al (2012) performed a cross sectional survey with 350 medical practitioners and identified conflicting and inconstant misperceptions about the importance of AMR, the causes thereof as well as solutions. She agrees that the awareness knowledge and beliefs of medical practitioners are key to reduce AMR.

The inappropriate use and misuse of antimicrobials by medical practitioners is not only a global concern, but a significant contributor to increased AMR (Bai et al, 2016). Shockingly, although the use of antimicrobials remains high in hospitals and although most infectious disease consultants agree that the inappropriate use thereof increases AMR, the majority believe that AMR is not a key factor to consider when selecting antibiotics for patients (Lucet, Nicolas-Chanoine, Roy, Riveros-Palacios, Diamantis, Le grand, Papy et al, 2011).
Chapter 2: Literature Review

In lower-income countries, AMR is driven by the irrational use of antimicrobials, the over- or unnecessary prescribing thereof (Threimer, Katuala, batoko, Alworonga, Devilieger, Van Geet, Ngbonda et al., 2013) and the lack of microbiology laboratories for antimicrobial susceptibility testing (Abera et al., 2014). Combined with high infection rates, AMR presents a particular challenge in these low income countries like South Africa (Abera et al., 2014).

South Africa faces an overwhelming burden of infectious disease, with the previously largely unnoticed AMR threat now becoming more visible and tangible to our medical practitioners (NDoH, 2015; Mendelson, 2015).

It can therefore be concluded that, by fully understanding the medical practitioners’ knowledge and perception on antimicrobials and what factors influence their prescribing patterns, effective interventions can be made (Kheder, 2012). Consequently, through assessing the knowledge and understanding the prescribing behaviour of medical practitioners (Threimer et al., 2013), the development of a strategy and effective interventions to improve antibiotic use and contain AMR may be permitted (Bai et al., 2016; Threimer et al., 2013; Abera et al., 2014).

Although studies have been performed on medical practitioners’ knowledge and belief of antibiotic use and AMR in higher-income countries, the results are not necessarily applicable to the lower-income countries (Abera et al., 2014). Limited data on this topic, targeted towards paediatrics, exist, therefore the aim of this study was to assess the knowledge and perception of medical practitioners regarding surgical antibiotic prophylaxis used in paediatric patients, by means of a survey.

To the researcher’s knowledge, no such study has been performed involving the medical practitioners’ knowledge and perception of antibiotic use in South Africa.

2.10 HEALTH CARE IN SOUTH AFRICA

Health care in South Africa consists of the public and the private health care system.

2.10.1 The public health care system

The public sector constitutes the majority of health care, catering for the lower–income, permanent residents of South Africa (Jobson, 2016).
Chapter 2: Literature Review

The public sector is funded by the government. Despite the 5% gross domestic product (GDP) recommendations by the WHO, this sector is consuming an estimated 11% of the total South African government budget, which reflects the striking burden of disease management and the treatment thereof (Jobson, 2016). The “high levels” of poverty and unemployment rates of the population further increase the burden on the NDoH. However, despite this level of expenditure, health care outcomes are poor and medical personnel are scarce (Jobson, 2016).

South Africa has 4,200 public health care facilities, with each facility providing services to an estimated 13,718 people. Again, this value exceeds the ratio of 10,000 per clinic, as recommended by the WHO. The National Health Laboratory Service (NHLS) is dedicated to deliver diagnostic and health services to public hospitals of South Africa. It is the largest pathology service, with 265 laboratories in the country, serving 80% of the population (Jobson, 2016).

The foundation of the public sector is primary health care clinics, providing free first-line care to those in need. If more “sophisticated” treatment is required, patients are referred to district and provincial hospitals. The last leg of the public health care system is at tertiary level, also referred to as teaching or academic hospitals (Jobson, 2016).

2.10.2 Teaching hospitals

A teaching hospital, also known as an academic or tertiary hospital, not only renders specialist and sub-specialist care, but also provides advanced diagnostic procedures and therapy, but more importantly, serves as training institutions for health care practitioners (Jobson, 2016; NDoH, 2016).

2.10.3 The private health care system

The private health care system is comprised of health care practitioners who provide privately-based services. These services are normally funded by individuals or medical scheme beneficiaries. The majority of patients making use of the private health care systems would be classified as middle- to high-income residents of South Africa, who are covered by a medical aid scheme. There is an estimated count of 110 registered medical schemes, serving around 3.4 million members and 7.8 million being beneficiaries, with an estimated annual contribution of R84,9 billion (Jobson, 2016; NDoH, 2015).
2.10.4 Basic landscape of South African health care

Prior to democratisation, private hospitals were defined as a medical scheme-funded sector, which consisted of 20% of the population, the majority being white (National drug policy for South Africa, 1996). However, since 1990, the incline of medical scheme beneficiaries contributes to a major shift in the use of private hospital care (Matsebula & Willie, 2016). Not only does private hospitals “alleviate the pressure from a substantially overburdened public hospital sector” but it also provides a short travelling distance to the nearest health care setting. However, despite being one of the “significant” role-players in the South African health care system, “access” to private hospitals is still very much limited. This is not only due to the notably high cost associated with private care, but also due to the demographical placing, as the majority of private hospitals are found in “major metropolitan areas”. As services provided by private hospitals cost more, it is only accessible to medical scheme beneficiaries or those wealthy enough to afford it (Matsebula et al, 2016). The remarkable difference in the amount of resources attributed to private hospitals in South Africa, a sector that caters for only seven million beneficiaries, exacerbates the affordability and accessibility imbalance between the public and private hospitals.

Contrary, the public health care system was regarded as a collapsing system due to the associated poor work circumstances, insufficient infrastructure and unreasonable use of resources. Furthermore, during 1990, private health care was accountable for 80% of the country’s total drug expenses. However, 60-70% of the total volume of pharmaceuticals was consumed by the public health care system. The pharmaceutical sector of the public health care system reflected the same picture. Quality of health care was impacted by the absence of fairness in the access to essential drugs. Poor pharmaceutical services were delivered due to rising drug prices, evidence of irrational drug use, negligence and poor security, all lead to damaging, cost-ineffective procurement and logistic practices (National drug policy for South Africa, 1996).

During the general household survey (2015) performed by Statistics South Africa, it was reported that an estimated seven out of every ten households (70.5%) of the South African population used public health care as their first access point. In comparison, only a quarter of the population said that they would make use of private health care. On the positive side, 81.1% of households that made use of public health care facilities were either very satisfied or satisfied with the service received, compared to the 97.7% obtained from private health care users. Unfortunately, a larger percentage of households, using public health care (6,1%) were very dissatisfied with the received service, compared to the 0,5% from private
health care. An estimated quarter (23.5%) of all South African households had at least one member belonging to a medical aid scheme, resulting in a relatively small proportion of 17.5%.

Table 2.12 outlines the demographics of public versus private health care. In both sectors there are 165,371 qualified and registered health care practitioners, however, 73% of the general medical practitioners practice in the private sector.

Table 2.12: Demographics of South Africa’s health care system

<table>
<thead>
<tr>
<th>Factor</th>
<th>Public</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hospitals</td>
<td>376</td>
<td>238</td>
</tr>
<tr>
<td>Urban hospitals</td>
<td>143</td>
<td>188</td>
</tr>
<tr>
<td>Rural hospitals</td>
<td>233</td>
<td>50</td>
</tr>
<tr>
<td>Total patients/doctor</td>
<td>4219</td>
<td>243</td>
</tr>
<tr>
<td>Annual expenditure</td>
<td>R122.4-billion</td>
<td>R120.8 billion</td>
</tr>
<tr>
<td>Total population served (%)</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>Total population served</td>
<td>42 million</td>
<td>8.2 million</td>
</tr>
</tbody>
</table>

As adapted from (Jobson, 2016).

2.11 ANTIMICROBIAL STEWARDSHIP

In the face of a post-antibiotic era, with declining efficacy in SAP and increased multi-drug resistance organisms, an urgent need for the implementation of AMS has been identified (Gould et al, 2016). The IDSA, the SHEA and the paediatric infectious disease society (PIDS) have agreed on a definition for AMS. In short, it involves specific interventions harmonised to ameliorate and measure the appropriate use of antimicrobials, through the encouragement of an optimal selection of antimicrobial regimens (dosing, duration of treatment and route of administration) (Barlam et al, 2016). Most importantly, AMS confronts antimicrobial resistance by improving antimicrobial susceptibility, but is also enhances patient outcomes and minimises adverse effects (Barlam et al, 2016).

This study wholly retrospectively represented the key components of AMS (Barlam et al, 2016).
2.12 CONCLUSION

A SSI is defined as a preventable leading cause of nosocomial infection, in which a wound infection occurs after an invasive surgical procedure and is further categorised as either incisional or organ/space. SSIs result in higher cost of care, decreased quality of life, increased hospital length of stay, risk of ICU admission and death. Paediatrics are defined as those younger than 18 years of age, and further classified into different categories ranging from neonates to infant, toddlers, childhood and adolescents, depending on their age. Paediatric mortality reflects not only the quality of care within health services, but also the true health status of a population. Globally, 5.9 million paediatrics, aged below five died in 2015, with Africa having the highest paediatric mortality risk. Importantly, South Africa’s population consists of 30% paediatric patients, which is a noteworthy point as the burden of surgical diseases in the paediatric population is a vital concern in developing countries. Worryingly, limited quality improvement programmes have been initiated to reduce SSIs in the paediatric population. The ASHP therapeutic guidelines (2013) define SAP as a method of preventing an infection by decreasing the load of organisms at the surgical site and thereby aiming to furthermore, decrease associated morbidity and mortality, length of stay and the accompanied cost. Paediatric SAP selection has been extrapolated from adult data. All recommendations for adults, unless otherwise specified, are the same for paediatrics, except the dosing of first- and second-generation cephalosporins being the agents of choice.

As appropriate SAP has been shown to reduce SSI-associated morbidity and mortality, key recommendations include: coverage of the most common pathogens associated with the type of surgery. A single dose SAP, 60 minutes prior to incision, redosing if surgical procedure exceeds two half-lives of the SAP or in extreme blood loss, and discontinuation of SAP should be within 24 hours.

As South Africa is battling with the growing emergence of resistant organisms and is facing several challenges, the significance of the consequences of both overuse (increased risk of resistant organism and side-effects) and underuse (increased risk for SSI) of SAP cannot be disregarded.

A change in social norms, attitudes and beliefs on antimicrobial use is of paramount importance if we want to modify the behaviour of our medical practitioners, especially those of the outliers.
In line with this current international movement, the study sought to address the gap and assess the current knowledge and perception as well as behaviour of the medical practitioners in both a teaching and a private hospital in South Africa.

2.13 SUMMARY

A comprehensive literature review was given regarding all aspects addressed by this study. The importance of SAP prophylaxis was highlighted, with a focus on the use in South Africa. The principles, recommendations and regimens of SAP use in paediatrics were outlined. As a final point, the important role of the pharmacist was discussed. The next chapter will give a systematic description of the methodology applied in the completion of this study.
CHAPTER 3
METHOD

3.1 INTRODUCTION

This chapter presents the methodology of this study in detail, starting with a discussion of the study site and the study period. The study design and the study population are described followed by the sample selection used. The data collection process and instrument, and the pilot study are explained in detail. This is followed by the description of data entry and analysis as well as methods used to ensure reliability and validity of the data collected. The chapter concludes with a discussion of the ethical considerations of this study.

3.2 STUDY DESIGN

The study followed two quantitative descriptive designs, one retrospectively, the other prospectively. This design assisted to answer both of the study’s research questions (see Chapter 1, 1.3) by primarily focusing on individuals and numerical assessments. The study design remained constant throughout the study period and is reproducible. A chart review was conducted retrospectively and a survey was administered to the medical practitioners prospectively.

3.2.1 Retrospective aspect

A retrospective quantitative descriptive design was used by conducting a retrospective chart review to evaluate compliance to SAP guidelines by medical practitioners treating paediatrics in a paediatric surgical ward, requiring surgical procedures in four different specialised areas, including; urology, ear, nose and throat (ENT), general surgery and maxillofacial in the paediatric surgical ward at a teaching and a private hospital. The study design is termed “retrospective” as the outcome investigated occurred before initiation of the investigation.

3.2.2 Prospective aspect

A prospective descriptive quantitative design was used by means of a survey to assess the knowledge and perception of the use of SAP of the medical practitioners from the same teaching and a private hospital used, whom treated paediatrics requiring surgical proce-
dures in four different specialised areas, including urology, ENT, general surgery and maxillofacial, in the paediatric surgical wards. The study design is termed "prospective" as a specific sample population was selected and variables of interested was measured.

### 3.3 STUDY SITE

The significance of this study identified the need for a larger study population, additionally, the ever-so contrasting health care setting in South Africa, motivated the need for another study site - a private hospital. The benefits of a multi-centre study outweighs the risks. Not only did a multi-centre study increase the study population, exposes different geographic locations, demographic information and the possibility of the inclusion of a wider range of population groups, but more importantly it provided the opportunity to compare results amongst the two health care settings in South Africa. This finally allowed for increased generalisation of the study findings.

#### 3.3.1 Retrospective aspect

The study was conducted through the use of files from the paediatric surgical ward at a teaching hospital. During the study period the ward consisted of four cubicles with a total of 40 beds. Paediatric surgical patient charts from a private hospital were also used. The private hospital used did not have a dedicated paediatric surgical ward, with patients being allocated to wards based on the type of surgery they underwent.

#### 3.3.2 Prospective aspect

The study was conducted at the same teaching and private hospitals as were used in the retrospective aspect of the study.

#### 3.3.3 The teaching hospital

DGMAH, formerly known as Ga-Rankuwa Hospital, was built in 1972 and is situated in Ga-Rankuwa, on the North-Western part of the Tshwane region of the Gauteng Province. This hospital initially served as a regional hospital. However, tertiary services were added with the establishment of the Medical University of Southern Africa (MEDUNSA) in 1976, serving as a teaching platform. In 2011, DGMAH gained academic status, followed by the establishment of Sefako Makgatho Health Sciences University (SMU), building on the legacy of the old MEDUNSA. The hospital has 28 clinical departments, rendering all three levels of
services. It is one of four academic institutions in the province. It provides a service to approximately 1.7 million people in the surrounding area. In addition to receiving referrals from Limpopo, North West and Mpumalanga, this facility further receives referrals from Southern African Development Community (SADC) countries, other tertiary academic hospitals, local specialists and general practitioners. The hospital has 1,650 active beds, 20 approved ICU beds, 60 high care beds and 17 surgical theatres (DGMAH, 2016).

This hospital has four paediatrics wards, namely the orthopaedics ward, surgical ward, oncology ward and the neonatal intensive care unit (NICU). This study primarily made use of the paediatric surgical ward (see Table 3.1).

**Table 3.1: The teaching hospital’s surgical ward**

<table>
<thead>
<tr>
<th>Ward</th>
<th>Number of Beds</th>
<th>Average number of admissions per month</th>
<th>Turn Over Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical ward</td>
<td>40</td>
<td>148</td>
<td>3.70</td>
</tr>
</tbody>
</table>

### 3.3.4 The private hospital

The private hospital used in this study is situated in the east of Pretoria, in the Gauteng Province of South Africa. It is part of the largest network of comprehensive private health care services in South Africa. This network comprises 52 hospitals. A total network revenue of R17.289-million was reported with an operating profit of R3.411-million in 2015. This is a 358-bed facility, with highly skilled and experienced specialist and professional nursing staff. Patients have access to the latest advances in medical and surgical technology, interventions and treatment across a broad spectrum of specialities. It has an average patient admission per month of 1,778. It has 17 wards, two ICUs, two high care facilities, and four operating theatres. Although this hospital does not have a dedicated paediatric ward, it does have three permanent and three temporary paediatricians. Furthermore, this hospital has an implemented AMS programme, which also evaluates surgical antibiotic prescribing. Table 3.2 outlines the specialists that work in the disciplines used in this study.
Chapter 3: Method

Table 3.2: Specialists working at both hospitals

<table>
<thead>
<tr>
<th>HOSPITAL</th>
<th>ENT</th>
<th>MAXILLO-FACIAL</th>
<th>UROLOGY</th>
<th>GENERAL</th>
<th>GASTROENTEROLOGIST</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teaching</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Private</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

3.4 STUDY PERIOD

3.4.1 Retrospective aspect

Ethical clearance obtained by SMUREC for this study allowed for a total study period of 12 months. Data collection was thus approved to commenced from 6 August 2015 to 6 August 2016.

The study period was broken down and used as follow:

6th of August, 2015: Initiation of study

September, 2015: Collection of patient GN numbers and submission thereof to DGMAH’s chart room

October, 2015: DGMAH prospective data collection

November, 2015: DGMAH retrospective aspect data collection

December, 2015: SMU Holiday

January and February, 2016: DGMAH retrospective aspect data collection continues

March and April, 2016: Private hospital’s retrospective and prospective data collection

May until 6th of August, 2016: Work up and final sorting of all data collected
3.4.2 Prospective aspect

Ethical clearance obtained by SMUREC for this study allowed for a total study period of 12 months. Data collection was thus approved to commenced from 6 August 2015 to 6 August 2016.

3.5 STUDY POPULATION

3.5.1 Retrospective aspect

The study population included all discharged paediatric patients aged 12 years or younger, who underwent surgery at a teaching and private hospital, who met the specified inclusion criteria. The NICHD classification is thoroughly discussed in Chapter 2, Section 2.3.

3.5.2 Prospective aspect

The study population included all the medical practitioners working with paediatric surgical patients at a teaching and a private hospital, who met the inclusion criteria.

3.5.3 Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>SPECIFIC TO</th>
<th>INCLUSION CRITERIA</th>
<th>EXCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective</td>
<td>Both male and female participants. Patients 12 years old or younger. Discharged patients of the teaching and private hospital who underwent surgery in urology, ENT, general surgery or maxillofacial.</td>
<td>Patients older than 12 years.</td>
</tr>
<tr>
<td>Prospective</td>
<td>Both male and female medical practitioners. Registrars, specialists, doctors, interns working in the paediatric surgical ward at the teaching and private hospital. Medical practitioners willing to provide informed consent.</td>
<td>Medical practitioners not working in the paediatric surgical ward at the teaching and private hospital during the time of the study. Medical practitioners not willing to provide informed consent</td>
</tr>
</tbody>
</table>
3.6 SAMPLE SELECTION

3.6.1 Retrospective aspect

All paediatric surgical patients who underwent surgery at a teaching and private hospitals, and who met the inclusion criteria.

1.5.1. Prospective aspect

Sampling was also done to include all medical practitioners working with paediatric surgical patients at the same teaching and private hospitals used for the retrospective aspect of the study, and who met the inclusion criteria.

1.5.2. Estimation of retrospective aspect sample size

The paediatric surgical ward of the teaching hospital was used to estimate the sample size, as the private hospital used did not have a dedicated ward for paediatric surgical patients. The paediatric surgical ward of the teaching hospital had an occupancy of 75% with an average of 30 patient admissions per month. Thus over 18–month period (January 2014 - June 2015) there was an estimated 540 admissions. A sample size of 112 patients was estimated at 95% confidence level and 5% confidence limits with 50% expected frequency. This estimation was performed on Epi Info™ 7.

3.6.2 Estimation of prospective aspect sample size

Sampling was also done to include all medical practitioners working in the paediatric surgical ward at a teaching and a private hospital who met the inclusion criteria. The estimated total number of medical practitioners who worked in the paediatric surgical ward at the teaching hospital during the study period was 15, which consisted of four ENT specialists, one maxillofacial specialist, five urology specialists and five specialists of other surgeries. Based on the number of medical practitioners per cubicle in the paediatric surgical ward at the teaching hospital, the sample size was estimated at 15 participants per hospital.

3.7 DATA COLLECTION PROCEDURE

3.7.1 Retrospective aspect

Paediatric surgical files from 2014 up until June 2015 were reviewed by the researcher of this study with the following objectives:
• To establish whether or not the documentation on antimicrobial administration included the name of the active ingredient, date, time of and route of administration;

• To confirm whether SAP was given within one hour prior to surgical incision (except for vancomycin, which should be given within two hours prior to surgical incision);

• To check whether the correct antimicrobial in the correct dosage was administered for the specific surgical procedure for the specific weight of the paediatric patient;

• To check whether intra-operative re-dosing was administered during procedures (>4 hours) to maintain adequate serum and tissue concentrations;

• To check whether antimicrobial prophylaxis for surgery was discontinued within 24 hours of surgical end-time.

In DGMAH a paper based system is used. Thus, in order to retrieve a discharged patient’s chart from DGMAH’s chart room, a GN number was required. Patients GN numbers were collected by the researcher and handwritten onto a sheet, from the surgical paediatrics ward’s nominal book according to the study period provide by the study size estimation (January 2014 - June 2015). The sheets were handed to chart room assistants for retrieval. The researcher was given an office in the chart room, where all of the charts were kept under lock and key and supervision. After all of the charts had been retrieved, the researcher collected all of the required data onto the paper hard copy data collection instrument. After which it was copied onto the relevant electronic Microsoft Excel® spreadsheets. The charts never left the chart room or hospital premises.

In order to retrieve charts from the private hospital’s chart room, a patient case number had to be obtained. The SAP® (Systems, Applications and Products in data processing) enterprise portal system was used. The SAP® system is a global system used in 190 different countries, with 85 million subscribers and it was applied in this study to obtain patient case numbers. For this study’s specific aims the M28 Procedure analysis report was selected in order to obtain the BW CO DRG report of the institution. This report is comprised out of all the theatre cases performed at the private hospital. In order to identify the specific surgeries recognised in this study in the theatre case report, procedure codes (CPT) first needed to be obtained. Table 3.3 shows the specific area of surgery identified in this study, with the main types of surgery interested in according to the study population and their relevant procedure code. After the appropriate CPT codes were obtained, the codes were used to identify the specific surgeries performed per month (within the study period). Furthermore,
Chapter 3: Method

the SAP easy access system granted permission to obtain selected patient information under the NP10 IS-H: Call case overview tab. Here each case number was used to identify whether or not the patient was 12 years old or younger at the time of surgery (The year 2003 was used as the cut-off date of birth year, as the study period was from January 2014 to June 2015 the max age would then be 12 years old). After the correct amount of patient case numbers were obtained, they were taken to the private hospitals chart room, where they were requested and received within 24 hours after all of the charts had been retrieved, the researcher collected all of the required data onto the paper hard copy data collection instrument. After which it was copied onto the relevant electronic Microsoft Excel® spread-sheets. The charts never left the chart room or hospital premises.

Table 3.3: Category of surgery, with the specific surgeries look at in that category and its specific CPT code

<table>
<thead>
<tr>
<th>Category of surgery</th>
<th>Type of surgery</th>
<th>CPT codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urology</td>
<td>Phimosis</td>
<td>54161</td>
</tr>
<tr>
<td></td>
<td>Circumcisions</td>
<td>54161</td>
</tr>
<tr>
<td></td>
<td>Undescended testicles</td>
<td>54640, 54520, 54530, 55040, 54041.</td>
</tr>
<tr>
<td>ENT</td>
<td>Tonsillectomy</td>
<td>42820, 42821, 42825, 42826</td>
</tr>
<tr>
<td></td>
<td>Papilloma (Laryngeal)</td>
<td>31511</td>
</tr>
<tr>
<td>General surgery</td>
<td>Hernia repair</td>
<td>49560, 49565, 49570, 49580, 49495, 49500</td>
</tr>
<tr>
<td></td>
<td>Appendectomy</td>
<td>44950, 44960, 44970</td>
</tr>
<tr>
<td></td>
<td>Colostomy</td>
<td>44345</td>
</tr>
<tr>
<td>Maxillofacial</td>
<td>Dental surgery</td>
<td>41899</td>
</tr>
</tbody>
</table>

3.7.2 Prospective aspect

This was done by means of a survey, to assess the knowledge and perception of medical practitioners working in the paediatric surgical ward at the teaching and private hospitals used.

On the first of October 2015, the researcher under supervision of her supervisor, scheduled a mass meeting with all the medical practitioners from DGMAH whom treats paediatrics
requiring surgical procedures in one of the four different specialised areas, including; urology, ENT, general surgery and maxillofacial, in the paediatric surgical ward. At this meeting a powerpoint presentation on the study was presented by the researcher. The power point presentation also covered the function of the survey, what it entailed and what knowledge and perceptions it aims to assess. The survey was then handed out to all of the medical practitioners, along with an informed consent page and a survey information letter. The researcher was able to assist with any questions regarding the survey. All surveys were completed during the mass meeting, on site, preventing bias due to discussions with peers or reference to literature under the supervision of the researcher and her co-supervisor. To ensure accuracy of all information collected on the data collection form, it was double-checked by the researcher’s supervisor, before it was electronically captured onto the data collection Microsoft Excel® spreadsheet. All errors identified were checked and discussed with the supervisor and another independent researcher.

At the private hospital, it was not possible to schedule a mass meeting with the medical practitioners whom treats paediatrics requiring surgical procedures in one of the four different specialised areas, including; urology, ENT, general surgery and maxillofacial, in the paediatric surgical ward. Instead, a list was compiled, with the help of a co-supervisor working at the private hospital, with all the medical practitioners working at the private hospital whom meets the inclusion criteria. After the final list was completed with all of the medical practitioners names, the researcher along with her co-supervisor, scheduled 20 minute personal appointments with each medical practitioner. The appointments started on the 6th of April 2016 and finished on the 8th of April 2016. In this appointment an overview of the study was given along with the powerpoint presentation slides, with an information letter that further thoroughly explained the purpose of the survey. The medical practitioner and the researcher was able to assist with any questions. The survey was completed during the appointments on site, preventing bias due to discussions with peers or reference to literature under the supervision of the researcher and her co-supervisor. To ensure accuracy of all information collected on the data collection form, it was double-checked by the researcher’s supervisor, before it was electronically captured onto the data collection Microsoft Excel® spreadsheets. All errors identified were checked and discussed with the supervisor and another independent researcher.
3.8 DATA COLLECTION INSTRUMENTS

3.8.1 Retrospective aspect

A data collection form was prepared, with a separate form used for each paediatric surgical file reviewed at both the teaching and a private hospital, during the study period. The data collection form was developed and compiled by the researcher, based on several previously published studies, with slight modifications (Ciofi, Spila, raschetti, Arace, Giusti, Spiazzi & Raponi, 2015; Khoshbin et al, 2015; Mohamoud & Yesuf, 2016; Sandora et al, 2016; So, Aleem, Tsang, Matlow & Wright, 2015; Sviestina, Mozgis & Mozgis, 2016). The designed form had a combination of “checking” and “fill-in” areas. The form recorded the patient’s demographics (age, date of birth, gender, weight and height), the primary diagnosis and clinical data, which included:

- The type of surgery;
- If SAP was administered;
- If it was, whether it was done one hour before, two hours before, or any other time, had to be specified;
- The name, ICD-10 code, ATC code, dosage, route of administration, date and time of the SAP were recorded, and whether the use thereof was discontinued within 24 hours, and if not, a reason had to be provided.

The aim of this data collection form was to record the SAP used in the paediatric surgical patients at both the teaching and private hospitals. This data collection form assisted the researcher by providing a framework for the summary of all information required for this study.

3.8.2 Prospective aspect

The survey form (see Appendix 2) was used for each medical practitioner who participated in the study from both the teaching and private hospitals used during the study period. The survey form, developed and compiled by the researcher, was based on several reference documents (Bai et al, 2016; Quet et al, 2015; Hsieh et al, 2011). The designed survey form was in a checklist form, although there was room for comments. Section A recorded the medical practitioners’ demographics (age, date of birth, gender, registration status and area of speciality). Anonymity was kept as medical practitioner were not required provided their
names and surnames or identity numbers. Instead, each survey that was handed out already had a study participant number allocated and written on.

Section B consisted of five key statements which covered antimicrobial costs, potential adverse reactions to antimicrobials, infection risk without SAP, reduction in infection risk with SAP and the potential AMR due to the use of antimicrobials. The medical practitioners had to indicate how each key factor affects the medical practitioners’ overall approach to SAP. This was done based on a grading scale ranging from one to five, as follows.

- One indicated “not at all important”;
- Two indicated “somewhat important”;
- Three indicated “important”;
- Four indicated “very important”;
- Five indicated “extremely important”

Section C was a “yes” or “no” checklist and medical practitioners had to indicate whether or not they administer pre- and/or post-operative antimicrobials for the following surgical subspecialties:

1. Urology- Phimosis, Circumcisions, Undescended testicles;
2. ENT- Tonsillectomy, Papilloma;
3. General surgery- Hernia repair, Appendectomy, Colostomy;
4. Maxillofacial- Dental surgery;
5. There was space to specify on any other.

The aim of this survey was to understand the current prescribing practices of the medical practitioners form both the teaching and private hospitals used, by recording their knowledge and perception with regards to SAP. The survey from assisted the researcher by providing a framework to summarise all information required for this study.
3.9 DATA CAPTURE AND ANALYSIS

Data were captured electronically from the completed data collection checklists onto Microsoft Excel® spreadsheets. All data captured from the paper hard copy data collection instruments were proof-read by the researcher’s supervisor for preciseness before captured electronically. Demographic details of paediatric patient files and medical practitioners were summarised descriptively by frequency tables and graphs. Frequency tables were constructed for types of antimicrobial use (see appendix 1 and sections B and C of appendix 2). Data were imported into Statistical Analysis System (SAS®) Release 9.3 for statistical analysis, which were calculated as a percentage with 95% confidence intervals (CIs). Results were descriptively summarised and presented in tables and figures.

3.10 METHODOLOGY TO ACCESS APPROPRIATE USE OF SAP

Based on the preceding literature review conducted (Chapter 2, section 2.6), the following criteria were used to access appropriateness of the SAP (and thus the compliance to guidelines) used if SAP was indicated and administered (ASHP, 2013; Choc Children’s guidelines, 2010; RHSC recommendations, 2014; SIGN guidelines, 2014; STGs/EML (Paediatrics), 2013). However, in this study, all five of the criteria had to be met in order for the use of SAP to be deemed complaint.

3.10.1 The five criteria

- Appropriate SAP agent selection, based on the surgical procedure performed;
- Appropriate dose of the selected SAP;
- Timing of administration of the SAP;
- Redosing of the SAP;
- Discontinuation of the SAP.

3.10.2 Appropriate SAP

The SAP guidelines used for the purposes of this study were defined from prior evidence-based guidelines. A comprehensive literature search was conducted by studying SAP recommendations of several guidelines (ASHP, 2013; Choc Children’s guidelines, 2010; RHSC recommendations, 2014; SIGN guidelines, 2014; STGs/EML (Paediatrics), 2013).
Table 3.4 shows the end result of the comprehensive literature search conducted in Chapter 2 on SAP recommendations based on the type of surgical procedure. If there was consensus on the SAP recommendations for a particular surgical procedure, a single statement was provided. If, however, there were discrepancies, the evidence-based recommendations were provided.
<table>
<thead>
<tr>
<th>TYPE OF SURGERY</th>
<th>SAP RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAR, NOSE AND THROAT (ENT) SURGERY</td>
<td></td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>SAP is not recommended</td>
</tr>
<tr>
<td>Adenoidectomy</td>
<td>SAP is not recommended</td>
</tr>
<tr>
<td>GENERAL SURGERY</td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>SAP is highly recommended</td>
</tr>
<tr>
<td>Cefoxitin or ampicillin/subactam or cefazolin plus Metronidazole. If major reaction to beta-lactams; clindamycin plus gentamycin</td>
<td></td>
</tr>
<tr>
<td>Cefoxitin, cefotetan, cefazolin plus metronidazole Clindamycin plus aminoglycosides or aztreonam or fluoroquinolones</td>
<td></td>
</tr>
<tr>
<td>Colorectal surgery</td>
<td>SAP is highly recommended</td>
</tr>
<tr>
<td>Gentamycin plus metronidazole</td>
<td></td>
</tr>
<tr>
<td>Hernia-repair groin (Inguinal/femoral with or without mesh)</td>
<td></td>
</tr>
<tr>
<td>SAP is not recommended</td>
<td></td>
</tr>
<tr>
<td>Hernia-repair groin (Laparoscopic with or without mesh)</td>
<td></td>
</tr>
<tr>
<td>SAP is not recommended</td>
<td></td>
</tr>
<tr>
<td>Hernia repair (Incisional with or without mesh)</td>
<td></td>
</tr>
<tr>
<td>SAP is not recommended</td>
<td></td>
</tr>
<tr>
<td>Obstructed hernia repair (hernioplasty and herniorrhaphy)</td>
<td></td>
</tr>
<tr>
<td>Cefazolin, clindamycin, vancomycin</td>
<td></td>
</tr>
<tr>
<td>UROLOGY SURGERY</td>
<td></td>
</tr>
<tr>
<td>Circumcision</td>
<td>SAP is not recommended</td>
</tr>
<tr>
<td>MAXILLOFACIAL</td>
<td></td>
</tr>
<tr>
<td>Extractions</td>
<td>SAP is not routinely recommended in healthy patients</td>
</tr>
</tbody>
</table>

SAP = SAP. As adapted from the different resources used (Choc Children’s Guidelines, 2015, ASHP Therapeutic Guidelines, 2013, Paediatric STGs/EML, 2013).
3.10.3 **Appropriate dose of the selected SAP**

Based on the comprehensive literature search performed (Choc Children’s guidelines, 2015; ASHP, 2013; Paediatric STGs/EML, 2013) Table 3.5 indicates the recommended doses/dosing range used per SAP agent for this study.

SAP should be administered in an appropriate dose to achieve adequate serum and tissue concentration for the time interval during which the surgical site is open. Paediatrics weighing more than 40kg will surpass the maximum recommended dosage for paediatrics and should use adult dosages (Anderson *et al*, 2016).
### Table 3.5: Recommended SAP dosages

<table>
<thead>
<tr>
<th>ANTIMICROBIAL</th>
<th>IV DOSE (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/sulbactam</td>
<td>50</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>50</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>30</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>25-30 (max 1g)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>50</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>50</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>40</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>40</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>50-75</td>
</tr>
<tr>
<td>Cefepime</td>
<td>50</td>
</tr>
<tr>
<td>Ciproflaxacin</td>
<td>10</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>10</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>15</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>6</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>2.5</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>10</td>
</tr>
</tbody>
</table>
| Metronidazole               | 10-15
  Neonates weighing
  $<1200$ g = 7.5 |
| Moxifloxacin                | 10              |
| Piperacillin-tazobactam     | Infants 2–9 mo: 80 mg/kg of the piperacillin component
  Children >9 mo and $\leq 40$ kg: 100 mg/kg of the piperacillin component |
| Vancomycin                  | 15              |
3.10.4 Timing of administration of the SAP agent

Based on the comprehensive literature review performed (Anderson et al, 2016, Salkind et al, 2011, ASHP, 2013) the researcher decided that the most optimal evidence-based time for SAP administration is within 60 minutes prior to surgical incision, except during the use of fluoroquinolones and vancomycin, where administration of over one to two hours is recommended.

3.10.5 Redosing of the SAP agent

During either surgical procedures surpassing two half-lives of the drug or excessive blood loss (more than 1500 ml), intra-operative redosing is necessary to ensure adequate serum and tissue concentrations. Redosing may also be necessary in patients with a shortened antimicrobial half-life, such as extensive burn patients. On the contrary, in patients with a prolonged half-life, such as renal failure patients, redosing is not required. The SAP dosing interval is measured from the time of the preoperative dose (Anderson et al, 2016).

Most study results support a single dose of SAP within one hour prior to incision. SAP should be redosed at one to two times the half-life of the drug.

Based on the comprehensive literature review performed (Salkind et al, 2011, ASHP, 2013; Choc Children’s guidelines, 2015; Paediatric STGs/EML, 2013) the following intra-operative recommendations were used in this study, as seen in Table 3.6.
Table 3.6: Intra-operative reducing of SAP

<table>
<thead>
<tr>
<th>ANTIMICROBIAL</th>
<th>INTRA-OPERATIVE REDOSING (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/sulbactam</td>
<td>2-3</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>2</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>4</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>4</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>4</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>3</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>2-3</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>6</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>N/A</td>
</tr>
<tr>
<td>Cefepime</td>
<td>4</td>
</tr>
<tr>
<td>Ciproflaxacin</td>
<td>N/A</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>6</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>N/A</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>N/A</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>8</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>N/A</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>6</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>N/A</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>2</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Recommended redosing intervals marked as “not applicable” (NA) are based on typical case length; for unusually long procedures, where redosing may be needed.
3.10.6 Discontinuation of the SAP agent

Based on the comprehensive literature review performed a discontinuation time of within 24 hours post-surgery is recommended. However, the society of thoracic surgeons recommend SAP continuation up to 48 hours after the completion of cardiothoracic surgery (Anderson et al, 2016; Salkind et al, 2011).

3.11 RELIABILITY, VALIDITY AND BIAS OF DATA

3.11.1 Pilot test for the retrospective aspect

As the data collection sheet had never been applied in practice, a pilot test was conducted to establish its efficacy. The purpose of this was to ensure that the data collection sheet was sufficient and contained every aspect that the researcher wanted to address in the study. By performing a pilot test on the data collection sheet the researcher was able to highlight any shortcomings, mistakes, unnecessary or insufficient aspects and to correct and adjust the data collection sheet accordingly. The pilot test was conducted once the protocol received ethical clearance.

3.11.2 Pilot test for the survey

As this survey had never been applied in practice, a pilot test was performed to find out whether or not it would be effective in practice. The pilot test was performed on medical practitioners who represented the intended sample. The purpose was to ensure that the survey was sufficient and contained every aspect that needed to be addressed in the study. The pilot test on the survey highlighted any shortcomings, errors, unnecessary or insufficient aspects. The survey was corrected and adjusted accordingly.

A retrospective interview was performed to ensure that the survey was understood correctly. The pilot test was done once the protocol received ethical clearance.

3.11.3 Reliability

Reliability is a measure of precision (Cherry, 2014) and refers to the consistency of a measure (Gravetter & Forzano, 2011). Inter-rater reliability is used to assess the degree to which different observers give consistent estimates of the same phenomenon (Zanarini, Frankenburg, Chauncey & Gunderson, 1987). To ensure precision, only data obtained from the data collection form and survey was used. To ensure accuracy of all information collected on the data collection form, it was double-checked by the researcher’s supervisor, before it was
electronically captured onto the data collection Microsoft Excel® spreadsheets. All errors identified were checked and discussed with the supervisor and another independent researcher.

### 3.11.4 Validity

Validity is a measure of accuracy (Cherry, 2014) and refers to whether the study was able to scientifically answer the questions that it was intended to answer (Gravetter et al., 2011). Internal validity is concerned with correctly concluding that an independent variable is responsible for variation of the dependent variable and can be affected when research participants try to figure out what is expected of them and perform accordingly (Kirk, 2009). External validity describes whether the causal relationship discovered can be generalised to other people, times and contexts (Rothwell, 2005). Validity was ensured by the use of a pilot-tested data collection sheet and a survey, which focused on the specific aim and objectives used to answer the research question and objectives. Only data obtained from the data collection form and survey for analysis was used to ensure precision. To ensure accuracy all information collected on the data collection form was double-checked. All errors identified were checked and discussed with the supervisor and another independent researcher.
### Table 3.7: Threats to Internal Validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to current study</th>
<th>What will be done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical Regression</td>
<td>Occur when researchers attempt to statistically equate groups.</td>
<td>Will occur during the study, because research participants have pre-existing differences.</td>
<td>Utilise analysis of covariance (ANCOVA) techniques that attempt to control statistically for pre-existing differences between the groups being studied.</td>
</tr>
<tr>
<td><strong>Data Interpretation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect Size</td>
<td>Involves the incorrect interpretation of statistical significance and related failure to interpret confidence intervals.</td>
<td>P-Values can be over- or under-interpreted if the sample size is not correct.</td>
<td>Statistician will be consulted to accurately define statistical significance of the data obtained.</td>
</tr>
<tr>
<td>Illusory Correlation</td>
<td>The tendency to overestimate the relationship between variables. This usually relates to confirmation bias.</td>
<td>Researcher can over or under estimate the relationship between variables.</td>
<td>External statistician will be consulted, so that predetermined views of the researcher has limited influence on the analyses of the data obtained.</td>
</tr>
</tbody>
</table>
Table 3.8: Threats to External Validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What will be done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Design / Data Collection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity</td>
<td>Refers to the extent to which the findings can be generalised from the sample group towards a larger target population.</td>
<td>The researcher could assume that the accessible population is representative of the target population.</td>
<td>Data collected will be specific to those who underwent surgical procedures in the four specified disciplines. Comparisons will not be drawn between those patients that participate in the study and the remaining study population, due to the difference in variables.</td>
</tr>
<tr>
<td>Ecological Validity</td>
<td>The extent to which the findings from a given study can be generalised across settings, conditions, variables and contexts.</td>
<td>Will influence the study, as the data and final results are dependent on the setting and location it which they are obtained in.</td>
<td>Researcher will not attempt to minimise this effect, as the aim of the study is focused within this specific context. Future research should aim to generalise to different setting where surgical prophylaxis is used.</td>
</tr>
<tr>
<td><strong>Data Analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity</td>
<td>Occurs when a researcher analyses a subset of data, the data from this subset is less likely to be generalised, compared to when the total sample would have been used.</td>
<td>Limited influence, as the total sample selected during the data collection phase, will be utilised during the data analysis phase of the study.</td>
<td>Where possible, standardised norms will be used so that variables can be transferable to a different context.</td>
</tr>
<tr>
<td>Specificity of variables</td>
<td>Relates to aspects such as location, time and type of participants used during the study.</td>
<td>Can influence external validity when variables are categorised using local norms.</td>
<td></td>
</tr>
<tr>
<td><strong>Data Interpretation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity, ecological validity and temporal validity</td>
<td>See internal validity.</td>
<td>Can occur when the researcher over-generalise the data obtained.</td>
<td>Results obtained will as comprehensively as possible be compared to extant literature so that the results can be placed in a realistic context.</td>
</tr>
</tbody>
</table>
3.11.5 Bias

Bias can be defined as any systematic error with a tendency for selectivity or influence, meaning that the research findings deviate from the ‘true findings’. Bias can occur at any stage of the research (Pannucci & Wilkins, 2010). Bias was ruled out and limited by using the data collection sheet after the pilot test has been successfully completed. As noted during the discussion on internal and external validity, various biases could have an influence on the current research study. These have been accounted for and, as far possible, various techniques will be employed to decrease or minimise the effect of bias on the data obtained.

Sampling bias occurs when the sample is collected in such a way that some members of the intended population are less likely to be included than others. This effect was minimised by including all paediatric surgical patients who underwent surgery from the paediatric surgical ward who met the inclusion criteria in this study. Analytical bias results from differences in methods and techniques used to evaluate the results. All results were analysed and evaluated using the same method and technique to capture and analyse data.
### Table 3.9: Threats to bias

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What will be done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation Bias</td>
<td>Occurs when the protocol designed for the intervention is not followed in the intended manner (also known as protocol bias)</td>
<td>Can occur if the protocol used for all patients are not the same, i.e. time of measurement, method of measurement.</td>
<td>The researcher will follow the same protocol throughout the research.</td>
</tr>
<tr>
<td>Researcher Bias</td>
<td>Occurs when the researcher has a personal bias/preference towards a particular result</td>
<td>The researcher may create predetermined hypothesis regarding the results that will be obtained.</td>
<td>The researcher will not discuss any pre-conceived notions regarding the possible results.</td>
</tr>
<tr>
<td></td>
<td>Usually occurs when the researcher evaluates open-ended responses and allows his/her prior knowledge of the research participants to influence the scores given.</td>
<td>No influence, as data analysis will be done by an objective statistician with no prior knowledge relating to the participants, with the use of objective data given to him.</td>
<td></td>
</tr>
<tr>
<td>Matching Bias</td>
<td>Occurs when the researcher only group patients after the data on the total sample group has been collected.</td>
<td>No influence, as research participants will already be grouped into the sample group during the data collection phase of the research study.</td>
<td></td>
</tr>
<tr>
<td>Confirmation Bias</td>
<td>Occurs when confirmation and conclusions made from the current data are overly consistent with the preliminary hypothesis.</td>
<td>Limited influence, as this study will not be approached with a predetermined hypothesis (due to a lack of previous studies), but rather a research question.</td>
<td></td>
</tr>
</tbody>
</table>

### 3.12 ETHICAL CONSIDERATIONS

Managerial approval from both hospitals were obtained. Ethical approval from Sefako Makgatho Health Sciences University research ethics committee (SMUREC) (SMUREC/H/185/2015: PG) as well as ethical clearance from the research operations committee of the private hospital used (UNIV-2016-0013) to perform the study. Personal patient information remained confidential, with a study number being assigned to each patient. Only the study number was used during data collection. All data was collected in the hospitals respectively, and the patient charts were not taken out of the hospital premises. All
documentation, captured data and data collection tools and informant consent forms (including incomplete forms) were locked away in the pharmacy department to be kept safe for 5 years under lock and key and supervision. After 5 years have past it will be destroyed in a suitable manner.

3.12.1 Retrospective aspect consent

Previous data obtained of patients who underwent surgery were studied, interpreted, analysed and finally documented, thus no patient consent was required.

3.12.2 Prospective aspect consent

Medical practitioners had to read and sign the consent form before they were allowed to participate in this study. No survey completed without a signed informed consent was used in this study. Consent was given for both the survey and the recording of the retrospective interview and medical practitioners could withdraw from the study at anytime.

3.13 CONCLUSION

The study was conducted on both paediatric surgical patient files and medical practitioners working with paediatric surgical patients at both the teaching and private hospitals used. This study comprised two different study designs, namely a retrospective charts review and a descriptive cross-sectional qualitative design. Data were captured using a data collection sheet for the retrospective aspect of the study, and a survey was used for data collection of the prospective aspect. Considerable thought and implementation went into the data collection process in order to obtain reliable and valuable results. It can be concluded that the methodology used was a perfect fit for the purpose of this study.

3.14 SUMMARY

A systematic discussion of the study’s methodology was given, as well as informative descriptions of the study design, study site and sample selection. The data collection instruments used in this study were described. This chapter ended with a definition and explanation of reliability, validity and bias, as well as the necessary ethical considerations, implemented throughout the study period. Chapter 4 will cover the results obtained in this study with a relevant discussion of the findings.
CHAPTER 4
MANUSCRIPT

4.1 INTRODUCTION

The results and discussion of this study is presented in the format of two manuscripts.

**Manuscript one** titled “Surgical antimicrobial prophylaxis in paediatrics: South Africa - "Comparer deux mondes différents"” will be submitted to the Journal of Antimicrobial Chemotherapy. A cover letter to the Editor-in-Chief of the selected journal is provided (see Appendix 7), followed by the guidelines for authors (see Appendix 9).

**Manuscript two** titled “Impetus for change: knowledge and perception of medical practitioners on surgical antimicrobial prophylaxis use in paediatrics, a multi-centre approach, South Africa” will be submitted to the Southern African Journal of Infectious Diseases. A cover letter to the Editor-in-Chief of the selected journal is provided (see Appendix 8) followed by the guidelines for authors (see Appendix 10).
4.2 MANUSCRIPT ONE

Surgical antimicrobial prophylaxis in Paediatrics: South Africa - “Comparer deux mondes différents”

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ABSTRACT

Objectives: To access compliance to surgical antimicrobial prophylaxis (SAP) guidelines for paediatrics undergoing surgery in one of four surgical sub-specialities (urology, ENT, maxillofacial and general surgery).

Methods: An eight month retrospective chart review study was conducted via a multi-centre and multi-health care system approach in South-Africa; DGMAH, a teaching hospital and a private hospital was used. The prescriptions of antimicrobials as SAP were compared to current SAP guidelines on appropriate antimicrobial selection, dosing, timing of administration, redosing and duration of treatment.

Results: The retrospective aspect utilised charts dated between February and August 2015. A total of 224 charts we reviewed, 112 each from the teaching and private hospitals respectively. The majority (p=1.000) of paediatrics from both hospitals received SAP when indicated (77.27% and 100% respectively). The minority of paediatrics from both hospitals received antimicrobials without an indication (21.11% and 45.88% respectively). Compliance to all five of the criteria was not met by either hospital. Overall, the teaching hospital met the most criteria (three out of five) in 58.82% of paediatrics.

Conclusion: The current SAP practices in South Africa’s teaching and private hospitals diverge from current SAP Guidelines. Inappropriate overuse of SAP occurs in both hospitals, whilst underuse is limited to the teaching hospital. Full compliance to the five criteria was not met by either hospital. Non-compliance was largely attributed to inappropriate selection and dosing. Quality improvement interventions, continued surveillance and local standardised evidence-based SAP guidelines are needed.

KEYWORDS: Surgical antimicrobial prophylaxis, paediatrics, South African health care, antimicrobial resistance, compliance, guidelines.
INTRODUCTION

Globally, antimicrobial resistance (AMR) threatens not only the fundamentals of modern medicine, but also the sustainability of an effective global health response to infectious diseases.\textsuperscript{1} Thus, a global action plan was initiated.\textsuperscript{2} In support of the global action plan, a high-level meeting, the fourth of its kind, was held by the General Assembly of the United Nations, primarily to summon and maintain strong national, regional and international political commitment in addressing AMR both comprehensively and multi-sectorally, and to improve awareness thereof.\textsuperscript{3}

Antimicrobials are the most commonly prescribed medicine, especially amongst paediatrics.\textsuperscript{4} Thus, an increasing desire to reduce practice pattern variation of antimicrobials has grown. One of the focus areas is surgical antimicrobial prophylaxis (SAP).\textsuperscript{5} SAP is a vital quality indicator, which illustrates how appropriately antimicrobials are utilised during surgery.\textsuperscript{6} The overall goal for SAP is to prevent surgical site infections (SSIs) by using an antimicrobial that is safe and cost-effective with a relevant spectrum of activity.\textsuperscript{7} Although half of SSIs are preventable, it remains not only one of the most common complications of paediatric surgery, but it is also associated with significant morbidity and mortality.\textsuperscript{8,9} One of the key interventions to reduce the incidence thereof is appropriate use of SAP.\textsuperscript{8} Furthermore, increasing evidence suggests that inappropriate use thereof (including selection, dosing, timing of administration and duration of use) contributes to the emergence of resistance.\textsuperscript{9,10}

Current available literature and recommendations on SAP pertain mostly to adults.\textsuperscript{9} Due to the inherent challenges in paediatric research, it is often observed in medicine that paediatric practices tends to follow those used in adults.\textsuperscript{5} This creates a void in knowledge, specifically pertaining to SAP indications in the paediatric population.\textsuperscript{11} Although paediatrics are commonly prescribed SAP, the trend of SAP use is poorly understood.\textsuperscript{9}

South Africa, which is situated at the southern tip of Africa, is a large (±1.2 million km\textsuperscript{2}), upper middle income country constituted of a two-tiered health system, i.e. the public and private health care systems. An estimated 54 million people comprise the population of South Africa.\textsuperscript{12} The public system is funded by government and constitutes the majority of health care, catering for the lower- to middle-income residents.\textsuperscript{13} One of the legs of the public health care system is teaching hospitals, also known as academic or tertiary hospitals.\textsuperscript{12} They provide specialist and sub-specialist care, perform advanced diagnostic proce-
dures and therapy, but more importantly serve as training institutions for health care practitioners (HCPs).13,14 Private healthcare services consist of HCPs, who provide privately-based services, normally funded by middle- to higher-income residents or medical aids (Figure 1).13,14,15

<table>
<thead>
<tr>
<th>SOUTH AFRICAN HEALTH CARE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Public health care</td>
<td>Private health care</td>
</tr>
<tr>
<td>• Funded by government</td>
<td>• Funded by individuals or medical aids</td>
</tr>
<tr>
<td>• ± 87 000 beds</td>
<td>• ± 31 000 beds</td>
</tr>
<tr>
<td>• Serves 82.5% (42 million) of the population</td>
<td>• Serves 17.5% (8.2 million) of the population</td>
</tr>
<tr>
<td>• Average spend per person per annum ZAR2857</td>
<td>• Average spend per beneficiary per annum ZAR12 859</td>
</tr>
<tr>
<td>• Annual expenditure ZAR122.4-billion</td>
<td>• Annual expenditure ZAR120.8-billion</td>
</tr>
<tr>
<td>• Mostly paper based system</td>
<td>• Electronic based system</td>
</tr>
</tbody>
</table>

Abbreviation used: ZAR=South African Rand

Figure 1: An overview of the South African health care system

NATIONAL TRENDS

In support of the global response, an AMR National Strategy Framework for 2014-2024 was developed by the National Department of Health (NDoH) in 2014. Prior to the AMR strategic framework a domain of patient safety, clinical governance and clinical care was established in 2011, termed the National Core Standards (NCS) for Health Establishments. This domain provided guidelines on how to ensure quality nursing, clinical care and ethical practice.16 By ensuring appropriate use of SAP, collateral damage is restricted, highlighting the importance thereof.16
KEY FOCUS

Globally, there is substantial variability in the overall and appropriate use of SAP in paediatrics at hospital level. Worldwide, medical prophylaxis used in paediatrics accounts for almost two thirds (64.3%) of all prophylactic antimicrobial prescribing. A study conducted in Italy, identified reasons for concern, as SAP administration was around 80% (81%) for paediatrics with an indication, of which only 8% was administered appropriately.\(^{17}\) Although a lower percentage (52%) of administration was found in the United States of America (USA), overall appropriateness was higher (64.6%). In Africa more than 80% (82.9%) of paediatrics receive prophylactic antimicrobials. In the Phillipines, a developing country like South Africa, a low percentage of paediatrics (13%) complying to all of the criteria (selection, dose, route, timing, reducing and duration) receive SAP.\(^{18}\) In Greece, although the majority of paediatrics (96.5%) with an indication received SAP, appropriateness was less than 6% (5.6%).\(^{19}\)

CONTRIBUTION TO THE FIELD

Limited research, studies and guidelines have been conducted and developed on SAP use in South Africa.\(^{20}\) However, no recently conducted comparable studies on SAP use in South Africa’s paediatric surgical population could be found, underlying the importance of this study to address this gap. To the best of our knowledge, this study was the first to specifically focus on the compliance to guidelines of SAP used in paediatric surgery in both health care systems of South Africa, thus innovatively highlighting the importance of optimised use of SAP to limit AMR.

Within the South African health care system, SAP use in paediatrics is not being actively surveyed, monitored nor reported on, creating a need for a study to investigate current practices of SAP use in paediatrics. The aim of this study was to access compliance to SAP guidelines for paediatrics undergoing surgery in one of four surgical sub-specialities. This study was designed to meet the following objectives: to describe SAP use in paediatrics at a teaching and a private hospital and to compare the compliance thereof to current national and international SAP guidelines.
METHODS

Study design, setting and study period

A retrospective chart review was conducted over an 8 month period, by studying the pre-
scribing patterns of discharged paediatrics requiring surgery in one of four surgical sub-
specialities, namely urology, Ear, Nose and Throat (ENT), maxillofacial or general surgery. 
The teaching hospital is one of four in the province and situated in Ga-Rankuwa, Pretoria, 
Gauteng Province. This is a 1,650-bed hospital with 28 clinical departments, 20 approved 
ICU beds, 60 high care beds and 17 surgical theatres, providing services to an estimated 
1.7 million people from the surrounding area. During the study period the teaching hospital’s 
paediatric surgical ward consisted of four cubicles with a total of 40 beds. The private 
hospital is situated in Pretoria, Gauteng Province, with 358 beds and 17 wards, two ICUs, 
two high care facilities and four surgical theatres. During the study period this hospital did 
not have a dedicated paediatric surgical ward and paediatrics were allocated to wards 
based on the type of surgery that they underwent.

Study population and sample

Sampling was done to include both male and female paediatrics from the teaching and 
private hospitals who were aged 12 years old or younger, and who underwent surgical 
procedures for the indications most frequently encountered in paediatrics in the four sur-
gical sub-specialities, before the 6th of August 2015.

Data assessment protocol

The appropriateness of the SAP was evaluated with regards to indication, administration 
and compliance to SAP guidelines. Compliance was defined as: appropriate selection of 
SAP, dose, timing of administration, re-dosing and duration of use. All five of the criteria 
had to be met, in order for SAP use to be deemed compliant (Table 1).
Table 1: Five criteria used to access compliance to guidelines

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Drug</td>
<td>Appropriate SAP selected for the surgical procedure performed&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2 Dose</td>
<td>Appropriate dose of the selected SAP administered based on participant’s body weight (in kg)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>3 Timing</td>
<td>SAP administered within 60 minutes prior to incision&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4 Redosing</td>
<td>If required, redose at one to two times the half-life of the drug&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>5 Duration</td>
<td>Within 24 hours post-surgery</td>
</tr>
</tbody>
</table>

Abbreviations used: SAP = surgical antimicrobial prophylaxis, <sup>a</sup> = based on SAP guidelines recommendations, <sup>b</sup> = except during the use of fluoroquinolones and vancomycin, where administration over one to two hours was recommended.

As adapted from<sup>7,17,23,24,25,26,27</sup>

In order to define in which surgical procedures SAP is indicated, a comprehensive literature search was conducted, using the following search engines; Scopus®, Science Direct®, Ebsco Host®, PubMed®, Medline® and Google Scholar®.

Keywords were identified that were used in the internet search related to SAP use in pediatrics.

The most appropriate literature sources were chosen from the results in order to fulfil the research objectives.


**DATA COLLECTION AND ANALYSIS**

The data collection form was developed and compiled by the researcher, based on several previously published studies,<sup>5,6,9,10,17,28</sup> with slight modifications to meet the objectives of
the study., The form recorded the pediatrics' demographics, the primary diagnosis and clinical data which included the type of surgery, if SAP was administered and if so, the name, ICD-10 code, ATC code, dosage, route, time and date of administration and discontinuation was recorded. Data from the collection forms were imported into Statistical Analysis System (SAS®). All statistical analyses were performed on SAS® (SAS® Institute Inc, Carey, NC, USA), release 9.4, with 95% confidence intervals (CIs), including the calculation of descriptive statistics by using the Fisher’s exact test (f) for comparisons of percentages, and the Student’s t test (t) for comparisons of mean values. All tests were two-sided and p-values ≤ 0.05 were considered significant.

ETHICAL CONSIDERATIONS

Data collection commenced after ethical consideration was granted from Sefako Makgatho Health Sciences University Research Ethics Committee (SMUREC) (SMUREC/H/185/2015: PG) as well as from the Research Operations Committee of the private hospital used (UNIV-2016-0013). Confidentiality and anonymity of paediatric information was maintained throughout the study, by means of allocating study numbers.

RESULTS

During the 8 month study period, a total 701 paediatric charts were reviewed; 164 from the teaching hospital and 537 from the private hospital. Thereafter a total of 224 charts, 112 from each hospital, were sampled. At the teaching hospital, paper-based charts are used, which are kept in the hospital filing room once a patient is discharged. In the private hospital a global electronic-based system (Systems, Applications and Products (SAP®) in data processing) is used.29

Demographics

Both groups were similar in terms of weight and gender (p <0.963 and p <0.591 respectively) but there was a statistically significant difference in terms of age (p <0.005) (Table 2). The mean age (SD, IQR) for the teaching hospital was 5.45 years (±3.1, ±3.00-7.5) compared to the private hospital’s 4.32 years (±2.7, ±2.0-6.0).
Table 2: Demographics of the study participants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Teaching n (%)</th>
<th>Private n (%)</th>
<th>Total n (%)</th>
<th>p-values f,t</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of paediatrics</td>
<td>112 (50)</td>
<td>112 (50)</td>
<td>224 (100)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>65 (58)</td>
<td>60 (54)</td>
<td>224 (100)</td>
<td>&lt;0.591f</td>
</tr>
<tr>
<td>Female</td>
<td>47 (42)</td>
<td>52 (46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (NICHD)</td>
<td></td>
<td></td>
<td>224 (100)</td>
<td>0.0099*f</td>
</tr>
<tr>
<td>Neonate</td>
<td>1 (0.89)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant</td>
<td>4 (3.57)</td>
<td>2 (1.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toddler</td>
<td>14 (12.50)</td>
<td>35 (31.25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early childhood</td>
<td>46 (41.07)</td>
<td>41 (36.61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle childhood</td>
<td>42 (37.50)</td>
<td>32 (28.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early adolescents</td>
<td>5 (4.46)</td>
<td>2 (1.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td>212a (100)</td>
<td>&lt;0.963t</td>
</tr>
<tr>
<td>Mean (± SD)</td>
<td>19.69 (±9.2)</td>
<td>19.76 (±9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>18.00 (13.5-23.0)</td>
<td>16.50 (14.0-24.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: NICHD = ages were categorised according to paediatric terminology developed by the Eunice Kennedy Shriver National Institute of Child Health and Human Development f = Fischer exact test, t = t-test, a = 102 Public, 110 Private, *statistically significant difference.

Surgical procedures performed

A total of 224 surgeries were performed, 112 for each hospital respectively. In both hospitals the majority of paediatrics who underwent ENT surgery were diagnosed with chronic adenotonsillitis (30, 54.55%; 90, 92.78%; for the teaching and private hospital respectively).

In the teaching hospital, the majority were diagnosed with undescended testicles (UDTs) (12, 36.36%) in urology, compared to redundant, prepuce phimosis and paraphimosis in the private hospital (7, 87.50%). In both hospitals, all maxillofacial surgical paediatrics (13, 100%; 4, 100% for the teaching and private hospital respectively) presented with dental caries. Acute appendicitis (5, 45.45%; 2, 66.67%), was the main diagnosis for those who
underwent general surgery respectively for both the teaching and the private hospital. It is evident from the data presented above that there were significant differences in the types of procedures performed for the disciplines ENT (p <0.0001) and urology (p =0.0157).

There was a statistically significant difference in the total number of surgeries performed per surgical discipline between the two study populations (p <0.0001) (Table 3).

Table 3: Total number of surgeries performed per surgical discipline

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Teaching n (%)</th>
<th>Private n (%)</th>
<th>Total n (%)</th>
<th>p-Value f</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Per discipline</td>
<td>Overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>55 (49.11)</td>
<td>97 (86.61)</td>
<td>152 (67.86)</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>Urology</td>
<td>33 (29.46)</td>
<td>8 (7.14)</td>
<td>41 (18.30)</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>Maxillofacial</td>
<td>13 (11.61)</td>
<td>4 (3.57)</td>
<td>17 (7.59)</td>
<td>0.0408*</td>
</tr>
<tr>
<td>General surgery</td>
<td>11 (9.82)</td>
<td>3 (2.68)</td>
<td>14 (6.25)</td>
<td>0.0498*</td>
</tr>
<tr>
<td>Total</td>
<td>112 (100)</td>
<td>112 (100)</td>
<td>224 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: ENT = Ear, Nose and Throat, f = Fisher Exact test, * statistically significant difference, ** highly statistically significant difference.

SURGICAL ANTIMICROBIAL PROPHYLAXIS USAGE

Antimicrobials used for surgical antimicrobial prophylaxis

A statistically significant difference was seen in the antimicrobial selection for the two hospitals (p <0.0001). The vast majority (32, 88.88%) from the teaching hospital received cefazolin, appropriately selected in one third (5, 29.41%) of the paediatrics, however, under-dosed in 60% (3). Further to this, 8.33% (3) of paediatrics, received amoxicillin-clavulanic acid and one paediatric received cefuroxime (2.77%). To the contrary, in the private hospital the vast majority received amoxicillin-clavulanic acid (47, 88.68%) and two paediatrics received ceftriaxone (3.77%). Four paediatrics received one of the following; cefuroxime (1.89%), azithromycin (1.89%), clindamycin (1.89%), and metronidazole (1.89%), respectively (Table 4).
<table>
<thead>
<tr>
<th>System</th>
<th>Class</th>
<th>ATC code</th>
<th>INN</th>
<th>Teaching n (%)</th>
<th>Private n (%)</th>
<th>p-valuef</th>
</tr>
</thead>
<tbody>
<tr>
<td>J</td>
<td>Anti-infectives for systemic use</td>
<td>J01</td>
<td>Anti-bacterials for systemic use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01C</td>
<td>Beta-lactam anti-bacterials</td>
<td>J01CR</td>
<td>Combo of penicillins, including beta-lactamase inhibitors</td>
<td>J01CR02</td>
<td>Amoxicillin-clavulanic acid</td>
<td>3 (8.33)</td>
</tr>
<tr>
<td>J01D</td>
<td>Other beta-lactam anti-bacterials</td>
<td>J01DB</td>
<td>First-generation cephalosporin</td>
<td>J01DB04</td>
<td>Cefazolin</td>
<td>32 (88.88)</td>
</tr>
<tr>
<td>J01DC</td>
<td>Second-generation cephalosporin</td>
<td>J01DC02</td>
<td>Cefuroxime</td>
<td>1 (2.77)</td>
<td>1 (1.89)</td>
<td>1.0000</td>
</tr>
<tr>
<td>J01DD</td>
<td>Third-generation cephalosporin</td>
<td>J01DD04</td>
<td>Ceftriaxone</td>
<td>0 (0)</td>
<td>2 (3.77)</td>
<td>0.5128</td>
</tr>
<tr>
<td>J01F</td>
<td>Macrolides, lincosamides and streptogramins</td>
<td>J01FA10</td>
<td>Azithromycin</td>
<td>0 (0)</td>
<td>1 (1.89)</td>
<td>1.0000</td>
</tr>
<tr>
<td>J01FF</td>
<td>Lincosamides</td>
<td>J01FF01</td>
<td>Clindamycin</td>
<td>0 (0)</td>
<td>1 (1.89)</td>
<td>1.0000</td>
</tr>
<tr>
<td>J01X</td>
<td>Other antibacterials</td>
<td>J01XD01</td>
<td>Metronidazole</td>
<td>0 (0)</td>
<td>1 (1.89)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>36 (100)</td>
<td>53 (100)</td>
<td></td>
</tr>
</tbody>
</table>

f= Fisher Exact test, ** highly statistically significant difference.

A statistically significant difference (p= 0.0399; p= 0.0130) was noted between the two hospitals, for both paediatrics who did not receive any antimicrobials as SAP and those who received one antimicrobial as SAP respectively. The majority, almost 70% (76, 67.86%), of
paediatrics from the teaching hospital, and just over 50% (59, 52.68%) for the private hospital did not receive any antimicrobials as SAP. Despite being construed to a small population (3, 2.86%; 1, 0.89% for the teaching and private hospital respectively) more antimicrobial combination use was seen in the teaching hospital (Figure 2).

**Figure 2: Number of antimicrobials administered**

a= Combination of amoxicillin-clavulanic acid and cefazolin, b= Combination of azithromycin and metronidazole, Fischer Exact test, *significant

**Assessment of surgical antimicrobial prophylaxis use**

In the teaching hospital, of the 112 paediatrics in the public hospital, SAP was indicated in 22 (19.64%) paediatrics, however, SAP was administered in 17 (77.27%). Compared to the private hospital where of the 112 paediatrics, SAP was indicated and administered in three (2.67%) paediatrics. A statistically significant difference was seen where SAP was not indicated nor administrated (p = 0.0003) (Table 5).
Table 5: Assessment of Surgical Antimicrobial Prophylaxis use

<table>
<thead>
<tr>
<th>Hospital</th>
<th>SAP indicated n=112 (100)</th>
<th>Administered</th>
<th>p-valuef</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teaching</td>
<td>22 (19.64)</td>
<td>17 (77.27)</td>
<td>1.000</td>
</tr>
<tr>
<td>Private</td>
<td>3 (2.67)</td>
<td>3 (100)</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>SAP not indicated n=112 (100)</td>
<td>Not administered</td>
<td>p-valuef</td>
</tr>
<tr>
<td>Teaching</td>
<td>90 (80.36)</td>
<td>71 (78.89)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Private</td>
<td>109 (97.32)</td>
<td>59 (54.12)</td>
<td></td>
</tr>
<tr>
<td>Total compliance</td>
<td>88 (78.57)</td>
<td>62 (55.36)</td>
<td>0.0003**</td>
</tr>
</tbody>
</table>

Abbreviations used: SAP = Surgical antimicrobial prophylaxis, f = Fischer Exact test, ** highly significant

Compliance to surgical antimicrobial prophylaxis

SAP was indicated and administered in three paediatrics (17, 77%) for the teaching hospital and 100% for the private hospital. Overall compliance to all five of the criteria (antimicrobial selection, dosing, timing of administration, redosing and duration) was not achieved by either hospital. Almost 60% (10; 58.82%) of paediatrics treated at the teaching hospital met three of the five criteria (Table 6). Comparative results between the teaching and private hospitals were demonstrated for selection and dosing (p = 0.5395, p = 1.0000 respectively). Compliance in terms of timing was only met by eight (47.06%) paediatrics at the teaching hospital. Of the three paediatrics from the private hospital, one received SAP 10 minutes prior to incision, one at the time of incision and the last paediatric’s timing of administration was not specified. Full compliance to redosing and duration of treatment was achieved by both hospitals.
Table 6: Compliance to the five criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Teaching n=17 (100)</th>
<th>Private n=3 (100)</th>
<th>p-value f</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Drug selection</td>
<td>5 (29.41)</td>
<td>0 (0)</td>
<td>0.5395</td>
</tr>
<tr>
<td>2 Dose</td>
<td>1 (5.88)</td>
<td>0 (0)</td>
<td>1.0000</td>
</tr>
<tr>
<td>3 Timing</td>
<td>8 (47.06)</td>
<td>0 (0)</td>
<td>0.2421</td>
</tr>
<tr>
<td>4 Redosing</td>
<td>17 (100)</td>
<td>3 (100)</td>
<td>n/a</td>
</tr>
<tr>
<td>5 Discontinuation</td>
<td>17 (100)</td>
<td>3 (100)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

f = Fischer Exact test

DISCUSSION

Retrospectively, this study aimed to access compliance to current evidence-based SAP guidelines\textsuperscript{23,24,25,26,27} for paediatrics requiring surgery in one of four surgical sub-specialities (urology, ENT, maxillofacial and general surgery). To our knowledge, this was the first study of its kind performed in paediatrics via a multi-centre approach in South Africa.

Statistically significant differences were seen in the paediatric patient characteristics, between the two hospitals in terms of age (p <0.005), primary diagnosis (p <0.0001) and total number of surgeries performed (p <0.0001). The largest proportion (41.07 \% and 36.61\% for the teaching and private hospital respectively) of paediatrics from both hospitals were in their early childhood, based on the NICHD classification.\textsuperscript{30} Furthermore, more elective ENT surgeries, specifically due to chronic adenotonsillitis (54.55\% and 92.78\% for the teaching and private hospital respectively), were performed in the private hospital. This finding is supported by the statement that in the over-crowded, under-funded, under-staffed and resource-limited public healthcare system, where there is poor access to health- and specialist care, adeno-/tonsillectomy is typically reserved for paediatrics with severe sleep disordered breathing (SDB).\textsuperscript{31} Additionally, due to a high unemployment and poverty rate (25\%; 86.8\% respectively for the public and private hospitals) in South Africa, the burden of acute tonsillitis disease is higher compared to developed countries, and is commonly seen in paediatrics of lower socio-economic status. As the teaching hospital is located in a rural area of Gauteng, serving around 1.7 million patients,\textsuperscript{21} other factors that may result in this variation of adeno-/tonsillectomy rates seen, is the HCPs-to-population ratio and geographical access barriers. Private health care paediatric patients under the age of seven
years are more likely to undergo adeno-/tonsillectomies than their public health care counterparts. It is possible that parents paying for health care may feel entitled to command specific treatment, thereby prompting surgical management. Likewise, reimbursed HCPs may feel pressured to accept their demands.\textsuperscript{31}

The majority (67.86% and 53.57% respectively of the teaching and private hospital) of paediatrics from both study groups did not receive any antimicrobials as part of SAP, regardless of whether it was indicated or not. The overall use of SAP (32.14%; 47.32% for the teaching and private hospital respectively) by both hospitals is lower compared to Africa (81%) but similar to what is prescribed worldwide (64.3%).

ENT surgical procedures were performed for the majority (49.11%; 86.61% for the teaching and private hospital respectively) of paediatrics in both groups, where SAP is not routinely recommended (ASHP therapeutic guidelines, 2013). The absence of antimicrobials as part of SAP for these procedures are in line with current guidelines (ASHP therapeutic guidelines, 2013). Use of SAP (32.14%; 47.32% for the teaching and private hospital respectively) by both hospitals is lower compared to Africa (81%) and the worldwide use (64.3%).

SAP, when indicated, was administered to the majority of the paediatric patients (77.27%, 100% for the teaching and private hospital respectively). These results are higher than similar studies conducted in the USA (72.2%)\textsuperscript{9} and Italy (18%).\textsuperscript{17} Despite the aforementioned and being limited to a small percentage of study patients in the teaching hospital (22.73%), the absence of SAP administration in paediatrics with an indication raises reason for concern.

The inappropriate and overuse of SAP without an indication occurred in both hospitals (21.11%; 45.88% for the teaching and private hospital respectively), resulting in a statistically significant difference (p= 0.0003). Either of these non-compliances may unwontedly expose paediatrics to an increased risk of SSIs and/or ADEs respectively.\textsuperscript{17}

In the two categories regarding SAP use (i.e indication and administration; no indication nor administration respectively), the teaching hospital had the highest overall compliance (78.57%) compared to the private hospital (55.36%). These findings are both lower than Italy 82\%\textsuperscript{17} and the USA (93.8%).\textsuperscript{9}

Compliance to all five of the criteria (selection, dosing, timing of administration, redosing and duration) was not met by either hospital. However, the teaching hospital complied to the most criteria (three out of the five criteria) in almost 60% (58.82%) of paediatrics.
Of all patients that received SAP with an indication from the private hospital, none of the cases complied with current SAP guidelines with regards to appropriate antimicrobial selection. In contrast, nearly a third (29.41%) of all paediatrics treated in the teaching hospital received an appropriate selected antimicrobial. These results are much lower than similar studies conducted in New York (97.1%)
 and Singapore (57%). One of the significant contributing modifiable drivers to AMR, is the appropriate selection of antimicrobials. Cefazolin was the SAP of choice in the majority (88.89%) of paediatrics from the teaching hospital, in contrast to amoxicillin-clavulanic acid (88.68%) in the private hospital. Based on current guidelines, cefazolin is the antimicrobial of choice for the majority of surgical procedures that require SAP, as the general principle of SAP is to use an antimicrobial with the narrowest spectrum active against the most suspected pathogens. Current guidelines do not routinely recommended the use of amoxicillin-clavulanic acid, which may contribute to the emergence of AMR and would either lead to a lack of further response or preclude the use of this antimicrobial for severe infections. This result, however, confirms the finding that broad-spectrum antimicrobials are excessively and inappropriately prescribed as SAP. A study described amoxicillin-clavulanic acid as preventing post-tonsillectomy morbidity, by reducing symptoms induced by the healing inflammatory process.

A third (29.41%) of the paediatrics from the teaching hospital, that appropriately received cefazolin, was under-dosed in 60% of the cases. This result is lower than the 77.5% of under-dosing reported in Greece. One of the modifiable drivers of AMR is the sub-therapeutic dosing of antimicrobials. By optimising antimicrobial dosing a contribution to reversing AMR is made.

It is thus evident that the majority of non-compliance for both hospitals was due to inappropriate antimicrobial selection and dosing.

Timing of administration of SAP complied with guidelines in less than 50% of paediatrics from both hospitals (47.06%; 0% for the teaching hospital and private hospital respectively). The teaching hospital's findings are in line with findings from a similar study conducted in Italy (47%), whereas the private hospital’s findings are lower than the findings from a study conducted in Israel (32%). Both hospitals' results are lower than that of Greece (83.3%), Singapore (76%) and the USA (75%).

One of the common failures to SAP described in literature, is compliance to redosing and duration of treatment beyond the recommended 24 hours post-surgery.
in the prevention of SSIs or additional benefits has been demonstrated. Instead, an increased risk for adverse effects, worsening of AMR and health care cost exists.\(^8,10,17\) Full compliance to both redosing and duration of treatment was found in both hospitals. These findings were higher in Greece (62.5% and 47.1% for redosing and duration of treatment respectively).\(^8\)

This study found substantial variation of SAP use in the teaching and private hospitals, especially on SAP selection, illustrating that overall compliance to national and international SAP guidelines is poor, and that interventions are required. A possible explanation for the variation in SAP use between the teaching and private hospitals is the lack of paediatric-specific SAP guidelines, both internationally and in South Africa. Another factor that plays a role is the disagreement that exists between adult-derived consensus guidelines and paediatric-focused observational data.

**LIMITATIONS**

Due to a small sample size and being limited to only four surgical sub-specialities, due care should be given in the generalisation of the study results for SAP practices across South Africa’s two health care systems. This study did not investigate the cause and relationship of the results. Additionally hospital charts were used for data collection, thus accuracy would depend on the accuracy of the hospital files. Further studies are needed which will take these limitations into consideration.

**CONCLUSION**

SAP practices in South Africa’s teaching and private hospitals diverge from current guidelines. Inappropriate overuse of SAP occurs in both hospitals, whilst underuse is limited to the teaching hospital. Full compliance to the five criteria was not met by either hospital. Non-compliance was largely attributed to inappropriate selection and dosing. Although literature is limited, findings are consistent with existing literature describing variation in SAP use amongst paediatrics. The importance of proper use of SAP cannot be over-emphasised, as it contributes to AMR and is associated with a significant decrease in SSI-associated morbidity and mortality. Reasons for concern have been identified and thus quality improvement interventions, continued surveillance and local standardised paediatric SAP guidelines in South Africa are needed.
FUNDING

Sefako Makgatho Health Sciences University

TRANSPARENCY DECLARATIONS

None to declare.
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4.3 MANUSCRIPT TWO

Impetus for change: knowledge and perception of medical practitioners on surgical antimicrobial prophylaxis use in paediatrics, a multi-centre approach, South Africa

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KEYWORDS Surgical antimicrobial prophylaxis, paediatrics, South African health care, knowledge and perception, behavioural change, medical practitioners

ABSTRACT

OBJECTIVES: To assess the knowledge and perceptions of medical practitioners, regarding surgical antimicrobial prophylaxis (SAP) used in paediatrics.

METHODS: A prospective survey was conducted using a multi-centre and -health care system approach in South-Africa. Knowledge on pre- and post-operative SAP use in pediatrics in four surgical sub-categories (urology, ear, nose and throat, general and maxillo-facial surgery) was compared to current SAP guidelines.

RESULTS: Over a two month study period (March to April 2016), 33 surveys were completed, 18 from the teaching and 15 from the private hospital. Comparative results were seen in both study populations regarding the consideration of potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR due to the use of antimicrobials (55.55%, 66.67%, 77.77% and 66.67% for the teaching hospital respectively, compared to 66.67%, 73.34%, 80% and 53.34% for the private hospital respectively). However, a statistically significant difference (p=0.0363) between the two study populations, in terms of SAP costs consideration when prescribing SAP was noted. Variations in ready knowledge of the medical practitioners, for pre- and post-operative SAP, was noted for the four surgical sub-categories in both hospitals.

CONCLUSION: Areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing in paediatrics has been identified. The areas in
most need of improvement include; pre- and post-operative SAP administration. Standardisation of education on SAP in paediatrics should receive attention from statutory bodies in South Africa as medical practitioners require further education to enhance ready knowledge pertaining to SAP use in paediatrics.
INTRODUCTION

Internationally, antimicrobial resistance (AMR) is an increasingly serious threat to public health that requires action across all government sectors and society.\textsuperscript{1} Thus, a global action plan was initiated to curb the increasingly serious threat towards a post-antimicrobial era and to ensure a sustainable investment in defying AMR.\textsuperscript{2} Recently, a high-level meeting on AMR was held by the general assembly of the United Nations. The primary objective of this meeting was to summon and maintain strong national, regional and international political commitment in addressing AMR both comprehensively and multi-sectorally, and additionally to increase and improve awareness of AMR. This meeting also recalled the “Global Action Plan on AMR”.\textsuperscript{3}

A significant driver to this threat in lower income countries, is the irrational use of antimicrobials, and importantly the over- or unnecessary prescribing thereof.\textsuperscript{4,5} Combined with high infection rates and AMR this presents a particular challenge in the lower income countries.\textsuperscript{6,7} Thus, throughout health care communities, an increasing desire to reduce these practices has grown, one of the focus areas being surgical antimicrobial prophylaxis (SAP).\textsuperscript{8} As SAP represents one-third of all antimicrobial use in paediatric hospitals\textsuperscript{9} and increasing evidence suggests that the inappropriate use thereof contributes to AMR.\textsuperscript{10} One of the factors contributing to inappropriate use is medical practitioner’s antimicrobial prescribing behaviour.\textsuperscript{11}

On a national front, South Africa faces an overwhelming burden of infectious disease, the previously largely unnoticed AMR threat is now becoming more visible and tangible to medical practitioners.\textsuperscript{12}

Although several interventions have proven to be cost-effective, the optimal method to address and optimise the use of antimicrobials remain uncertain.\textsuperscript{13} Although, appropriate SAP reduces surgical site infection (SSI) incidences and available SAP guidelines improve quality of care, compliance by medical practitioners remains poor.\textsuperscript{14}

To facilitate behavioural modification, various barriers needs to be addressed.\textsuperscript{14} However since antimicrobials are prescribed by medical practitioners, any action aimed at improving the use thereof must be targeted at the medical practitioner level.\textsuperscript{13} What is known is that interventions are required to identify and change antimicrobial use behaviour of medical practitioners, to rationalise the further use of antimicrobials and to contain the growing emergence of resistance.\textsuperscript{11} Factors influencing prescribing behaviour may include training,
their environment, patient demands and medical reimbursement structures.\textsuperscript{10} And thus, behavioural change in medical practitioners would necessitate multiple dissemination strategies to address all of listed factors.\textsuperscript{14}

However, most importantly, one of the key factors identified that affects individual prescribing behaviour and provides reason for the improper use of antimicrobials\textsuperscript{15} is the medical practitioner’s knowledge, perception and experience of antimicrobials and AMR.\textsuperscript{4,15} As this may either facilitate or hamper the use of SAP guidelines.\textsuperscript{14}

**NATIONAL TRENDS**

In order to compliment the international response to AMR, an AMR National Strategy Framework for 2014-2024 was constructed in South Africa.\textsuperscript{16}

Finally, to the research team’s knowledge, this study was the first to specifically assess medical practitioners’ knowledge and perception of SAP use in paediatrics, via a multi-centre approach. This study consequently provided the opportunity to establish if medical practitioners have both equitable and evidence-based perceptions, and knowledge on recommended SAP use in paediatrics.

**KEY FOCUS**

A dire need for change in the prescribing practices of medical practitioners,\textsuperscript{4} has been identified and the importance of understanding the current knowledge of prescribers highlighted. In order to establish a fundamental change in the medical practitioner’s behaviour, control antimicrobial utilisation and decrease the emergence of AMR, a change in their personal knowledge and perception would be required.\textsuperscript{4,5,6,7,15} For this type of intervention, information may be obtained through knowledge, attitude and practice surveys of the prescribers to access their antimicrobial prescribing behaviour.\textsuperscript{11}

The need for future studies has been identified to assess the best ways of improving SAP use.\textsuperscript{9} Although studies have been performed on the medical practitioner’s knowledge and belief of antimicrobial use and AMR in higher income countries, the results are not necessarily applicable to the lower-income countries.\textsuperscript{6}

South Africa, situated at the southern tip of Africa, is a large (estimated at 1.2 million km$^2$), upper middle income country, consisting of a two tiered system: the public- and the private health care system (Figure 1).\textsuperscript{17}
The significance of this study thus lied in addressing specific needs highlighted both internationally and nationally, using a multi-centre approach. This approach ensured an increased study population, exposure to different geographic locations, demographic information and the possibility of a wider range of population groups.

**CONTRIBUTION TO THE FIELD**

Limited information is available on medical practitioner’s knowledge on SAP use in paediatrics, in both systems of the South African health care. Further to this evidence on SAP use in paediatrics is not readily available. However, in a country like South Africa, there is a substantial need for intensified research in this area.

The aim of this study was thus to assess the knowledge and perception of medical practitioners, regarding SAP use in paediatrics, by means of a survey, at both a teaching and a private hospital in South Africa. By accessing the knowledge and perception of medical practitioners on SAP, a powerful tool is utilised contributing to strategies aimed at improving antimicrobial use.⁴

**METHODS**

**Study design, setting and population**

A descriptive cross-sectional quantitative study by means of a survey with medical practitioners was conducted prospectively. Sampling was done to include all medical practitioners working with paediatric surgical patients at the teaching and private hospital used. Medical practitioners, who were registered at the Health Professions Council of South Africa (HPCSA) working within the discipline of paediatric surgery at either the teaching and private hospital, who were willing to provide informed consent was included. Estimation of sample size was based on the total number of medical practitioners working in the teaching and private hospital’s paediatric surgical units, and was estimated at 15 participants per hospital (Table 1).
Table 1: Number of Medical Practitioners at the respective facilities

<table>
<thead>
<tr>
<th>Area of speciality</th>
<th>Teaching n (%)</th>
<th>Private n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENT</td>
<td>4 (26.67)</td>
<td>4 (25)</td>
</tr>
<tr>
<td>Maxillofacial</td>
<td>1 (6.67)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Urology</td>
<td>5 (33.33)</td>
<td>3 (18.75)</td>
</tr>
<tr>
<td>General surgery</td>
<td>5 (33.33)</td>
<td>5 (31.25)</td>
</tr>
<tr>
<td>Gastroenterologist</td>
<td>0 (0)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (100)</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

Abbreviations used: ENT = Ear, Nose and Throat

Study period, procedures and data collection instrument

A self-administer survey, in the form of a checklist with open ended questions, was used in this study over a period of two months. The survey was adopted from similar studies\(^4,11,18\) and adapted to fit the setting used in this study and modified to meet the outlined aim and objectives. The survey was distributed and completed on site, preventing bias due to discussions with peers or reference to literature. The survey was pretested for readability, length and relevance amongst a sample of medical practitioners from neighboring hospitals.

The survey was divided into three sections;

Section A: demographics (age, date of birth, gender, registration status and area of specialty).

Section B consisted of five key statements which covered antimicrobial costs, potential adverse reactions to antimicrobials, infection risk without SAP, reduction in infection risk with SAP and the potential AMR due to the use of antimicrobials. The medical practitioners had to indicated how each key factor affects the medical practitioners' overall approach to SAP.

Section C was a “yes” or “no” checklist and covered questions based on whether the medical practitioner administers pre- and/or post-operative SAP for certain surgical specialties.
Table 2: Grading scale

<table>
<thead>
<tr>
<th></th>
<th>Grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not at all important</td>
</tr>
<tr>
<td>2</td>
<td>Somewhat important</td>
</tr>
<tr>
<td>3</td>
<td>Important</td>
</tr>
<tr>
<td>4</td>
<td>Very important</td>
</tr>
<tr>
<td>5</td>
<td>Extremely important</td>
</tr>
</tbody>
</table>

Data Analysis

Data was captured electronically from the completed data collection form onto Microsoft Excel® spread sheets. All data were proof-read by a second independent researcher for preciseness and correctness. Corrections were made prior to any analysis. All statistical analyses were performed on SAS® (SAS® Institute Inc, Carey, NC, USA), Release 9.4, with 95% confidence intervals (CIs), including the calculation of descriptive statistics by using the Fisher Exact test for comparisons of percentages, and the Student t test for comparisons of mean values. All tests were two-sided and p values ≤ 0.05 were considered significant.

ETHICAL CONSIDERATION

Data collection commenced after ethical consideration was granted from Sefako Makgatho Health Sciences University’s Research and Ethics Committee (SMUREC) (SMUREC/H/185/2015: PG) as well as from the Research Operations Committee of the private hospital used (UNIV-2016-0013). Participation was voluntary and responses were anonymous and signed consent was obtained from each medical practitioner.

RESULTS

Response

A total of 33 medical practitioners completed the survey, 18 from the teaching hospital and 15 from the private hospital, this was the total number of medical practitioners for both facilities. Thus, the overall response rate was 100% for both hospitals.
Participant study characteristics

Both groups differed significantly (p <0.001) in terms of age, HPCSA registration status and area of specialty. The mean age (± SD) was 34.94 (±9.77) and 51.50 (±11.59) years, and the median (IQR) was 31.00 (±29.50-35.30) and 49.00 (±46.00-55.00) years respectively for the teaching and private hospital. The majority (66.67%) of teaching hospital participants were registered at the HPCSA, as registrars specialising in paediatrics, compared to the private hospital, where all participants were already registered as specialists. Statistically significant differences noted in area of sub-specialisation were noted, between the two hospitals (Table 3).
Table 3: Demographics of survey participants at both hospitals

<table>
<thead>
<tr>
<th></th>
<th>Teaching</th>
<th>Private</th>
<th>p-Value</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number n (%)</td>
<td>18 (100)</td>
<td>15 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 (11.11)</td>
<td>14 (93.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6 (33.33)</td>
<td>1 (6.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>10 (55.56)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Mean (± SD)</td>
<td>34.94 (±9.77)</td>
<td>51.50 (±11.59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>31.00 (±29.50-35.50)</td>
<td>49.00 (±46.00-55.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPCSA* registration Status n (%)</td>
<td></td>
<td></td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Intern</td>
<td>2 (11.11)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Registrar</td>
<td>12 (66.67)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist</td>
<td>4 (22.22)</td>
<td>15 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area of sub-specialty</td>
<td></td>
<td></td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Urology</td>
<td>0 (0)</td>
<td>3 (20.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>0 (0)</td>
<td>4 (26.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General surgery</td>
<td>1 (5.56)</td>
<td>4 (26.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillofacial</td>
<td>0 (0)</td>
<td>1 (6.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (5.56)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatology</td>
<td>1 (5.56)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paediatrics</td>
<td>15 (83.33)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plastic surgeons</td>
<td>0 (0)</td>
<td>3 (20.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: ENT= Ear, Nose and Throat, χ² Chi-Square test done, *Highly statistically significant difference
Factors influencing overall approach to SAP use

Comparative results were seen in both study populations regarding the consideration of potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR due to the use of antimicrobials (55.55%, 66.67%, 77.77% and 66.67% for the teaching hospital respectively, compared to 66.67%, 73.34%, 80% and 53.34% for the private hospital respectively). However, a statistically significant difference (p=0.0363) between the two study populations, in terms of SAP costs consideration when prescribing SAP was noted. Less than 10% (7.69%) of private hospital participants compared to 50% of participants from the teaching hospital, considered cost as a very to extremely important consideration, when prescribing SAP (Figure 2).

PRE-OPERATIVE SAP ADMINISTRATION

This formed part of section C of the survey and was not consistently completed by all medical practitioners. The response was relatively low ranging from 33.33% to 38.88% (6; 7 respectively for pre- and post-operatively) from the teaching hospital, compared to a high participation ranging from 86.67% to 93.33% (12; 13 respectively for pre- and post-operatively) for the private hospital.

Urology

According to SAP guidelines19,20,21,22,23 SAP is not routinely recommended for either one of the three surgical sub-categories (phimosis, circumcisions, UDT’s).

One medical practitioner from the teaching hospital and five from the private hospital completed this section. The teaching hospital’s medical practitioner stated that SAP should not be administered for both phimosis and circumcision. In contrast, the majority (66.67%; 75%) of medical practitioners from the private hospital stated that SAP should be administered for the aforementioned conditions. With UDTs all medical practitioners from the teaching and private hospital stated that UDT’s require SAP.

Ear, nose and throat

According to SAP guidelines19,20,21,22,23 SAP is not routinely recommended for either one of the two surgical sub-categories (papillomas and tonsillectomies).
One medical practitioner from the teaching hospital and four from the private hospital completed this section. The teaching hospital’s medical practitioner stated that SAP for tonsillectomies should be administered for both surgical sub-categories. The majority (66.7%; 75%) of medical practitioners from the private hospital, stated that SAP should not be administered for either of these conditions.

**General surgery**

According to SAP guidelines\(^{19,20,21,22,23}\) SAP is highly recommended for all three of the surgical sub-categories (hernia repair, appendectomies and colostomies)

Six medical practitioners from the teaching hospital and four from the private hospital completed this section. All medical practitioners from both study populations indicated that they administer SAP for hernia repairs and colostomies. All medical practitioners from the private hospital administer SAP for appendectomies.

**Maxillofacial surgery**

According to SAP guideline\(^{19,20,21,22,23}\) SAP is not routinely recommended for dental caries.

One medical practitioner from the teaching hospital and one from the private hospital completed this section. The medical practitioner from the teaching hospital stated that SAP should be administered for dental caries, whereas, the private hospital’s medical practitioner does not.

**POST-OPERATIVE SAP ADMINISTRATION**

According to current literature\(^{19,20,21,22,23}\) post-operative SAP administration provides no additional benefit in preventing SSIs, and thus routine administration thereof should be abandoned.

**Urology**

One medical practitioner from the teaching hospital and four from the private hospital completed this section. The teaching hospital’s medical practitioner administers for all three surgical sub-categories, in contrast, the majority (66.67%) of medical practitioners in the private hospital, does not administer SAP. 
**Ear, nose and throat**

One medical practitioner from the teaching hospital and three from the private hospital completed this section. All medical practitioners from both hospitals administers SAP for tonsillectomies. One medical practitioner from the private hospital, indicated that SAP should not be administered for papillomas.

**General surgery**

Four medical practitioners from both hospitals completed this section. SAP is not administered by any medical practitioners from the private hospital for hernia repairs. The majority (75%) of medical practitioners from the private hospital administer SAP for appendectomies. All medical practitioners from the teaching hospitals administers SAP for colostomies, compared to only one in the private hospital.

**Maxillofacial surgery**

Only one medical practitioner from the private hospital completed this section, stating that SAP should be administered for dental caries.

**General comments provided**

The following statements are quoted per verbatim regarding the use of SAP.

**Teaching hospital**

“Paediatrics are given antimicrobials on arrival of ward and metronidazole prior to surgery”.

**Private hospital**

“Beta-lactams are administered in the case of balanitis under the foreskin, however antimicrobials are used with caution because of resistance”.

“occasional post-operative SAP is administered for appendectomies”.

**DISCUSSION**

This study evaluated knowledge and perceptions of medical practitioners regarding SAP use in paediatrics. To the best of our knowledge, this study is the first to assess these
aspects amongst medical practitioners in both a private and teaching hospital in South Africa.

Statistically significant differences were seen in age, HPCSA registration status, and area of specialty. This may be due to the misdistribution of the available health care practitioners (HPCs) between the private and the public health care system. Statistics from 2013, indicated that of 39 847 medical practitioners registered at the HPCSA, including a total of 14 021 specialists, scarcely 13 614 (34%) were distributed over the entire public health care system (Gray et al, 2016). The public health care system is funded by government and constitutes the majority of health care in South Africa, serving an estimated 82.5% (42 million) of the lower to middle income residents. One of the legs of the public health care system is teaching hospitals, also known as academic or tertiary hospitals. They serve as training institutions for medical and allied health universities, and provide in-practice training for interns and registrars.

The majority of medical practitioners from both hospitals shared the same approach to potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR due to the use of antimicrobials. Similar results were found in a study conducted in the USA, highlighting the fact that AMR is a key factor to consider when selecting antimicrobials for patients. A statistically significant difference (p=0.0363) between the two study populations was noted, in terms of costs consideration when prescribing SAP. Medical practitioners from the teaching hospital had greater cost-considerations to SAP use as part of their overall treatment approach. The results are thus in line with the South African Health policy, developed in accordance with the 1996 National Drug Policy, which is directed towards the delivery of cost-effective medicines and health care services.

Although a lower response rate to general knowledge regarding SAP administration pre-and post-operatively was obtained, key findings noted will be described. In urology, the majority of the medical practitioners from the private hospital’s knowledge on pre-operative SAP administration for circumcision was lacking, and there was an absolute shortage in knowledge at both hospitals that UDT’s do not require SAP administration. With post-operative SAP administration the teaching hospital’s medical practitioners had an absolute lack of knowledge regarding all three surgical sub-categories, compared to a clear understanding at the private hospital. Regarding knowledge on ENT pre-operative SAP administration, medical practitioners from the teaching hospital seems to lack ready knowledge that both papillomas and tonsillectomies do not require SAP. In contrast, the majority of medical
practitioners from the private hospital has accurate knowledge on the aforementioned. With post-operative SAP administration the opposite was seen where the majority of medical practitioners from the private hospital lack knowledge that both tonsillectomies and papillomas does not require SAP administration. A similar trend was noted in the teaching hospital regarding tonsillectomies. In general surgery, all medical practitioners had accurate knowledge on the pre-operative administration of SAP. However, unnecessary post-operative SAP is administered by the majority of teaching hospital medical practitioners for colostomies. The same is seen for appendectomies by private hospital’s medical practitioners. Appropriate use of SAP is vital because haphazard use thereof increases the prevalence of AMR\textsuperscript{4,5} and may predispose patients to unwanted super-infections like Clostridium difficile.\textsuperscript{24} Thus, by ensuring appropriate use of SAP, medical practitioners are not only supporting both national and international goals on the fight against AMR,\textsuperscript{1,2,3} but additionally restricting collateral damage.\textsuperscript{25}

With maxillofacial surgery, medical practitioners from the private hospital had a better understanding of pre-operative SAP recommendations, however lacked understanding of post-operative SAP administration. Other similar studies conducted in developed countries, found that medical practitioners working with maxillofacial patients had good knowledge of SAP use. In contrast, developing countries showed abuse of SAP, typically to prevent SSIs, cover up non-aseptic technique used or due to the ‘just in case’ principle.\textsuperscript{26}

It is evident from the findings that medical practitioners require further education to enhance ready knowledge pertaining to SAP use in paediatrics. In the teaching hospital, it could be included as part of specilisation training as the results points to a need for targeted educational interventions.

LIMITATIONS AND RECOMMENDATIONS

A limited number of study sites were included as part of this study, and thus the results should be generalised with caution. Furthermore, section C was not completed by all of the medical practitioners consistently and may thus not provide a true reflection of medical practitioners' knowledge.

The results found in this study can motivate reasons for training on SAP and AMR in paediatrics, in order to promote behavioural change in prescribing patterns. It further identified the need for targeted interventions on education. Surveys demonstrates a snapshot of the
current situation, however, additional qualitative research would allow for a more comprehensive understanding of knowledge, perceptions of antimicrobial prescribing.

CONCLUSION

This study to the best of our knowledge, was the first of its kind in South Africa, to address factors influencing the overall approach of medical practitioners towards prescribing SAP in paediatrics. Areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing has been identified. The areas in most need of increased and improved targeted interventions and education programs include; pre- and post-operative SAP initiation of antimicrobials. Standardisation of education on SAP in paediatrics should receive attention from statutory bodies in South Africa to ensure quality healthcare for all the children regardless of the health care setting.

FUNDING

Sefako Makgatho Health Sciences University

TRANSPARENCY DECLARATIONS

None to declare.
REFERENCES


Abbreviations used for Figure 1:

ADRs = Adverse drug reactions,

AMR = Antimicrobial resistance,

SAP = surgical antimicrobial prophylaxis,

SSIs = surgical site infections.

Circle size corresponds to the number of answers per grade on the grading scale.

Figure 1: Difference between the two hospitals use

<table>
<thead>
<tr>
<th>South African health care</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Teaching hospital</td>
<td>Private hospital</td>
</tr>
<tr>
<td>Serves as teaching platform for medical and allied health universities</td>
<td>Qualified and experienced specialist and professional nursing staff</td>
</tr>
<tr>
<td>Provide specialist and sub-specialist public health care, performs advanced diagnostic procedures and therapy</td>
<td>Provides the latest advances in medical and surgical technology, interventions and treatment across a broad spectrum of specialities</td>
</tr>
<tr>
<td>AMR National Strategy Framework for 2014-2024 was constructed by NDoH</td>
<td>Has an implemented AMS program which also evaluates SAP prescribing</td>
</tr>
</tbody>
</table>
Abbreviations used for Figure 2:

ADRs= Adverse drug reactions,

AMR= Antimicrobial resistance,

SAP= surgical antimicrobial prophylaxis,

SSIs= surgical site infections.

Circle size corresponds to the number of answers per grade on the grading scale.

Figure 2: Overall approach to SAP

<table>
<thead>
<tr>
<th>Not at all important</th>
<th>Teaching hospital</th>
<th>Extremely important</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Private hospital</td>
<td></td>
</tr>
</tbody>
</table>

SAP costs

Potential ADRs to SAP

SSI infection risk without SAP

Reduction of SSI risk without SAP

Potential AMR due to the use of antimicrobials
CHAPTER 5

SUMMARY OF RESULTS, CONCLUSION AND RECOMMENDATIONS

5.1 INTRODUCTION

The limitations and recommendations of this study are discussed followed by a conclusion. A summary for the study ends this chapter.

5.2 LIMITATIONS AND RECOMMENDATIONS

5.2.1 Retrospective aspect

Due to a small sample size and being limited to only four surgical sub-categories, due care should be given to the generalisation of study results for SAP practices across South Africa’s two health care systems. This study did not investigate the cause and relationship of the results. Hospital charts were used for data collection, thus accuracy depended on the accuracy of the hospital files. Further studies, which will take these limitations into consideration, are needed.

The need for quality improvement interventions has been identified, together with the need for continued surveillance of SAP practices in both health care systems of South Africa, the urgent need for local standardised SAP guidelines, based on the latest evidence with consideration of local tenders, availability and costs.

5.2.2 Prospective aspect

A limited number of study sites were included as part of this study, and thus the results should be generalised with caution. Furthermore, section C was not completed consistently by all medical practitioners and may therefore not provide a true reflection of the knowledge of medical practitioners.

The results found in this study can motivate reasons for training on SAP and AMR in paediatrics, in order to promote behavioural change in prescribing patterns. It further identified the need for targeted interventions on education. Surveys demonstrate a snapshot of the current situation, however, additional qualitative research would allow for a more comprehensive understanding of knowledge and perceptions of antimicrobial prescribing.
Chapter 5: Summary of Results, Conclusion and Recommendations

5.3 CONCLUSION

5.3.1 Retrospective aspect

SAP practices in South Africa’s teaching and private hospitals diverge from current guidelines. Inappropriate over-use of SAP occurs in both hospitals, whilst under-use is limited to the teaching hospital. Full compliance to the five criteria was not met by either hospital. Non-compliance was largely attributed to inappropriate selection and dosing. Although literature is limited, findings were consistent with existing literature, which described variation in SAP use amongst paediatrics. The importance of the proper use of SAP cannot be over emphasised, as it contributes to AMR and is associated with a significant decreases in SSI-associated morbidity and mortality. Reasons for concern have been identified and therefore quality improvement interventions, continued surveillance and local standardised paediatric SAP guidelines in South Africa are needed.

5.3.2 Prospective aspect

Areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing have been identified. The areas most in need of increased and improved targeted interventions and education programmes, include pre- and post-operative SAP initiation of antimicrobials. Standardisation of education on SAP use in paediatrics should receive attention from statutory bodies in South Africa to ensure quality health care for all children regardless of the health care setting.

5.4 SUMMARY

5.4.1 Retrospective aspect

A retrospective chart review was conducted with a multi-centre and health care system approach in South Africa. The aim of this study was to access compliance to SAP guidelines for paediatrics undergoing surgery in one of four surgical sub-categories (i.e. urology, ENT, maxillofacial and general surgery). It was designed to meet the following objectives: to describe SAP use in paediatrics at a teaching and private hospital and to compare the compliance thereof to current national and international SAP guidelines. To our knowledge, this was the first study of its kind performed in paediatrics via a multi-centre approach in South Africa. Between February and August 2015, 224 charts were reviewed, 112 charts each from the teaching and private hospitals respectively. The majority (p=1.000) of paediatrics from both hospitals received SAP when indicated (77.27% and 100% respectively). The
minority of paediatrics from both hospitals received antimicrobials without an indication (21.11% and 45.88% respectively). Compliance to all five of the criteria was not met by either hospital. Overall, the teaching hospital met the most criteria (three out of five) in 58.82% of paediatrics. It was thus concluded that the current SAP practices in South Africa’s teaching and private hospitals diverge from current SAP guidelines. Inappropriate over-use of SAP occurs in both hospitals, whilst under-use is limited to the teaching hospital. Non-compliance was largely attributed to inappropriate selection and dosing. Quality improvement interventions, continued surveillance and local standardised evidence-based SAP guidelines are needed.

5.4.2 Prospective aspect

A prospective survey was conducted to address factors influencing the overall approach of medical practitioners towards prescribing SAP in paediatrics. Knowledge on pre- and post-operative SAP use in paediatrics in four surgical sub-categories (i.e urology, ENT, general and maxillofacial surgery) was compared to current SAP guidelines. Over a two-month study period (March to April 2016), 33 surveys were completed, 18 from the teaching and 15 from the private hospital. Comparative results were seen in both study populations regarding the consideration of potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR, due to the use of antimicrobials (55.55%, 66.67%, 77.77% and 66.67% respectively for the teaching hospital, compared to 66.67%, 73.34%, 80% and 53.34% respectively for the private hospital). However, a statistically significant difference (p=0.0363) between the two study populations, in terms of SAP cost consideration when prescribing SAP, was noted. A variety of pre- and post-operative knowledge exists over the four surgical sub-categories in both hospitals. In conclusion, areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing in paediatrics have been identified. The areas most in need of improvement include pre- and post-operative SAP administration. Standardisation of education on SAP use in paediatrics should receive attention from statutory bodies in South Africa, as medical practitioners require further education to enhance ready knowledge pertaining to SAP use in paediatrics.


Goldstein, E., Goff, D., Reeve, W., Naumovski, S., Epson, E., Zenilman, J., Kaye, K., File, T. 2016. Approaches to modifying the behavior of clinicians who are noncompliant with Antimicrobial Stewardship Program Guidelines. Clinical Infectious Diseases, 63(4):532-538.


### Appendix 1: Data collection form for paediatric charts

#### Patient demographics

<table>
<thead>
<tr>
<th>Study no.</th>
<th>Gender</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Height</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of birth</th>
<th>Weight</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Clinical diagnosis

#### Clinical data

**Type of surgery**

<table>
<thead>
<tr>
<th>Was surgical prophylaxis administered?</th>
<th>Yes</th>
<th>If Yes, when was it administered</th>
<th>1 hour before</th>
<th>2 hours before</th>
<th>Another time? Specify</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotics used</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>ICD-10 code</th>
<th>ATC code</th>
<th>Dosage</th>
<th>Route</th>
<th>Date of dose</th>
<th>Time of dose</th>
<th>How long before surgery?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Was the prophylactic antibiotics discontinued within 24 hours</th>
<th>Yes</th>
<th>No</th>
<th>If not, reason?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| | | | |</p>
<table>
<thead>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# APPENDICES
<table>
<thead>
<tr>
<th>Classification</th>
<th>Active ingredient</th>
<th>ATC-code</th>
<th>DDD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-lactam antibacterials, penicillin</td>
<td>Ampicillin/ Sulbactam</td>
<td>J01C/J01GG</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>First-generation cephalosporin</td>
<td>Cefazolin</td>
<td>J01DB</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Second-generation cephalosporin</td>
<td>Cefoxitin</td>
<td>J01DC</td>
<td>40 mg/kg</td>
</tr>
<tr>
<td>Lincosamide</td>
<td>Clindamycin</td>
<td>J01FF</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td>Fourth-generation cephalosporin</td>
<td>Cefepime</td>
<td>J01DE</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Ciprofloxacin</td>
<td>J01MA02</td>
<td></td>
</tr>
<tr>
<td>Glycopeptide antibacterials</td>
<td>Vancomycin</td>
<td>J01XA</td>
<td>15 mg/kg</td>
</tr>
<tr>
<td>Imidazole derivatives</td>
<td>Metronidazole</td>
<td>J01XD</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>Gentamycin</td>
<td>J01G</td>
<td>2.5 mg/kg</td>
</tr>
</tbody>
</table>

Adapted from ASHP Therapeutic guidelines (2013), ChocChildren’s (2015).
Appendices

Appendix 2: Survey form for medical practitioners

### Section A: Demographics

<table>
<thead>
<tr>
<th>Study no</th>
<th>Intern</th>
<th>Age</th>
<th>CS MP</th>
<th>Date of birth</th>
<th>Registrar</th>
<th>Male</th>
<th>Female</th>
<th>Specialist</th>
</tr>
</thead>
</table>

Please specify in which area you practice

<table>
<thead>
<tr>
<th>Urology</th>
<th>ENT</th>
<th>Maxillofacial</th>
<th>Other? Specify</th>
</tr>
</thead>
</table>

### Grading scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not at all important</td>
</tr>
<tr>
<td>2</td>
<td>Somewhat important</td>
</tr>
<tr>
<td>3</td>
<td>Important</td>
</tr>
<tr>
<td>4</td>
<td>Very important</td>
</tr>
<tr>
<td>5</td>
<td>Extremely important</td>
</tr>
</tbody>
</table>

### Section B: According to the grading scale, please grade how does the following aspects affect your overall approach to surgical antibiotic prophylaxis?

<table>
<thead>
<tr>
<th>Antibiotic costs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic costs</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Potential adverse reactions to antibiotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection risk without antibiotic prophylaxis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction of infection risk with antibiotic prophylaxis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential antibiotic resistance due to use of antibiotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Section C: Do you administer pre-- and/or post-operative antibiotics for the following surgical specialities?

<table>
<thead>
<tr>
<th>Specialised areas</th>
<th>Procedure</th>
<th>Pre-operative</th>
<th>Postoperative</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urology</td>
<td>Phimosis</td>
<td>YES</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Circumcisions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Undescended testicles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>Tonsillectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Papilloma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>Hernia repair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Appendectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colostomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillofacial</td>
<td>Dental surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other? (please specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendices

Appendix 3: SMUREC clearance certificate

Ms N van der Sandt  
Department of Pharmacy  
P.O Box 216  
Medunsa  
0204  

Dear Ms van der Sandt  

RE: MREC/H/105/2015: PG – PROTOCOL AMENDMENT  

MREC approved title: Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr George Mukhari Academic hospital, Pretoria, Gauteng Province  

New title: Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr George Mukhari Academic Hospital and private hospital  

SMUREC NOTED a letter dated 27 January 2016 requesting the following minor amendments to the abovementioned protocol:  

a) Questionnaire for medical practitioners-section A: The addition of an option for the participants to indicate whether they are male or female (Appendix 2)  

b) Questionnaire for medical practitioners-section C: The addition of an option to indicate and specify whether pre- and/or post-operative antibiotics are administered for any other surgical specialties not listed in the questionnaire (Appendix 2)  

Motivation: In the protocol researcher stated that a pilot test will be performed on the questionnaire for medical practitioners (Appendix 2) as it has never been applied in practice. In order to identify whether it would work in practice the pilot test was conducted on the medical practitioners who represent my intended sample, where after an interview followed. The interview done during the pilot study, established whether or not the questionnaire was understandable, sufficient and if it reliably measures the same construct.  

After performing the pilot test, researcher was able to highlight certain shortcomings. The first shortcomings was the need for the medical practitioners to have an option in order to indicate whether pre- and/or post-operative antibiotics are administered for any other surgical specialties which are not provided for on the questionnaire. Secondly there was no option for the medical practitioners to indicate their gender, which is important for demographical data.
c) To change the single study site Dr. George Mukhari Academic Hospital (DGMAH) to a multi-center study site, which involves DGMAH and Netcare Pretoria East hospital.

d) To change the title: Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr. George Mukhari Academic Hospital (DGMAH) and a Private Hospital (Protocol page 1).

**Motivation:** Since the data collection has commenced, I have recognized the need for a larger study population. It would be ideal to broaden the study population by adding another study site (Netcare Pretoria East). The researcher trusts that the benefits of a multicentre study outweigh the risks. Not only will a multicentre study increase my study population, expose me to different geographic locations, demographic information and the possibility of the inclusion of a wider range of population groups, but more importantly will provide me with the ability to compare results among centres. This finally will contribute to an increased generalisation of the study findings. Netcare’s Standard Operating Procedure (SOP) requires that the researcher will not disclose Netcare’s name in the research without written consent from, nor will Netcare’s name be mentioned in the results and in publication.

**SMUREC NOTED and APPROVED** the following:

- minor amendments under questionnaire
- to change the single study site Dr. George Mukhari Academic Hospital (DGMAH) to a multi-center study site, which involves DGMAH and Netcare Pretoria East hospital.
- to change the title: Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr. George Mukhari Academic Hospital (DGMAH) and a Private Hospital

**SMUREC REQUESTED** the researcher to obtain a letter of intent from the Private Hospital.

Yours Sincerely,

[Signature]

DR C BAKER
DEPUTY CHAIRPERSON SMUREC

04 February 2016

Cc: Prof N Schellack
Appendix 4: Research Operations Committee Clearance Certificate

RESEARCH OPERATIONS COMMITTEE FINAL APPROVAL OF RESEARCH

Approval number: UNIV-2016-0013

Ms N van der Sandt

E-mail: nicolene.vdsandt@gmail.com

Dear Ms Van der Sandt

RE: PRESCRIBING PRACTICES OF ANTIBIOTIC PROPHYLAXIS USED IN SURGICAL PROCEDURES IN PAEDIATRIC PATIENTS AT DR GEORGE MUKHARI ACADEMIC HOSPITAL AND PRIVATE HOSPITAL

The above-mentioned research was reviewed by the Research Operations Committee’s delegated members and it is with pleasure that we inform you that your application to conduct this research at private Hospital, has been approved, subject to the following:

i) Research may now commence with this FINAL APPROVAL from the Committee.

ii) All information regarding the Company will be treated as legally privileged and confidential.

iii) The Company’s name will not be mentioned without written consent from the Committee.

iv) All legal requirements regarding patient / participant’s rights and confidentiality will be complied with.

v) The research will be conducted in compliance with the GUIDELINES FOR GOOD PRACTICE IN THE CONDUCT OF CLINICAL TRIALS IN HUMAN PARTICIPANTS IN SOUTH AFRICA (2006)

vi) The Company must be furnished with a STATUS REPORT on the progress of the study at least annually on 30th September irrespective of the date of approval from the Committee as well as a FINAL REPORT with reference to intention to publish and probable journals for publication, on completion of the study.

vii) A copy of the research report will be provided to the Committee once it is finally approved by the relevant primary party or tertiary institution, or once complete or if discontinued for any reason whatsoever prior to the expected completion date.
vii) The Company has the right to implement any recommendations from the research.

ix) The Company reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects/ Company or should the researcher not comply with the conditions of approval.

x) APPROVAL IS VALID FOR A PERIOD OF 36 MONTHS FROM DATE OF THIS LETTER OR COMPLETION OR DISCONTINUATION OF THE TRIAL, WHICHEVER IS THE FIRST.

We wish you success in your research.

Yours faithfully

[Signature]

Prof Dion du Plessis
Full member: Research Operations Committee & Medical Practitioner evaluating research applications as per Management and Governance Policy

[Signature]

Shannon Nell
Chairperson: Research Operations Committee
Date: 9/3/2016

This letter has been anonymised to ensure confidentiality in the research report. The original letter is available with author of research
Dear Dr Holum

Dr. George Mukhari Academic Hospital

Request permission to conduct a study at Dr. George Mukhari Academic Hospital.

I am a post-graduate student at the Department of Pharmacy, Sefako Makgatho University of Health Sciences. As part of the requirements for my MPharm post graduate qualification, I have to conduct a research project. The name of my study is “Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr. George Mukhari Academic Hospital, Pretoria, Gauteng province” I kindly request your permission to conduct the study at Dr. George Mukhari Academic Hospital. Please find a copy of the protocol attached, which will be submitted to the Sefako Makgatho University of Health Sciences Research and Ethics Committee for ethical approval.

I trust that you will find the above in order. Please feel free to contact me or my supervisor, should you require additional information.

Yours faithfully

Ms Nicoline van der Sandt
25 May 2015

Dr N Shellack (Supervisor)
(012) 521 3286

Department of Pharmacy: Post Graduate Division
Appendices

Appendix 6: Amendment Letter

Dear Prof Ogunbanjo,

Protocol amendment: Prescribing practices of antibiotic prophylaxis used for surgical procedures in paediatric patients at Dr. George Mukhari Academic Hospital (DGMAH), Pretoria, Gauteng province.

The above mentioned protocol received ethical clearance from the Sefako Makgatho University Research Ethics Committee (SMUREC) on 06 August 2015 (SMREC/H/185/2015: PG).

I hereby request the following minor amendments to the above protocol:

a) Questionnaire for medical practitioners-section A: The addition of an option for the participants to indicate whether they are male or female (Appendix 2).

b) Questionnaire for medical practitioners-section C: The addition of an option to indicate and specify whether pre- and/or post-operative antibiotics are administered for any other surgical specialties not listed in the questionnaire (Appendix 2).

Motivation: In my protocol I stated that a pilot test will be performed on the questionnaire for medical practitioners (Appendix 2) as it has never been applied in practice. In order to identify whether it would work in practice the pilot test was piloted on the medical practitioners who represent my intended sample, where after a retrospective interview followed. The interview establish whether or not the questionnaire was understandable, sufficient and that it contains every aspect that I would like to address in my study.

After performing the pilot test and retrospective interview, I was able to highlight certain shortcomings. The first shortcomings was the need for the medical practitioners to have an option in order to indicate whether pre- and/or post-operative antibiotics are administered for any other surgical specialties which are not provided for on the questionnaire. Secondly there was no option for the medical practitioners to indicate their sex, which is important for demographical data.

MISSION OF THE SCHOOL OF PHARMACY
Our mission is to improve the health and well-being of the people of Southern Africa through innovative pharmacy-related learning programmes, research and support services
c) To change the single study site Dr. George Mukhari Academic Hospital (DGMAH) to a multi-center study site, which involves DGMAH and Netcare Pretoria East hospital.

**Motivation:** Since my data collection has commenced, I have recognized the need for a larger study population. It would be ideal to broaden the study population by adding another study site (Netcare Pretoria East). I trust that the benefits of a multicentre study outweigh the risks. Not only will a multicentre study increase my study population, expose me to different geographic locations, demographic information and the possibility of the inclusion of a wider range of population groups, but more importantly will provide me with the ability to compare results among centres. This finally will contribute to an increased comparability of the study.

Since there is a generalized perception that private healthcare sectors delivers more efficient, accountable, and sustainable health care compared to the public sector, it would be perfect to investigate and compare the prescribing patterns with regards to surgical prophylaxis in the paediatric population of a private to a public sector hospital. This will permit me to establish if equitable and evidence-based care is provided as it should be in both sectors.

I believe that the above amendments will strengthen the ethical considerations for the study as well as benefit South African medical literature, especially in the paediatric population where data is limited.

All changes to the text in the protocol, as a result of the above amendments, have been highlighted. Attached please kindly find a copy of the original protocol dated June 2015, the revised protocol dated October 2015 and the SMUREC clearance certificate.

Thank you for your valuable time and input into reviewing this study, if there is any more questions please do not hesitate to contact me.

Kind regards

Nicolene van der Sandt

Master’s Degree Candidate

Cc:  Prof N Schellack (supervisor)

Mrs LA Mabope (Co-supervisor)
Appendix 7: Covering letter for the Journal of Antimicrobial Chemotherapy

Dr. Peter Donnelly
Editor-in-Chief
Journal of Antimicrobial Chemotherapy of the British Society

Dear Dr. Peter Donnelly,

I am pleased to submit an original research article titled: Surgical antimicrobial prophylaxis in Paediatrics: South Africa. “Comparer deux mondes différents” by Nicolene van der Sandt, Natalie Schellack, Lindi Matope, P Mawela and Dane Kruger, for consideration for publication in the Journal of Antimicrobial Chemotherapy of the British Society. This manuscript investigated the current practices of Surgical Antimicrobial Prophylaxis (SAP) used in paediatrics whom underwent surgery procedures in one of four surgical sub-specialities (urology, ENT, general and maxillofacial surgery). This was a comparative study done via a retrospective charts review, conducted in both health care systems of South Africa (a teaching and a private hospital).

In this manuscript, we found that the current SAP practices in South Africa’s teaching and private hospitals is divergent from the latest evidence based SAP guidelines. Although the majority of paediatrics receive SAP when indicated, and the minority receives antimicrobials without an indication. Compliance to all five of the criteria (SAP selection, dosing, re-dosing, timing of administration and duration of treatment) was not found in either hospital.

We believe that this manuscript is appropriate for publication by the Journal of Antimicrobial Chemotherapy of the British Society because it speaks to the importance of antimicrobial research, by identifying reason for concern with regard to SAP use in paediatrics. As well as the urgent need for quality improvement, monitoring of SAP practices and standardised SAP guidelines specifically in the paediatric population.

This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose. The research was funded by Seftak Nkgathi Health Sciences University (SMU). If you feel that the manuscript is appropriate for your journal, we suggest the following reviewers:

N Schellack: BCU, BPharm, PhD (Pharmacy), Associate Professor, natalie.schellack@smu.ac.za
L Matope: lindimatope@gmail.com

Thank you for your consideration.

Sincerely,

Nicolene van der Sandt
Corresponding author
Appendix 8: Covering letter for the Southern African Journal of Infectious Diseases

Professor Charles Feldman
Editor-in-Chief
The Southern African Journal of Infectious Diseases

Dear Professor Charles Feldman,

I am pleased to submit an original research article titled; “Impetus for change: knowledge and perception of medical practitioners on surgical antimicrobial prophylaxis use in paediatrics, a multi-centre approach, South Africa” by Nicolene van der Sandt, Natalie Schellack, Lindi Mabope, P Mawela and Danie Kruger, for consideration for publication in the Southern African Journal of Infectious Diseases. This manuscript investigated the knowledge and perceptions of medical practitioners, regarding surgical antimicrobial prophylaxis (SAP) used in paediatrics. This was a comparative study done via a prospective survey, conducted in both health care systems of South Africa (a teaching and a private hospital).

In this manuscript, we found comparative results in both study populations regarding the consideration of potential adverse reactions of SAP, SSI infection risk without SAP, reduction of SSI risk without SAP as well as potential AMR due to the use of antimicrobials. However, a statistically significant difference between the two study populations, in terms of SAP costs consideration when prescribing SAP was noted. Additionally, that variations in ready knowledge of the medical practitioners, for pre- and post-operative SAP exits.

We believe that this manuscript is appropriate for publication by the Southern African Journal of Infectious Diseases because it speaks to the importance of antimicrobial research, by identifying areas for improvement in the perception and knowledge of medical practitioners with regards to SAP prescribing in paediatrics.

This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose. The research was funded by Sefako Makgatho Health Sciences University (SMU). If you feel that the manuscript is appropriate for your journal, we suggest the following reviewer:

N Schellack: BCur, BPharm, PhD (Pharmacy), Associate Professor, natalie.schellack@smu.ac.za

Thank you for your consideration.

Sincerely,

Nicolene van der Sandt
Corresponding author
Appendix 9: Guidelines for authors for the Journal of Antimicrobial Chemotherapy

BACKGROUND AND SCOPE OF THE JOURNAL

Background

The Journal of Antimicrobial Chemotherapy was founded in 1975 by the British Society for Antimicrobial Chemotherapy (BSAC) as part of its mission to facilitate the acquisition and dissemination of knowledge in the field of antimicrobial chemotherapy. Proceeds from the Journal are used by the BSAC to further these objectives. Articles are published continuously online in JAC Advance Access and assembled into monthly printed and online issues. The Journal has an Impact Factor of 5.313 in 2014.

Aims

The Journal publishes articles that further knowledge and advance the science and application of antimicrobial chemotherapy with antibiotics and antifungal, antiviral and antiprotozoal agents. The Journal publishes primarily in human medicine, and articles in veterinary medicine likely to have an impact on global health.

Scope

The Journal particularly welcomes manuscripts on:

• the practice of evidence-based medicine relating to antimicrobials (clinical trials, systematic reviews and meta-analyses)

• antimicrobial treatment (pharmacokinetics, pharmacodynamics and prescribing practices)

• the action of antimicrobial agents and the mechanisms, genetics and epidemiology of antimicrobial resistance

• antimicrobial stewardship

• the genetic basis of antimicrobial resistance

In addition, the Journal is very keen to publish articles that:

• offer evidence-based synthesis of knowledge and data useful for clinical practice

• analyse, reflect and comment on the current state of the art and practice

• consolidate our knowledge of antimicrobial agents and their use
• consider the future of antimicrobial chemotherapy

The Journal will consider publishing articles on:

• new approaches to improving antimicrobial chemotherapy

• new compounds provided evidence is offered of selective antimicrobial activity and comparative cytotoxicity data

• previously unreported antimicrobial activity relating to a marketed drug product but such studies must take into account the exposure to the drug that can be safely achieved with clinically acceptable doses

• articles reporting the activity of bacteriophages

The Journal will not usually consider publishing material on:

• the chemical synthesis or characterization of compounds. These are better suited to chemistry journals.

• the use and activity of biocides or disinfectants. These require specialist methodology and are generally better suited to more specialist journals.

• the process of turning antimicrobials into a medication i.e. pharmaceutics. These are better suited to a pharmacy journal

• drug stability studies

• naturally occurring substances or extracts that exhibit antimicrobial activity but for which no specific active ingredient has been chemically defined

Authors who are unsure about whether their intended submission meets the aims and scope of the Journal are welcome to contact directly the Editor-in-Chief (jac@bsac.org.uk).

Open Access

Authors can choose open access publication, otherwise journal articles are typically available only to subscribers for 12 months from the month of publication in print and online. Thereafter, all articles are freely available online. This balances the desire for broad access to research with the need to retain revenue for the Journal. JAC is compliant with the NIH funding mandate.

Acceptance rate and processing times
There are almost four times the number of submissions to the Journal than it can accommodate. Hence the rejection rate is high and is likely to remain so. Articles that are not judged to meet the aims and scope of the Journal, or which are judged from the beginning to be unlikely to achieve high enough priority for publication, will be returned to the authors without external peer review. All remaining submissions will be subjected to peer review as rapidly as possible. Our aim is to keep the time from submission to first decision within 4–6 weeks. Once accepted, the time from acceptance to publication online ahead of print is also around 4–5 weeks.

Appeals

Authors wishing to lodge an appeal against a decision can do so by contacting the Senior Editor responsible for the decision directly and by copying in the Editorial Office.

EDITORIAL OFFICE CONTACT INFORMATION

The contact details for the JAC Editorial Office are as follows:

Griffin House

53 Regent Place

Birmingham

B1 3NJ

UK

Tel: +44 121 262 1830

E-mail: jac@bsac.org.uk

PROCESSING OF PAPERS

Where to submit

All material to be considered for publication should be submitted in electronic form via the Journal’s online submission system at:

http://mc.manuscriptcentral.com/jac

Given that you can produce a file of your paper through a word processing package of some description, you only need the three following items to access and use the system: access to the website via a web browser, Adobe Acrobat Reader (which can be downloaded free of
charge from [http://www.adobe.com/](http://www.adobe.com/) and an e-mail account. For more guidance see the section ONLINE SUBMISSION DETAILS.

In addition to submitting your paper online you should simultaneously provide a written statement, signed by all the authors indicating that you have complied with the stipulations in the Instructions to Authors. A copy with the original signatures must be faxed to the Editorial Office as soon as possible after online submission. A blank form is available at [http://www.oxfordjournals.org/jac/for_authors/signature.pdf](http://www.oxfordjournals.org/jac/for_authors/signature.pdf). If at any stage during consideration the authorship of the article changes, the authors must supply a signed statement from ALL the authors (including any whose names are being removed) explicitly indicating the nature of the changes and their agreement. Please note that copied and pasted ‘graphics’ of signatures are NOT permitted owing to the possibility of fraud. Digital signatures, properly verified by the issuing organization (such as Adobe for instance) are permitted.

Article types and format

All documents should be double spaced, and the margins should not be excessively wide. A clear, legible single font (which is readily available internationally) and point size should be employed throughout. For symbols, please use the ‘insert symbol’ function and ONLY select characters from the ‘normal text’ subset. All submitted articles should be line numbered (using continuous line numbers). To do this in Word, use File, Page Setup, Layout, Line Numbers and select continuous line numbering. Please DO NOT insert page numbers (as the pdf proof created by the online submission system will automatically be page numbered).

All articles should include a title page comprising: article title; author names and their affiliations (each affiliation address must be given separately and in full); telephone, fax and e-mail contact details for the corresponding author; and a short running title. In addition, all articles must include a Funding section (if reporting original research) and a Transparency declarations section.

Article titles. All articles reporting the results of original research must have a descriptive title. For example ‘Effect of streptomycin in tuberculosis’ is acceptable; ‘Streptomycin cures tuberculosis’ is not acceptable. Leading articles, which are expressions of opinion, are permitted to have declarative titles. Please note that claims of priority are not permitted in article titles as such claims are impossible to verify; only history will reveal the first example. For instance ‘First NDM-1 Escherichia coli isolated in Andorra’ would not be permitted. Authors are permitted to indicate in the article that, to the best of their knowledge, a finding is the first of its kind.
Appendices

Original articles and Brief reports must have a structured synopsis. The headings for the structured synopsis are as follows: Background (optional), Objectives, Patients and methods (or Methods), Results, and Conclusions.

Original articles. There is a limit of 3500 words in the main text of the article (everything from the Introduction to the end of the Discussion). Papers must be written as concisely as possible. Original articles are divided into the following sections: Synopsis (250 words maximum), Introduction, Materials (or Patients) and methods, Results, Discussion, Acknowledgements, Funding, Transparency declarations and References. Repetition of content between sections must be avoided. A combined Results and Discussion section is acceptable.

Brief reports. These should have the same format as Original articles, but should have no more than two figures/tables, should have a maximum of 20 references and should not exceed 1500 words of main text.

Antimicrobial practice. Articles on topics related to the use of antimicrobials, format as for Original articles/Brief reports.

Correspondence. Letters on topics of concern or interest in the field of antimicrobial chemotherapy, particularly arising from papers or letters already published in the Journal. These should be addressed to the Editor-in-Chief and must not exceed 800 words, one figure or table and 10 references.

Case reports. JAC will publish Case reports that are of sufficient calibre and potential importance, and they should be submitted in the form of Correspondence (see above). Please note that patient anonymity MUST be preserved in Case reports (see the later section on Ethics approval and patient consent/privacy).

Systematic review articles. There is no length limit for this format. A systematic review, as defined by the Cochrane Handbook, is ‘A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarize the results of the included studies.’ They should include a structured synopsis (with appropriate headings; these may differ from the headings used for Original articles etc.).

Review articles. There is no length limit for this format. These generally aim to give an overview of a field suitable for a wide audience, and they should include a synopsis (250 words
maximum). Most reviews are invited. We are pleased to consider unsolicited reviews, but authors are encouraged to consult the Editor-in-Chief in advance of writing to avoid duplicating commissioned material.

Leading articles. These articles are usually in the region of 800-1000 words and may contain the expression of opinion as well as fact. They should address a topical subject, perhaps taking a particular viewpoint and throwing new light on a current debate. A leading article should include a short synopsis (150 words maximum) that should convey the topics and ideas the article covers. Those wishing to contribute a Leading article are encouraged to contact the Editor-in-Chief to discuss their ideas before writing to avoid clashes with any articles already in the pipeline.

For debate. These articles should air contentious issues or discuss controversies so as to stimulate discussion in the Journal on any given topic on antimicrobial chemotherapy. Articles should be as clear and concise as possible, consist of 800-2500 words and must be accompanied by an unstructured synopsis of up to 150 words.

The Editor-in-Chief particularly welcomes pairs of For debate articles offering two opposing viewpoints that aim to persuade readers of their cases. The two resultant articles will be published side by side in the same issue.

Those wishing to contribute a For debate article should first contact the Editor-in-Chief to discuss their ideas and secure a clear agreement before submission. Unsolicited For debate articles will not be considered.

Please note that on publication all Original articles and Brief reports, as well as Antimicrobial practice papers, will be published under the heading of Original research so that articles on similar topics can be grouped together when assigned to an issue. In addition each piece of Correspondence will be published as either a Research letter or a Letter to the Editor.

Peer review

After preliminary examination of the submission by Editorial Office staff to check that all the necessary elements are present, the paper is passed to the Editor-in-Chief. The Editor-in-Chief then assigns the paper to an appropriate Senior Editor. The Senior Editor is then responsible for selecting an Editor to handle the article. Articles can be rejected immediately by the Editor-in-Chief, a Senior Editor or an Editor without further peer review. The assigned Editor is responsible for selecting referees and obtaining referee reports.
The usual number of referees is two, however, the Editors reserve the right to make a decision on a paper on the basis of one referee report, or seek the opinion of more than two referees if they judge this to be necessary or desirable. Leading articles and Correspondence are not routinely sent for external refereeing, but the Editor-in-Chief, Senior Editors and Editors reserve the right to seek the opinion of one or more external referees if they judge this to be necessary or desirable.

Senior Editors, Editors and referees are asked to consider whether they have any conflicts of interest when they are assigned a paper, and if necessary to decline to handle the paper. See the section 'Conflicts of interest' for more information on this subject.

If an Editor decides upon rejection of a paper, it is passed back to the handling Senior Editor for approval of this decision. All rejection correspondence therefore originates from a Senior Editor. Authors should regard rejection as final and only resubmit if they have been invited to do so. Papers may be rejected for a number of reasons, including: (i) they may be of only peripheral interest and perhaps more suitable for submission to a different journal; (ii) they may be, in the opinion of the reviewers, scientifically flawed; (iii) they may be unclear or overly long; or (iv) they may not make a significant contribution to the literature.

Requests that a revised version of a paper be submitted for consideration are sent direct to the corresponding author from the Editor responsible. Any revised version should be submitted within 6 weeks of the revision request or the Journal reserves the right to consider the manuscript as a new submission that may be subject to further refereeing.

The Editor-in-Chief, Senior Editors and Editors reserve the right to request more rounds of revision and resubmission/refereeing, or reject a paper outright, if they judge that any revised version does not adequately address the concerns raised by the referees and the Editor. Once the Editor is satisfied that a revised version has adequately dealt with any points raised they may accept the paper.

Authors can appeal against a decision by contacting the handling Senior Editor, but unless there has been a gross misunderstanding of the submitted article by the Editor and referees, rejection appeals are not likely to be successful. Authors should appreciate that if they resubmit an article that has been rejected without substantially modifying it in line with the suggestions of the Editor and referees, it is almost certain to be rejected again.

After acceptance the paper is sent for copy-editing and typesetting prior to production of proofs for author correction.
The Journal maintains the right to edit any paper to the extent necessary to achieve clarity and precision of expression and to conform with English usage and the Journal's conventions. Please note that if authors ignore requests to conform with Journal style at the revision stage, these changes may be enforced during copy-editing and proof production.

Articles submitted by Editors of the Journal

JAC does not bar Editors (including Senior Editors and the Editor-in-Chief) from submitting articles to the Journal. Articles submitted by Editors are handled in the same fashion as other articles subject to the following considerations: these articles are never assigned to the submitting Editor, or an Editor from the same institution; the submitting Editor is unable to access details of their article through the online submission system; and, like other authors, the submitting Editor will not know the identity of the handling Editor (in cases of rejection) or referees.

Supplement articles

Supplement articles are subject to peer review and may be rejected. Unless specialist external expertise is required, this peer review is conducted among the team of Editors that is dealing with the Supplement.

Proofs

An e-mail containing a link to the proof is sent to the corresponding author. The proof should be read carefully, paying particular attention to any tables, figures and references, and corrections (and answers to any queries) should be submitted to the JAC Editorial Office as soon as possible. Authors should pay particular attention that they check any dosage directions, owing to the seriousness of any error entering the printed record. Extensive changes at the proof stage are not permitted. Authors may be charged for correction of their non-typographical errors. The Journal reserves the right not to comply with changes marked on the Author's proof if these are contrary to the style set down in the Instructions to Authors.

In the event of important developments in a field that affect the paper arising after the final revision, a 'Note added in proof' may be permitted. Please note that Supplementary data files are largely unedited and are not proofed out.

Once all the corrections have been made by the typesetters, the article is then posted on JAC Advance Access

Late corrections, Advance Access and Errata
Appendices

Authors should check articles carefully before submission and resubmission to ensure errors are kept to an absolute minimum. Authors must treat the proof as the LAST CHANCE they will have to make corrections to their article. Corrections that are requested once an article has appeared in Advance Access will entail a higher level of scrutiny. The Journal takes a very dim view of corrections requested at this stage that should have been dealt with earlier, and reserves the right to refuse to make further changes.

After publication in print, the only avenue available to correct an article is the publication of a linked Erratum. The purpose of an Erratum is to correct items that affect the scientific validity of a piece of research. The Journal will refuse to publish an Erratum if the correction requested does not affect the scientific validity of the article (hence requests to correct author names or address details, funding information, or collaborator names or locations, for example, will be refused). This is why it is of the utmost importance that authors pay the necessary attention to ensuring articles are correct at every stage and treat the proof as the last available opportunity for corrections.

JAC Advance Access

JAC Advance Access is the Journal's system for the early online publication of articles ahead of the monthly printed journal issue. Advance Access papers are posted as soon as possible, in exactly the same format as they appear in the issue (i.e. once author and proof-reader corrections have been incorporated) – in order to protect the integrity and accuracy of the scientific record we believe that it is very important that articles are only published once they have been copy-edited, typeset and proof-checked. JAC Advance Access significantly reduces time from acceptance to publication for JAC articles (to approximately 4-6 weeks). If you are a subscriber to the Journal you can view the Advance Access papers by visiting www.jac.oxfordjournals.org and clicking the Advance Access link.

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Material offered for publication must be original, unpublished and not under simultaneous consideration by another journal. Any previous publication of the material (including abstracts in conference proceedings or posters, or in a clinical trials results database) must be declared in the covering letter, as well as in the Acknowledgements section of the paper. For these purposes the posting of essentially raw data on a website without significant analysis, is not considered to represent prior publication. In addition, authors must include in the covering letter details of ANY previous submission of the work to JAC that has been rejected. The manuscript number of the earlier submission must be provided, as well as a point-by-point response to the comments made in the decision e-mail for the previous submission.

Authors should not fragment their research into least publishable units. Authors must be aware that JAC may decline to publish articles if this approach becomes evident.

Authors are fully responsible for the accuracy of all data in their articles.

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In-press papers or papers under editorial consideration

In-press and submitted papers that are important for the review of a paper MUST be uploaded when the paper is submitted and referred to in the covering letter that accompanies the submission. Authors should be aware of the issues of redundant/duplicate publication. For further information, please see the following Editorial:


Sequence data
When reporting sequences they must be submitted to one of the three major databases and an accession number must be provided at latest in the first revised version.

If a sequence has been submitted but an accession number has not yet been provided or the sequence is not yet available to the public then authors must submit the annotated sequence data as Supplementary data for scrutiny by the Editor and referees. Articles will not be permitted to enter the review process without the sequence data.

Supplementary data

Please note that it is also possible to submit files containing Supplementary data. The Supplementary data (for example large tables of MICs, or a survey) can be lodged with the version of the paper published online as an extra resource for readers. Supplementary data is largely unedited and is not proofed out so authors should ensure that they provide high quality, accurate files. In addition, authors must ensure that they cite the Supplementary data within the article. Please contact the Editorial Office if you require further details.

Authorship

The authorship of the paper should be confined to those who have made a significant contribution to the design and execution of the work described. In the case of clinical trials/randomized control trials it is compulsory for the contribution of each author to be clearly stated in the Transparency declarations section, after the information on conflicts of interest. Authors of other types of article may indicate the contribution made by each author if they wish.

JAC recommends that authors review the ICMJE criteria for authorship before submission (http://www.icmje.org/#author).

Author signed submission forms

When submitting a paper online authors should simultaneously provide a written statement, signed by all the authors indicating that they have complied with the stipulations in the Instructions to Authors (the statement MUST include the title of the paper and the COMPLETE list of authors). A copy (or copies) with the original signatures must be scanned and e-mailed to the Editorial Office as soon as possible after online submission (jac@bsac.org.uk). A blank form is available at http://www.oxfordjournals.org/jac/for_authors/signature.pdf. If at any stage during consideration the authorship of the article changes, the authors must supply a signed statement from ALL the authors (including any whose names are being removed) explicitly indicating the nature of the changes and their agreement.
Please note that the Journal requires the original handwritten signatures of ALL authors. This is the only way in which the Journal can be certain that all authors agree with the submission. If it is impossible to obtain the signature of a particular author (owing to death, loss of contact or other reasons), the corresponding author should explain the circumstances.

Please note that copied and pasted signatures are not acceptable.

Changes in authorship

The author list of any submission should be decided upon and fixed BEFORE submission. Other than in exceptional circumstances the Journal does not allow addition or removal of author names after submission. A satisfactory explanation for any proposed changes in authorship will be required and ALL authors will be required to supply new signed consent forms that reflect the changes. We will also require a signed consent form from any person whose name has been removed indicating that they agree to the removal of their name from the author list. Owing to the complexity of these rules we strongly advise authors to fix the author list before submission and not to attempt to make changes later.

‘Umbrella’ groups and authorship

Many large collaborative studies are organized under a group name that represents all of the participants. JAC will not accept a group name as an ‘author’ of an article. All articles must have at least one named individual as author. Authors of large collaborative studies should list the author(s) of the article and follow this with ‘on behalf of the [GROUP NAME]’. The names of all of the participants should then be listed in the Acknowledgements section.

Professional medical writers and editorial assistance

Professional medical writers and other forms of writing assistance have an important role to play in the clear communication of scientific results. However, unless this role is openly explained and acknowledged unfounded suspicions about this role will continue. JAC encourages the open and precise description of any such assistance received by authors in relation to any article. It is possible that writers may qualify for authorship of a manuscript, we recommend that authors review the ICMJE criteria for authorship before submission (http://www.icmje.org/#author).

The precise role of the writer or service in the origin or preparation of the manuscript must be declared in the Transparency declarations section; we recommend that the name of the writer (and their agency where applicable) or the service is provided. If this support was funded, the source must be declared in the Funding section.
Responsibilities of the corresponding author

For each paper submitted to JAC there must be a single corresponding author. As the representative of the authors, the corresponding author must ensure that all authors are given access to submitted and revised versions of papers. The corresponding author is responsible for the collation of the authors’ signatures on submission letters and also the collation and communication of proof corrections to the Journal. The corresponding author should be the signatory of the publication licence form. As the authors’ nominated representative, the corresponding author will be held primarily accountable for any failure to comply with the Instructions to Authors or generally accepted standards of good practice. This does not absolve other authors of responsibility, however.

The corresponding author will act as the primary contact for correspondence regarding the paper, and as such authors should take care not to appoint a corresponding author likely to be absent for extended periods (such as a sabbatical) during the consideration of the paper as this is likely to cause unacceptable delays.

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Ethics

All articles in JAC describing research in humans or animals must include an ‘Ethics’ heading as the first section in the Patients and methods or Methods section. Authors must include in this section all relevant statements regarding approvals, licences, informed consent and so on, as applicable.

Research involving humans

Authors must indicate in the Ethics section whether the research was conducted in accordance with the Declaration of Helsinki and national and institutional standards. If approval was obtained from an Ethics Committee the authors must clearly name the ethics committee responsible if more than one institution is involved. The approval/reference number must be listed in the Ethics section of the article. Written informed consent must be obtained from study
participants and the existence of this consent must be stated in the article. Authors must supply the relevant approval numbers from Ethics committees or other bodies.

Patient privacy. Patients have a right to privacy. Any information that might result in identification of individuals must be omitted, especially if it is not directly clinically relevant. Patient age, sex, admission dates and co-morbidities should be removed as far as possible. If it is possible that a patient could be identified, the authors must obtain written informed consent from the individual(s) concerned and state that this has been obtained in the article. Publication consent forms should be retained by the authors and not supplied to the Journal. If the patient is deceased the next of kin should be contacted. If consent cannot be obtained the authors must explain the circumstances briefly in the article, as well as in detail in the covering letter. In rare circumstances where relevant clinical details mean that the patient can be identified, the patient/next of kin must be shown the manuscript before submission and made aware as part of the informed consent process that the article may appear on the internet.

Case reports. Authors must avoid the temptation to recite the entire clinical history of the patient at the start of a case report and should retain only the clinical history that is pertinent. Reciting the entire clinical history greatly increases the chances that the patient could be identified. Date of treatment must be removed or converted to timespans for the same reason.

Research involving animals

Authors must state their compliance with relevant institutional and national standards for animal care and experimentation, together with the details of any authorities that licensed the experiments.

JAC supports the use of the ARRIVE Guidelines (https://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/NC3Rs%20ARRIVE%20Guidelines%20Checklist%20(fillable).pdf) and articles reporting research in animals must include a completed ARRIVE checklist (https://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/NC3Rs%20ARRIVE%20Guidelines%20Checklist%20(fillable).pdf) which must be uploaded with the article so it is available for the scrutiny of the Editor and referees.

Funding

ALL papers submitted to JAC reporting original research MUST include a ‘Funding’ section. This section should appear after the ‘Acknowledgements’ section.

Details of all funding sources for the work in question must be given.
Authors must list any internal funding. If no specific funding has been received then this should be clearly stated; equally if data have been generated as part of the routine work of an organization, this too should be stated. Ongoing financial support for any of the authors should also be included under the Funding heading.

If a professional medical writer or similar service was involved in the origin or preparation of a manuscript and this support was funded, the source must be declared in the Funding section.

Sources of funding may of course still be thanked in the Acknowledgements section, but should not be listed again in the Transparency declarations (see below), unless there is an important reason for doing so. For example if the funder played any decision-making role in the research this must be stated.

The following rules should be followed:

• The sentence should begin: ‘This work was supported by …’

• The full official funding agency name should be given, i.e. ‘the National Cancer Institute at the National Institutes of Health’ or simply ‘National Institutes of Health’ not ‘NCI’ (one of the 27 subinstitutions) or ‘NCI at NIH’ (full RIN-approved list of UK funding agencies is at http://www.rin.ac.uk/files/List-of-major-UK-research-funders.pdf)

• Grant numbers should be complete and accurate and provided in brackets as follows: ‘(grant number ABX CDXXXXXX)’

• Multiple grant numbers should be separated by a comma as follows: ‘(grant numbers ABX CDXXXXXX, EFX GHXXXXXX)’

• Agencies should be separated by a semi-colon (plus ‘and’ before the last funding agency)

• Where individuals need to be specified for certain sources of funding the following text should be added after the relevant agency or grant number ‘to (author initials)’.

An example is given here: ‘This work was supported by the National Institutes of Health (P50 CA098252 and CA118790 to R. B. S. R.) and the Alcohol & Education Research Council (HFY GR667789).

Crossref Funding Data Registry
In order to meet your funding requirements authors are required to name their funding sources, or state if there are none, during the submission process. For further information on this process or to find out more about the CHORUS initiative please click [here](#).

Conflicts of interest

Conflicts of interest have the potential to affect authors, referees and Editors (including Senior Editors and the Editor-in-Chief). JAC has the following systems in place to deal with conflicts of interest:

Authors. Authors are required to include a Transparency declarations section in every submission to the Journal (for details see below).

Referees. When invited to act, and again when they agree to act, referees are reminded to consider whether they have any potential conflicts of interest. Referees are asked to discuss any perceived potential conflict with the Editor of the article who will reach a decision as to whether it is appropriate that the referee acts on the article or whether they should withdraw.

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Transparency declarations

In the interests of openness, ALL papers submitted to JAC MUST include a 'Transparency declarations' section (which should appear at the end of the paper, before the 'References' section). We suggest authors concentrate on transparency declarations (i.e. conflicts of interest) of a financial nature, although relevant non-financial disclosures can also be made. Authors should consider making a declaration if they answer 'Yes' to any of the following questions:

1. Have you in the period of research leading up to this publication accepted any of the following from an organization (including government departments or granting bodies) that may in any way be financially affected by the conclusions of your article (e.g. reimbursement for attending a symposium, a fee for speaking, a consultancy fee, funds for research other than directly for this work, funds for a member of staff, any other substantial material benefit)?
2. Do you directly own any stocks or shares in a company that might be financially affected by the conclusions of your article?

3. Has the funder of the research played any decision-making role in the design, execution, analysis or reporting of the research?

4. Have you received the assistance of a professional medical writer or similar service? [The precise role of the writer or service in the origin or preparation of the manuscript must be declared and we recommend that the name of the writer (and their agency where applicable) or the service is provided.]

5. Have you accepted any reimbursement for preparing your article?

Authors should either include appropriate declarations or state ‘None to declare’. Importantly, the declarations should be kept as concise as possible, should avoid giving financial details (e.g. sums received, numbers of shares owned etc.), and should be restricted to declarations that are specific to the paper in question. Authors will of course need to consider whether or not the transparency declarations need to be amended when revisions are submitted.

The burden of responsibility rests with all authors, who must ensure that appropriate declarations are included. The corresponding author will be responsible for obtaining the relevant information from all of their co-authors. By signing a submission form each author is stating that they have made any necessary transparency declaration. All authors should carefully consider the embarrassment and potential damage to their reputation that could result should they fail to declare an interest that is revealed subsequently.

If only some authors need to make a declaration it must be made clear that the remaining authors have nothing to declare, for example:

'A.B. has received funds for speaking at symposia organized on behalf of Panacea Ltd and has also received funds for research from Panacea. C.D. is a member of the Panacea advisory board for fantastazole. All other authors: none to declare.'

All papers submitted to JAC must include a transparency declarations section; papers that do not include such a section will not enter the review process; they will be returned to the corresponding author so that the appropriate section can be added. Following resubmission the paper will then be progressed to peer review.

In the case of clinical trials/randomized control trials it is compulsory for the contribution of each author to be clearly stated in the Transparency declarations section, after the information
on conflicts of interest. Authors of other types of article may indicate the contribution made by each author if they wish.

Other useful information

In some instances (often when the authors themselves have no interests to declare) it may be helpful to readers as background information to give brief details of organizations that do have an interest but do not appear elsewhere in the article, for example ‘Fantastazole is owned by Wonder Pharmaceuticals’.

Misconduct

We will energetically pursue accusations of misconduct directed at authors, Editors or referees and have a number of sanctions at our disposal including the option to inform employers about accusations and ask them to mount their own internal investigations. Accusations should not be made lightly or in the absence of the likelihood of supporting evidence being obtainable. The Journal may take the view that accusations are malicious if supporting evidence cannot be found and may direct sanctions against accusers in such cases. Any accusation of misconduct should be addressed to the Editor-in-Chief (unless it involves the Editor-in-Chief, in which case it should be directed to the President of BSAC). JAC is a member of COPE and will follow its guidelines on the handling of investigations into research misconduct.

Clinical trials/Randomized controlled trials

Registration and data publication

Authors must register their trials in one of the databases dedicated to registration of trials. In addition, authors must state the database and provide the unique registration number – both in the abstract and in the main body of the paper.

JAC will consider for publication clinical trials for which there has been prior publication of trial data in results databases (such as http://www.clinicalstudyresults.org/about/ or others), however, authors MUST declare in the covering letter and the Acknowledgements section of the article that they have previously published data in a results database.

Contributions

The contribution of each author must be clearly stated in the Transparency declarations section, after the information on conflicts of interest.

Reporting standards
All involved in the publication of health intervention research have a duty to patients and society at large to ensure that this research is reported in a complete, accurate and transparent fashion. This includes authors, referees, Editors and Journals. JAC takes this responsibility seriously and endorses the work of organizations such as the EQUATOR network (http://www.equator-network.org/), an international initiative that seeks to improve the reliability and value of the medical research literature.

There is a wide range of reporting guidelines, each specific for different types of study. Some of those for study types that are frequent in JAC are mentioned specifically below. Authors should consult the EQUATOR network website (http://www.equator-network.org/) for links to the latest versions of guidelines, which are organized by the study type.

Randomized controlled trials

Authors should comply with the Consolidated Standards of Reporting Trials (CONSORT) statement (www.consort-statement.org/) and use the resources within it (for example the checklist and flow diagram) to ensure they have addressed potential criticisms and provided all necessary information. Authors should include a CONSORT flow diagram in their article, and provide a copy of the completed checklist.

Systematic reviews and meta-analyses

For systematic reviews and meta-analyses of randomized controlled trials authors should comply with the PRISMA statement (which replaces the QUORUM statement), which consists of a checklist and flow diagram (http://www.prisma-statement.org/index.htm). Authors should include a PRISMA flow diagram in their article, and provide a copy of the completed checklist.

Outbreaks and intervention studies in nosocomial infection

Authors should comply with the ORION statement (www.idrn.org/orion.php), which is the CONSORT equivalent for infection control studies. Its purpose is to increase the quality of research and reporting in the area of nosocomial infection.

Economic evaluations

Authors of articles describing economic evaluations of antimicrobial interventions are encouraged to make use of the following resources, where applicable, in order to ensure that their work is both optimal and adequately described.
International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Checklist for retrospective database studies, which can be accessed at: http://www.ispor.org/workpaper/healthscience/ret_dbTFR0203.asp


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JOURNAL STYLE

General

In addition to reading the information provided here, authors should consult a recent issue of the Journal for the layout and conventions used.

The past tense should be used throughout for description of the results of the paper, the present tense should be used when referring to previously established and generally accepted results.

Where possible SI units should be used.

Please ensure that characters with a similar appearance are consistent throughout the document and not from different Unicode sub ranges as with the Greek Delta.

Language editing

Particularly if English is not your first language, before submitting your manuscript you may wish to have it edited for correct usage of English. This is not a mandatory step, but may help
to ensure that the academic content of your paper is fully understood by journal editors and reviewers. Language editing does not guarantee that your manuscript will be accepted for publication. If you would like information about one such service provided by SPi, please click http://www.oxfordjournals.org/for_authors/language_services.html. There are other specialist language editing companies that offer similar services and you can also use any of these. Authors are liable for all costs associated with such services.

Spelling

British spelling should be used. Spelling should follow that of the Oxford Dictionary for Scientific Writers and Editors and where this gives no guidance the Concise Oxford Dictionary. Spelling of drug names should conform with that given in the latest edition of the British National Formulary (published by the British Medical Association and the Royal Pharmaceutical Society of Great Britain and available online at http://www.bnf.org/bnf), but please note that JAC will continue to use methicillin (not meticillin).

Abbreviations

Non-standard abbreviations should be defined at the first occurrence and introduced only where multiple use is made. See here for abbreviations that may be used without definition, as well as antimicrobial abbreviations (which may be used in Tables and Figures).

Dosage frequencies and routes of administration

Latin dosage frequency abbreviations are not permitted (qd, bd, bid, tds etc.), however, constructions q12h, q8h and so on are permitted as there is less likelihood of confusion. Routes of administration other than intramuscular (im) and intravenous (iv), which may be abbreviated after definition, should be given in full in English.

MICs

Please note that all MIC data in JAC must be expressed in terms of mg/L (not μg/mL).

Nomenclature

Authors are required to check and ensure that in all instances the most up to date nomenclature is being used.

Bacterial nomenclature

When genus and species are given together use a capital letter for the genus and a lowercase letter for the species and italicize both e.g. Staphylococcus aureus. After the initial use in the
text of the full name of an organism the generic name should then be abbreviated to the initial letter, e.g. E. coli.

When the genus is used as a noun or adjective use lowercase roman unless the genus is specifically referred to e.g. 'staphylococci and streptococci' but 'organisms of the genera Staphylococcus and Streptococcus'.

The name of an order has an initial capital but is not italicized, e.g. Enterobacteriaceae. For genera in the plural, use lowercase roman, e.g. salmonellae.

When the species is used alone use lowercase e.g. viridans streptococci. For trivial names, use lowercase roman e.g. meningococcus.


Genetic and amino acid nomenclature

Bacterial genetics. Genotype designations are indicated with italic lowercase three-letter locus codes (e.g. par, his, ara). If several loci are involved in a related function the individual loci are designated by the addition of an uppercase italic letter to the locus code (parC, ompF).

Phenotype designations (for example the protein product of a bacterial gene) are given in roman type with an initial capital letter (OmpF, LacZ).


Yeast genetics. Wild-type alleles are all uppercase and italicized (LEU2), mutant alleles are all lowercase and italicized (leu2), and gene products are capitalized on the first letter and are not italicized (Leu2).

General. Authors should ensure that they confine discussion of changes in amino acid sequence to the context of the protein (e.g. OmpF) and nucleotide changes to the context of the
gene (e.g. ompF). Please also be aware of the difference between a mutant (a strain with one or more mutations) and a mutation (a change in the sequence of the genetic material).

Amino acids. The full residue names or three-letter abbreviations are preferred in the text (e.g. a methionine residue at position 184 should be symbolized Met-184). The single letter codes may be used in figures. Amino acid changes should be designated Met-184→Val or M184V.

When comparing nucleotide or amino acid sequences authors should exercise care in the use of the term homology. Homology should only be used when a common evolutionary origin is being implied; it is incorrect to give a percentage homology between two sequences. The wing of a bird and the human arm are homologous structures (they are believed to have a common evolutionary origin), homology cannot be quantified. For sequence comparison authors should use the terms identity and similarity. Sometimes 'equivalent' or 'counterpart' is more appropriate than 'homologue'.

Beta-lactamase nomenclature

Authors submitting articles reporting the identification of new beta-lactamases must provide evidence that they have contacted the relevant clearinghouse (http://www.lahey.org/Studies/) to deposit the new sequence data and receive a unique designation for the new enzyme.

Macrolide-lincosamide-streptogramin resistance determinant nomenclature

Nomenclature for macrolide-lincosamide-streptogramin resistance determinants should follow the structure suggested by: Roberts MC, Sutcliffe J, Courvalin P et al. Nomenclature for macrolide and macrolide-lincosamide-streptogramin B antibiotic resistance determinants. Antimicrob Agents Chemother 1999; 43: 2823-30. A new gene must have ≤79% amino acid identity with all previously characterized MLS genes before receiving a new unique name. Adding subscripts or superscripts to established genes is not acceptable. See: http://faculty.washington.edu/marilynr/. Before submitting a sequence to GenBank or submitting a manuscript for publication, please contact Professor Marilyn Roberts (marilynr@u.washington.edu). Once a new name has been assigned you must indicate in your article that you have received approval by the nomenclature centre for the new gene name.

Tetracycline resistance determinant nomenclature

Adding subscripts or superscripts to established genes is not acceptable. See: http://faculty.washington.edu/marilynr/. The Levy Group is responsible for coordinating the naming of new tet genes and before submitting a sequence to GenBank or submitting a manuscript for publication, please contact Laura McMurry (laura.mcmurry@tufts.edu). Once a new name has been assigned you must indicate in your article that you have received approval by the nomenclature centre for the new gene name.

qnr gene/allele nomenclature

Authors submitting articles reporting the identification of new qnr genes or alleles must provide evidence that they have contacted the relevant clearinghouse (http://www.lahey.org/qnrStudies/) to deposit the new sequence data and receive a unique designation. Authors should consult Jacoby G, Cattoir V, Hooper D et al. qnr gene nomenclature. Antimicrob Agents Chemother 2008; 52: 2297-9.

FICI data

Fractional inhibitory concentration index (FICI) experiments are performed in order to study drug interactions and they must be interpreted in the following way:

FICI<=0.5 = synergy

FICI>4.0 = antagonism

FICI>0.5-4 = no interaction

For further information please see the following Editorial:


Microarray data

Authors of articles containing microarray data must ensure that the full datasets are lodged with an appropriate publicly available online database (the data must not be supplied for publication as Supplementary data alongside the article). The data should be supplied with the submitted article if they are not already publicly available. The name of the database and the accession numbers should be provided in the article. Authors must ensure that their data are available for public scrutiny from the online publication date of their article at the latest.

Chemistry
General nomenclature. The IUPAC recommendations on chemical nomenclature should be followed (IUPAC Compendium of Chemical Terminology (1987, ISBN 0 632 01767 8, Blackwell Scientific Publications, Oxford). All chemical names are run together except those of acids, acetals, esters, ethers, glycosides, ketones and salts, which are printed as separate words; hyphens are used to separate numbers, Greek letters and some configurational prefixes, e.g. p-nitrophenol. Italics are used for certain prefixes, e.g. cis-, trans- and N. Small capitals are used for dextro- and laevo- prefixes, e.g. L-glutamine.

Drugs. Spelling of drug names should conform with that given in the latest edition of the British National Formulary. Chemical or generic names of drugs should be used; trade names may be referred to once only upon first use of the generic or chemical name. The content of proprietary formulations should be given if relevant. Generic names should not be abbreviated in the text; abbreviations may be used in Tables if there is limited space. If compounds are referred to by code name or company number either the structure or a reference to a paper illustrating the structure must be given, any previous code names or designations should be given on first use.

Supplier locations are required for all smaller/local suppliers.

References

Authors are responsible for the accuracy of all references, which must be checked against the original material. Reference citations should be restricted to those that are essential for introducing the purpose and context of the paper, describing methods that are not given in detail, and for discussing the results and any relevant issues raised by them. Authors are responsible for ensuring that references are quoted accurately and not taken out of context. References must not be cited in the synopsis.

Where possible authors should avoid citing conference abstracts or posters (partly because they are not peer reviewed and also because they often report interim findings and the final published studies can often come to substantially different conclusions) and authors MUST NOT cite abstracts that are more than 2 years old without excellent justification for doing so. In addition, abstracts must only be cited if they appear in published abstract books, journal supplements or in a permanent online archive.

References should be cited in the text using sequential numbers. Superscript numbers should be used and should be placed after any punctuation. When referring to several references, separate individual numerals by a comma or a hyphen for a range greater than two references.
For instance: This was first discovered by Jones, 1 and later confirmed by several other groups of investigators. 2,3,5-7

Papers accepted for publication, but not yet published, may be included in the reference list; they should be listed as 'in press', with the name of the journal and the likely year of publication. Submitted work should be quoted as 'unpublished results'. Personal communications and unpublished results, which are permitted in the text only, must include the initials and surnames of all the workers involved; for the former citation, the person’s affiliation must be stated, e.g. ‘(J. Bloggs, NIH, personal communication)’, and documentary evidence (an e-mail will suffice) from the person quoted, showing their agreement to be so quoted, must be provided (the agreement must include the exact wording that appears in the paper).

All references should be listed numerically at the end of the text. Each reference should be preceded by a number (not superscript) followed by a full stop. Please see the following examples. Failure to conform to Journal style will result in the manuscript being returned to authors.

Examples

Journal reference (<= three authors)


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Whole book


Book chapter

NCCLS/CLSI methods


Meeting abstract


Online material

References to online material should be given in the reference list. Please note that URLs for the suppliers of materials must not be given in either the text or the references. The Journal does not accept any responsibility for the content of web pages cited.

NB – it is no longer necessary to provide the ‘date last accessed’ for URLs.


Tables

These should be employed sparingly and should be generally comprehensible without reference to the text. Each table should be supplied on a separate sheet and numbered consecutively using Arabic numerals in the order they are referred to in the text. Each must have a brief descriptive heading. Column headings must clearly explain the content of the column and indicate any units used. Footnotes should be kept to a minimum.

Tables must be created using the Table function in Word; they must not be inserted as images. Each data item should occupy a single cell and return characters should not be used within
Appendices

any Table. JAC reserves the right to move complicated Tables to online-only Supplementary data.

Figures

These must be employed sparingly to demonstrate important specific points. Figures should be numbered using Arabic numerals in the order in which they are referred to in the text. In figure LEGENDS, symbols should be described in words (e.g. filled circles, open squares etc.). Wherever possible, figures should be two-dimensional. Authors should NOT supply ‘three-dimensional’ figures unless this is actually necessary to represent the data.

The quality of reproduction in JAC is limited by the quality of the submitted material. All figures must be of high quality - they should be sharply focused, have good contrast and any lettering must be clear and legible. Colour illustrations can be reproduced if there is sufficient scientific merit in doing so. Authors will be expected to pay for the cost of colour origination in the print version of the Journal (£350/US$600/€525.00 per figure). Alternatively, black and white figures can appear in the printed version of an article with colour versions appearing online (for which there is no charge) – figure legends will need to be suitably worded, e.g. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC. Please state your preferred option (i.e. agreement to pay £350/US$600/€525.00 per figure for print and online colour or preference for online-only colour with no charge) in your covering letter.

Guidance for preparation of Figures

Figures should be sized to fit a single column of the Journal where possible (88 mm) or a double column if necessary (180 mm). The preferred font for lettering is Times; lettering should have an upper case height of 2 mm and a lower case height of 1 mm at publication size (corresponding to point size 8). Line thickness should be set at 0.5 points. Shading used on line drawings should be clear and distinctive; shades of grey and heavy stippling do not reproduce well. Lines and symbols should be drawn boldly enough to withstand reduction. The preferred symbols are filled circles, open circles, filled squares, open squares, filled triangles and open triangles, and should be no smaller than 1 mm (height/diameter) at publication size. Part labels should be lower case letters within parentheses, e.g. (a), (b), (c) etc.

Authors must be ready to supply original gel pictures if requested to do so.

ONLINE SUBMISSION DETAILS
Appendices

The URL for JAC's online submission and peer review site is: http://mc.manuscriptcentral.com/jac

For online submission instructions, please follow this link.

Revised March 2016.
Appendix 10: Guidelines for authors for the Southern African Journal of Infectious Diseases

Manuscripts submitted to the SAJID must be in the form of Research Articles, Brief Reports, Clinical Case Studies, Correspondence, Reviews, State-of-the-Art Articles, Commentaries and Opinion Papers, Editorials or Supplement Articles. The Journal welcomes the publication of Guidelines, Conference Proceedings Newsletters or Press Releases, and Book Reviews. Articles, Brief reports and Reviews are peer reviewed; other categories are reviewed by the Editors. Commentaries and Editorials are generally invited contributions, indicating the authors’ identity, while manuscripts in the form of Reviews, and State-of-the-Art Articles may also be requested by the Editors.

All manuscripts must have conflict of interest and funding statements. When authors submit a manuscript, whether an article or a letter, they are responsible for disclosing all financial and personal relationships that might bias their work. To prevent ambiguity, authors must state explicitly whether potential conflicts do or do not exist. Authors should do so in the manuscript on a conflict-of-interest notification page that follows the title page.

Manuscripts describing research in human subjects or animals must indicate ethics clearance from appropriate research review committees. When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

Articles describe original investigations at an acceptable degree of completion, constituting an advance in the field. Articles must not exceed 3500 words of text, without counting the abstract, references or legends, and illustrations and tables must be limited to the minimum necessary for clear and concise presentation. The abstract must either be structured, using Background, Methods, Results, and Conclusions as headings and comprising no more than 250 words, or unstructured with a 200 word limit. Articles are limited to a maximum of 7 insets (tables and figures combined) and 50 references.

Brief Reports present complete studies that are narrower in scope than those described in Articles or that present new developments. Manuscripts that are descriptive or primarily methodological in nature, or that describe in vitro chemotherapeutic studies should, in general, be submitted as Brief Reports. Brief Reports include an abstract (no more than 100 words) and
are limited to a total of no more than 2000 words of text, a total of 2 inserts (tables or figures), and 15 references.

Correspondence (letters) must be submitted in reference to a previous publication in SAJID (within the previous 12 months), or relate to a topical matter in line with the interests of FIDSSSA, PHASA or their affiliated societies. Please prepare the letter in manuscript format, including a title page. The letter must not exceed 750 words of text, 1 insert (table or figure) and 10 references.

Commentaries and Editorials are generally invited by the Editor and are overviews of articles in SAJID, or of other research in epidemiology or infectious diseases, or matters relating to public health and other issues of special interest to FIDSSSA, PHASA or their associated societies. Unsolicited commentaries are also considered.

Reviews and State-of-the-Art Articles that are research oriented or fall within the fields of interests of FIDSSSA, PHASA or any of their affiliated societies will be considered for publication by SAJID. Prospective authors of such manuscripts are advised to communicate with the Editor in advance to ensure that a specific contribution is deemed appropriate and timely. Manuscripts of Reviews and State-of-the-Art Articles will be peer-reviewed.

Reviewers

The Journal would encourage authors to supply the names of at least 2 potential reviewers for their manuscript, as well as to indicate any reviewers they would feel may have a potential conflict of interest with regard to their submission.

Supplements

Requirements for supplement manuscripts generally follow those for SAJID manuscripts, including conflict of interest and funding statements. Inquiries relating to suitability of topic, programme organisation, production and costs should be made to the Editor.

Evaluation of manuscripts

Review procedure. The Editor-in-Chief and Emeritus Editor screen all unsolicited manuscript submissions and some of these are rejected without further review. All other manuscripts are sent to a minimum of two outside experts for review. After receipt of the reviewers’ reports, the Editor-in-Chief and the Emeritus Editor with administrative assistance of the Journal Secretary discuss the merits of the manuscripts and the Editor-in-Chief makes the final decision.
to accept, reject, or request revision of the manuscript. A request for revision does not guarantee ultimate acceptance of the revised manuscript.

Related manuscripts. If there appears to be significant overlap between a manuscript submitted to SAJID and another submitted manuscript by the same authors to SAJID or another journal, the editors will take the matter up with the corresponding author, and based on the response, take appropriate action (ask for modification, or reject with detailed explanation). Further action may include informing the appropriate authority in the authors’ resident institution and if overlapping is discovered after publication in SAJID, publishing an appropriate announcement to that effect in the journal.

DOCUMENT REQUIREMENTS

Checklist

The following are required for your manuscript to be processed:

Covering letter

Word count limits

Conflict of interest statement

Funding statement

List of potential reviewers

Covering Letter

All manuscripts submitted to SAJID must be accompanied by a letter declaring that the manuscript has not been submitted or accepted for publication elsewhere. This letter must confirm and declare that all authors have seen and approved the content and have contributed significantly to the work. Authors should suggest potential unbiased reviewers who are qualified to review their manuscript. A covering letter must also accompany a revised submission and must address issues raised in the review process.

Manuscript Preparation

The SAJID complies with the Uniform Requirements for Manuscripts Submitted to Biomedical Journal Journals (Ann Intern Med 2000; 133:229-231 [editorial]; http://www.icmje.org, full text). Text, tables, references, and legends must be double-spaced. Italicics should be used for genus and species names and for genes but not for in vivo, in vitro, in situ, et al, or other Latin-
derived expressions. For layout of manuscript and appropriate style see a recent issue of SAJID.

Title page. On the title page, please supply a running head of not more than 40 characters and spaces, a title of not more than 160 characters and spaces, the names and affiliations of all the authors, and word counts of the abstract and text. Each author’s first name, subsequent initials and surname must be used.

Footnote page. Footnotes must include:

Statement that authors either have or have not a commercial or other association that might pose a conflict of interest (e.g. pharmaceutical stock ownership, consultancy, advisory board membership, relevant patents, or research funding)

Statement naming sources of financial support (including grant numbers)

Name, date (month and year), and location (city, and country if not South Africa) of a meeting at which all or part of the information has been presented (include an abstract number, if available)

Name, address, telephone and fax numbers, and e-mail address of the person to whom correspondence should be addressed

Current affiliations and addresses for authors whose affiliations have changed since completion of the study

Abstract. The abstract for an Article may be structured with the headings Background, Methods, Results, and Conclusions (250-word limit) or unstructured (200-word limit). Abstracts of Brief Reports should be no more than 100 words. Whether structured or unstructured, the abstract must state the purpose of the research, the methods used, the results, and the conclusions. Do not cite references in the abstract. Include up to 10 key words, separate from the abstract. Please remember that the abstract is particularly useful for literature retrieval purposes.

Text. The text of Articles must be no longer than 3500 words, and that of Brief Reports no longer than 2000 words. The Methods section must include a statement that informed consent was obtained from patients or their parents or guardians, and human experimentation guidelines of the National Department of Health (http://www.doh.gov.za) or the South African Medical Research Council (MRC; http://www.sahealthinfo.org/ethics/index.htm) and /or those of
the authors’ institution(s) were followed in the conduct of clinical research or that animal experimentation guidelines (see MRC website above) were followed in animal studies.

References. Articles are generally limited to 50 references, Brief Reports to 15 references. Only works that have been published or accepted for publication can be included in the reference list. Unpublished observations by the authors (authors’ unpublished data) personal communications (SP Stanley, personal communication), and manuscripts submitted for publication (J Odendaal, S Coovadia and J Radebe, submitted) should be mentioned parenthetically in the text Please number references in order of appearance; those cited only or first in tables or figures are numbered according to the order in which the table or figure is cited in the text. Example: If table 3 is cited in the text after reference 20, a new reference cited in table 3 will be reference 21.

References must follow the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org, full text). Provide all authors’ (or editors’) names when there are fewer than 7; for 7 or more, list the first 3 and add “et al.” Titles of journals not listed in Index Medicus should be spelt out in full. Reference to a doctoral thesis or Master’s dissertation should include the author, title, institution, location, year and publication information, if published. For online resources, include a URL and date accessed. Accuracy of references is the responsibility of the authors.

Examples of the proper format are as follows:


Acknowledgment(s). The page preceding the references may include a statement thanking those who assisted substantially with work relevant to the study.

Statistical analysis. The statistical analyses used should be identified both in the text and in all tables and figures where the results of statistical comparison are shown.

Units of measure. All Data should be expressed in metric units; use of SI units is encouraged. Use °C for temperature.

Tables and figures. Articles are limited to a maximum of seven inserts (tables and figures combined), Brief Reports to a maximum of two inserts. Data should not be repeated in both a table and a figure. Abbreviations and acronyms used in tables and figures must be explained in the table footnotes and figure legends, even if already defined in the text.

Tables should be numbered in the order of mention in the text. Tables should be typed double-spaced throughout, with no vertical or internal rules. Footnotes and accompanying explanatory material should be kept to a minimum. Footnotes should be placed below the table and designated by superscript lowercase letters (listed in order of location when the table is read horizontally). Each column must have an appropriate heading describing the data in the column below, and units of measure must be clearly indicated. For further instructions on the preparation of tables in Word, consult the Special Instructions for Tables.

Figures should be also numbered in the order of mention in the text and should appear at the end of the manuscript and references. Your figures should be prepared in accordance with the Guidelines for Submission of Artwork. Letters, numbers, and symbols should be clear and of sufficient size to be legible when the figures are reduced. Photomicrographs should have internal scale markers. Figures reproduced from other publications must be accompanied by permission from the copyright holder. If the manuscript is accepted, the author will be required to send one complete set of glossy, hard-copy figures.

Figure legends should be double-spaced and appear on a separate page preceding the figures. Any abbreviations or symbols used but not defined in the figure itself must be defined in the legend.

Appendices

For commercially obtained products mentioned in the text, list the full names of manufacturers. Generic names of drugs and other chemical compounds should be used.

Nomenclature. SAJID recommends the latest widely accepted nomenclature, as set out in documents prepared by recognised international agencies e.g. the International Journal of Systematic and Evolutionary Microbiology, Bergey's Manual of Determinative Bacteriology (9th ed., revised, Williams& Wilkins, 1993), Virus Taxonomy – The Classification and Nomenclature of Viruses: Sixth Report of the International Committee on Taxonomy of Viruses (Springer-Verlag, 1995). The latter document also supplies standard abbreviations for virus species.

Clinical trials registration. All clinical trials must be registered in a registry that is electronically accessible to the public, free of charge. Registration should occur before patient enrolment and the registry’s URL and the trial’s registration number must be supplied at the end of the manuscript's abstract. For information on acceptable registries, consult the ICMJE Web site, http://www.icmje.org. The National Library of Medicine’s registry which is free and open to all investigators, generally meets with the requirements of journals for the publication of clinical trials.

MANUSCRIPT SUBMISSION

Procedure

Authors are advised to retain a copy of submitted manuscripts, including tables, figures and photomicrographs. The journal is not responsible for manuscripts lost or damaged.

All manuscripts must be submitted online at www.sajei.co.za. Register as an author, login in and click on CLICK HERE TO FOLLOW THE FIVE STEP SUBMISSION PROCESS. The covering letter must please be submitted as a supplementary file. For assistance to upload your manuscript or further instructions please contact Ms Robyn Marais at toc@sajei.co.za.

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Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

The submission has not been previously published, nor is it before another journal for consideration (or an explanation has been provided in Comments to the Editor).

The submission file is in Microsoft Word, RTF document file format.

Where available, URLs for the references have been provided.

The text is one and a half-spaced; uses a 12-point font; employs italics, rather than underlining (except with URL addresses); and all illustrations, figures, and tables are placed within the text at the appropriate points, rather than at the end.

The text adheres to the stylistic and bibliographic requirements outlined in the Author Guidelines, which is found in About the Journal.

The following is required for your manuscript to be processed:

Covering letter

Word count limits
Appendices

Conflict of interest statement

Funding statement

List of potential reviewers

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