EVALUATION OF THE COMPLIANCE OF ANTIBIOTIC PRESCRIBING WITH INTERNATIONAL CLINICAL PRACTICE GUIDELINES FOR SURGICAL ANTIBIOTIC PROPHYLAXIS AT INTERMEDIATE HOSPITAL RUNDU, NAMIBIA

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ABSTRACT

Compliance with guidelines of surgical antibiotic prophylaxis (SAP) has been shown to reduce the prevalence of surgical site infections by approximately 40%. However, globally, 30 to 90% of antibiotics used for SAP purposes, are irrationally utilized. The aim of this study was to estimate the level of compliance with international clinical practice (ICP) guidelines for SAP and determine predictors of non-compliance at Intermediate Hospital Rundu (IHR).

This was a quantitative, analytical retrospective clinical record review. Data were collected from April 2019 to June 2019 from the clinical records of post-operative patients in theatre unit using a standardized assessment form. Compliance was evaluated in terms of correct antibiotic prophylaxis choice, timing, route of administration, dose and discontinuation.

A total of 153 surgical procedures were evaluated. Of these, 149 warranted SAP but only 92.0% received antibiotic prophylaxis. The level of compliance with SAP guidelines was high with regards to correct route (99.3%) and moderate with respect to timing of administration (38.7%). Compliance with SAP guidelines was low with regards to correct antibiotic choice (15.3%), dosing (9.5%) and antibiotic discontinuation within 24 hours (0.7%). None of the records complied with the parameters of ICP guidelines for SAP. The main predictors of non-compliance to prescribing correct SAP were general medical officers OR = 34.29 (95% CI 8.71 to 134.95) and specialists OR = 6.35 (95% CI 2.63 to 37.61). Elective surgical procedures OR = 2.96 (95% CI 1.32 to 6.65) independently predicted non-compliance to appropriate timing of antibiotic administration. General medical officers OR = 53.03 (95% CI 8.35 to 336.66), specialist OR = 14.11 (95% CI 2.4 to 83.24) and age of patient OR = 1.09 (95% CI 1.02 to 1.16) were predictors of non-compliance to correct dosing of prophylactic antibiotics.

Compliance with internationally recognized guidelines was sub-optimal. There is need to develop local SAP guidelines and access to improve rational antibiotics use in surgery at IHR.

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LIST OF ABBREVIATIONS/ACRONYMS

AMR antimicrobial resistance

ASHP American society of Health-System Pharmacists

CDI *Clostridium difficile* infection

CD Caesarean delivery

CS Caesarean section

HAI health-care-associated infections

IHR Intermediate Hospital Rundu

MoHSS Ministry of Health and Social Services

NICE National Institute for Health and Care Excellence

SAP surgical antibiotic prophylaxis

SIGN Scottish Intercollegiate Guidelines Network

SSI surgical site infections

WHO World Health Organization

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DEDICATION

This work is dedicated to my children Sarah and Samuel whom I deprived most of precious time. To my wife Kabwe, your encouragement and support kept me motivated when I felt like giving up and I will forever cherish your patience.

DECLARATIONS

I, Brian Chola, hereby declare that this study is my own work and is a true reflection of my research, and that this work, or any part thereof has not been submitted for a degree at any other institution.

Brian Chola		May, 2022
Name of Student	**Signature**	**Date**

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Surgical site infections (SSIs) are common postoperative complications (1) and account for most health-care-associated infections (HAI) in low and middle-income countries (LMICs) such as Namibia (1,2). Although SSIs are mostly preventable, approximately 30% of surgical patients develop post-operative infections in resource-limited settings (1). The estimated incidence of SSIs is 5.6 per 100 surgical procedures (1,3). SSIs negatively impact patient outcomes in terms of morbidity and mortality, and financial resources of health-care systems, mostly in LMIC due to prolonged hospitalisation of patients (4).

However, studies have shown that the risk of SSIs may be reduced by approximately 40% through the appropriate use of surgical antibiotic prophylaxis (SAP) (5,6). As a result, about 12 – 50% of antibiotics in some hospitals are utilised for SAP (7,8). In Namibia, there is a dearth of data on the proportion of antibiotics utilized for SAP, however, in the Kavango region for example, antimicrobials accounted for approximately 30% of annual pharmaceutical expenditure in 2015 (9).

Current evidence-based guidelines (10–13) recommend SAP in post-operative patients when there is an indication, with consideration for the choice of antibiotic agent, dosing, route of administration, timing and discontinuation. Despite the availability of these guidelines, recent studies (14–16) suggest that globally, 30 to 90% of antibiotics utilized for SAP are used irrationally. These studies suggest that antibiotic use in SAP is mostly inappropriate with regard to timing of administration

and duration (discontinuation) of prophylactic antibiotic therapy (14–16). For instance, a recent systematic review reported that compliance of antibiotic prescribing with SAP guideline with respect to timing and duration parameters ranged from 12.7% to 100% and 5.8% to 91.4%, respectively (17). This systematic review did not include studies undertaken in Sub-Saharan Africa. However, the findings of several studies conducted in Africa are consistent with those of the systematic review (18–20).

Although there is paucity of data on studies around SAP in Namibia, Rushubiza evaluated antibiotic prophylactic use at Windhoek Central Hospital Main theatre and found a dismal overall compliance with the local hospital protocol of 8.5% (21). Besides, some local studies focusing on other aspects of antibiotic use have also shown low compliance of antibiotic use with guidelines and policies ranging from 30% to 62% (22,23).

Non-compliance with national guidelines, policies or hospital protocols may lead to indiscriminate use of antibiotic prophylaxis. Low level compliance with recommendations of SAP guidelines raises concerns as it not only accelerates the development of antimicrobial resistance (AMR) but also unnecessarily predisposes patients to adverse outcomes such as *Clostridium difficile* infection (CDI) (24–26). The global health and economic gravity of AMR projected that AMR-attributable mortality could rise to about 10 million annually accompanied by a global economic cost of approximately 100 trillion United States (US) dollars (27). Therefore, concerted efforts are required to curb the rise of AMR by optimising antibiotic use given that two local studies have demonstrated an increase in emergence of AMR (28,29).

As previously stated, sub-optimal SAP prescribing is partly attributed to a global challenge of non-compliance with clinical practice guidelines (17). This situation may be dire in settings which lack a dedicated SAP guideline such as Namibia. The reasons for non-compliance with clinical guidelines are complex and multiple (30).

Therefore, this study aimed to estimate compliance levels of surgical antibiotic prophylaxis with the international clinical practice guidelines of the Scottish Intercollegiate Guidelines Network (SIGN) and the American Society of Health-System Pharmacists (ASHP) at Intermediate Hospital Rundu in the Kavango East Region of Namibia. The SIGN (10) and ASHP (11) guidelines were used as they have a broad scope in terms of antibiotic options besides being both evidence-based and internationally recognised.

1.2 Statement of the Problem

Most studies conducted in Sub-Saharan Africa have demonstrated poor overall compliance of SAP prescribing with clinical guidelines. Generally, overall compliance is estimated at less than 3% (18,31). The problem may be compounded by lack of a dedicated SAP guideline as is the case with Namibia. Furthermore, excessive antibiotic prescribing has been reported in Namibia's public and private health sectors (32,33).

Irrational use of antibiotics for SAP has been associated with increased risk of AMR, wastage of resources and predisposition of surgical patients to poor outcomes (34). Collection of baseline antibiotic prescribing data to inform implementation of intervention strategies has been recommended as a way of improving rational antimicrobial use in the health care system (35,36). Therefore, this study intended to

fill this gap by exploring prescribing practices in SAP and its compliance with SIGN and ASHP guidelines.

1.3 Objectives of the Study

1.3.1 Main objective

To estimate the level of compliance of antibiotics prescribed as surgical antibiotic prophylaxis in selected elective and emergency surgical procedures with SIGN and ASHP guidelines at Intermediate Hospital Rundu.

1.3.2 Specific objectives

i. To estimate the level of compliance with guidelines in terms of appropriateness of indication, choice of antibiotic, timing, route of administration, dose and discontinuation of SAP

ii. To identify predictors associated with non-compliance with guidelines

1.4 Significance of the study

This study explored SAP prescribing practices in patients undergoing surgical procedures. The study highlights aspects of antibiotic prescribing in SAP that require interventions to improve clinical care and reduce SSIs in health facilities. The findings of this study also provide baseline information required for the development of a local guideline for SAP to standardize prescribing practices in surgery and reduce wastage of antimicrobials.

CHAPTER 2:

LITERATURE REVIEW

2.1 Search strategy

A literature search of multiple databases subscribed to by the University of Namibia (UNAM) online library such as MEDLINE (PubMed), Hinari, and ScienceDirect was conducted. Open access articles were retrieved from databases such as ResearchGate and other authoritative websites on the subject of interest. The UNAM library and an author provided a few articles on request. The search focused on recent literature pertaining to SAP from January 2013 to September 2019. However, due to the scarcity of published studies, the search was extended to January 1990 since most evidence-based guidelines on the subject were generally published in the previous 20 years (37).

The language was restricted to English. However, articles with English translation were also considered**.** Medical subject headings (Mesh) terms and keywords such as 'surgical antibiotic prophylaxis' or 'SAP', 'antibiotic prophylaxis', 'surgical site infections or 'SSI', 'adherence', 'compliance' 'guidelines', 'Sub-Saharan Africa' and 'Namibia' were used to search databases. There was a paucity of published studies from Africa, and no article of a study conducted in Namibia was retrieved, although one unpublished study was obtained (21).

2.2 Introduction

This chapter explores the literature related to the use of surgical antibiotic prophylaxis as an adjunctive measure in reducing surgical site infections. The fundamental principles of antibiotic prophylaxis in surgery and the importance of compliance with evidence-based clinical practice guidelines that aim to maximise the potential benefits of antimicrobials while slowing the emergence of AMR are introduced in this chapter. The global challenge of non-compliance of antibiotic prescribing with SAP guidelines and the predictors of non-compliance are also highlighted.

2.3 The rationale of surgical antibiotic prophylaxis

The overall objective of surgical antibiotic prophylaxis is to provide appropriate prophylactic coverage to reduce the incidence of SSIs in patients undergoing operations with risk of infection while minimising the emergence of AMR (10). The evidence supporting SAP use is well established and spans more than 50 years following clinical studies conducted by Bernard and Cole, and later Polk and Lopez-Mayor that demonstrated the significance of antibiotic prophylaxis in reducing the prevalence of SSIs in surgery (38,39). These landmark studies were further supported by another study by Stone and colleagues (40).

SAP is not indicated in all surgical procedures. For instance, there is no indication for SAP in most minor surgeries (41). SAP should only be used according to wound classification, mostly in clean-contaminated and contaminated procedures (10). Equally important, the risk of infection associated with the surgical operation should be considered before the use of SAP (10). For example, it is widely accepted that SAP is not required in most clean surgical procedures other than those involving

implantation of prosthetic materials due to the perceived low risk of SSI in such operations (10,12,42). Nonetheless, several studies (15,43–46) have demonstrated various results of compliance with indication for SAP. In a study by Nabor *et al* (15), compliance with indication for SAP was demonstrated in 93% of surgical interventions. Two recent retrospective studies (43,44) have equally showed a high level of compliance with indication for SAP and appropriate administration of prophylactic antibiotics ranging from 91.3% to 98.7%.

On the contrary, compliance with indication for SAP and appropriate administration of prophylactic antibiotics has been shown to be lower than acceptable in some settings (45,46). For instance, a study conducted in Iran found a percentage compliance of 53% in terms of compliance with indication for SAP assessed against the ASHP guidelines (46). The study further showed that 47% of patients were administered prophylactic antibiotics without a valid indication. Similarly, Mohamoud and colleagues (45) reported a percentage compliance of 58.7% with respect to compliance of antibiotic prophylaxis with ASHP guidelines on indication for SAP. Further, Mohamoud *et al,* found that the proportion of patients that received prophylactic antibiotics without indication was only 3.6%, lower than that reported by the study conducted in Iran. In summary, the findings suggest a global challenge of implementing evidence-based practices in most settings.

2.4 Fundamental principles of SAP use in surgery

The five quality parameters of appropriate prophylactic antibiotic use such as choice of antibiotic based on surgery type, dosing, timing, route and duration of not more than 24 hours post-operatively underscores antimicrobial stewardship in the context of SAP use (47,48). Compliance with these principles has been shown to not only decrease the SSIs rates but also to slow the emergence of AMR (49). It is, therefore, important for surgeons' antibiotic prescribing to comply with local or national guidelines for SAP and where none exist, as in the case of Namibia, use of reputable international guidelines has been suggested (35).

2.4.1 Appropriate choice of SAP

The critical consideration when selecting an appropriate antibiotic for SAP in surgery is knowledge of the most likely microorganism associated with SSI at the incision site (50). According to recent reports, *Staphylococcus aureus, Escherichia coli, Coagulase-negative Staphylococcus* and *Enterococcus faecalis* are the most frequently isolated pathogens associated with SSIs (51,52). Nonetheless, a systematic review undertaken by Nejad *et al* revealed that *Klebsiella* species and *Pseudomonas aeruginosa* were among the commonly isolated pathogens in SSIs in African countries (3). Given these findings, it is imperative that prescribers took the local epidemiology of bacteria and their resistance patterns into account when selecting an appropriate antibiotic for SAP.

Moreover, most of these pathogens are normal flora commonly found on the skin. Therefore, the goal of an antibiotic agent of choice should be to reduce the bacterial contaminating load with minimal alteration of nonpathogenic commensal microbial flora (53). In light of this, available evidence strongly supports the use of narrow-

spectrum antibiotics, particularly first-generation cephalosporins such as cefazolin (50). Further considerations include the safety and cost of the antibiotic (54).

Current literature suggests that SAP should target gram-positive bacteria such as *S. aureus* and *streptococci* for operations above the waist whereas for operations under the waistline, the antibiotic of choice should cover both gram-positive and gram-negative bacteria. Additionally, coverage with an agent such as metronidazole for anaerobic bacteria is recommended for abdominal procedures (53). Studies, however, suggest that irrational selection of antibiotics for SAP is common despite the availability of guidelines (55,56). Abdel-Aziz *et al* undertook a descriptive, retrospective, observational analysis of data obtained from different surgical units to assess the standard practice of care of surgeons in SAP at Hamad General Hospital in Qatar, which found that among 101 patients in whom SAP was indicated, the selection of antibiotics was inappropriate in 31.5% of the patients (57). Cefazolin was the most widely used antibiotic (44.6%) and its selection complied with hospital guidelines in 53.3% of the cases. The use of amoxicillin/clavulanic acid was totally non-compliant with recommendations of a hospital guideline. Similarly, an observational prospective study carried out by Durando and colleagues in a tertiary referral teaching hospital in Liguria, Italy, to evaluate adherence of perioperative procedures for prevention of SSIs to international and national standards reported that the choice of antibiotics for SAP was inappropriate in 55.2% of 703 patients who underwent 717 surgical procedures (56). Further, Durando *et al* noted that approximately 60% of the antibiotics used were broad-spectrum contrary to the guideline recommendations relating to the use of narrow-spectrum antibiotics.

2.4.2 Dose, timing, route and duration of SAP

The prudent use of antibiotics for SAP entails appropriateness of selection, dose, timing, route and duration of antibiotic prophylaxis in line with recommendations of a SAP guideline. Therefore, appropriate use of antibiotics for SAP optimises surgical patients' outcomes and safety.

2.4.3 Dose

The recommended dose of an antibiotic indicated for SAP should reach the minimum inhibitory concentration (MIC) against the targeted microorganism for it to be considered effective in preventing SSIs.Thus, most guidelines recommend the use of usual treatment doses for prophylaxis against SSIs (10,11). Zelenitsky *et al* conducted a study to characterize the relationship between gentamicin concentrations during surgery and the development of wound infection following colorectal operations among 134 subjects, using data from a previous prospective, randomised, double-blind trial of patients that underwent colorectal surgery. They found that patients administered a single high dose of gentamicin 4.5mg/kg (high concentrations) had significantly reduced rates of SSIs compared to those administered 8 hourly standard gentamicin dose of 1.5mk/kg (low concentrations) (58). However, 12 subjects were excluded from the original sample size of 146 due to missing data. Nevertheless, the findings by Zelenitsky *et al* underscore the importance of pharmacokinetic and pharmacodynamic considerations in addition to patient factors in the determination of appropriate doses of antibiotics used for SAP (59).

2.4.4 Timing

Timing of SAP administration is arguably the most critical predictor for developing SSI. The importance of the timing of SAP administration in surgery was initially highlighted through experimental studies conducted by Burke and later supported by findings of a landmark clinical study undertaken by Classen *et al* (60,61). The rationale behind timing of SAP administration is premised on the fact that in order to achieve effective MIC in tissues that can avert development of SSI; the antibiotic must be administered at an appropriate time before skin incision.

In a prospective, single-centre, observational study involving 2,847 patients at a large community hospital in the USA, Classen and colleagues evaluated the relationship between SAP timing and occurrence of SSI. Classen *et al* found that the risk of SSIs was lowest (0.6%) in patients who received SAP preoperatively (0 to 2 hours before the initial surgical incision) and moderate (1.4%) for those who received SAP perioperatively (within 3 hours after the incision) (61). The risk of SSI was highest in patients who received SAP early (3.8%) or late (3.3%). Early and late administration of SAP were defined as administration of SAP 2 to 24 hours before incision, and 3 to less than 24 hours after incision, respectively. The study by Classen *et al* confirmed the assertion that administering the prophylactic antibiotic either too early or too late may result in sub-optimal antibiotic concentration at the incision site and subsequently increase risk of SSI. Classen *et al* suggested that administration of SAP in the two hours before surgery reduces the risk of wound infection. Global guidelines for the prevention of SSI developed by WHO recommend administration of SAP within 120 minutes time frame before incision (42). Classen *et al* noted that cefazolin was the most commonly used antibiotic (56%). Most clinical guidelines

suggest that the half-life of an antibiotic in relation to the timing of SAP administration should be considered when selecting an appropriate antibiotic (10,11,42).

de Jonge *et al* recently undertook systematic review and meta-analysis to assess the effect of timing of preoperative SAP on SSIs and compared the different timing intervals (62). de Jonge *et al* emphasised the importance of pharmacokinetic consideration for most antibiotics with a short half-life particularly, cephalosporins and penicillins, and consequently recommended that antibiotics with short half-lives should be administered as close to incision time as possible (< 60 minutes) (42,62). This systematic review and meta-analysis included 14 observational studies. WHO global guidelines for SSI prevention were based on the findings of the systematic review and meta-analysis. Although the WHO's global guidelines for the prevention of SSIs adopted and generally recommend SAP administration within 120 minutes time frame before incision, the SIGN, ASHP and European Centre for Disease Prevention and Control (ECDC) recommend administration of SAP within 1-hour time frame before the scheduled surgical procedure (10,11,63). Given that recommendations on the timing of SAP in the global guidelines for the prevention of SSI were based on observational studies, WHO further proposed the need for randomised controlled trials (RCT) studies to assess the effectiveness of various pre-incision SAP administration timings within the 120 minutes window.

Weber *et al* conducted a phase 3 randomised controlled superiority trial to establish the precise optimum timing of SAP by comparing early versus late administration of SAP before surgery (64). A total of 5175 patients who underwent general surgery, orthopaedic and vascular operations were analysed. Patients were given a single dose

of 1.5g cefuroxime infusion or combined with 500mg metronidazole for colorectal surgery patients. Patients were equally randomly assigned to receive SAP early (30 – 75 minutes) in the anaesthesia room or late (0 – 30 minutes) in the operating room before surgical incision. The overall SSIs rate was 5.1%. The SSIs rate in the early group was 4.9% compared to 5.3% in the late group. No statistically significant difference in SSIs rate was observed whether SAP was administered early or late (OR = 0·93, 95% CI: 0·72-1·21, p = 0·601). Therefore, Weber *et al* concluded that there was no justification for narrowing the 60 minutes window of SAP timing for antibiotics with a short half-life.

2.4.4.1 Timing of SAP in caesarean section

Although the 60-minute window for pre-incision antibiotic prophylaxis has received wide acceptance, controversy still surrounds its application in caesarean section (CS) (42). The contention is on whether prophylactic antibiotics should be administered before or after umbilical cord clamping. Pre-incision SAP administration before umbilical cord clamping is opposed due to concerns over neonatal exposure to antibiotics and subsequent poor outcomes such as alteration of the normal gut microbiome, masked neonatal sepsis and emergence of AMR in this population (65). However, current evidence has not conclusively demonstrated these adverse neonatal outcomes. As a consequence, the WHO global guidelines for the prevention of SSIs and SIGN guidelines have not explicitly provided guidance on SAP timing in CS (10,42). In contrast, the ASHP and the National Institute for Health and Care Excellence (NICE) unequivocally recommend pre-incision SAP administration in CS (11,66). Furthermore, recommendations for administration of SAP before skin

incision in CS are based on studies that demonstrated an overall risk reduction in maternal infections (67,68).

Several studies (69–72), however, have reported conflicting findings of maternal and neonatal outcomes. A systematic review of five RCTs involving 1777 patients conducted by Heesen *et al* showed no difference in maternal and neonatal outcomes between SAP administration before skin incision in CS and after umbilical cord clamping (69). Nonetheless, a significant risk reduction in the rate of endometritis was noted in patients who received SAP before skin incision in CS (RR 0.48, 95% CI: 0.27 - 0.87). Limitations of Heesen and colleagues' systematic review and meta-analysis included the use of only two databases for literature search and inclusion of few trials with relatively smaller sample sizes.

Zhang *et al* conducted a multicentre RCT and meta-analysis at three hospitals in western China involving 410 patients to compare the effectiveness of antibiotic prophylaxis before skin incision with that after umbilical cord clamping in elective caesarean delivery (CD) (70). Zhang *et al* did not find any statistically significant differences in the incidence of postpartum endometritis (RR 0.34, 95% CI: 0.04 - 3.24), wound infections (RR = 3.06, 95% CI: 0.13 - 74.69) and total puerperal morbidity (RR 1.02, 95% CI: 0.47 - 2.22). Moreover, there was no significant difference in the incidence of neonatal sepsis (RR = 0.65, 95% CI: 0.35 - 1.20), septic workup (RR 0.88, 95% CI: 0.50 - 1.54), or neonatal intensive-care unit (NICU) admission (RR = 0.91, 95% CI: 0.70 - 1.18). Zhang *et al* further reported that there was no difference in neonatal stool bacterial flora among patients in whom SAP was administered before skin incision or after umbilical cord clamping (p=0.48). Only two of the nine RCTs included in the meta-analysis undertaken by Zhang *et al* were double-blinded hence increasing the risk of bias. Despite this

limitation, findings by Zhang and colleagues were similar to those reported by Heesen *et al* (69).

On the contrary, Dlamini *et al* conducted a RCT in Uganda to compare the effect of antibiotic prophylaxis within 1 hour before skin incision and after skin incision on the incidence of SSIs among 432 patients that underwent CS. Dlamini *et al* demonstrated statistically significant reduction in overall maternal infections and endometritis (RR= 0.77; 95% CI: 0.62 - 0.97; $p = 0.022$) and (RR 0.62; 95% CI: 0.39 - 0.99; $p = 0.036$), respectively (71). The disparity in neonatal outcomes between the two arms of the trial was not statistically significant. However, this RCT was a single blind; one centre study and patients were only followed up for ten days in contrast to the 30 days recommended for SSIs. Moreover, the follow-up period for observation of neonatal outcomes was inadequate.

Jyothirmayi *et al* (72) carried out a double blind RCT on 1096 women and neonates, and found that administering SAP before incision in CS was associated with statistically significant reductions in SSIs (RR = 0.14, 95% CI: 0.04 - 0.53, $p < 0.001$). Significant reductions in rates of endometritis (RR = 0.49, 95% CI: 0.23 - 1.05, $p = 0.02$) and febrile illness (RR = 0.48, 95% CI: 0.29 - 0.80, $p = 0.005$) were also noted. There were no significant differences in neonatal outcomes with respect to sepsis and readmission in both arms of the trial, though this study was not powered for this secondary outcome. Thus, this double-blind RCT supports the findings of Dlamini and colleagues (71). Additionally, the findings of this study are similar to those reported by two systematic reviews and meta-analyses (5,68). Baaqeel and Baaqeel (68) undertook a systematic review and meta-analysis to examine maternal and neonatal infectious morbidity in women who received preoperative prophylactic antibiotics compared with those who received

intraoperative administration. Six RCTs involving 2313 women and 2345 newborns were included. Baaqeel and Baaqeel reported that administration of SAP before CS was associated with a 41% significant reduction in rates of endometritis (RR 0.59, 95% CI: 0.37 - 0.94) (68). The rates of SSIs (wound infections), febrile illness, neonatal sepsis, neonatal septic workup and NICU admissions were comparable and non-significant in both preoperative and postoperative SAP groups. Similarly, Martin *et al* (5) in a more recent systematic review of reviews and meta-analyses, recommended pre-incision administration of SAP in CS as part of an infection control bundle for CS.

In light of the conflicting evidence emanating from various studies, evolving concepts will likely continue to emerge in this domain, and the debate is unlikely to be abated any time soon. This has implications locally given that approximately fourteen percent of women undergo CD in Namibia (73). Therefore, the adoption of a recommendation for SAP timing should be based on current rigorous evidence. The appropriate recommendation should be cost-effective and maximally optimise maternal and neonatal outcomes.

2.4.5 Route of administration and duration

Traditionally, parenteral administration of SAP has been the generally accepted standard for the majority of surgical procedures as it assures predictable pharmacokinetics (11). However, the intravenous route may not be optimal for specific procedures such as colorectal and cataract surgeries which may require oral and intracameral administration, respectively (10). The WHO recommendation on the use of orally administered antibiotics in combination with mechanical bowel preparation (MBP) in colorectal surgery is based on findings of a meta-analysis of 11

RCTs (74). A combination of MBP and oral antibiotic use reduced the rates of SSI in colorectal surgery compared to MBP alone (OR 1·31; 95% CI: 0·99 –1·72) (74). However, Allegranz *et al* could not specifically recommend the choice of antibiotic and dose due to a wide range of antibiotics that were used in the assessed RCTs.

A single dose of an appropriate antibiotic or administration of the antibiotic for a duration of less than 24 hours is sufficient as SAP for most surgical procedures, provided that the half-life of the selected antibiotic covers the period of surgery (48,75). A systematic review of SAP in maxillofacial fracture surgery showed that a single dose or doses of various antibiotics given within 24 hours post-operation was non-inferior to multiple doses (76). Andreasen *et al* concluded that a single dose or doses within a day of surgery was superior to multiple doses in reducing SSIs (76). The main limitation of this study was that only four RCTs were reviewed. Loozen *et al* demonstrated the non-inferiority of single dose SAP versus extended antibiotic prophylaxis in patients with mild acute cholecystitis that underwent cholecystectomy. A randomized controlled non-inferiority trial conducted by Loozen *et al* evaluated 150 patients who underwent cholecystectomy at six teaching hospitals in the Netherlands. Loozen and colleagues found that a single preoperative 2 gram dose of cefazolin did not increase the risk of SSIs compared to extended antibiotic prophylaxis (intravenous cefuroxime 750 mg plus metronidazole 500 mg, three times daily in addition to the single dose) for 3 days after surgery (77). Although the sample size of this RCT was small, its findings are in agreement with those noted by Andreasen and colleagues (76).

2.5 Compliance with SAP guidelines

Despite the availability of best-practice SAP guidelines and protocols, most studies have shown that compliance with guidelines remains sub-optimal (43,78–81). For instance, in a single-centre prospective study carried out on 400 surgical patients in Botswana, Mwita *et al* reported non-compliance with respect to timing, appropriate antibiotic choice and duration of SAP (82). Mwita *et al* did not report the level of non-compliance with these parameters to ascertain which element was least or most compliant. This might have been because their primary measure of outcome was the occurrence of SSI (82).

Most studies, however, have reported the rate of non-compliance with SAP guidelines (18,19,43,45,78). For instance, two prospective studies conducted in Ethiopia and Sudan on various surgical procedures showed that compliance with correct antibiotic choice ranged from 43.7% to 89.5%. Compliance with timing was as low as 9.3% (18,45). A study conducted in Sudan by Elbur *et al* reported compliance with dose and appropriate discontinuation of 29% and 3%, respectively (18). Overall compliance with the SIGN guideline was 2.7% (18). Elbur and colleagues did not evaluate route of prophylactic antibiotic administration parameter in their study. Moreover, the study by Elbur *et al* was limited to clean and clean-contaminated elective surgical procedures.

However, the study by Mohamoud *et al* in Ethiopia (45) showed better compliance with dose and discontinuation (89.6% and 36.5%, respectively) than Elbur *et al*. Overall compliance with the local guideline, however, was 0% controlling for indication. In addition, Mohamoud and colleagues included route of SAP administration in their evaluation of SAP compliance and their assessment of wounds

was expanded to include contaminated wounds. Pharmacy students and nurses collected data in the studies undertaken in Ethiopia and Sudan, respectively. Elbur *et al* and Mohamoud *et al* did not state whether independent experts cross-checked the collected data for face validity in their studies, thus raising the possibility of bias inherent to such study designs.

Another similar study in Ethiopia also demonstrated non-compliance with local and international SAP guidelines (19). Though route and dose parameters were not assessed, the study by Alemkere showed that 80.4% of patients were given prophylactic antibiotic with indication but only 10% of this proportion complied to correct choice of prophylactic antibiotics (19). Additionally, slightly above half of the patients (52.3%) were administered prophylactic antibiotics at the appropriate time. Alemkere also reported that discontinuation of SAP was non-compliant in more than 75% of patients and third-generation cephalosporin (ceftriaxone) was the mostly used antibiotic in 84% of patients. Since Alemkere used convenience sampling, selection bias could not be ruled out in the final analysis.

In a recent retrospective study of 265 surgical patients, Bunduki and colleagues reported compliance levels in terms of choice of antibiotic, dose, timing, route and discontinuation of 18.1%, 76.2%, 79.2%, 83% and 30.9%, respectively (43). Twenty-two patients developed SSIs (OR = 0.4, 95% CI: 0.09 – 1.9, p = 0.386) and in 20 (90.9%) of these patients, non-compliance with SAP guidelines was observed. Similar to the present study, compliance was assessed against two authoritative guidelines but in this case, NICE and Stanford Health Care were used, and overall compliance with these consensus guidelines was sub-optimal (18.1%). Ampicillin was the most widely used antibiotic accounting for 43.8%. Bunduki *et al* recommended the use of ampicillin, mostly on the basis of availability and cost (43).

However, their recommendation is not supported by most guidelines (10–12,83). In contrast, Mousavi and colleagues (46) observed a major use of cefazolin (66%) in their single centre study conducted in Iran and reported overall compliance with ASHP guideline of 22%.

The observed poor compliance with SAP guidelines is not unique to LMICs, as studies in developed countries have also shown irrational use of SAP, though to a better extent than in most developing countries. For example, non-compliance with choice of prophylactic antibiotics and timing was reported to be around 7% and 35%, respectively in a study by Muller *et al* at a French teaching hospital. Muller and colleagues further noted compliance of 84.6% in terms antibiotic dosing but did not assess compliance with SAP discontinuation due to data collection methods used. However, overall compliance with the amalgamated local and French Society of Anaesthesia and Intensive Care (SFAR) guidelines used in the study was 51.6%. The findings by Muller *et al* showed better compliance than a 7-year surveillance of SSI in 149 French hospitals that reported overall compliance with SFAR of 19.4% (79). Nevertheless, the 7 year surveillance by Miliani and colleagues (79) included appropriate SAP discontinuation in their study and found non-compliance with prophylactic antibiotic discontinuation in 65% of patients.

In a study of 760 patients with SSI at a US hospital, Goede *et al* assessed compliance with four critical parameters of SAP besides antibiotic discontinuation. They reported an overall compliance of 75.4% with repeat dosing being the most non-compliant parameter (45.1%) (84). Repeat dosing or re-dosing is recommended for prolonged procedures (> 4 hours) that exceed the half-life of a prophylactic antibiotic (85). In the current study, this aspect was not investigated as none of the surgical procedures included in the study exceeded 4 hours.

Another study conducted in Australia by Lavers *et al* (86) reported poor overall compliance of 49.2%, although only one surgical procedure (breast surgery) was assessed thus limiting its generalizability. Prior to Lavers and colleagues' study (86), another study undertaken in Australia by Friedman *et al* (78) showed varying trends of SAP compliance with selection, timing and discontinuation in three surgical categories (cardiac, orthopaedic and colorectal) evaluated. Friedman *et al* noted that non-compliance with national guidelines was mostly observed with respect to prophylactic antibiotic discontinuation in cardiac and colorectal surgeries (21% and 13%, respectively). Bonello and Starfrace assessed SAP compliance with a local hospital guideline in Malta and found a percentage compliance of 24% in terms of selection, dose and route of administration (87). This level of compliance was lower than the compliance levels reported by Muller *et al* (88). Moreover, compliance with prophylactic antibiotic discontinuation was 9.3% but better than that reported in a study undertaken in Sudan (18).

Though most of these studies excluded children, the few studies conducted in the paediatric population have shown similar findings of sub-optimal compliance with guidelines (89–91). In a study of 224 charts of paediatric patients that underwent 4 selected surgical procedures at 2 South African hospitals (public teaching hospital and private hospital), van der Sandt *et al* (92) reported overall non-compliance (0%) at both hospitals. Although both hospital settings fully complied with re-dosing and duration modalities of SAP, significant differences were noted regarding appropriate antibiotic choice ($p < 0.0001$). The teaching hospital mostly complied with antibiotic choice by using the recommended narrow-spectrum cefazolin (88.9%) whereas the broad-spectrum amoxicillin-clavulanic acid was the most commonly used antibiotic

in the private hospital (88.7%). However, van der Sandt and colleagues did not assess predictors of non-compliance with the SAP guidelines.

Although Mohamed *et al* (93), recently reported higher overall compliance (39.6%) with the local guideline compared to the van der Sandt study (92), the compliance level was not optimal. Both studies (92,93) evaluated the same SAP parameters such as choice of antibiotic, dose, re-dosing, timing and discontinuation but differed in that Mohamed *et al* undertook a single centre study. Nevertheless, Mohamed and colleagues further reported better level of compliance with SAP choice of antibiotic (81.2%) compared to a study by Dona *et al* (89) that found a percentage compliance of 48.9% with respect to choice of prophylactic antibiotics in the pre-intervention phase of the study.

2.6 Predictors of non-compliance with SAP guidelines

Many obstacles hamper the efforts to improve prophylactic antimicrobial prescribing in surgery and specifically, compliance with SAP guidelines. For instance, a retrospective study at a university hospital in France (88) analyzed data of 1312 patients that underwent different surgical procedures categorized as priority by the SSI national surveillance. Patient characteristics such as age (OR = 0.99, 95% CI: 0.981 - 0.996, $p = 0.002$) was significantly associated with non-compliance with the local guidelines (88). Type of surgery such as digestive and gynaecological/obstetric procedures were also significantly associated with non-compliance with SAP guidelines (OR = 4.56, 95% CI: 3.05 to 6.80, $p = 0.001$) and (OR = 7.10 95% CI: 4.19 - 12.03, $p = 0.001$) respectively. Of note, is that the findings relating to digestive surgery is likely to have been overestimated, as the local guideline used in this study

was not updated to correspond with the national guideline (SFAR) for this type of surgery.

The findings by Muller *et al* support the earlier findings by Simon and colleagues (94) who prospectively assessed physicians' compliance with SAP guidelines and evaluated predictors of non-compliance. The findings revealed poor overall compliance (37%) with the guideline. The findings by Simon *et al* further demonstrated that surgeon prescription (RR: 3.4; 95% CI: 1.6 - 7.5), type of surgery (RR; 3.7; 95% CI: 1.8 - 7.5) and wound classification (RR: 2.2; 95% CI: 1.4 - 3.7) and emergency status of surgery (RR: 0.96; 95% CI: 0.52 - 1.76, p = 0.005) were predictors of non-compliance with SAP guidelines. However, there was no significant association between patient age and non-compliance with guidelines.

Despite some variations in predictors of non-compliance with rational SAP use, several studies have demonstrated convergence in certain drivers of irrational SAP use across the globe (43,93,95,96). For example, a study conducted in Ethiopia (19) showed that department or ward (gynaecological/obstetric) significantly impacted non-compliance with SAP discontinuation (AOR = 0.07, 95% CI: 0.01 - 0.81, p = 0.033). This finding is supported by a recent study conducted in the Democratic Republic of the Congo (DRC) (43).

Providers of surgical care have been reported to influence compliance with SAP prescribing as earlier shown in a study by Simon and colleagues (94). In another study by Lavers *et al*, significant association was reported between prescribers and non-compliance with administration of postoperative antibiotics (p=0.05), with 11.2% of patients given postoperative antibiotics against guideline recommendation (86). Nonetheless, no significant association between prescribers of SAP and the level of overall compliance with the national guideline (p=0.631) was observed

among the 7 surgeons involved in the 250 interventions assessed in the study (86). Conversely, Musmar *et al* reported a significant relationship between provider of SAP and compliance with appropriate timing, choice and duration of SAP (97). In their study, Musmar and colleagues showed that anaesthetic technicians were more likely to comply with timing ($p = 0.001$), prophylactic antibiotic selection ($p = 0.005$) and duration of SAP ($p = 0.001$) than nurses (97). Equally, Abdel Jalil *et al* reported variations in compliance with dose of prophylactic antibiotics among nine consultants involved in the surgical procedures that were studied (98). Only two of the nine consultants were less likely to be non-compliant to appropriate dosing of SAP (OR = 0.45, 95% CI: 0.26 - 0.75, $p = 0.002$ and OR = 0.50, 95% CI: 0.30 - 0.84, $p = 0.009$) (98). Nevertheless, Abdel Jalil and colleagues only assessed caesarean sections.

2.7 Gaps in the current literature

In summary, literature shows that despite the availability of guidelines, injudicious use of SAP is prevalent but varies across settings. Non-compliance with evidence-based guidelines has negative consequences especially on the patient but also on the health-care system. Most single centre studies reviewed were conducted at university-affiliated settings that are likely to be better equipped than district or regional hospitals as in the case of the present study. Moreover, most of these studies excluded children < 18years and in most cases, there was availability of a local or national guideline unlike the present study. Further, the largest study among similar studies undertaken in sub-Saharan Africa, with more than 1700 patients was the study (18) conducted in Sudan thus illustrating the need of more studies to better

understand the practice given that only one unpublished study in Namibia (21) was retrieved.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Study design

This was a retrospective quantitative, analytical, study. The study was quantitative as numeric data such as patient age, operative minutes and duration of antibiotic use was collected to describe the relationships among these different variables. The current study was also analytical as predictors of non-compliance with SAP guidelines were identified. Due to limited time and logistics, only baseline data from clinical records of post-operative patients were collected at one time point thus qualifying the study as retrospective in design.

3.2 Study setting

The study was conducted in the theatre unit at Intermediate Hospital Rundu (IHR) by review of SAP prescribing in clinical records of post-operative patients. Intermediate Hospital Rundu is a 330 - bed capacity hospital and is situated in the Kavango East region of Namibia. The hospital serves as a referral centre for three regions, namely Kavango East and West, and Zambezi. The hospital theatre performs approximately over 2500 surgical procedures annually. The hospital also serves as a teaching hospital for intern pharmacists, dentists, nursing students and other healthcare professions.

3.3 Study population

The population was records of post-operative patients from all age groups who underwent clean, clean-contaminated and contaminated surgical procedures between 1st April 2018 and 31st March 2019 at Intermediate Hospital Rundu. The theatre daily

statistics showed that an estimated 230 clean, clean-contaminated and contaminated surgical procedures were conducted per month. The accessible population was 958 clinical records of surgical procedures. In this study, clinical records of post-operative patients were considered as those of patients that had undergone a surgical procedure as defined by WHO (42) while wounds were classified according to SIGN guideline shown in **Appendix A**: Extract of Scottish Intercollegiate Guidelines Network (SIGN) 104 guideline Data sources were clinical records of patients that had undergone surgical procedures.

3.4 Sample size

With estimated compliance with guidelines at 10% (99), power of the study at 80%, level of significance, $\alpha = 0.05$ and a critical value of 1.96 for a two-tailed test, the sample size was determined as follows:

Sample size $n = Z^2_{(1-\alpha)}\, p\,(1-p)/d^2$

Where n = sample size, p = prevalence or level of compliance with guidelines estimated at 10% Z = critical value at 95% confidence interval, d = level of precision at 5%

Therefore, $n = (1.96)^2 * 0.10(1-0.10) / (0.05)^2 = 138.3$

Therefore, the calculated sample size was 139. A 10% allowance was added to account for clinical records with missing data, thus a sample size of 153 clinical records of surgical procedures was determined.

3.5 Sampling

- A total of 958 clinical record of surgical procedures that met the eligibility criteria were retrieved over the study period. The clinical records of the surgical procedures conducted on patients were firstly stratified according to the type of surgical procedure meeting eligibility criteria using the probability proportional to size based on the average total number of surgeries (958) conducted over the specified 12 months study period. Secondly, a systematic random sampling technique was used to select clinical records to be included in the study (**Table 1**). Lastly, the sampling intervals for each stratum depended on the total number of clinical records representing the respective surgical procedures. Ten eligible surgical procedures were included in the sample (**Table 1**).

Table 1: Sampling of clinical records

surgical procedure	surgical procedure (Population)	Strata (sample)	Sampling interval
Caesarean section	504	80	6
Appendicectomy	173	28	6
Hysterectomy	78	12	6
Fracture	85	14	6
Tonsillectomy	26	4	6
Colorectal surgery	7	1	6
Gall bladder surgery	6	1	6
Stomach and duodenal surgery	47	8	6
Lower limb amputation	32	5	6
TOTAL	**958**	**153**	

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3.5.1 Inclusion criteria

Clinical records of elective and emergency surgical procedures referred from the maternity unit (obstetrics and gynaecology) and general surgical ward were included. Only surgical procedures classified as clean, clean-contaminated and contaminated were included in the study.

Additionally, only surgical operations clearly falling under SIGN and ASHP guidelines recommendations on the use of SAP were included.

3.5.2 Exclusion criteria

Clinical records of patients who underwent otolaryngological, ophthalmological and dirty surgical procedures or were on therapeutic antibiotics before surgery were excluded. Clinical records of patients who underwent more than one surgical procedure were also excluded. Surgical operations without clear SIGN and ASHP guidelines recommendations on the use of SAP were excluded.

3.6 Study instruments

A Surgical Antibiotic Prophylaxis Assessment Form (**Appendix C**: Data collection tool based on the SIGN and ASHP guidelines (**Appendix A**: Extract of Scottish Intercollegiate Guidelines Network (SIGN) 104 guideline and **Appendix B**: Extract of American Society of Health System Pharmacist guideline respectively) was used to collect data. The form had four sections containing variables relevant to the objectives of the study. Compliance of antibiotic prescribing in SAP with recommendations of clinical guidelines was assessed using the SIGN and ASHP guidelines since these clinical practice guidelines are internationally recognised and recommended for investigating antimicrobial use in hospitals in the absence of local guidelines (35). Moreover, these two guidelines (SIGN and ASHP) were used so as not to be too stringent given that the objective was to collect baseline data.

3.7 Reliability and validity of the research instrument

The Surgical Antibiotic Prophylaxis Assessment Form (data abstraction tool) was independently assessed by experienced surgeons /medical officers in Surgery and Theatre for face and content validity in terms of patient data to be collected. The data collection tool was also reviewed by research supervisors and piloted on 20 clinical records to ensure validity and reliability and adjustments were made accordingly.

3.8 Procedure

The researcher solely collected data from April 2019 to June 2019 from clinical records of patients that had undergone surgical procedures. First, eligible surgical procedures were identified by reviewing the Operation Theatre books in Theatre department. Second, the selected clinical records of surgical procedures (Medical Notes, Operation Theatre Notes, Medication Charts and Administration Records) were then retrieved from the archive records department and reviewed by the researcher.

Data such as patient demographics, type of surgical operation, surgeon specific details and surgical antibiotic prophylaxis were collected using the Epicollect 5® software developed by Imperial College London (100). The Epicollect 5® software is an electronic data collection tool that facilitates easy data collection in a hierarchical order, real-time visualization of data and secure storage. The software can be installed on a smart phone or tablet computer. In the current study, a tablet computer with installed Epicollect 5® software and password protected was used to collect data.

3.9 Data analysis

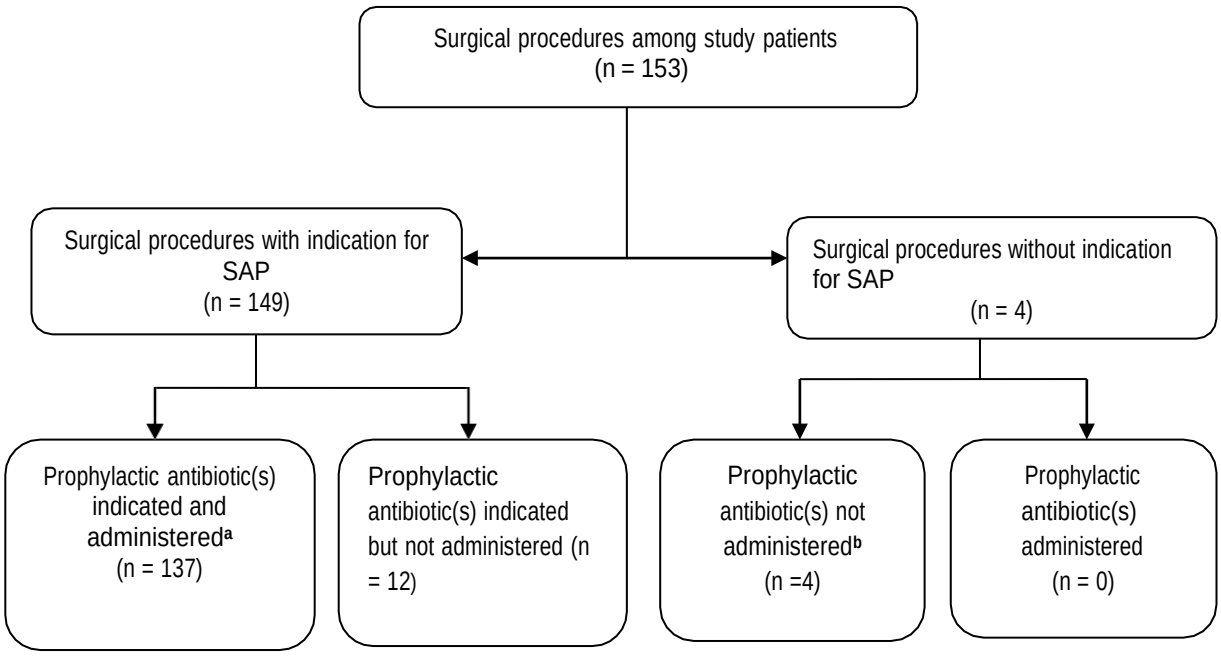
The Data were analyzed using IBM® SPSS® Statistics version 22 (IBM Corporation, Chicago, IL, USA). The primary outcome measure of the study was compliance of antibiotic prescribing in surgical antibiotic prophylaxis with recommendations of SIGN and ASHP guidelines with respect to appropriateness of SAP in terms of, choice of antibiotic, timing, route of administration, dose and discontinuation among surgical procedures with indication for SAP. **Figure 1** shows the flow chart used to analyse the data. Categorical variables such as gender of study patients, type of

surgical operation, type of surgical wound and compliance of antibiotic prescribing with the guidelines were analyzed using descriptive statistics, and presented as frequencies and proportions. Normally distributed continuous variables were expressed as mean and standard deviation (SD). Additionally, the results of various types of operations conducted were summarized and presented as bar charts.

In order to select the best predictor variables of non-compliance of antibiotic prescribing with the guidelines as a secondary outcome measure, bivariate analysis was first used with the chi-square or fisher's exact test at the significance level of 5%. Multivariate binary logistic regression was then used to analyse the output of bivariate analysis for independent variables of interest that had a *p*-value < 0.05 against the outcome variable. The forward stepwise likelihood ratio (LR) method was used for modeling. Multicollinearity was checked for multivariate logistic model output with more than one predictor. In addition, to validate the observed model, a model of fit assessment using Hosmer-Lemeshow chi-square test and area under Receiver Operating Characteristics (ROC) curve was conducted. Lastly, data from the multivariate analysis were expressed as odds ratios (OR) with the respective 95% confidence intervals (CI). A *p*-value < 0.05 was considered statistically significant. Results with more than one predictor of the outcome measure were presented in table format.

Compliance of antibiotic prescribing with SAP guidelines was defined as correspondence of the prescribed antibiotic in terms of indication, selection, timing, and route of administration, dose, and discontinuation with recommendations of the SIGN and ASHP guidelines. Therefore, non-compliance was regarded as any deviation from the recommendations outlined in the guidelines. For instance,

administration of an antibiotic not recommended by either SIGN or ASHP guideline in surgical procedures with an indication for SAP would imply non-compliance.



1. Compliance with indication for SAP = **a** + **b**

Figure 1: Flow chart showing surgical procedures with respect to SAP parameters among study patients.

3.10 Research ethics

The need for ethical clearance was waived by the Human Research Ethics Committee (HREC) at University of Namibia due to minimal risk of harm or injury to patients since the study involved retrospective review of clinical records (**Appendix D**: University of Namibia ethical clearance exemption letter. The Ministry of Health and Social Services granted permission to conduct the study (**Appendix E**: Ministry of Health and Social Services approval letter. Permission to conduct the study at the IHR was also granted by the management (Appendix F: Intermediate Hospital Rundu approval letter. Confidentiality of participants was ensured by recording anonymized data.

CHAPTER 4

RESULTS

4.1 Demographics of study population

A total of 153 clinical records of eligible surgical procedures were included in the study as shown in **Figure 1**. Most of the surgical procedures were done on females (77.8%). The median age of the post-operative patients was 26.0 (IQR: 4 – 89) years. Only 22.9% (35/153) of the patients that had undergone the surgical procedures had comorbidity. The demographics of the post-operative patients are shown in **Table 2**.

4.2 Demographics of medical practitioners

Ten medical practitioners conducted the 153 surgical procedures evaluated. All the medical practitioners were male. Two of the medical practitioners were volunteer specialists; two were senior medical officers while six were general medical officers. Eight of the medical practitioners had more than 10 years' experience. Medical practitioners in the age range of 40 to 49 years performed most of the surgical procedures signifying 68.0% (104/153) of all procedures. Mainly practitioners with more than 10 years of medical experience, 88.2% (135/153), conducted the surgical procedures. General medical officers, 53.6% (82/153), performed about half of the surgical operations. Specialists and senior medical officers conducted 33.3% and 13.1% of operations, respectively.

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Table 2: Demographics of the study population

Patient characteristics	153 (100%)
Age	
Mean (SD) (years)	29.2 (15.9)
Range (years)	4 - 89
Gender	
Male, n (%)	34 (22.2)
Female, n (%)	119 (77.8)
Co-morbidities	
Cancer, n (%)	8 (5.2)
Cancer/HIV, n (%)	2 (1.3)
HIV, n (%)	15 (9.8)
Hypertension, n (%)	5 (3.3)
Other*, n (%)	5 (3.3)
No recorded comorbidity, n (%)	118 (77.1)
Patient residence status	
Rundu, n (%)	109 (71.2)
Not from Rundu, n (%)	44 (28.8)

* Included asthma, epilepsy, fibroids and peptic ulcer disease.

4.3 Characteristics of surgical procedures

Most of the surgical procedures (73.2%) took less than 60 minutes to perform (mean 52.0, SD ± 24.8 minutes). About 3% (5/153) of the surgical procedures took two to two and half hours. Most of the surgical procedures (52.3%) were from maternity ward (obstetrics and gynaecology) (**Table 3**). The other wards including surgery, general medicine (male and female) and paediatric accounted for 32.0%, 11.8% and 3.9%, respectively.

Emergency procedures accounted for more than half of surgical procedures (57%) compared to elective surgeries that accounted for 43%. The characteristics of the surgical procedures undertaken among the studied clinical records of post-operative patients are shown in **Table 3**. The majority of surgical procedures (79.1%) conducted were clean-contaminated and mostly had an indication for SAP. Less than a third of surgical procedures were conducted at night (27.5%).

Table 3: Characteristics of surgical procedures (n = 153)

Surgical procedures among departments	Number (%)
General surgery	47 (30.7)
Obs/gynaecology	92 (60.1)
Orthopaedic	14 (9.2)
Status of surgery	
Elective	66 (43.1)
Emergency	87 (56.9)
Type of surgical wound	
Clean	23 (15.0)
Clean contaminated	121 (79.1)
Contaminated	9 (5.9)
Time surgical procedure undertaken	
Day	111 (72.5)
Night	42 (27.5)

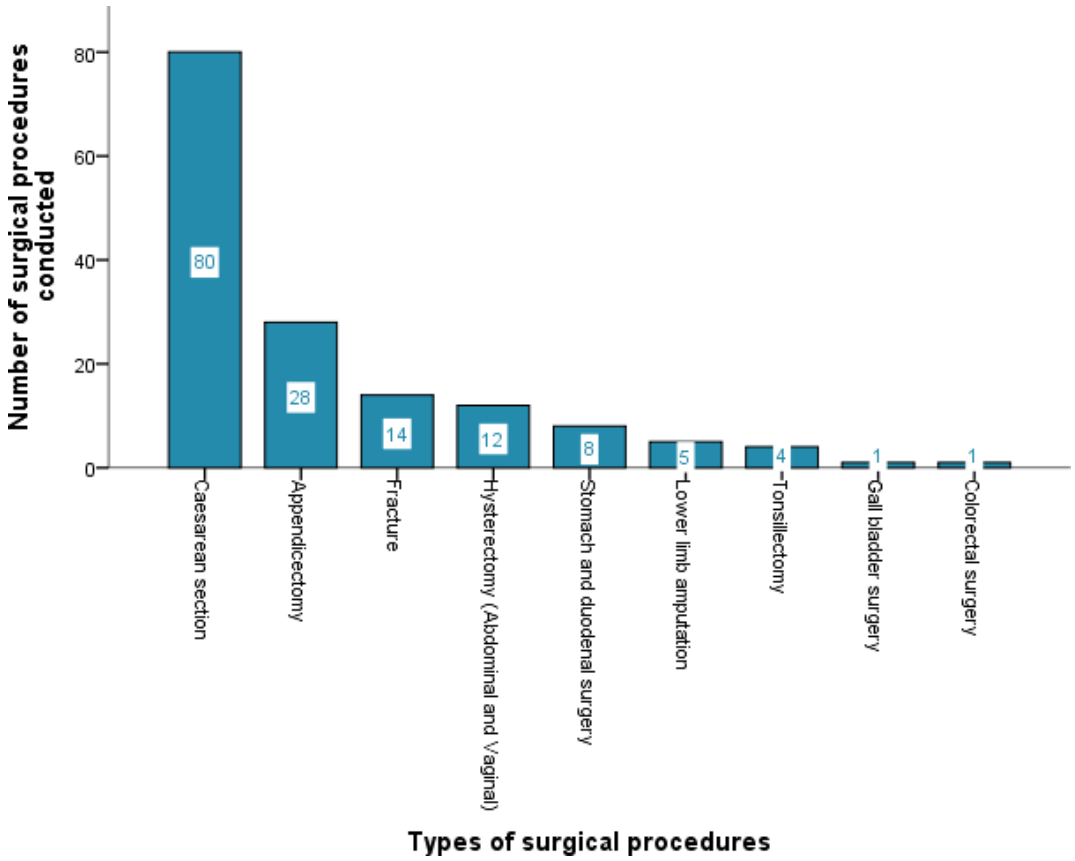

Figure 2: Types of surgical procedures among clinical records of post-operative study patients (n=153).

The types of surgical procedures conducted among the reviewed clinical records of post-operative patients are depicted in **Figure 2**. Caesarean section was the most common surgery performed 52.3% (80/153) followed by appendicectomy 18.3% (28/153). Fracture and hysterectomy (abdominal and vaginal) accounted for 9.2% (14/153) and 7.8% (12/153), respectively.

4.4 Antibiotics used for SAP among study patients

Among the 137 surgical procedures in which SAP was indicated and administered, ampicillin was the most utilized prophylactic antibiotic and was used in 58.4% (80/137) of patients. Cefuroxime alone or in combination with metronidazole was administered in 18.2% (25/137) of patients. Ceftriaxone and broad-spectrum antibiotic namely amoxicillin-clavulanic acid were used in 6.6% (9/137) and 3.0% (4/137) of operations, respectively. The pattern of prophylactic antibiotics used is shown in **Table 4** below.

Table 4: Pattern of prophylactic antibiotics use among study patients (n = 137)

ATC Code	Prophylactic antibiotic used	Number of surgical procedures (n = 137)	Percentage (%)
J01CA01	Ampicillin	80	58.4
J01RA01	Ampicillin + Metronidazole	12	8.8
J01CA04	Amoxicillin	1	0.7
J01CR02	Amoxicillin-clavulanate	4	3.0
J01DD04	Ceftriaxone	6	4.4
J01RA01	Ceftriaxone + Metronidazole	3	2.2
J01DC02	Cefuroxime	7	5.1
J01RA03	Cefuroxime + Metronidazole	18	13.1
J01MA02	Ciprofloxacin	1	0.7
J01CF02	Cloxacillin	2	1.5
J01RA01	Cloxacillin + Metronidazole	1	0.7
J01GB03	Gentamicin	1	0.7
J01RA01	Gentamicin + Metronidazole	1	0.7

4.5 Compliance with correct indication for SAP

Of the 153 surgical procedures whose clinical records were reviewed, SAP was indicated in 149 surgical procedures. However, only 92.0% (137/149) of these received prophylactic antibiotics. **Table 5** shows the level of compliance of antibiotic prescribing with respect to appropriate indication for SAP as per guidelines recommendation.

Table 5: Compliance of antibiotic prescribing with indication for SAP (n = 153)

Parameter	Number of procedures (n)	Frequency (%)
Indication for SAP (n = 153)		
Indicated	149	97.4
Not indicated and not administered [a]	4	2.6
SAP indication and administration of prophylactic antibiotics (n = 149)		
Indicated and administered [b]	137	91.9
Indicated and not administered	12	8.1
compliance with indication according to SIGN / ASHP Guidelines [c] (n =153)	141	92.2

NOTE: c = a + b

4.6 Compliance with SAP guidelines with regards to choice of prophylactic antibiotics

Most of the surgical procedures (84.7%) in whom SAP was indicated were prescribed antibiotics that were not recommended by SIGN and ASHP guidelines (**Table 6**). Ampicillin was the most prescribed antibiotic in 58.4% of procedures as shown in **Table 4** and was mainly administered as 1g single dose. The selection of prophylactic antibiotics was appropriate in approximately 15.3% of the study patients.

4.7 Compliance with SAP guidelines with regards to route of administration of prophylactic antibiotics

The level of compliance of antibiotic prescribing in SAP with SIGN and ASHP guidelines with respect to the route of administration of prophylactic antibiotics was 99.3% (**Table 6**). Non-compliance was observed in one patient who was administered oral antibiotic contrary to recommendation of guidelines.

4.8 Compliance with SAP guidelines with regards to timing of administration of prophylactic antibiotics

Compliance in terms of prophylactic antibiotic administration within 60 minutes before incision was observed in only 38.7% (53/137) of the surgical procedures as shown in **Table 6** below. Prophylactic antibiotics were administered more than 60 to 120 minutes before skin incision in 27.7% of the surgical procedures. A third of the patients (33.6%) received prophylactic antibiotics more than 60 minutes to 24 hours after incision.

4.9 Compliance with SAP guidelines with regards to dosing of prophylactic antibiotics

Appropriate doses of prophylactic antibiotics were administered in only 9.5% (13/137) of the surgical procedures (**Table 6**). Among the procedures in which the selection of prophylactic antibiotics was appropriate but dosing was non-compliant, incorrect dosing was chiefly due to administration of low doses.

4.10 Compliance with SAP guidelines with regards to discontinuation of prophylactic antibiotics

De-escalation of prophylactic antibiotics within less than 24 hours was appropriately undertaken in 0.7% (1/137) surgical procedure with indication for SAP. Among the post-operative patients in whom prophylactic antibiotics were continued post-operatively (range 2 to 29 days), 115 (83.9%) were prescribed two antibiotics (**Table 6**).

4.11 Overall compliance with guidelines in surgical procedures with indication for SAP

Overall compliance with assessed SAP parameters with regards to choice of antibiotic, timing of antibiotic administration, route of administration, dosing and discontinuation was not achieved among surgical procedures with SAP indication and administered in the present study. **Table 6** shows the summary of the main findings regarding compliance of antibiotic prescribing in SAP with SIGN and ASHP guidelines.

Table 6: Compliance of antibiotic prescribing with SAP parameters (n=137)

Parameter	SIGN /ASHP Guidelines compliance	SIGN /ASHP Guidelines non-compliance
Choice of antibiotic, n (%)	21 (15.3)	116 (84.7)
Administration route, n (%)	136 (99.3)	1 (0.7)
Dose, n (%)	13 (9.5)	124(90.5)
Timing, n (%)	53 (38.7)	84 (61.3)
Discontinuation, n (%)	1 (0.7)	136 (99.3)
Overall compliance, n (%)	0 (0)	137 (100)

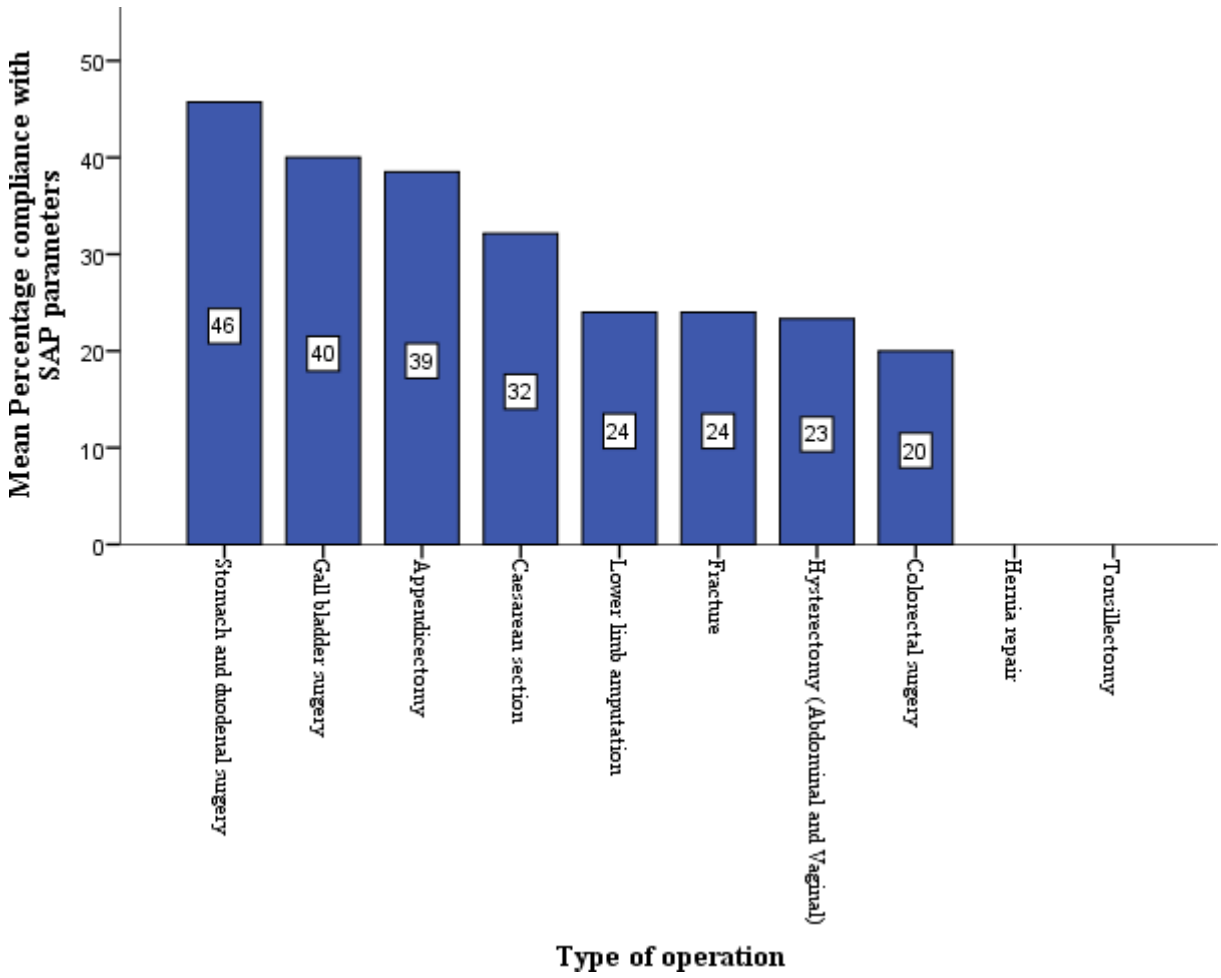

Figure 3: Level of compliance with guidelines among surgical procedures with indication for SAP

Compliance with SIGN and ASHP guidelines in terms prophylactic antibiotic choice, timing, dose, route and discontinuation was higher among upper gastrointestinal surgical procedures (>40%) than surgical procedures in other categories (**Figure 3**).

4.12 Predictors of non-compliance with SAP guidelines in terms of choice of prophylactic antibiotics

Female gender of post-operative patient, CDC wound classification and primary surgeon's rank, were all statistically significant in the bivariate analysis as shown in **Table 7**. The results of the multivariate logistic regression model (**Table 8**) indicated

that the three-predictor model imparted a statistically significant improvement compared to the constant only model, X^2 (2, n=137) = 31.81, $p < 0.001$. Nagelkerke R^2 explained approximately 36% of the variance in the model. The overall prediction rate was 88.3%. The Hosmer and Lemeshow test showed a *p*-value of 1.00 indicating good model fit. Only primary surgeon's rank (general medical officer, $p < 0.0001$; specialist, $p = 0.001$) was shown to be significantly associated with non-compliance with appropriate selection of prophylactic antibiotic in multivariate analysis.

The results below (**Table 8**) show that patients undergoing surgical procedures conducted by general medical officers were more likely not to receive appropriate choice of SAP than those operated on by specialists or senior medical officers. Furthermore, patients operated by specialist were 6 times more likely not to receive appropriate choice of SAP compared to senior medical officers.

4.13 Predictors of non-compliance with SAP guidelines in terms of route of administering prophylactic antibiotics

In the bivariate analysis, all the independent variables were not significantly associated with non-compliance to SAP guidelines in terms of route of administering prophylactic antibiotics ($p > 0.05$) and therefore, a multivariate analysis was not performed.

4.14 Predictors of non-compliance with SAP guidelines in terms of timing of administering prophylactic antibiotics

The results of the bivariate analysis showed that post-operative patient's age and female gender, status of surgery (elective), surgical procedures conducted during daytime and primary surgeon's rank (general medical officer) were significant

predictors ($p < 0.05$) of non-compliance with appropriate timing of administering prophylactic antibiotics (**Table 7**). The results of multivariate logistic regression showed that the final five predictor model had a statistically significant improvement over the constant only model, X^2 (2, n=137) = 37.6, $p < 0.0001$. Approximately 23.4% of the variance in the model was explained by Nagelkerke R^2. The Hosmer and Lemeshow test showed a *p*-value of 0.829 indicating good model fit and supported by the correct prediction rate of 66.4% and the area under the ROC curve of 71%. The Wald test showed that female gender of post-operative patient and elective surgical procedures significantly predicted non-compliance with appropriate timing of giving prophylactic antibiotics. Moreover, the Wald test showed no significant interaction effect between female gender of post-operative patient and elective surgical procedures on non-compliance with appropriate timing of giving prophylactic antibiotics outcome.

Non-compliance with appropriate timing of administering prophylactic antibiotics was significantly associated with elective surgical procedures (OR = 2.96, 95% CI: 1.32 – 6.65, $p = 0.009$) as shown in **Table 8** below. Female gender of post-operative patients (OR = 0.053, 95% CI: 0.01 - 0.41, $p = 0.005$) were less likely to be given prophylactic antibiotics at the wrong time than male patients.

Table 7: Predictors of non-compliance to SAP parameters using bivariate regression analysis

Variable	Choice of SAP		Timing of SAP administration		Dosing of SAP		Low compliance to SAP parameters	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	-	-	1.03 (1.01 to 1.06)	0.019	1.07 (1.01 to 1.14)	0.025	1.07 (1.09 to 1.14)	0.025
Female gender	6.62 (2.34 to 18.41)	< 0.0001	0.05 (0.01 to 0.37)	0.004	7.34 (2.20 to 24.50)	0.001	6.87 (2.07 to 22.80)	0.002
Status of surgery								
Elective	-	-	3.11 (1.43 to 6.73)	0.004	-	-	-	-
CDC wound classification								
Clean	27.00 (1.98 to 368.38)	0.013	-	-	-	-	-	-
Clean-contaminated	22.5 (4.13 to 122.51)	< 0.001	-	-	6.54 (1.36 to 31.47)	0.019	-	-
Time of operation								
Day	-	-	2.10 (1.00 to 4.42)	0.051	-	-	-	-
Primary surgeon's rank								
General medical officer	34.29 (8.71 to 134.95)	< 0.0001	0.282(0.06 to 1.46)	0.13	29.82 (5.64 to 158.78)	< 0.0001	28.73 (5.39 to 153.06)	< 0.0001
Specialist	9.94 (2.63 to 37.61)	< 0.001	0.12 (0.03 to 0.57)	0.007	7.52 (1.69 to 33.50)	0.008	8.24 (1.86 to 36.61)	0.006

Table 8: Predictors of non-compliance to SAP parameters using multivariate logistic regression analysis

Variable	Choice of SAP		Timing of SAP administration		Dosing of SAP		Low compliance to SAP paratmeters	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	-	-	-	-	1.09 (1.02 to 1.16)	0.01	1.09 (1.02 to 1.16)	0.011
Female gender	-	-	0.05 (0.01 to 0.39)	0.005	-	-	-	-
Status of surgery								
Elective	-	-	2.96 (1.32 to 6.65)	0.009	-	-	-	-
Primary surgeon's rank								
General medical officer	34.29 (8.71 to 134.95)	< 0.0001	-	-	53.03 (8.35 to 336.66)	< 0.0001	48.44 (7.77 to 301.82)	< 0.0001
Specialist	6.35 (2.63 to 37.61)	< 0.001	-	-	14.11 (2.40 to 83.24)	0.003	14.11 (2.39 to 83.24)	0.003

4.15 Predictors of non-compliance with SAP guidelines in terms dosing of prophylactic antibiotics

Post-operative patient's age, patient gender, CDC wound classification and primary surgeon's rank were the only significant predictors of non-compliance with appropriate dosing of prophylactic antibiotic in bivariate analysis (**Table 7**). The output of the multivariate regression showed that the four predictor model was significantly improved compared to the constant only model, X^2 (3, n=137) = 31.07, $p < 0.001$. Nagelkerke R^2 explained approximately 43.5% of the variance in the model. The overall prediction rate was 93.4%. The Hosmer and Lemeshow test showed a *p* value of 0.372 indicating good model fit that was supported by the area under the ROC curve of 89.1%. In the multivariate analysis (**Table 8**), non-compliance with dosing was significantly associated with patient's age (OR = 1.14,

95% CI: 1.14 to 1.26, $p = 0.007$). Surgical procedures conducted by general medical officers (OR = 14.44, 95% CI: 7.77 to 301.82, $p < 0.0001$) and specialists (OR = 43.60, 95% CI: 5.6440 to 336.91, $p < 0.0001$) were also significantly associated with non-compliance with appropriate dosing of prophylactic antibiotics. The Wald test showed that patient's age and primary surgeon's rank significantly predicted non-compliance with appropriate dosing of prophylactic antibiotics.

4.16 Predictors of non-compliance with SAP guidelines in terms of discontinuation of prophylactic antibiotics

All the independent variables were not significantly associated ($p > 0.05$) in the bivariate analysis and thus, a multivariate analysis was not performed.

4.17 Predictors of low compliance with SAP parameters

Compliance with SAP parameters using the SIGN and ASHP guidelines was generally poor in this baseline study as anticipated. Therefore, a summed scale was used to determine overall percentage compliance, with one point allocated to compliance with each of the five parameters namely; selection, dosing, timing, route and discontinuation. Similarly, a no point was awarded for non-compliance. Compliance with three or more parameters (> 50%) was considered high-level compliance while compliance with less than three parameters (< 50%) was considered low-level compliance. Compliance of more than 50% was only achieved in 9.5% (13/137) of the surgical procedures. Compliance with SAP parameters was mostly low with 90.5% (124/137) of surgical procedures complying with less than three SAP parameters.

Post-operative patient's age, patient gender and primary surgeon's rank were predictors of low compliance in bivariate analysis (**Table 7**). The output of the multivariate regression as presented in **Table 8** showed that the three predictor model was significantly improved compared to the constant only model, X^2 (3, n=137) = 30.31, $p < 0.001$. Approximately 42.6% of the variance in the model was explained by Nagelkerke R^2. The overall prediction rate was 93.4%. The Hosmer and Lemeshow test showed a p value of 0.394 indicating good model fit. In the multivariate analysis, low compliance was significantly associated with patient's age (OR = 1.09, 95% CI: 1.02 to 1.16, $p = 0.011$). Surgical procedures conducted by general medical officers (OR = 48.44, 95% CI: 7.77 to 301.82, $p < 0.0001$) and specialists (OR = 14.11, 95% CI: 2.40 to 83.24, $p = 0.003$).

CHAPTER 5

DISCUSSION

5.1 Characteristics of the study population

In the current study, post-operative patient and surgical procedures characteristics were similar to those reported by a recent study conducted in the Democratic Republic of the Congo (DRC) (43). However, in the current study, a higher proportion of gynaecological surgical procedures were conducted. This may have been due to the high volume of caesarean sections that were conducted (**Figure 2**). Similarly, a study undertaken by Weiser *et al* showed that caesarean section accounted for an estimated 30% of surgical procedures in LMIC (101) of which Namibia is part of the setting. More than half of the surgical procedures conducted in the current study were emergency surgeries similar to the findings by Simon *et al* (94) and Klinger *et al* (95). In contrast, most studies evaluated compliance with SAP guidelines in elective surgical procedures only (43,45,82). Moreover, a significant number of surgical procedures were performed during the day shift in the current study.

Ten medical doctors were involved in conducting the surgical procedures assessed in the present study similar to a study by Abdel Jalil *et al* (98). However, in the present study, only two of the medical doctors were specialist and more than half of the surgical procedures were conducted by general medical doctors contrary to a study by Abdel Jalil and colleagues in Jordan (98) and also by Mohammed *et al* in Australia (93).

5.2 Compliance with correct indication for SAP in the study population

The present study revealed that the majority of patients with an indication for SAP were given prophylactic antibiotics in compliance with SIGN and ASHP guidelines recommendation. The probable explanation for this finding could be that on one hand, the presence of a training manual that was used as a reference in Obstetrics/Gynecology department may partly explain this observation given that CS comprised more than half of surgical procedures assessed. On the other hand, it is likely that the medical practitioners were aware of the risks of SSIs despite the absence of a local or national guideline and thus were inclined to prescribe prophylactic antibiotics. However, a small proportion of these patients with an indication for SAP still did not receive any antibiotic for prophylaxis (**Table 5**) and this was higher than the proportion reported by Bunduki *et al.*, (43). This finding suggests that the proportion of patients in whom prophylactic antibiotics were not administered despite SAP being indicated according to the SIGN and ASHP guidelines, might have been at increased risk of developing SSI (10,40) and other sequelae secondary to SSIs. Nonetheless, the findings of the present study are comparable to those of Nabor *et al* that showed 93% compliance with SAP indication and administration (15) but lower than 98.7% compliance reported by Uppendahl and colleagues (44). However, the findings of the current study significantly differ from those reported by Mohamoud *et al* (45) and Mousavi *et al* (46) in which percentage compliance was 58.7% and 53%, respectively, lower than the current study.

5.3 Compliance with SAP guidelines with regards to choice of prophylactic antibiotics

The present study revealed sub-optimal compliance with the choice of the recommended prophylactic antibiotic (**Table 6**). The observed non-compliance was mostly related to the administration of ampicillin in more than two-thirds of surgical procedures either alone or in combination with metronidazole. Given that ampicillin is a broad-spectrum penicillin, its use was in contrast to the recommended antibiotics that target the microorganisms likely to cause SSIs based on the type of surgical procedure according to the SIGN and ASHP guidelines (10,11). For instance, the ASHP guideline recommends cefazolin, or second-generation cephalosprins in most surgical procedures as shown in **Appendix B**: Extract of American Society of Health System Pharmacist guideline In addition, in the absence of local antimicrobial susceptibility data in surgical patients and considering the review by Nejad and colleagues (3) and two other local studies (28,29); it may be presumed that ampicillin use in this study could have been inappropriate.

Although cefazolin is a commonly recommended narrow-spectrum antibiotic of choice in most of the surgical procedures (11,83) and is included in the Namibia Essential Medicines List (102), it was not used in any of the surgical procedures assessed in the present study. The non-use of cefazolin may suggest the lack of an evidence-based guideline or lack of prescriber awareness of its availability. However, a recently published Namibian antimicrobial guideline, though not available at the time of study also advocates for use of cefazolin in most cases (103). The findings of the current study are consistent with the results reported by three other similar studies conducted in Ethiopia (19,45) and the DRC (43) in which non-compliance with selection of an appropriate antibiotic for SAP was observed in

89.5%, 89.4% and 81.9% of the study population, respectively. However, in the studies conducted in Ethiopia, ceftriaxone was the antibiotic of choice in more than 80% of surgical procedures unlike in the present study where ampicillin alone or in combination was used in over 67% of the surgical procedures (**Table 4**). Aiken and colleagues also reported preferential use of ampicillin for SAP in a study conducted in Kenya citing availability and cost as reasons for its selection (31). Recently, ampicillin was also shown to be the preferred prophylactic antibiotic in 43.8% of surgical procedures in a study undertaken by Bunduki *et al* (43).

Compliance with SAP guidelines in terms of antibiotic choice at IHR was, however, lower than the compliance levels of 43.7% and 44% reported by Elbur *et al* (18) and Nabor *et al* (15), respectively. Other larger studies in developed settings, however, have demonstrated even higher compliance levels of 92% reported by van Kasteren and colleagues (104) than the current study. Similarly, a national survey in France reported compliance with national guideline of 83.3% with respect to appropriate prophylactic antibiotic choice.

5.4 Compliance with SAP guidelines with regards to route of administration of prophylactic antibiotics

Of all the five parameters of appropriate SAP use assessed in surgical procedures with indication for prophylactic antibiotics, compliance with the route of administration was the highest complied to parameter observed in accordance with guidelines (10,11). Prophylactic antibiotics for SAP were mostly administered intravenously in compliance with guidelines as illustrated in **Table 6** (10,11) in most surgical procedures in the present study although oral prophylactic antibiotic was administered in one case. Therefore, the current study showed that almost all the

post-operative patients were administered prophylactic antibiotics through the appropriate route that ensures therapeutic blood levels of antibiotics are attained in order to prevent SSI (10).

Few studies have assessed this parameter; however, studies conducted in Ethiopia and the Philippines have revealed similar findings, though, with a slightly higher percentage compliance of 100% (15,45). In contrast, lower compliance levels of 49% were reported in a study be Mousavi *et al* (46) and recently, Bunduki *et al* reported compliance of 83% (43).

5.5 Compliance with SAP guidelines with regards to timing of administration of prophylactic antibiotics

Compliance with timing of administering prophylactic antibiotics was moderately low in the present study as only slightly more than a third of post-operative patients were given prophylactic antibiotics within 60 minutes before skin incision as recommended by ASHP guideline (11). Therefore, most of the patients that underwent different surgical procedures were likely at high risk of developing SSIs. Though the reasons for this observation may not be fully ascertained in the present study, it clearly shows the gaps in optimal timing of SAP and the need for a multifaceted approach to improve antimicrobial prescribing in addition to developing and availing of a local guideline for SAP (105,106).

Several studies from both underdeveloped and developed countries have shown wide variations in the level of compliance with appropriate timing of administering prophylactic antibiotics in patients undergoing surgical procedures (17). For instance, a study conducted by Muller *et al* at a university teaching hospital in France showed that the level of compliance with correct injection time before the incision was 35%

(88) and was the most non-compliant SAP parameter. Another study performed by Elbur *et al* in Sudan with a higher sample size than Muller and colleagues reported an even lower percentage compliance of 9.3% (18). The findings of the present study are comparable with those of the study undertaken by Muller *et al* in spite of the lack of a local guideline for SAP. A recent study undertaken in Nigeria by Abubakar *et al* (20) reported a percentage compliance of 16.5% with respect to appropriate timing in obstetric and gynaecological surgical procedures, which is lower than the current study's finding of 38.7% (**Table 6**). However, compliance with appropriate timing was lower in the present study than the compliance levels of 52.3% and 79.2% reported by Alemkere (19) and Bunduki *et al* respectively (43).

In the present study, majority of the patients who underwent CS were administered antibiotics before skin incision. In contrast to guideline recommendations and findings of the present study, prophylactic antibiotics were given after incision in 98.2% of CS in a study by Muller *et al.* The practice of administering prophylactic antibiotics before skin incision in CS is based on evidence from recent studies that seem to show favourable maternal and neonatal outcomes in patients (5,71,72).

5.6 Compliance with SAP guidelines with regards to dosing of prophylactic antibiotics

The present study found that relatively few patients received appropriate doses of the recommended prophylactic antibiotics. The low compliance was mostly attributed to under-dosing of the recommended prophylactic antibiotics. This observation suggests a probable lack of information among practitioners involved in surgery concerning proper dosing of prophylactic antibiotics and is a modifiable risk factor that can be addressed. The current study's level of compliance with SIGN and ASHP SAP

guidelines concerning appropriate dosing of prophylactic antibiotics is lower than that reported by Elbur *et al* in Sudan (18) and van Kasteren and colleagues who undertook a larger study in the Netherlands (104). Elbur *et al* and, van Kasteren *et al* reported compliance levels of 29% and 89%, respectively. Unlike Elbur *et al* who used a similar clinical guideline (SIGN) as the present study, van Kasteren *et al* used a local hospital guideline. The use of a local hospital guideline may explain the high level of compliance with respect to both antibiotic choice (92%) and dosing reported by van Kasteren *et al* (104).

The majority of the patients (90.5%) in the present study were under-dosed thus predisposing them to undesired outcomes such as SSIs and AMR. However, the percentage compliance of antimicrobial prescribing with appropriate dosing of prophylactic antibiotics was higher than 5.9% reported by van der Sandt *et al* who carried out a study among paediatric patients in South Africa (92).

5.7 Compliance with SAP guidelines with regards to discontinuation of prophylactic antibiotics

A high rate of non-compliance with appropriate discontinuation of SAP within 24 hours was noted in the present study (**Table 6)**. Almost all patients that received prophylactic antibiotics before surgical incision continued the medication until discharge. Current evidence does not support prolonged use of prophylactic antibiotics beyond 24 hours after wound closure for the prevention of SSIs (48,76,77). This finding has serious implication for the patients and the hospital. Firstly, prolonged use of prophylactic antibiotics has been shown to increase the risk of CDI in a time-dependent manner (26). Secondly, unnecessary use of prophylactic antibiotics may predispose patients to emergence of AMR. Lastly, single doses of

prophylactic antibiotics has been shown to be effective in reducing the risk of SSIs (77). Therefore, the prolonged use of prophylactic antibiotics was a waste of medication and resources to the hospital.

Compliance with SAP guidelines regarding prophylactic antibiotic discontinuation is lower in the present study than that reported in studies conducted in other settings. For instance, a study undertaken by Abdel-Aziz in Qatar (57) showed that the level of compliance with the discontinuation of antibiotic prophylaxis was 40.7%. Similarly, Friedman and colleagues reported that more than 20% of patients with cardiac surgery received postoperative antibiotics (78). However, the findings of the present study are similar to those revealed by a study conducted by Abubakar *et al* in Nigeria (20) and did not differ much with those reported by similar studies carried out in Sudan and Iran which found percentage compliance of 3% and 14%, respectively (18,46).

In the present study, antibiotics were inappropriately continued for a longer duration of 2 to 29 days compared to the 5 to 12 days reported by Abubakar *et al* (20). Further, the findings of the present study support previous local studies on antibiotics which reported excessive and unnecessary use of antibiotics (22,33). Lack of antibiotic de-escalation observed in the present study may be due to a knowledge gap in the rational use of antibiotics in preventing SSIs among healthcare workers involved in the surgical care pathway.

5.8 Overall compliance of antimicrobial prescribing with SAP parameters

In the present study, none of the records complied with the ASHP and SIGN SAP guidelines for the five parameters assessed. Numerous studies and reviews have also reported non-compliance with appropriate SAP parameters according to internationally recommended guidelines and in some instances, national or facility guidelines (45,79,92). For example, overall compliance of 0% with all SAP parameters has been reported in studies conducted by Al-Momany *et al* (81) in Jordan and van der Sandt *et al* (92) in South Africa. These findings are similar to those of the present study.

Overall compliance of antimicrobial prescribing with SAP parameters in the present study was lower than that reported by studies undertaken in other LMIC countries (15,18,45) and a local study at WCH (21). A local or national SAP guideline was available in study settings in other LMIC countries unlike the present study and this may partly explain the difference in overall compliance with guidelines. Another reason for the poor overall compliance could probably be due to the absence of a robust antimicrobial stewardship programme (AMS) at the facility given the observed low compliance.

5.9 Predictors of non-compliance with SAP guidelines in terms of choice of antibiotics

The present study found that surgical procedures conducted by general medical officers (OR = 34.29, 95% CI: 8.71 to 134.95) and specialists (OR = 6.35, 95% CI: 2.63 to 7.61) were more likely to receive prophylactic antibiotics not recommended by guidelines (**Table 8**). These findings reflect irrational antibiotic use with respect to appropriate selection of SAP among medical practitioners and may possibly

predispose surgical patients to poor outcomes. The findings may be partly explained by the lack of local guideline or failure to adhere to the WHO Checklist (107). Another possible explanation could be the high volume of surgical procedures (workload). A study conducted in Japan identified workload as a predictor of poor compliance with appropriate selection of prophylactic antibiotics (96).

The findings of the present study are similar to those of a study conducted in French Guiana which showed significant association between type of prescriber (surgeon) and non-compliance with SAP guideline (94). On the contrary, the findings of the present study differ from those reported by a study undertaken by Lavers *et al* in Australia which showed no significant association between prescribers of SAP and non-compliance with national guidelines (86).

The relatively higher likelihood of most general medical officers to offer inappropriate choice of prophylactic antibiotics compared to consultants and senior medical officers may further suggest a knowledge disparity among the medical practitioners and a possible lack of mentorship. In contrast, Broom and colleagues (108) concluded that junior doctors were influenced by the prescribing practice of their seniors and consultants. Another similar study also reported surgeon specialty as a determinant of non-compliance with SAP guidelines (94). Moreover, the findings of the current study suggest a void in leadership role of prescribing SAP. Therefore, consultants being in positions of clinical leadership have a vital role in taking responsibility of SAP prescribing and positively influencing junior doctors and other healthcare workers involved in conducting surgical procedures.

5.10 Predictors of non-compliance with SAP guidelines in terms of timing of administering prophylactic antibiotics

Elective surgical procedures were the main predictor of non-compliance to SIGN and ASHP SAP guidelines in terms of timing of administering prophylactic antibiotics. This finding is contrary to expectations given the ample time available for preparing elective cases. As already mentioned above such practice likely reflects knowledge gap and the tendency to continue with the old practice rather than using evidence-based guidelines. Another reason could be system challenges since prophylactic antibiotics are not administered in operating theatre but rather in admitting wards at IHR. However, antibiotic prescribing in surgical procedures conducted on female surgical patients was less likely not to comply with optimal timing than that undertaken in male patients. The possible explanation for a relatively higher level of compliance of antibiotic prescribing with guidelines among female surgical patients could have been due to the availability of a training manual in the maternity ward (obstetrics/gynaecology). The training manual as a reference resource for CS cases was intended to improve maternal and neonatal outcomes. In addition, most of the surgical procedures (52.3%) assessed in the present study were CS. Therefore, based on this observation, it may be inferred that the availability of a local protocol or national SAP guideline may likely improve rational use of prophylactic antibiotics in surgery.

The findings of the present study are similar those reported by a study conducted by Mohamed *et al* (93) which showed that the status of surgery (elective surgical procedures, *p* value = 0.012), was a significant predictor of poor compliance with SAP guideline. Alemkere (19) also reported a significant correlation between gender (male, *p*-value = 0.001) and non-compliance with timing of SAP administration.

However, emergency surgical procedures were predictors of non-compliance to timing of administering prophylactic antibiotics (19) unlike in the present study.

5.11 Predictors of non-compliance with SAP guidelines in terms of dosing of prophylactic antibiotics

In the multivariate analysis, general medical officers ($p < 0.0001$) and specialist ($p < 0.0001$), were predictors of non-compliance with SIGN and ASHP guidelines with regards to appropriate dosing of prophylactic antibiotics. Thus, the finding of this study demonstrates knowledge gap in determining the correct dose of prophylactic antibiotics among providers of surgery at the study facility. Again, this may largely be attributed to lack of a guideline since medical practitioners were at liberty to follow their own judgments. This highlights the need for implementation of evidence-based practice at the study facility. Moreover, failure to follow evidence-based practice has been cited as a factor in most studies (43,78,88).

The findings of the present study are comparable to observations reported by Simon and colleagues who found that the type of prescriber (surgeon) was significantly associated with non-compliance with guidelines (94). Similarly, Musmar *et al* also reported variations in level of compliance with SAP guidelines among surgical care providers (97). The findings of the present study are also consistent with those by Abdel Jalil and colleagues who revealed that surgeon characteristics were associated with compliance with appropriate dosing of SAP (98). In their study, Abdel Jalil *et al* (98) reported that only two of the nine surgeons involved in 1173 CS procedures were more likely comply with appropriate dosing of prophylactic antibiotics ($p = 0.002$ and $p = 0.009$).

However, finding of the present study should be interpreted with caution, given the wide confidence interval, which could be due to sample size underestimation for this outcome measure.

5.12 Predictors of low compliance with SAP parameters

Due to almost absolute overall non-compliance with SIGN and ASHP guidelines for the evaluated five SAP parameters, it was difficult to understand factors contributing to this outcome in the present baseline study. Therefore, to determine predictors of overall non-compliance with SIGN and ASHP guidelines, compliance with three or more (> 50%) SAP parameters was deemed high compliance while compliance with less than two (< 50%) SAP parameters was considered low compliance. The present study revealed that 90.5% of the surgical procedures had low compliance. Few studies have reported the level of compliance based on the number of SAP parameters adhered to but a higher level of 58.8% compliance with three SAP parameters was reported by van der Sandt *et al* (92). However, Ciofi and colleagues observed a decrease in the level of compliance from 40.3% (compliance with two SAP parameters i.e., selection of prophylactic antibiotics and timing of administration) to 8.3% (compliance with three SAP parameters i.e. selection of prophylactic antibiotics, timing of administration and duration of SAP). This finding highlights the challenge with attaining high overall compliance with guidelines in a baseline study (91). Nonetheless, the level of compliance with three SAP parameters of 8.3% reported by Ciofi *et al* is lower than that revealed by the present study that found a percentage compliance of 9.5%. Unlike the present study, Ciofi *et al* carried out a multicentre study.

The studies by van der Sandt *et al* and Ciofi *et al* did not evaluate predictors of overall non-compliance with SAP parameters unlike the present study. The current study found that patient's age, general medical officers and specialists, were independent predictors of low overall compliance with SAP parameters. A tendency in decrease of surgeon's rank was noted to increase non-compliance to ASHP and SIGN guidelines suggesting the need of mentoring graduate doctors and probably those with less experience that are involved in surgical care pathway. This finding could be partly explained by lack of standardization due to the unavailability of local guidelines at the time of the study. Moreover, there was no antimicrobial stewardship programme in place at the facility at the time of the study. Further, the hospital lacked anaesthetists, clinical pharmacists, and infectious disease specialists that are key members of AMS.

5.13 Study limitations

The present study had several limitations. Firstly, this was a single centre study and therefore, the findings may not be generalizable to other settings. Due to lack of a database, only a representative sample of the surgical procedures was evaluated. Inclusion of all surgical procedures undertaken would have been more impactful. Secondly, compliance was based on two comprehensive international guidelines (10,11) which may not reflect the local context in terms of appropriate antibiotic selection with respect to local antibiotic susceptibility patterns and cost of antibiotics. Lastly, the sample size was likely underestimated to investigate predictors of non-compliance to SAP guidelines. However, as baseline research, the findings of the present study provides robust data that may be used to develop protocols and SAP

guideline to improve rational use of prophylactic antibiotics in surgery both locally and in Namibia at large.

CHAPTER 6

CONCLUSIONS

6.1 Compliance of surgical antimicrobial prophylaxis use with international guidelines

The findings of this study have revealed poor compliance with international clinical practice guidelines for SAP in terms of choice of prophylactic antibiotics at the hospital. Contrary to recommendations of guidelines, there was indiscriminate use of broad-spectrum antibiotics as well as use of antibiotics without full antibacterial coverage of suspected organisms. Although, compliance with regard to the timing of prophylactic antibiotic administration was moderate, poor compliance to dosing was observed thus further predisposing patients to risk of SSIs.

Another critical observation was that there was extended use of prophylactic antibiotics beyond the recommended 24-hour period in almost all the surgical procedures assessed. Therefore, it can be concluded that surgical patients were unnecessarily predisposed to risk of side effects and possible AMR. Moreover, non-compliance with duration of SAP signified a waste of resources, as it offered no additional benefits to surgical patients. However, the study also showed high compliance of antibiotic prescribing in terms of administering SAP through the appropriate route and needs to be encouraged. The overall compliance to the five parameters of SAP assessed in this study in surgical procedures that were administered prophylactic antibiotic with indication as recommended by SIGN and ASHP guidelines was not achieved.

6.2 Predictors of poor compliance with guidelines recommendation

Although the analysis of factors associated with poor compliance with rational SAP use showed that patient characteristics such as age and gender and primary surgeon's rank were all significant predictors of non-compliance with guidelines, other factors not explored in this study are likely to be involved. In summary, findings of this study suggest that the lack of SAP guidelines and limited knowledge of appropriate SAP use among the prescribers may account for the non-compliance with rational antibiotic use in surgery. Additionally, this study is the first at the hospital to establish baseline data of SAP prescribing practices.

CHAPTER 7

RECOMMENDATIONS

Based on the findings of the present study, it is recommended that multiple intervention measures must be implemented to improve compliance with SAP guidelines. These strategies may be interim measures aimed at optimizing patient outcomes or long-term measures that strengthen the health systems in terms of rational use of antibiotics for SAP. Therefore, the following recommendations are proposed:

a) Hospital management to strengthen antimicrobial stewardship program to optimise antibiotic use in surgical patients at IHR.

b) Develop a local SAP policy through the Hospital Therapeutics Committee and the Infection Control Committee and enforce implementation of the WHO checklist (5).

c) The MoHSS to conduct training on rational use of antibiotics for SAP and awareness on inappropriate use of antibiotics in SAP among surgeons, anaesthetists, pharmacists and nurses.

d) MoHSS to incorporate SAP indicators in the national Pharmaceutical Management Information System (PMIS) for hospitals to audit rational antibiotic use in surgery.

e) Further research to explore the effectiveness of SAP; describe antimicrobial susceptibility patterns of antibiotics for SAP and determine health system factors associated with non-compliance with SAP guidelines should be encouraged by the MoHSS.

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APPENDICES

Appendix A: Extract of Scottish Intercollegiate Guidelines Network (SIGN) 104 guideline

Table 2 ASA classification of physical status[17]

ASA score	Physical status
1	A normal healthy patient
2	A patient with a mild systemic disease
3	A patient with a severe systemic disease that limits activity, but is not incapacitating
4	A patient with an incapacitating systemic disease that is a constant threat to life
5	A moribund patient not expected to survive 24 hours with or without operation

3.1.2 WOUND CLASS

Operations can be categorised into four classes (see *Table 3*) with an increasing incidence of bacterial contamination and subsequent incidence of postoperative infection.[18]

Table 3 Classification of operation[18]

Class	Definition
Clean	Operations in which no inflammation is encountered and the respiratory, alimentary or genitourinary tracts are not entered. There is no break in aseptic operating theatre technique.
Clean–contaminated	Operations in which the respiratory, alimentary or genitourinary tracts are entered but without significant spillage.
Contaminated	Operations where acute inflammation (without pus) is encountered, or where there is visible contamination of the wound. Examples include gross spillage from a hollow viscus during the operation or compound/open injuries operated on within four hours.
Dirty	Operations in the presence of pus, where there is a previously perforated hollow viscus, or compound/open injuries more than four hours old.

This guideline applies to all elective operations in the clean, clean-contaminated or contaminated categories. Recommendations for prophylaxis of emergency surgery are limited to clean operations (for example, emergency repair of abdominal aortic aneurysm or open fixation of a closed fracture) and clean-contaminated operations (for example emergency caesarean section and facial trauma).

The guideline development group considered that antibiotic therapy for emergency operations with contaminated or dirty wounds is standard therapy rather than prophylaxis and as such is beyond the scope of this guideline.

3.1.3 DURATION OF SURGERY

Duration of surgery is positively associated with risk of wound infection and this risk is additional to that of the classification of operation.[19] In this study operations that lasted longer than the 75th percentile for the procedure were classified as prolonged.

3.1.4 EXTRINSIC RISK FACTORS

Guidelines for the prevention of SSI, outlining optimum practice, have been published by the CDC.[14] Extrinsic risks or patient care practices include preoperative skin care, perioperative practices and postoperative wound care (see Table 1).

3.1.5 PROCEDURE SPECIFIC RISKS

Some surgical procedures are associated with specific risks, for example, the insertion of an orthopaedic implant increases the risk of SSI.[20] Procedures performed endoscopically have been associated with a lower risk of infection.[21]

a|

5.2 RECOMMENDED INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS TO PREVENT SSI

Operation		Recommendation	Odds Ratio	ARR	Outcome	Evidence level
HEAD AND NECK Intracranial						
Craniotomy	A	Antibiotic prophylaxis is recommended	0.24	17	Wound infection	1++[48]
Cerebrospinal fluid (CSF) shunt	A	Antibiotic prophylaxis is recommended	0.48 0.52	16 16	Wound and shunt infection	1+[49,50]
Spinal surgery	A	Antibiotic prophylaxis is recommended	0.36	28	Wound infection	1++[48]
Ophthalmic						
Cataract surgery	A	Antibiotic prophylaxis is highly recommended	0.36	451	Endophthalmitis	1++[48]
Glaucoma or corneal grafts	B	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about cataract surgery*			1+[48]
Lacrimal surgery	C	Antibiotic prophylaxis is recommended	0.03	9	Wound infection	2+[51]
Penetrating eye injury	B	Antibiotic prophylaxis is recommended	0.20	16	Endophthalmitis	1+[48,52]
Facial						
Open reduction and internal fixation of compound mandibular fractures	A	Antibiotic prophylaxis is recommended	0.26	5	Wound infection	1++, 1+[53,54]
	A	The duration of prophylactic antibiotics should not be more than 24 hours				1++[55]
Intraoral bone grafting procedures	B	Antibiotic prophylaxis is recommended	*There was no direct comparison of prophylactic antibiotic with no antibiotic*			1++[56]
Orthognathic surgery	A	Antibiotic prophylaxis is recommended	0.21	4	Wound infection	1+[57,58]
	A	The duration of prophylactic antibiotics should not be more than 24 hours				1+[59,60]
	B	Broad spectrum antibiotics appropriate to oral flora should be given				1+[57,58]
Facial surgery (clean)	✓	Antibiotic prophylaxis is not recommended				
Facial plastic surgery (with implant)	✓	Antibiotic prophylaxis should be considered	*Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices*			4[61]
Ear, nose and throat – benign						
Ear surgery (clean/ clean-contaminated)	A	Antibiotic prophylaxis is not recommended	*There was no subgroup of analysis of clean and clean-contaminated surgery*			1++[62]
Routine nose, sinus and endoscopic sinus surgery	A	Antibiotic prophylaxis is not recommended				1+[63]
Complex septorhinoplasty (including grafts)	A	The duration of prophylactic antibiotics should not be more than 24 hours				1++[64]

Operation		Recommendation	Odds Ratio	ANT	Outcome	Evidence level
HEAD AND NECK **Ear, nose and throat – benign**						
Tonsillectomy	✓	Antibiotic prophylaxis is not recommended	*No studies were identified showing evidence of effectiveness of prophylaxis*			
Adenoidectomy (by curettage)	A	Antibiotic prophylaxis is not recommended				1+[79]
Grommet insertion	B	Antibiotic prophylaxis (a single dose of topical antibiotic) is recommended	0.46	13	Otorrhea	1++, 1+, 2+[80-82]
Head and neck						
Head and neck surgery *(clean, benign)*	D	Antibiotic prophylaxis is not recommended				4[83,84]
Head and neck surgery *(clean, malignant) neck dissection)*	C	Antibiotic prophylaxis should be considered	1.26 0.12	–29 9	Wound infection	2+[85,86]
Head and neck surgery *(contaminated/clean-contaminated)*	A	Antibiotic prophylaxis is recommended	0.37	6	Wound infection	1++[87-90]
	C	The duration of prophylactic antibiotics should not be more than 24 hours				2+[91,92]
	D	Ensured broad spectrum antimicrobial cover for aerobic and anaerobic organisms				4[93]
THORAX						
Breast cancer surgery	A	Antibiotic prophylaxis should be considered				1++[94]
Breast reshaping procedures	C	Antibiotic prophylaxis should be considered	0.86	14	Infection at 6 weeks	2+[95]
Breast surgery with implant *(reconstructive or aesthetic)*	C	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about breast cancer surgery and other procedures involving insertion of prosthetic devices*			1++[96], 4[97]
Cardiac pacemaker insertion	A	Antibiotic prophylaxis is recommended	0.26	58	Any infection	1++[98]
Open heart surgery	C	Antibiotic prophylaxis is recommended	0.83 2.52 0.86	5 –27 8	Wound infection	2+[99-101]
	C	The duration of prophylactic antibiotics should not be more than 48 hours				2++, 2+, 4[102,103]
Pulmonary resection	A	Antibiotic prophylaxis is recommended	0.20	8	Surgical site infection	1++[104-106]
UPPER GASTROINTESTINAL						
Oesophageal surgery	D	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[107]
Stomach and duodenal surgery	A	Antibiotic prophylaxis is recommended	0.17	5	Wound infection	1+[108-114]
Gastric bypass surgery	D	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[115]
Small intestine surgery	D	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[115]

Operation		Recommendation	Odds Ratio	ANT	Outcome	Evidence level
HEPATOBILIARY						
Bile duct surgery	A	Antibiotic prophylaxis is recommended	0.30	11	Wound infection	1++[MA]
Pancreatic surgery	B	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about biliary surgery*			1++[MA]
Liver surgery	B	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about biliary surgery*			1++[MA]
Gall bladder surgery (open)	A	Antibiotic prophylaxis is recommended	0.30	11	Wound infection	1++[MA]
Gall bladder surgery (laparoscopic)	A	Antibiotic prophylaxis is not recommended				1+[MA]
	✓	Antibiotic prophylaxis should be considered in high risk patients				
		High risk: intraoperative cholangiogram, bile spillage, conversion to laparotomy, acute cholecystitis/pancreatitis, jaundice, pregnancy, immunosuppression, insertion of prosthetic devices				
LOWER GASTROINTESTINAL						
Appendicectomy	A	Antibiotic prophylaxis is highly recommended	0.83 0.43	11 105	Wound infection Intra-abdominal abscesses	1++[MA]
Colorectal surgery	A	Antibiotic prophylaxis is highly recommended	0.24	4	Wound infection Intra-abdominal abscesses	1++[MA]
ABDOMEN						
Hernia repair-groin (inguinal/femoral with or without mesh)	A	Antibiotic prophylaxis is not recommended				1++[MA,RCT]
Hernia repair-groin (laparoscopic with or without mesh)	B	Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[MA,RCT]
Hernia repair (incisional with or without mesh)	C	Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[MA,RCT]
Open/laparoscopic surgery with mesh (eg gastric band or rectopexy)	B	Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[MA,RCT]
	✓	Antibiotic prophylaxis should be considered in high risk patients (see section 9.7)				
Diagnostic endoscopic procedures	D	Antibiotic prophylaxis is not recommended				4[EP]
Therapeutic endoscopic procedures (endoscopic retrograde cholangio-pancreatography and percutaneous endoscopic gastrostomy)	D	Antibiotic prophylaxis should be considered in high risk patients				4[EP]
		High risk: pancreatic pseudocyst, immunosuppression, incomplete biliary drainage (eg primary sclerosing cholangitis or cholangiocarcinoma)				

Operation		Recommendation	Odds Ratio	ANT	Outcome	Evidence level
ABDOMEN						
Spleen						
Splenectomy	✓	Antibiotic prophylaxis is not recommended	*Post-splenectomy prophylaxis is covered elsewhere*[133]			
	✓	Antibiotic prophylaxis should be considered in high risk patients *High risk: immunosuppression*				
Gynaecological						
Abdominal hysterectomy	A	Antibiotic prophylaxis is recommended				1++[118,119,134]
Vaginal hysterectomy	A	Antibiotic prophylaxis is recommended	0.17	4	Pelvic infection	1++[118,119,134]
Caesarean section	A	Antibiotic prophylaxis is highly recommended	0.41	19	Wound infection	1++[117]
Assisted delivery	A	Antibiotic prophylaxis is not recommended				1++[118]
Perineal tear	D	Antibiotic prophylaxis is recommended for third/fourth degree perineal tears involving the anal sphincter/rectal mucosa			Wound infection	4[135]
Manual removal of the placenta	D	Antibiotic prophylaxis should be considered				4[136]
	D	Antibiotic prophylaxis is recommended for patients with proven chlamydia or gonorrhoea infection				4[136]
Induced abortion	A	Antibiotic prophylaxis is highly recommended	0.58	25	Upper genital tract infection	1++[131]
Evacuation of incomplete miscarriage	A	Antibiotic prophylaxis is not recommended				1++[132]
Intrauterine contraceptive device (IUCD) insertion	A	Antibiotic prophylaxis is not recommended				1++[130]
Urogenital						
Transrectal prostate biopsy	A	Antibiotic prophylaxis is recommended	0.76	27	Bacteriuria	1+[124,125]
Shock wave lithotripsy	A	Antibiotic prophylaxis is recommended	0.45	28	Urinary tract infection	1++[126]
Percutaneous nephrolithotomy	B	Antibiotic prophylaxis is recommended for patients with stone ≥20 mm or with pelvicalyceal dilation	0.24	4	Urosepsis	1+[127]
	B	Oral quinolone for one week preoperatively is recommended				1+[127]
Endoscopic ureteric stone fragmentation/ removal	B	Antibiotic prophylaxis is recommended	0.13 2.75	10 –15	Bacteriuria	1+, 2+[128,129]
Transurethral resection of the prostate	A	Antibiotic prophylaxis is highly recommended	0.35	8	Bacteriuria Infective complications	1++[120]

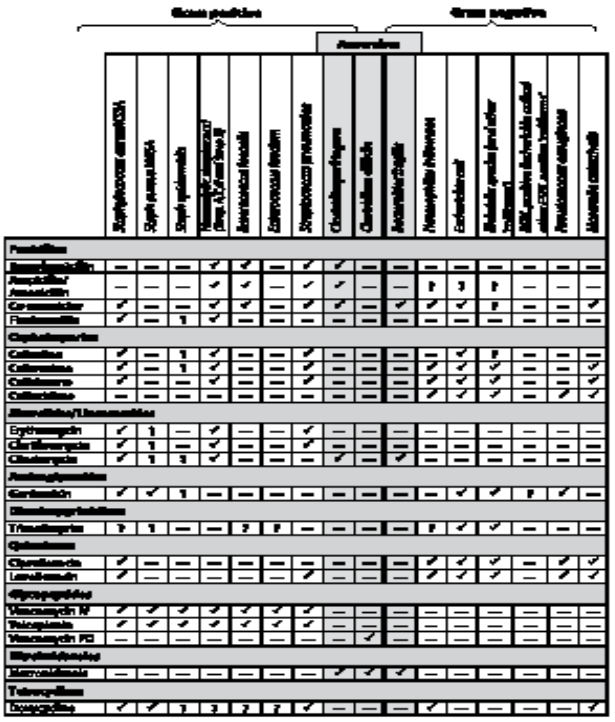
Operation		Recommendation	Odds Ratio	ARR	Outcome	Evidence level
ABDOMEN Urogenital						
Transurethral resection of bladder tumours	D	Antibiotic prophylaxis is not recommended				4[131]
Radical cystectomy	✓	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence that SSI is high post-cystectomy*			5[132]
LIMB						
Arthroplasty	B	Antibiotic prophylaxis is highly recommended	0.27 0.25	42 57	Hip infection Joint infection	1++, 1+, 2++[133-135]
	B	Antibiotic-loaded cement is recommended in addition to intravenous antibiotics				2++[136-138]
	B	Up to 24 hours of antibiotic prophylaxis should be considered				2++[139]
Open fracture	A	Antibiotic prophylaxis is highly recommended	0.41	14	Wound infection	1++[137]
Open surgery for closed fracture	A	Antibiotic prophylaxis is highly recommended	0.36	38	Deep wound infection	1++[139]
Hip fracture	A	Antibiotic prophylaxis is highly recommended	0.55	23	Deep wound infection	1++[139]
Orthopaedic surgery *(without implant)*	D	Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[89]
Lower limb amputation	A	Antibiotic prophylaxis is recommended	0.32	5	Wound infection	1++[140]
Vascular surgery *(abdominal and lower limb arterial reconstruction)*	A	Antibiotic prophylaxis is recommended	0.12 0.10	18 4	Wound infection Wound infection	1++[141]
Soft tissue surgery of the hand	B	Antibiotic prophylaxis should be considered	Effectiveness is inferred from evidence about orthopaedic and vascular surgery			1++[136,139]
NON-OPERATIVE INTERVENTIONS						
Intravascular catheter insertion • non-tunnelled central venous catheter (CVC) • tunnelled CVC	D D A	Antibiotic prophylaxis is not recommended Antibiotic prophylaxis is not recommended				4[142], 1++[143]
GENERAL						
Clean-contaminated procedures *–where no specific evidence is available*	D	Antibiotic prophylaxis is recommended				4[89]
Insertion of a prosthetic device or implant *–where no specific evidence is available*	D	Antibiotic prophylaxis is recommended				4[89]

Operation		Recommendation	Odds Ratio	NNT	Outcome	Evidence level
UROGENITAL						
Hydrocoeles/Tears in repair	C	Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair in adults*			1++[38, 39]
Shock wave lithotripsy	B	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence in adults*			1++[38]
Percutaneous nephrolithotomy	C	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence in adults*			1+[37]
Endoscopic ureteric stone fragmentation/ removal	C	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence in adults*			1+, 2+[38, 39]
Cystoscopy	✓	Antibiotic prophylaxis is not recommended				
	✓	Antibiotic prophylaxis should be considered if there is a high risk of UTI				
Nephrectomy	✓	Antibiotic prophylaxis is not recommended				
Pyeloplasty	✓	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about other clean-contaminated procedures in adults*			4[40]
Surgery for vesicoureteric reflux *(endoscopic or open)*	✓	Antibiotic prophylaxis is recommended	*Effectiveness is inferred from evidence about other procedures involving insertion of a prosthetic device in adults*			4[40]
NON-OPERATIVE INTERVENTIONS						
Intravascular catheter insertion • non-tunnelled central venous catheter (CVC) • tunnelled CVC	D D A	Antibiotic prophylaxis is not recommended Antibiotic prophylaxis is not recommended	*Effectiveness is inferred from evidence in adults* *Effectiveness is inferred from evidence in adults*			4[40], 1++[41]
GENERAL						
Clean-contaminated procedures – *where no specific evidence is available*	D	Antibiotic prophylaxis is recommended				4[40]
Insertion of a prosthetic device or implant – *where no specific evidence is available*	D	Antibiotic prophylaxis is recommended				4[40]

Annex 5

In vitro activity of antibiotics, which may be considered for antibiotic prophylaxis

(reproduced by kind permission of V Wallroth, V Weston and T Hills)[77]



✓ In vitro activity (usually sensitive)

— Intrinsic resistance (always or usually resistant)

? Variable sensitivity

Appendix B: Extract of American Society of Health System Pharmacist guideline

Table 2.
Recommendations for Surgical Antimicrobial Prophylaxis

Type of Procedure	Recommended Agents[a,b]	Alternative Agents in Pts With β-Lactam Allergy	Strength of Evidence[c]
Cardiac			
Coronary artery bypass	Cefazolin, cefuroxime	Clindamycin,[d] vancomycin[d]	A
Cardiac device insertion procedures (e.g., pacemaker implantation)	Cefazolin, cefuroxime	Clindamycin, vancomycin	A
Ventricular assist devices	Cefazolin, cefuroxime	Clindamycin, vancomycin	C
Thoracic			
Noncardiac procedures, including lobectomy, pneumonectomy, lung resection, and thoracotomy	Cefazolin, ampicillin–sulbactam	Clindamycin,[d] vancomycin[d]	A
Video-assisted thoracoscopic surgery	Cefazolin, ampicillin–sulbactam	Clindamycin,[d] vancomycin[d]	C
Gastroduodenal[e]			
Procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy[f])	Cefazolin	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j]	A
Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients	Cefazolin	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j]	A
Biliary tract			
Open procedure	Cefazolin, cefoxitin, cefotetan, ceftriaxone,[k] ampicillin–sulbactam[h]	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j] Metronidazole + aminoglycoside[g] or fluoroquinolone[h-j]	A
Laparoscopic procedure			
Elective, low-risk[l]	None	None	A
Elective, high-risk[l]	Cefazolin, cefoxitin, cefotetan, ceftriaxone,[k] ampicillin–sulbactam[h]	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j] Metronidazole + aminoglycoside[g] or fluoroquinolone[h-j]	A
Appendectomy for uncomplicated appendicitis	Cefoxitin, cefotetan, cefazolin + metronidazole	Clindamycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j] Metronidazole + aminoglycoside[g] or fluoroquinolone[h-j]	A
Small intestine			
Nonobstructed	Cefazolin	Clindamycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h-j]	C

Continued on next page

Table 2 (continued)

Type of Procedure	Recommended Agents[a]	Alternative Agents in Pts with β-Lactam Allergy	Strength of Evidence[b]
Obstructed	Cefoxitin + metronidazole, cefmetazole, cefotetan	Metronidazole + aminoglycoside[c] or fluoroquinolone[d]	C
Hernia repair (hernioplasty and herniorrhaphy)	Cefoxitin	Clindamycin, vancomycin	A
Colorectal[e]	Cefoxitin + metronidazole, cefmetazole, cefotetan, ampicillin–sulbactam, ertapenem + metronidazole	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone[d], metronidazole + aminoglycoside[c] or fluoroquinolone[d]	A
Head and neck			
Clean	None	None	B
Clean with placement of prosthesis (excludes tympanostomy tube)	Cefazolin, cefuroxime	Clindamycin[f]	C
Clean-contaminated cancer surgery	Cefazolin + metronidazole, cefuroxime + metronidazole, ampicillin–sulbactam	Clindamycin[f]	A
Other clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	Cefazolin + metronidazole, cefuroxime + metronidazole, ampicillin–sulbactam	Clindamycin[f]	B
Neurosurgery			
Elective craniotomy and ventriculoperitoneal fluid-shunting procedures	Cefazolin	Clindamycin,[f] vancomycin[f]	A
Implantation of intrathecal pumps	Cefazolin	Clindamycin,[f] vancomycin[f]	C
Cesarean delivery	Cefazolin	Clindamycin + aminoglycoside[g]	A
Hysterectomy (vaginal or abdominal)	Cefazolin, cefotetan, cefoxitin, ampicillin–sulbactam[h]	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[d] + metronidazole + aminoglycoside[c] or fluoroquinolone[d]	A
Ophthalmic	Topical neomycin–polymyxin B–gramicidin or fourth-generation topical fluoroquinolones (gatifloxacin or moxifloxacin) given as 1 drop every 5–15 min for 3 doses[i] Addition of cefazolin 100 mg by subconjunctival injection or intracameral cefazolin 1–2.5 mg or cefuroxime 1 mg at the end of procedure is optional	None	B
Orthopedic			
Clean operations involving hand, knee, or foot and not involving implantation of foreign materials	None	None	C
Spinal procedures with and without instrumentation	Cefazolin	Clindamycin,[f] vancomycin[f]	A

Continued on next page

Table 2 (continued)

Type of Procedure	Recommended Agents[a,b]	Alternative Agents in Pts With β-Lactam Allergy[c]	Strength of Evidence[d]
Hip fracture repair	Cefazolin	Clindamycin,[e] vancomycin[f]	A
Implantation of internal fixation devices (e.g., nails, screws, plates, wires)	Cefazolin	Clindamycin,[e] vancomycin[f]	C
Total joint replacement	Cefazolin	Clindamycin,[e] vancomycin[f]	A
Urologic			
Lower tract instrumentation with risk factors for infection (includes transrectal prostate biopsy)	Fluoroquinolone,[g,h] trimethoprim–sulfamethoxazole, cefazolin	Aminoglycoside[i] with or without clindamycin	A
Clean without entry into urinary tract	Cefazolin (the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material [e.g., penile prosthesis])	Clindamycin,[e] vancomycin[f]	A
Involving implanted prosthesis	Cefazolin ± aminoglycoside, cefazolin ± aztreonam, ampicillin–sulbactam	Clindamycin ± aminoglycoside or aztreonam, vancomycin ± aminoglycoside or aztreonam	A
Clean with entry into urinary tract	Cefazolin (the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material [e.g., penile prosthesis])	Fluoroquinolone,[g,h] aminoglycoside[i] with or without clindamycin	A
Clean–contaminated	Cefazolin + metronidazole, cefoxitin	Fluoroquinolone,[g,h] aminoglycoside[i] + metronidazole or clindamycin	A
Vascular[j]	Cefazolin	Clindamycin,[e] vancomycin[f]	A
Heart, lung, heart–lung transplantation[k] Heart transplantation[l]	Cefazolin	Clindamycin,[e] vancomycin[f]	A (listed on cardiac procedures)
Lung and heart–lung transplantation[m]	Cefazolin	Clindamycin,[e] vancomycin[f]	A (listed on cardiac procedures)
Liver transplantation[n]	Piperacillin–tazobactam, cefotaxime + ampicillin	Clindamycin or vancomycin + aminoglycoside[i] or aztreonam or fluoroquinolone[g,h]	B
Pancreas and pancreas–kidney transplantation[o]	Cefazolin, fluconazole (for patients at high risk of fungal infection [e.g., those with enteric drainage of the pancreas])	Clindamycin or vancomycin + aminoglycoside[i] or aztreonam or fluoroquinolone[g,h]	A
	Cefazolin	Clindamycin or vancomycin + aminoglycoside[i] or aztreonam or fluoroquinolone[g,h]	A

Continued on next page

Appendix C: Data collection tool

ID #:	Ward:_____	Length of stay (hrs):	Date:_____	
SECTION A: Patients' demographics				
Gender □ Female □ Male	**Age:____** □ Child □ Adult	**Weight (kg):**	**Co-morbidity** □ HIV □ Cancer □ Diabetes mellitus □ Hypertension □ Other (specify):____	**Referral status** □ Resident □ District referral □ Unknown
SECTION B: Surgery category (tick from list given below) and state for type of operation				
Department □ General surgery □ Obs/gynaecology □ Orthopaedics	**Status of surgery** □ Elective □ Emergency	**Type of wound** □ Clean □ Clean contaminated □ Contaminated	**Time of operation** □ Day □ Night	**ASA score** □ □ No record
Type of operation:	Incision time:	Finish time:		
SECTION C: Details of medical officer conducting surgery				
Primary Surgeon's rank □ Specialist □ Senior medical officer □ medical officer	**Gender** □ Male □ Female	**Age group** □ 20 - 29 □ 30 - 39 □ 40 - 49 □ > 50	**Years of experience** □ < 5 □ 5 - 9 □ > 10	
SECTION D: Surgical antimicrobial prophylaxis				
Prophylaxis indicated? □ Yes □ No	**Name of antibiotic(s) given:_____**	**Antibiotic dose (mg):_____**	**Time of antibiotic administration:_____**	**Route and # of doses given:** □ IV single dose □ IV > single dose □ Other (specify):____
Antibiotics continued post operatively? □ Yes □ No **If yes:** Name of antibiotic(s):_____ Duration:___				

Appendix D: University of Namibia ethical clearance exemption letter

SCHOOL OF PHARMACY
University of Namibia, Private Bag 13301, Windhoek, Namibia
Pioneers Shilongo Street, Windhoek North
URL: http://www.unam.edu.na

UNAM

28 March, 2019

Prof. Tim Rennie
Associate Dean
School of Pharmacy

SUBJECT: M.Pharm. Research Proposal of Mr. Brian Chola

Dear Prof. Rennie,

I read the M.Pharm. Research Proposal of Mr. Brian Chola entitled "EVALUATION OF COMPLIANCE TO INTERNATIONAL GUIDELINES OF ANTIMICROBIAL PRESCRIBING IN SURGICAL PROPHYLAXIS AT INTERMEDIATE HOSPITAL RUNDU".

There are not really any human ethics concerns since the data will be retroactively collected from an existing patient data files. Obviously, the anonymity of the patients whose data will be used in the study should be guaranteed, but that aspect is clearly addressed in the proposal under point 4. Research Ethics.

Consequently, I do not see any need for this proposal to be evaluated by the Human Research Ethics Committee (HREC).

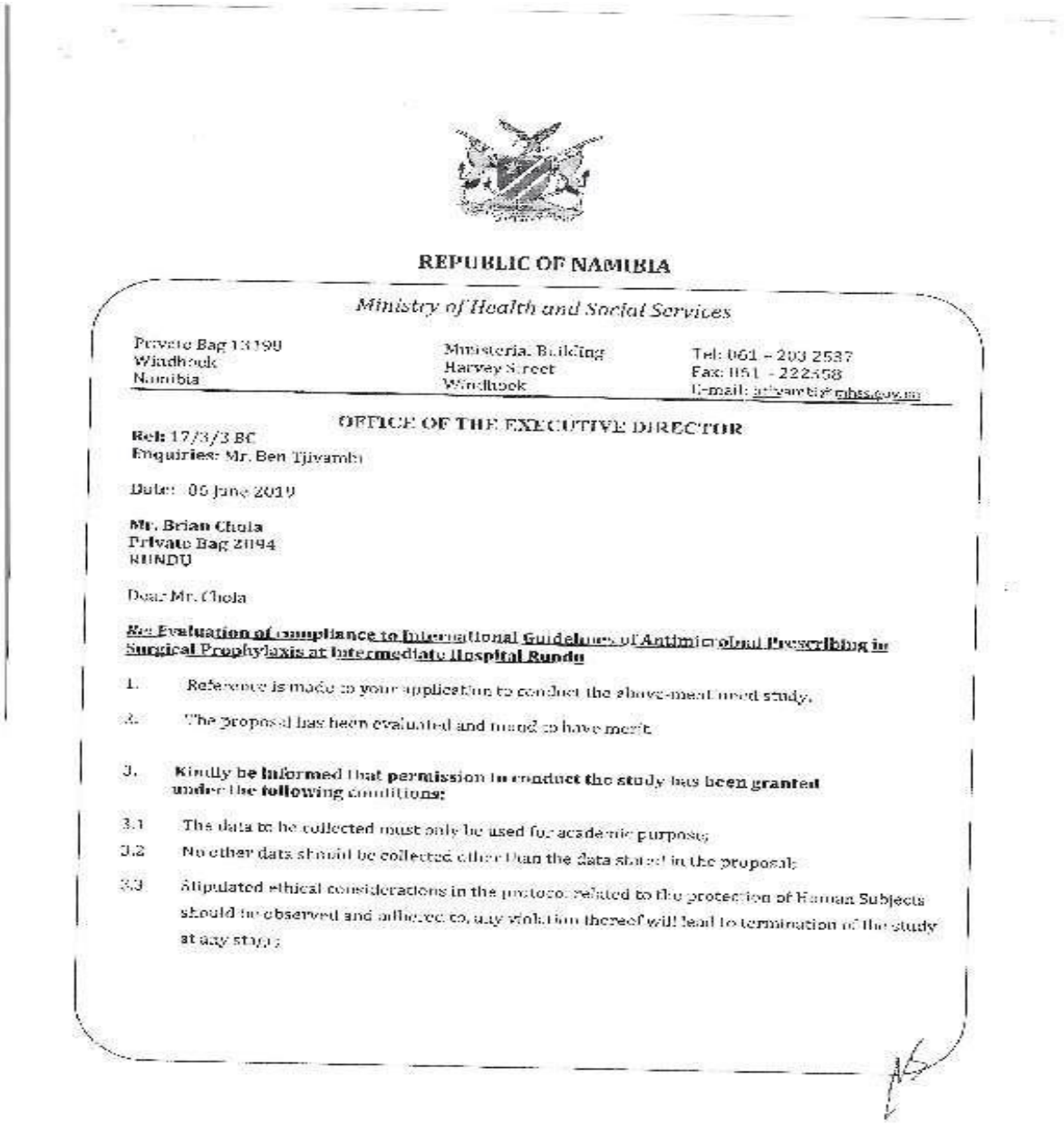
Kind regards.

UNIVERSITY OF NAMIBIA
Faculty of Health Sciences
School of Medicine
28 MAR 2019
Private Bag 13301
Windhoek, Namibia
ASSOCIATE DEAN SCHOOL OF PHARMACY

Professor Roger Verbeeck
Faculty Representative of the Human Ethics Research Committee

Faculty of Health Sciences
School of Pharmacy
Hage Geingob Campus

Appendix E: Ministry of Health and Social Services approval letter



REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198
Windhoek
Namibia

Ministeria. Building
Harvey Street
Windhoek

Tel: 061 – 203 2537
Fax: 061 – 222458
E-mail: ptjivambi@mhss.gov.na

OFFICE OF THE EXECUTIVE DIRECTOR

Ref: 17/3/3 BC
Enquiries: Mr. Ben Tjivambi

Date: 06 June 2019

Mr. Brian Chola
Private Bag 2094
RUNDU

Dear Mr. Chola

Re: Evaluation of compliance to International Guidelines of Antimicrobial Prescribing in Surgical Prophylaxis at Intermediate Hospital Rundu

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for academic purposes;

3.2 No other data should be collected other than the data stated in the proposal;

3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;

3.4 A quarterly report to be submitted to the Ministry's Research Unit;

3.5 Preliminary findings to be submitted upon completion of the study;

3.6 Final report to be submitted upon completion of the study;

3.7 Separate permission should be sought from the Ministry for the publication of the findings.

4 All the costs implications that will result from this study will be the responsibility of the applicant and not of the MoHSS.

Yours sincerely,

PERMANENT SECRETARY MINISTRY OF HEALTH & SOCIAL SERVICES

MR. BENJAMIN MBE
EXECUTIVE DIRECTOR OF HEALTH & SOCIAL SERVICES

"Health for All"

Appendix F: Intermediate Hospital Rundu approval letter

9 - 0 / 0001

REPUBLIC OF NAMIBIA

MINISTRY OF HEALTH AND SOCIAL SERVICES

Rundu Intermediate Hospital Rundu Namibia	Private Bag 2094 Rundu Namibia	Tel: +264 66 265500 Fax: +264 66 255037 Ext: 554

OFFICE OF THE MEDICAL SUPERINTENDENT

Ref: P/F
Date: 24 April 2019

TO WHOM IT MAY CONCERN

RE: APPROVAL TO CONDUCT RESEARCH PROJECT FOR MR. BRIAN CHOLA

The Management of Rundu Intermediate Referral Hospital grants permission for Brian Chola a student of the University of Namibia to carry out research in our institution in relation to his field of study entitled: *Evaluation of Compliance to International Guidelines of Antimicrobial Prescribing in Surgical Prophylaxis.*

Kindly be informed that permission has been granted under the following condition:

No other data should be collected other than for the stated purpose in the permission request to conduct research.

Wishing you success during your stay

Thank you.

.....

DR. JOSEPH MUKERENGE
MEDICAL SUPERINTENDENT

"YOUR HEALTH, OUR CONCERN"