University of Nairobi

PRACTICE OF PROPHYLACTIC ANTIBIOTIC USE IN ELECTIVE ORTHOPEDIC PROCEDURES AT THE KENYATTA NATIONAL HOSPITAL

Dr. Shabir Adamjee Najmudin

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University of Nairobi

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DECLARATION

This proposal is my original work and has not been presented for a degree in any other university for examination.

Name: DR SHABIR NAJMUDIN ADAMJEE

Signature: .....

Date 2/8/23

SUPERVISORS APPROVAL

This proposal has been submitted for examination with our approval as university supervisors

Fred Sitati (MBChB, Mmed (ortho), FCS (ECSA), Dip SICOT, Fellowship (Arthroscopy and Arthroplasty) and Doctor of Philosophy in Orthopedic Surgery)
Consultant Orthopedic and Trauma Surgeon,
Senior Lecturer, Department of Orthopedic Surgery,
University of Nairobi
Email: fredsitati@yahoo.com

Signature.....Date 03-08-2023

Edward Gakuya (MBChB, Mmed surgery and Fellowship Reconstruction and Trauma Surgery)
Consultant Orthopedic and Trauma Surgeon,
Lecturer, Department of Orthopedic Surgery,
University of Nairobi
Email: kibaka62@gmail.com

Signature.....Date 03/08/2023

DEPARTMENTAL APPROVAL

This dissertation was presented at the Department of Surgery, Orthopedic Thematic unit on 6th of December 2022 at the University of Nairobi. It was subsequently approved by the Kenyatta National Hospital – university of Nairobi, ethics and research committee (KNH-UON ERC) on 28th march 2023.

Vincent M Mutiso MBChB, MMED (Surgery), FCS (ECSA), AO Fellow (Trauma and Orthopedics), Fellowship Arthroplasty and Arthroscopy (U.K)
Consultant Orthopedic Surgeon and Senior Lecturer
Orthopedic Thematic Unit Head
University of Nairobi.

Signature ..... Date 10/08/2023

This dissertation is hereby submitted for examination with my approval as the Chairman, of the Department of Surgery

Julius G. Kiboi
Chairman, Department of Surgery
Senior Lecturer and Consultant Neurosurgeon
Faculty of Health science
University of Nairobi

Signature ..... Date 15-8-2023

DEPARTMENT OF SURGERY
FACULTY OF HEALTH SCIENCES
P O Box 19676 - 00202, KNH
NAIROBI
Tel: 020 4915043

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ABBREVIATIONS

AAOS – American academy of orthopedic surgeons

AMR- Antimicrobial Resistance

ASA- American Society of Anesthesiologists classification of Physical Health

ASB- Asymptomatic bacteriuria

ASHP-American Society of Health System Pharmacists

CDC- Centers for Disease Control and Prevention

CL- Total clearance

FDA- Food and Drug Administration

GFR – Glomerular filtration rate

HAI- Hospital acquired infection

IV- Intravenous

KNH- Kenyatta National Hospital

MRSA- Methicillin resistant Staphylococcus Aureus

NHS- National Health Services

PJI- Prosthetic Joint Infection

PMMA – Polymethylmethacrylate

PSAP- Prolonged surgical antibiotic prophylaxis

SAP- Surgical Antibiotic Prophylaxis

SPSS – Statistical package for social sciences

SSI- Surgical Site Infection

TJA- Total Joint Arthroplasty

U.S- United States of America

Vd – Volume of distribution

VRE- Vancomycin resistant Enterococci

WHO- World Health Organization

OPERATIONAL DEFINITIONS

Prophylaxis is an action performed to maintain health and stop the spread of disease. Focus is on antibiotic prophylaxis**.**

Care bundle includes a group of interventions usually three to five evidence-based interventions that when performed together have better outcomes than if performed individually.

Perioperative period refers to the three phases of surgery: preoperative, intraoperative and postoperative.

Surgical site infection is defined as microbial contamination of the surgical wound within 30 days of an operation or within one year after surgery if an implant is placed in a patient.

Volume of distribution is a proportionality constant that relates the total amount of drug in the body to the plasma concentration of the drug at a given time.

Half-life refers to the time required for plasma concentration of a drug to decrease by 50%.

ABSTRACT

Background: Orthopedic surgeries require the use of implants and these may cause an increased risk of infection. Surgical site infections are associated with high morbidity, death, and increased cost burden. The judicious use of prophylactic antibiotics following evidence-based guidelines leads to optimum outcomes, which includes reduced infection rate and also prevent antimicrobial resistance which is a rapidly progressing global crisis.

Study objective: The practice of prophylactic antibiotic use in elective orthopedic procedures at level 6 Kenyatta National Referral Hospital.

Design: Descriptive cross-sectional type of study.

Study Area: Kenyatta National Hospital orthopedic inpatient wards and operating theaters.

Methodology: Participants awaiting elective orthopedic surgery in KNH orthopedic wards were recruited using a consecutive sampling approach. Data collected from the patients in the operating room and wards included age, comorbidities, any allergies to antibiotics, alcohol and smoking history. Data was gathered from the treatment sheets and from antibiotic prescribers. Comparison to the available local guidelines was made and reasons for the choice of surgical antibiotic prophylaxis was sought from the prescribers.

Data analysis: The collected data was analyzed using statistical package of social sciences version 24 and presented as tables, graphs and pie charts as appropriate. Bivariate analysis involving specific respondent characteristics on the variables of interest was used to perform tests of independence and association using Chi-square and T-test/ Analysis of Variance (ANOVA) respectively. All the statistical calculations were done at 95 percent confidence level and any statistic associated with a priori probabilities less than 5% were deemed statistically significant.

Results: A total of 161 patients participated. Out of this patients Cefazolin was the most commonly used antibiotic 99% preoperatively and 86% post operatively. 87% of the antibiotics were given within one hour from start of operation and all antibiotics were given before application of tourniquet. varied dosages of antibiotics were given according to the ages. 16% of total operations used intraoperative vancomycin at wound site. The study showed spine and arthroplasty had the highest percent of use of vancomycin. 79% of the cases prolonged antibiotic were used. 19% of the prescribers post operatively did not have knowledge of KNH guidelines. the most common indication according to the prescribers for prolonged surgical antibiotic found in this study was due to preventing surgical site infection (33%) and case complexity (22%), other factors found were cefazolin being not available, surgeon's preference, long duration and multiple procedures.

Conclusion: There is an alarming high rate of prolonged surgical antibiotic prophylaxis despite this high rate of PSAP, the prescribing practices of antibiotics in terms of choice of drug, dosage, pre-operative timings were found mostly to be in line with the recommendations in the KNH guidelines.

CHAPTER 1: INTRODUCTION

According to the CDC recommendations, antibiotic prophylaxis should only be used, when necessary. In theory, adequate tissue concentrations of the antibiotic above the minimal inhibitory concentration are needed to be beneficial in SSI prophylaxis, according to the CDC. (1) Despite these recommendations, prolonged surgical antibiotic prophylaxis and improper antibiotic use are common. (2)

Surgical antibiotic prophylaxis (SAP) has no role after one day from start of operation. There is still controversy and debate in high-risk surgeries like cardiovascular operations where some reports show that prolonged use of antibiotics actually reduces the risk of SSI in these select high-risk surgeries. However, multiple bodies including CDC, advocate for single dose antibiotic prophylaxis for operations that are classified as clean or clean contaminated and does not depend on the complexity or type of surgery. (3)

American Society of Pharmacist advocate for single dose SAP. Despite this recommendation, SAP can be readministered in a setting of extended time of operation, increased bleeding and its hemodilution effect due to increased pumping of fluids to maintain intravascular volume, demanding operations that have risks of contamination and when creating another surgical incision on the same patient. (4)

PJI agreement report proceedings advocate heavily that SAP should not exceed 24 hours from the first antibiotic given. (5)

A descriptive cross-sectional study carried out at KNH on SAP for all surgical patients, including emergencies found PSAP in 76.9% of patients who took antibiotics longer than 48 hours. This study also revealed that antibiotics are used inconsistently and with little regard for local recommendations. (6)

In one point prevalence study across Europe, the percentage of inappropriate use of SAP was close to 25% meaning one in every four subjects was given PSAP. (7) There are reports that PSAP in some centers are extremely high so variable results present across Europe, but in general inappropriate SAP is unacceptable. (8)

This inappropriate use does not only affect Europe but is a worldwide issue. In Asian countries, there is a preference of PSAP and the orthopedic surgeons in these centers were not aware of any guidelines or recommendations of the appropriate use of SAP. (9) This shows lack of knowledge and surgeon preferences are factors that can lead to PSAP.

One study report ascertained that extended use of SAP resulted in reducing the rate of SSI, however, this study lacked credibility as it was retrospective with possible biases as it looked at arthroplasty cases only though it is worth mentioning it had a huge sample population with statistically significant results. (10) However, there are similar studies done on arthroplasty patients including RCTs that actually show no added advantage of PSAP. (11)
Another cross-sectional analysis study done shows the prevalence of PSAP use was 12%. (12)
Despite these recommendations and guidelines, it is still unclear of the factors that are associated with the high rates of PSAP. In our study, the major goal was to assess the knowledge of these guidelines among practitioners of appropriate SAP as well as the reasons that lead to PSAP depending upon the patient, surgical or practitioner related factors.

Study Question: What is the practice of antibiotic prophylaxis in orthopedic surgical patients at the Kenyatta national hospital?

Hypothesis: There is high level of prolonged surgical antibiotic prophylaxis use in orthopedic surgical patients.

Objectives

Broad objective:

To assess the practice of prophylactic antibiotic use in elective orthopedic procedures at Kenyatta National Hospital.

Specific objectives

1. To establish the choice and dosage of surgical antibiotic prophylaxis
2. To determine the duration of surgical antibiotic prophylaxis
3. To determine the prevalence of extended SAP
4. To identify factors associated with prescribing practices of SAP

Study Justification

There are gaps in appropriate prophylactic antibiotic use and prolonged surgical antibiotic prophylaxis is one of the fuels that lead to AMR. Most studies look at the relation of SSI and SAP, no local studies are available that look at the prevalence of PSAP in the orthopedic practice.

This study set out to find the prescribing practices of prophylactic antibiotics and determine the factors that affect the choice of antibiotics. This shall enable us to focus on areas and tackle factors that lead to these variable antibiotic prophylactic practices that enables relevant bodies develop policies in SAP at KNH.

Problem Statement

There is a high incidence of antimicrobial resistance, seen as increased cases of MRSA. This is a fundamental threat as this is creating a challenge for the efficient delivery of universal health as AMR causes extended time of illness, higher morbidity, mortality and the cost of health care. Part of the solution is antimicrobial stewardship that entails the correct antibiotic type that matches the organism causing the disease and does not harm the patient. The accurate time as mentioned in guidelines, with the precise dosage and route.

CHAPTER 2: LITERATURE REVIEW

2.1 Background

According to the Greek language, the word "antibiotic" means "against or opposed to life." Antimicrobial refers to a substance that eliminates microbes, which can include bacteria, viruses, fungi, and other microorganisms. In contrast, the term antibiotic refers to a particular class of medications used to treat bacterial infections. They can either destroy the bacteria by killing or by inhibiting their growth. (13) Antibiotics can be used in orthopedic surgery in five different ways: prophylaxis, pre-emptive therapy, empiric therapy, targeted therapy, and suppressive therapy. (14)

Since 1928, when Alexander Fleming made the first antibiotic discovery, antibiotics have been human medicine's most successful treatments and, to this day, have played a crucial role in prevention and management of microbial related infections. (15)

In the 17th century wound infection was extremely common. In mid-1800s, the first step towards control of this infection was brought about by Semmelweis when he postulated hand washing and this technique remarkably reduced bacteremia. Lister used of carbolic acid spray as an antiseptic on skin before an incision in 1867 that further reduced rates of intrawound infections. The next major advance in prevention of surgical wound infection was brought about by antibiotics. However, there is no question about SAP’s effectiveness against SSI there are arguments on the best timing and dosing regimens. (16)

The magnitude and cost of infection in orthopedics is alarming. In the United States the average yearly rate of SSI is slightly higher than 1%, an alarming 8000 dying yearly specifically attributable to this condition and approximately an extra 10 billion dollars each year in terms of additional treatment cost. Comparing the U.S to the United Kingdom, the additional cost of a single patient with SSI is more than three thousand dollars and a rise by up to 17 additional hospital in-patient days. (17) According to the WHO, surgical site infections are the type of hospital acquired infection that is most frequently assessed and encountered in low- and middle-income countries. (18) This is hence a universal problem.

Staphylococcus aureus is the most frequent organism responsible for SSI in all surgical operations, especially orthopedics. Other organisms are less frequent but do cause an infection include, Staphylococcus epidermidis which is a coagulase-negative organism, beta-hemolytic streptococci and gram-negative bacilli. In a recent period, there is an exponential rise in microorganisms that are resistant to commonly used antibiotics, Methicillin Resistant

Staphylococcus aureus is one example that causes SSIs and this cannot be treated by common antibiotics that are used routinely. (19)

Numerous SSI causes can be avoided, and if the correct actions are followed, the incidence may be reduced. The environment and equipment in the operating room, along with the patients, doctors, and nurses, are among the many factors that need to be considered. Although numerous techniques and measures are taken in minimizing rate of SSI after any operation, especially those that require use of implant fixation, infections do happen. SAP might not be enough to win this battle on their own. (17)

Since the 1980s, cefazolin prophylaxis has been proven to drastically lower the number of prosthetic joint infections. The schedule and dosage of cefazolin is altered, nevertheless. Adverse effects such allergies, antibiotic-associated diarrhea, and antimicrobial resistance can result with the use of SAP. Alternative antibiotics can be used in allergy cases. (20)

According to a U.S. study, 16 novel antibacterial compounds were found between the years 1983 and 1987, indicating that the discovery of antibiotics is decreasing. From 2008 to 2012, this number decreased to just 2. (13) Bacterial resistance is a major issue that is becoming more and more prevalent, and its severity is heightened by the fact that in recent years, fewer antibiotics have been created and released onto the market. A comparison of antibiotics to other medications like antihypertensives and cholesterol reducing drugs, antibiotics are given for a short period of time. In addition, there is a high likelihood that resistance would develop. Due to the above concerns majority of pharmaceutical corporations are not interested in producing them because there is less financial advantage. (21)

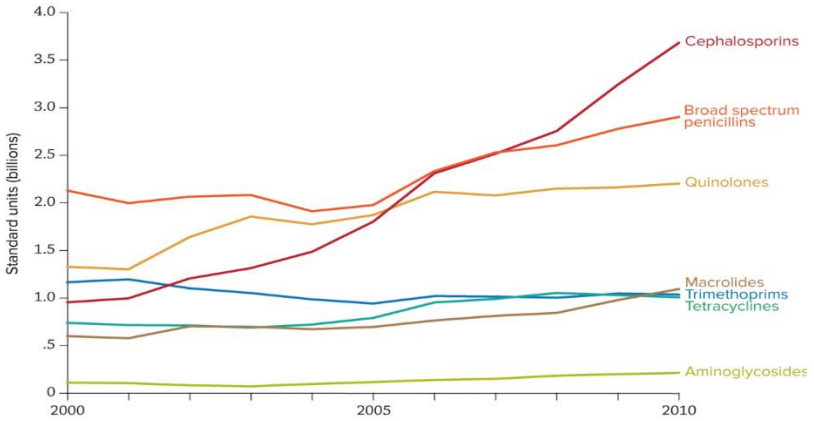

Figure 1 The graph depicts the rate of rising AMR from 2000 to 2010 for the most widely prescribed antibiotics. Cephalosporins are the first line used in SAP which clearly shows the highest trend in resistance compared to other antibiotics. (22,23)

A study in Jaipur, India carried out to study the pattern of antibiotic resistance in 50 clinical isolates of staphylococcus Aureus and concluded that most bacteria were found to be resistant towards common antibiotics such as cephalosporins, however, isolates were found to be susceptible to vancomycin. (24)

Kenya, an African nation, was utilized to examine bacteria from intestinal tracts of healthy people and sick people, and the researchers discovered an alarming incidence of bacterium strains of commensal klebsiella species resistant to frequently used antibiotics. This organism, however, is not common cause of infection in orthopedics. (25)

First-line antibiotic resistance is on the rise, and second-line antibiotic resistance is also becoming more visible. This demonstrates the necessity for antibiotic management and antimicrobial surveillance to prevent the rising tide of antimicrobial resistance. (26)
A protracted sickness and a higher chance of complications including septicemia, non-union/pathological fractures, which could increase morbidity and mortality, are the effects of bacterial resistance on health. The financial effects include lost wages and rising medical expenses due to an increase in the length of hospital stays, consultations, diagnostic tests, and antibiotic treatments. (27)

Local research carried out in 2002 at KNH on the impact of a single dose of antibiotic pre-operatively in clean major general surgical operations and the results showed SSI rates were lowered from 1.6% to 0.5%. (28)

2.2 Antimicrobial prophylaxis

Antibiotic prophylaxis has been taken into consideration as a way to reduce the significant morbidity, mortality, and higher expenses that are linked to infection in orthopedic surgery. (29)

In a recent comprehensive analysis, AlBuhairan et al revealed that SAP in arthroplasty operations decreases chances of wound infection at 8%. This was in contrast to subjects who did not receive SAP. (30)

A care bundled approach consists of important evidence-based interventions that, when administered collectively, improve clinical outcomes. For the purpose of prescription antibiotics for surgical prophylaxis, a proposed antibiotic care bundle consists of the chosen agent that complies with regional recommendations for particular operation. Appropriate

Time for start amounts of drug is given 30 minutes to an hour before the incision and stop using antibiotics 24 hours after the preoperative dose (or a first dose after operation). (31,32) Intra operative time greater than four hours and excessive bleeding of 1500mls or greater requires another shot of antibiotic intraoperatively due to the dilution effect. (33) Standard recommendations mention, adults that Weigh more than 120 kilograms require different amount of drug compared to normal adult. For cefazolin 3grams instead of the normal 2 grams is recommended. (34)

The pharmacodynamic and pharmacokinetic features of an antibiotic are used to calculate the dosage, frequency, and duration of a specific antibiotic. The term "pharmacokinetic" refers to the link between a drug's dose and the time course of the drug's concentration at various bodily sites of interest is the bones, muscle and joints (synovium). This involves absorption into the bloodstream from the administration site (with the exception of direct administration into the bloodstream), distribution in tissues after leaving the bloodstream, and elimination through renal excretion, metabolism, or both. In terms of pharmacodynamics, the link between concentration and antibacterial effect is described. (35)

Orally administered antibiotics in contrast to Intravenous antibiotics undergo different pharmacokinetics and pharmacodynamics as the oral has to pass the gastrointestinal and hepatic circulation to be available at the surgical site which is not the case for IV antibiotics hence preferred choice of SAP. Antibiotic prophylaxis is given intravenously for practical reasons, and because of higher absorption. Several recommendations, including those of the American Academy of Orthopedic Surgeons, propose cefazolin or cefuroxime. (36)

A randomized double-blind study carried out on the application of oral versus intravenous antibiotic in gall bladder surgeries. The amount of drug in bile was higher in a subject who had taken the drug by mouth compared to intravenous and the cost of intravenous medication was 20 times higher. It concluded that in laparoscopic cholecystectomy SAP taken by mouth was not only cheaper but effective compared to intravenous use. (37) However, no studies done comparing oral versus intravenous SAP and effect on SSI in orthopedic procedures.

2.2.1 Dosing strategies and Timing of antibiotic administration.

In the study of drugs three pharmacokinetic values need to be understood. These parameters have a clinical value and explains the basis of how a particular drug is distributed and maintained in the tissues but also the physiology of the patient will affect these parameters like in case of patients with reduced renal functions. (38)

The first is the apparent volume of dilution abbreviated as Vd and it means the amount of drug levels in the tissues and is correlated with the amount of initial drug given and its ability to distribute in plasma and body tissues. (39) Pharmacokinetic metric, which is reliant on physiochemistry. Antibiotics can be categorized physiochemically with its affinity for water. Drugs with high affinity to water cannot move through the cell like cephalosporins which primarily circulate in the extracellular body water rather than inside of cells. Number of adipose tissues greatly influences how lipophilic antibiotics like fluoroquinolones are distributed. An antibiotic that is habiting in the plasma has a modest Vd hence clinically for drug to be present at the site of incision to prevent contaminations a higher amount of start dose needs to be given if the drug has higher Vd. Vd is affected by albumin levels. In cases of low albumin such as chronic liver disease, these drugs escape faster into the tissues compared to intravascular component. In Obesity there is increased adipose tissues and due to this change in physiology, adjustments to the amount of drug have to be made in order to achieve minimal inhibitory concentration at the surgical site. Pregnancy, condition where the water content and normal body physiology changes, with this change, the Vd is raised hence need for similar adjustments to the drug given. (40)

Drug clearance is the second parameter once Vd is considered, the aim of any SAP is to have its concentration in the tissue levels maintained from start to closure of skin and drug clearance is key as this will ensure balance in terms of dispensing to the tissues and removing from the tissues. From a clinical perspective this is important when consideration re-dosing of the antibiotic to enable the concentrations of antibiotic to be always above the MIC. (15) Systemic clearance of drug is dependent majorly by the hepatic or renal systems. Just as Vd, the route of elimination is also dependent on the physiochemistry. Antibiotics that have affinity to water are removed by the renal system and drugs which freely pass into the cells are eliminated by the liver. CL can be estimated by measuring GFR (creatinine clearance). For example, penicillin has affinity to water and since primarily removed by the renal system, if the renal is only working half as efficient as it should then the drug will stay at the site for a longer time, therefore this will double the time to repeat the same amount of drug. Hence dosing should be adjusted according to renal / liver functions. (38)

Half-life, the third value that is dependent on the apparent volume of dilution and creatinine clearance. This value defines a time scale where the drug value lowers at a fixed and calculated rate and this is known for each antibiotic and also available in the guidelines. (38) There is no set amount of time for antibiotics; instead, this is typically dependent on their

half-lives. Until skin closure, the antibiotic's concentration must be kept above the minimal inhibitory concentration of the infectious organisms. (31) This does not take into effects of occult hematogenous infection, deep tissue contamination and hematoma accumulation after skin closure that may justify continuing use of antibiotics after skin closure. An antibiotic's half-life may be impacted by conditions including renal insufficiency and severe burns. Cephalosporins need to be repeated in contrast to single dose that will depend on operation hours and also the bleeding levels during the surgery. (15)

One study done to show levels of antibiotic in the plasma and skeletal muscle after infusion of the antibiotic. The levels were measured at interval of half an hour and 1 hour from the start of infusion. The levels of antibiotic at half an hour were almost close to 100% while at one hour the concentration was almost halved. Although this study lacks high level of evidence, it does confirm that antibiotic given 30 to 60 minutes before start of operation is beneficial and effective. (41)

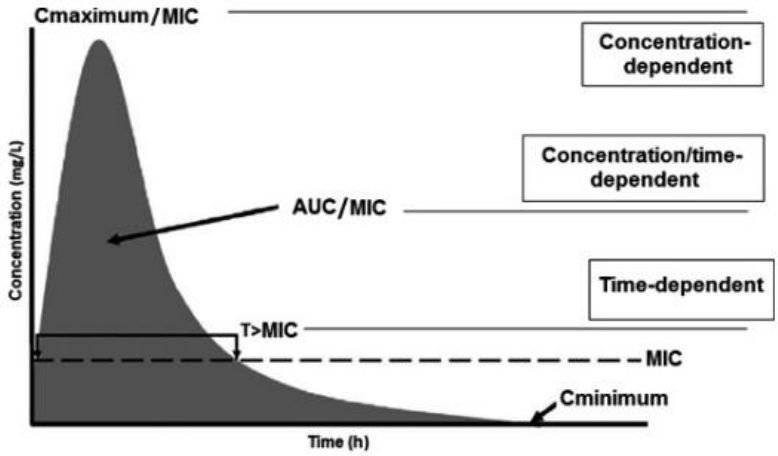

Figure 2: Pharmacokinetic-pharmacodynamic relationship of different antibiotics. (42)

The figure above shows different classes of pharmacodynamic properties of antibiotics. Pharmacodynamics is a part of pharmacology which studies the effect of the drug on the body, cephalosporins exhibit time-dependent characteristics which entails that as long as the amount of drug is greater than MIC than its effect will be positive in our study case prevent contamination hence infection. Aminoglycoside show concentration-dependent characteristics and this means that the amount of drug higher in the curve above the MIC will lead to more effective response. (42.43)

Out of the 19 items on the WHO's surgical safety checklist, one asks whether an antibiotic given in period less than one hour from start of operation because this has shown as accepted standard of care practice in surgical operations. (44)

The timing of antibiotics generally varies from 15 minutes to 120 minutes, if SAP are given after the 120-minute period before start of operation the risk of infection post operative is six times higher than if SAP given within the above range. (45)

It has been advocated in several studies that 30 – 60 minutes before surgery and 10 minutes before inflation of tourniquet. Scientific explanation to this is due to pharmacokinetics and pharmacodynamic of antibiotics such as cephalosporin. (46,47) Antibiotic is least effective if given after the application of a tourniquet. Initiating antibiotics after a skin incision is ineffective. (48)

Two studies reported on effects of combination of two different antibiotics is better than one in SAP and results of this study revealed that use of two compared to one reduced rates of post-operative infection. These studies however, were retrospective studies looking at arthroplasty orthopedic elective cases. The study also concluded that combination would not result in any harm such as renal impairment. (49,50)

TABLE 1 : Recommendation of appropriate timing of Surgical Antibiotic Prophylaxis. (18)

Specifications (Year published)	**Directions on use of antibiotic prophylaxis**
Society For Healthcare Epidemiology of America (SHEA)/ Infectious Diseases Society of America (IDSA) (2014)	Administer only when indicated. Drug given within 30 minutes have better outcomes in terms of infection rates compared to within 60 minutes
American Society Health-Care Pharmacists (2013)	Giving SAP in the first hour except for vancomycin and fluoroquinolones which can be given at 2hrs before surgery is advocated.
The Royal College of Physicians Ireland (2012)	SAP to be given in the first hour and only repeated in case of operation is extended.

	In operation with torniquet SAP should be given before inflation
USA Institute of Health Improvement: Surgical Site Infection (2012)	Administration of first dose of antibiotic in first hour before start of operation. To give further two doses
Health Protection Scotland Bundle/ Scottish Intercollegiate Guidelines Network (SIGN) (2013)	Administration of single amount in first hour. A second dose if given may not cause any major consequences to the patient.
UK high impact intervention care bundle (2011)	Administration of first dose of antibiotic fist hour before start of surgery.

2.2.2 Type of antibiotics to choose from

The most common organisms causing SSIs include gram positive organism. In special cases for operations around axilla, then Cutibacterium is common. (15)

SAP use depends on the microorganisms likely to cause SSI in the planned surgery and according to the care bundle this depends on local guidelines available but most frequently it is Staphylococcus aureus. (20)

If a patient has an allergy to -lactam antibiotics, they can utilize vancomycin (600-900 mg intravenously) or clindamycin (1 g intravenously). Vancomycin is related with VRE colonization and infection, hence its routine usage for surgical site infection prevention, or any form of surgery is not advised. (51)

Antibiotics ought to be readily available, inexpensive, non-toxic to the body, and with a constrained spectrum. According to local research done at KNH, Staphylococcus aureus was the most common isolate. High levels of resistance to widely used antimicrobials were present. One or more drugs were resistant in 60.2% of isolates. There are suggestions for continued surveillance to monitor etiology and antimicrobial susceptibility patterns, which will help direct the empirical utilization of these drugs. (26)

Gram-negative bacteria made up more bacterial isolates (73%) than gram-positive bacteria (27%), and they had high levels of antimicrobial resistance to the standard preventive antibiotics. (52)

In the view of the American Society of Pharmacists, the choice is based on the most common organism which is staphylococcus aureus. Antibiotics like gentamycin and ceftriaxone are not advocated as they do not cover for the most common organism and because of their wide coverage this will lead to AMR. On the other hand, first generation cephalosporin is the drug of choice. (53)

In Malaysia, recommendation of use of penicillin as the initial appropriate choice of SAP. Cloxacillin was advocated as the initial course of treatment or prevention by a Swedish orthopedic teaching hospital. (54)

The pharmacodynamics of antibiotics in surgical prophylaxis is key as this will enable to maintaining sufficient concentration of antibiotics at the end of the operation hence preventing microbial infection. (55)

TABLE 2: Antibiotics and factors associated with the choice of antibiotic use. (31)

Drug	**Organisms responsive to**	**Advantages over other drugs**	**Recommendations**
cefazolin	Gram positive organisms	good safety profile, superior efficacy on musculoskeletal system	Most commonly used across all boards as choice of surgical antibiotic prophylaxis In UK is no longer first line
Flucloxacillin	Staphylococcus aureus	When given IV, at 60 minutes it has excellent bactericidal effect.	This has fallen out of favor due to better pharmacokinetics and pharmacodynamics or first generation cephalosporins
Amoxicillin/clavulanic acid	Effective against organisms producing beta-lactamases	effective against resistant strains to amoxicillin.	Due to the extended spectrum, it is not routinely used as prophylaxis. British Organizations do advocate its use in open injuries
Clindamycin	Gram-positive and anaerobic cover	Beneficial for musculoskeletal infections.	Can be used for prophylaxis, preferred by surgeons, recommendations by KNH national guidelines in open fractures.
Quinolones	Wide range of cover of	excellent oral bioavailability	This are not used as stand-alone drugs, mainly given in combinations to prevent AMR

	common organism		
Mupirocin	Staphylococci and most Streptococci	excellent activity against staphylococci and most streptococci	Eradication of nasal colonization with MRSA in patients and health workers. Preoperative use in arthroplasty surgery
Gentamycin	Wide coverage of organisms	Combined in Cement due to it pharmacokinetic characteristics, used as empiric management in severe open trauma	Caution as can lead to renal system damage and hearing defects

2.2.3 Duration of antibiotics

SAP not used longer than a 24-hour duration. (20) There are study reports that advice on twice giving SAP, the first given before operation and the subsequent infusion after six hours this has shown to be effective and also reduce hepatotoxicity, nephrotoxicity, costs and rate of AMR. (56)

A local study done in KNH on SAP for open injuries reported no benefits in the extended antibiotic patients compared to subjects who received antibiotics for one day. (57)

A five-year safety and outcome retrospective study from Singapore General Hospital Antimicrobial Stewardship Program concluded SAP administered for greater than one day resulted in no different outcomes compared to those who were given and stopped after one day. (58)

2.3 Special situations

2.3.1 Diabetes

Diabetes is an illness that causes high sugar levels in the body and at the same time decreases immunity and predispose them to infections. This immunosuppression state causes surgeon to take extra precautions to avoid SSI which may lead to extended use of SAP. However, studies advocate no advantage of extended use. Contrary what has shown to reduce the rate of SSI is ensuring good glucose levels, nutrition and exercise in other to reduce weight, these measures can be taken especially in elective cases due to the luxury of time. (31)

2.3.2 HIV patients

Seropositive patients on anti-retroviral treatment with undetectable viral loads are similar to patient who are seronegative and need no extended of special precautions in terms of SAP.

(59,60) There is scarcity in studies for seropositive patients with high viral loads or treatment failures, but studies have not shown any advantage of PSAP in this group of patients

2.3.3 Rheumatoid arthritis

Rheumatoid arthritis is an inflammatory condition mainly affecting joints. Patients are usually on NSAIDs and DMARDs that can cause immunosuppression and it is advised to change or stop some of these medications pre-operatively. However, no studies have recommended extended use of SAP. (31)

2.3.4 Antibiotics and urinary catheter

Patients with asymptomatic bacteriuria do not need treatment before elective surgery. There is no advantage of PSAP in these cases.

Patients with urinary catheter preoperatively, have confirmed UTIs, have catheter placed for more than 3 weeks then some reports advocate for specific antibiotic cover perioperative, there is role of treating infection before elective procedure. (61,62)

No studies have shown advantages of PSAP in these select cases.

2.3.5 Patient with implants such as heart valves

The same prophylactic antibiotics as in patients without earlier implanted prosthesis can be used. (20)

2.3.6 Obesity

The KNH National guidelines 2021 publication states that for obese patients' dosage should be adjusted, patient >120 kg should receive 3g cefazolin. Further consultation with infectious disease specialist should be sought.

2.4 Prolonged surgical antibiotic prophylaxis (PSAP)

Prolonged means extended use of antibiotics not following the guidelines stipulated time-line. (12) Reason as to why extended use is dangerous to all, is due to its direct link to antimicrobial resistance. (63) PSAP leads to hazardous side effects such as acute kidney injury and Clostridium difficile infection. (64) in contrast, no studies have shown that PSAP is advantageous in reducing SSI.

One survey Study carried out on orthopedic trauma association surgeons, 297 member and found heterogeneity in the use of antibiotic prophylaxis where 4% of surgeons advocated for

use of antibiotics at 48 hours or more after operative intervention whereas 59% used at least one additional postoperative dose. In the study, cefazolin was the most preferred first-line antibiotic favored by 96% of surgeons. (4)

American Society of Pharmacist advocate for single dose SAP. Despite this recommendation, SAP can be readministered in setting of extended time of operation, increased bleeding and its hemodilution effect due to increased pumping of fluids to maintain intravascular volume, demanding operations that have risks of contamination and when creating another surgical incision on same patient. (4)

In one point prevalence study across Europe, percentage of inappropriate use of SAP was close to 25% meaning one in every four subjects were given PSAP. (9) there are reports that PSAP in some centers are extremely high so variable results present across Europe, but in general inappropriate SAP is unacceptable. This inappropriate use does not only affect Europe but a worldwide issue. In Asian countries there is preference of PSAP and the orthopedic surgeons in these centers were not aware of any guidelines or recommendations of appropriate use of SAP. (9) This shows lack of knowledge and surgeon preferences are factors that can lead to PSAP.

PJI agreement report proceedings advocate heavily that SAP should not exceed 24 hours from first antibiotic given. (5)

One study report ascertained that extended use of SAP resulted in reducing rate of SSI, however this study lacked credibility as it was retrospective with possible biasness as looked at arthroplasty cases only though it is worth mentioning as had a huge sample population with statistically significant results. (11) however, there are similar studies done on arthroplasty patients including RCTs that actually show no added advantage of PSAP. (11)

Another cross-sectional analysis study done shows the prevalence of PSAP use was 12%. (11)

Factors related to the high rate of PSAP are summarized below, (65,66,67,68)

PATIENT FACTOR	**SURGEON FACTORS**
Older Age	Presence of wound drain
BMI >29KG/M2	Type of surgery
American society of anesthesiologist classification- 3 or more	Experience of surgeon practices – own feeling and comfort
Malnutrition, low nutrition risk score	Availability of strong evidence

Immunosuppression including diabetes	duration of operation
Fever	Amount of blood loss
Leukocytosis	Avoiding conflicts with patient
Alcohol and smoking history	

SAP has no role after one day from start of operation. There is still controversy and debate in high-risk surgeries like cardiovascular operations where some reports show that prolonged use of antibiotics actually reduce the risk of SSI in these select high risk surgeries. However, multiple bodies including CDC, advocate for single dose antibiotic prophylaxis for operations that are classified as clean or clean contaminated and does not depend on the complexity or type of surgery. (3)

2.5 Other routes of administration of antibiotics

2.5.1 Topical administration

As mentioned, staphylococcus Aureus is the most common cause of SSI in orthopedic surgery, in up to half of the healthy adults this organism colonizes usually in the anterior nares. The use of preoperative intranasal mupirocin in the reduction of SSI has brough inconclusive results, however, its use reduced the risk of non- general surgery studies with no effect on general surgery patients (surgeries in which gram negative and anaerobic organisms play a bigger role). (69)

2.5.2 Antibiotic impregnated bone cement

The Scottish Intercollegiate Guidelines Network (SIGN) 2014 does recommend impregnated cement in addition to intravenous antibiotics for cemented joint replacements. Study shows combination of the two-regimen had lower revision rates, aseptic loosening and infections. (70)

2.5.3 Intrawound vancomycin powder

Vancomycin is approved for the treatment of infections caused organisms that retain the purple color of crystal violet dye described by bacteriologist Hans Gram hence called gram positive. It continues to be the drug of choice in treating most MRSA infections with low side effects. Its topical use is well studied in spine and orthopedic surgery in reducing SSIs. (71) However, studies carried out so far do not pass the threshold to conclusively recommend vancomycin as an antibiotic for use at the surgical site. Use of vancomycin at surgical site is not advised by the pharmaceutical companies and the food and drug administration body do

not advocate for its use either. Routine application has shown that it can promote emergence of resistant bacteria. In some reports its use was described as toxic to osteoblasts. The reports differed in their usage of vancomycin dosage and how it was administered. (72)

Despite this controversy orthopedic surgeons use this drug at the surgical wound site especially in arthroplasty cases or spine instrumentation cases as it is believed to reduce rate SSI and at the same time has minimal side effects. The U.S Preventive Services Task Force does advocate on its use on basis that patients that received vancomycin were at a lesser risk of contracting severe surgical wound infections in contrast to those who did not receive but there is lack of high-level evidence on the same. (73)

In summary looking at the above literature review prophylactic antibiotic use reduces the incidence of surgical site infection. Following guidelines strictly on use of antibiotics will lead to best outcomes as well as reduce rate of AMR, reduce excess cost to the patient incurred in the case of prolonged use of antibiotics and prevent toxic effects of antibiotics. There are areas that are yet inconclusive such as use of local antibiotics at the wound site, hence motivating the aspect of this study as these are areas that need further studies.

CONCEPTUAL FRAMEWORK

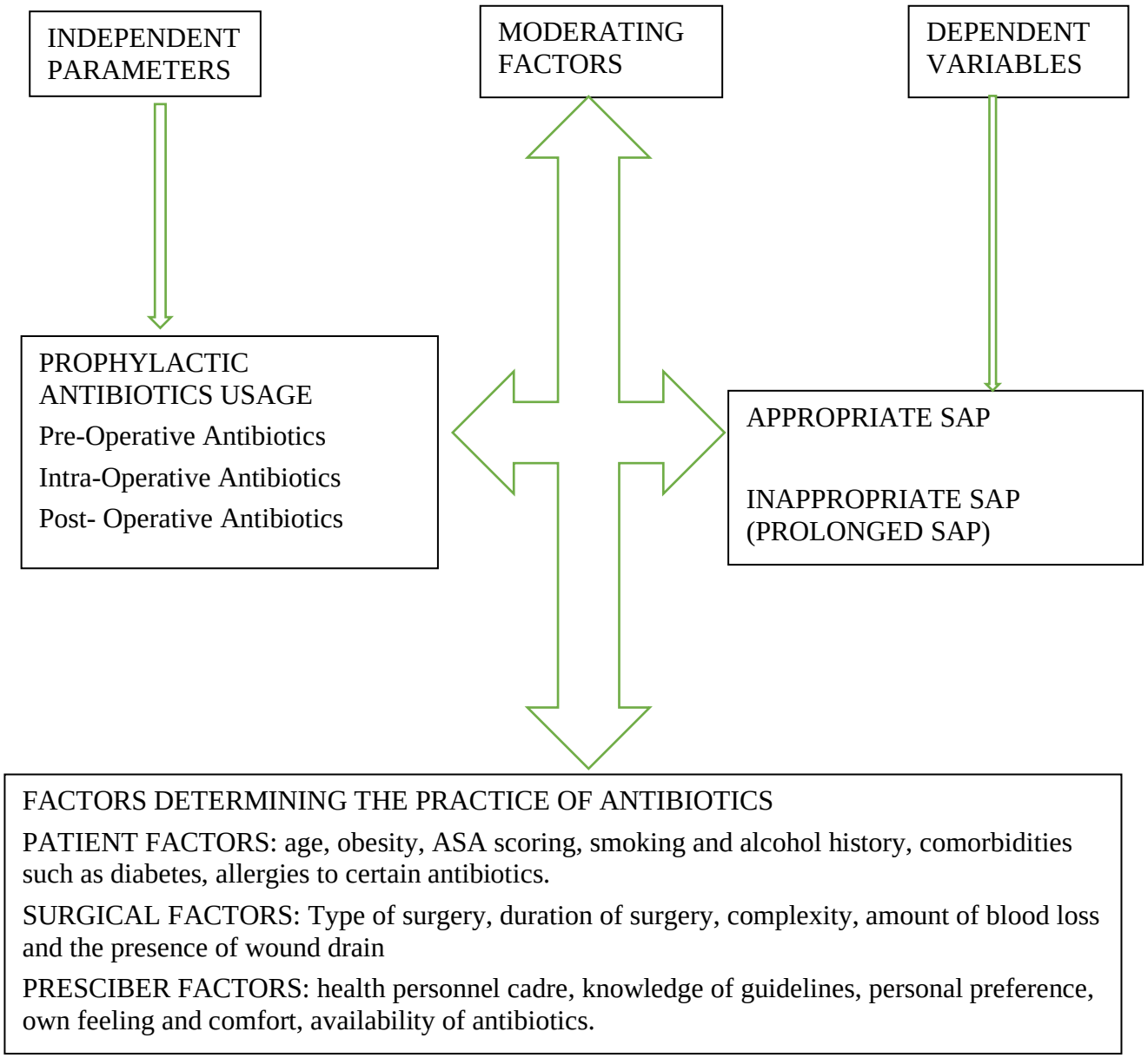

Figure 3: the above shows the link between the independent and dependent parameters and how moderating factors influence these variables. This is a summary representation of variables in the study and summarizes the above literature review and guiding on the research methodology

CHAPTER 3: RESEARCH METHODOLOGY

3.1 STUDY DESIGN: Descriptive cross-sectional study

3.2 STUDY SETTING

This research was carried out at the major referral hospital in Kenya. Situated in the capital city Nairobi, being a tertiary level 6 hospital, it receives all cases from emergencies to complex referrals from other areas within and also outside the country. Currently, the orthopedic unit is divided into sub specialized thematic units that include trauma, spine, arthroplasty, pelvis and sports, orthopedic oncology, foot and ankle, hand, ortho-plastics and pediatric orthopedic units. Each of these units have specialized surgeons, this has enabled the hospital to receive and manage a wide area of orthopedic issues. The orthopedic inpatient is situated at the 6^{th} floor for adults and pediatric is on the 1^{st} floor at the KNH. There is trauma theatre that runs 24hrs and deals with mainly trauma and emergencies as well as two specialized theatres where special orthopedic and trauma cases are handled. The hospital has a bed capacity of 2400 beds with over 30 orthopedic consultants and approximately 60 orthopedic residents.

3.3 STUDY POPULATION:

All orthopedic patients who were not on antibiotics and awaiting elective orthopedic surgery admitted to the Kenyatta national Hospital.

3.3.1 Inclusion Criteria

Orthopedic elective surgical patients who were not taking any antibiotics at the time of recruitment.

All orthopedic treatments that involved the implantation of foreign material, including those for joint prosthesis, closed fractures, bone grafts, ligament reconstruction, spine surgery, arthroscopy, and clean procedures without the use of foreign material

3.3.2 Exclusion Criteria

Patients who declined to give consent.

Situations where prolonged post-operative antibiotic used, persistent osteomyelitis, open fractures, cases that required ICU stay, etc.

3.4 SAMPLE SIZE

The magnitude of the number of participants for this study was determined using historical data for the number of KNH elective orthopedic surgery patients, from January to December, 2021 resulting into 890. From literature, the formula for such a closed environment using, the Scheaffer et al. 2011 (74) was adopted and modified to cater for statistical power and nonresponse rate.

The formulae for estimating the sample size $n = DEFF \frac{Npq}{\frac{d^2}{z^2_{1-a/2}+Z_\beta}(N-1)+pq} * NR$

Where N is the total orthopedic patients admitted in KNH, n is the calculated sample size, $DEFF$ is the design effect, p is the estimated prevalence (PSAP=86.3%) (9), q is $1-p$, d is the desired absolute level of precision, $Z^2_{1-a/2}$ is the critical value for the standard normal distribution corresponding to a type-1 error of α=0.05 for a two tailed test, Z_β=0.84 is the statistical power associated with type-2 error and NR is the 10% estimated nonresponse rate. Using these formulae and at 95% level of confidence, the calculated sample size was 151 which can be amplified to 161 to cater for nonresponse.

Computed sample size was as follows:

Total population	N	890
	N-1	889
Z value at 95% CL	Z(1-alpha/2) for two tailed	1.96
Statistical power (beta)	Z(beta)=0.84	84%
Prevalence	p (86.3%)	86%
	q=1-p	14%
DEFF	design effect	1
NR	Non response rate (10%)	110.0%
margin of error	Error (5%)	5.0%
Numerator	Npq	105.2256
Denominator	(d^2/(Z^21-a/2+Z^2b) (N-1)+pq	0.697
Sample size	Un amplified (n)	151
	Amplified with 10% NR rate	161

N- The population of total elective procedures done in the year 2021. This information was sought from the Health Information Department-KNH Health Records Statistics Section.

3.5 SAMPLING PROCEDURE

The sampling procedure used was consecutive sampling. A type of non-probability sampling where every patient meeting the inclusion criteria is selected until sample size of 161 was completed.

3.6 RECRUITMENT AND CONSENTING PROCEDURE

Initial recruitment of the patient was done in the orthopedic wards at the Kenyatta National Hospital while patients were waiting for theatre. Once the patient had fit the inclusion criteria, consent was taken. For the pediatric patient, the next of kin/guardian provided consent.

3.7 VARIABLES AND DATA COLLECTION PROCEDURE

3.7.1 Independent Variables

A formatted data collection tool was filled by the research assistant on the demographic data, comorbidities, history of alcohol or cigarette smoking previous history of use of antibiotics and any adverse effects, diagnosis, and type of surgery carried out, the ASA score which was given by the pre-anesthetic review.

In theater preoperative time of antibiotic, the type of antibiotic used, tourniquet used were filled. Intraoperative duration of procedure, the estimated blood loss, fluids or blood transfusions given any, the use of an implant, use of any topical antibiotics mentioned, the application of wound drain, any repeat doses of antibiotics with time, dosage and reason. The level of training of the antibiotic prescriber was indicated.

During the data collection, the research assistant cross-referenced the available Kenyatta National Hospital guidelines on surgical antibiotic prophylaxis for orthopedic procedures that was available to them. In cases, where the data received did not comply with the guidelines then specific questions were asked to the prescriber at the moment and recorded in the data collection tool.

Immediate Post-operative period information was obtained from the post-operative treatment sheet on the prescription of antibiotics, the prescriber level of training, and duration of antibiotic use. Patient were followed in the wards until patient stopped using antibiotics in the ward or discharged and if any prescription of antibiotics given to patient upon discharge this data was collected.

3.7.2 Dependent variables

Two groups were then made, as one with SAP stopped less than 24 hours after the start of operation. The other was the PSAP group, in the case of PSAP, the assistant asked the prescriber questions as written on the data collection tool.

3.8 TRAINING PROCEDURE AND QUALITY ASSURANCE

Three Research assistants were used to collect data using data collection tools. They were clinical officers who were trained on the data collection procedure. Three assistants each divided among the three theatres at the Kenyatta National Hospital, which included one in the trauma theatre and 2 research assistants in the main theatre. Before actual data collection, a pilot study for one week was done where training for the research assistants was done from recruitment till the end of data collection. This ensured quality in terms of accuracy, validity and reliability of results

3.9 ETHICAL CONSIDERATION

Informed written consent was sought from all patients included in the study. For those underaged of 18 years consent was taken from the parent/guardian or next of kin. Information was held in utmost confidentiality and kept in a locked briefcase. KNH-UoN Ethics and Research Committee was consulted and after approval by the committee was when data collection was initiated.

There were no risks involved for the patient that were undergoing this study as there was no influence directly or indirectly to the management during the study, a data collection tool was used and this did not harm or incur any costs to the participants of the study.

Covid-19 prevention guidelines were strictly followed, sanitizing and wearing of masks were mandatory throughout the study procedure.

3.10 DATA MANAGEMENT AND ANALYSIS

This data was cleaned for any errors identified before inserting the data for reviewing with the use of the S.P.S.S version 21. Presentation methods such as charts, tables, and histograms are used. Any antibiotic that was given inappropriately or prolonged use of SAP was read and documented as a percentage of the entire study sample population.

The pre-operative start time of SAP administration and the full period of SAP use was read and results displayed as measures of the central tendency and measure of variation. Compliance with the surgical guidelines analyzed and presented as proportions. Demographics and clinical characteristics and operative details were presented as interquartile ranges and means where applicable and variance and student T-test were used to access comparisons and deduct patient and surgical factors for PSAP.

Data was cleaned for accuracy before entry in order to avoid errors and analyzed with the help of a statistician.

3.11 STUDY TIME FRAME

ACTIVITY					
2022-2023	APRIL-DEC	DECEMBER-FEB	FEB-MARCH	APRIL	APRIL-MAY
PROPOSAL WRITING, PRESENTATION					
ETHICS APPROVAL					
DATA COLLECTION					
DATA ANALYSIS AND THESIS WRITE UP					
CORRECTION BY SUPERVISORS AND SUBMISSION					

CHAPTER 4: STUDY FINDINGS

4.1 Demographic characteristics of the patients

This study was anchored on a broad objective of assessing the practice of prophylactic antibiotic use in elective orthopedic procedures at the Kenyatta National Hospital. To achieve this objective, all the targeted 161 patients who were scheduled for elective surgery were interviewed and they comprised of 121 males (75%) and 40 females (25%). The distribution by gender is shown below

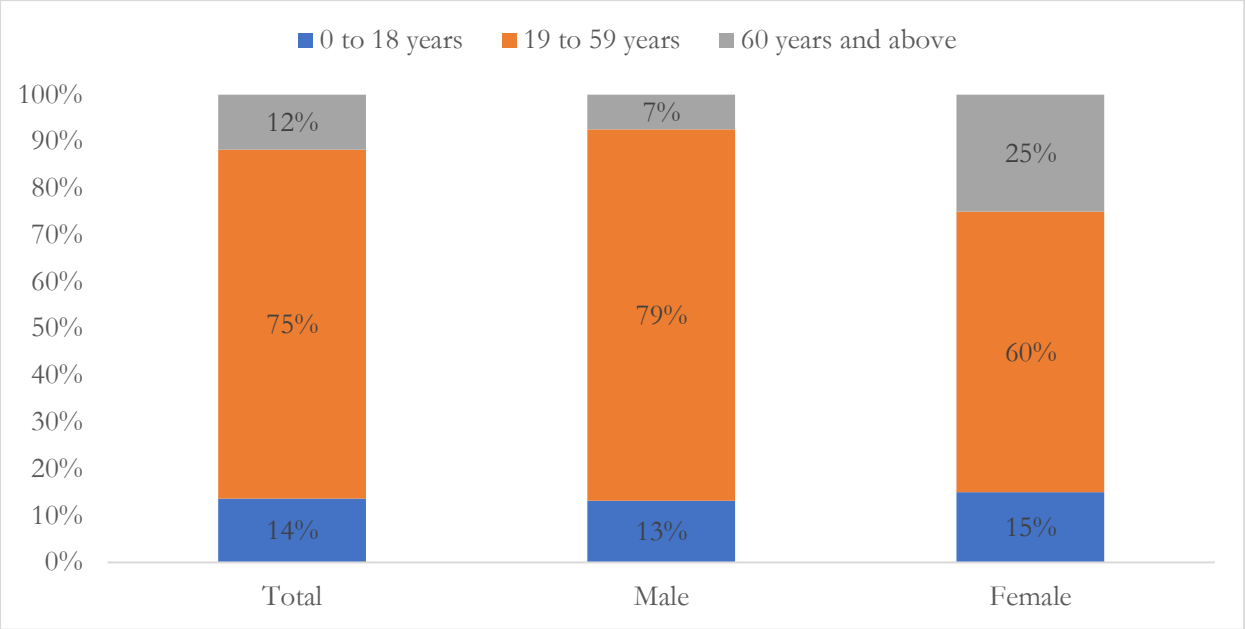

Figure 4: Patient's age category by gender

As shown in figure above the largest numbers of patients fall in the middle age group meaning three in every four were aged 19 to 59 years. For the elderly age group those above 60 years the female group was slightly higher compared to the other similar age groups meaning one in every four women were above 60 years. Chi-square analysis indicates that there is significant difference on age distribution within both genders (χ=0.861, p-value=0.012).

The patients were planned for elective surgery according to different thematic units distributed by gender is shown in table 3

Table 3: Total cases by thematic unit showing gender distribution of the patient

	Total (N)	Total (%)	Male	Female
	161	100%	121 (75%)	40 (25%)
Trauma	87	54%	59%	40%
Hand	30	19%	22%	8%
Arthroplasty and sports	15	9%	2%	30%
Spine	11	7%	7%	8%
Oncology	8	5%	3%	10%
Pediatric	6	4%	4%	3%
Foot and ankle	4	2%	2%	3%

The results indicate that over half of the patients had trauma, 19 percent with hand injuries and 7 percent had spine conditions. The reported diagnosis by gender indicates that males reported more trauma cases than females while females, reported more arthroplasty and sports related surgeries.

4.2 Prevalence of extended SAP

The prime objective of this study was to determine the prevalence of prolonged surgical antibiotic prophylaxis (PSAP) among patients planned for elective surgery in KNH. This indicator is achieved by assessing the patients whose prescription of antibiotic post operation is more than 1 day and the results are shown in Figure 5.

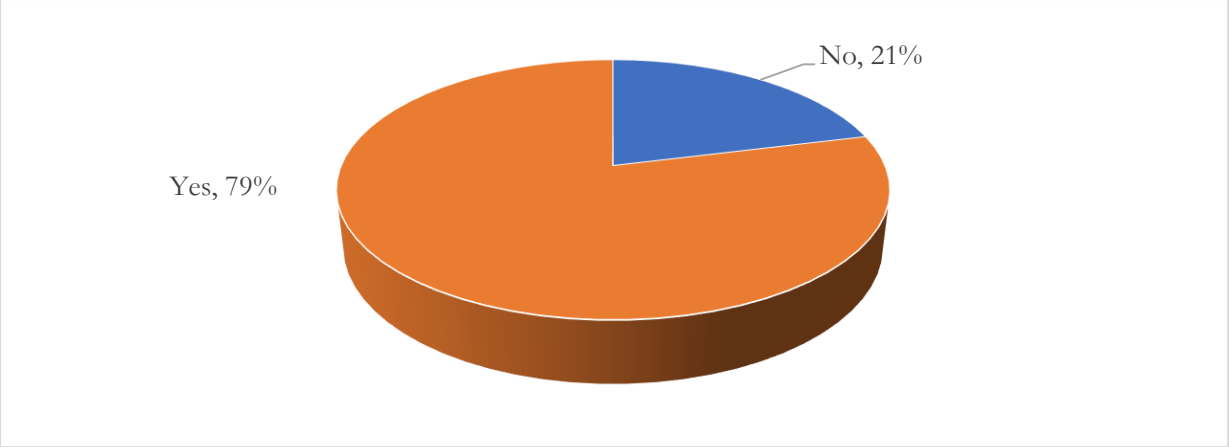

Figure 5: Prevalence of prolonged surgical antibiotic prophylaxis

The results indicate 34 patients (21%) received their antibiotic within one day while 127 patients (79%) received their antibiotic post operation in more than one day. This is an implication that the prevalence of prolonged surgical antibiotic prophylaxis among the patients planned for an elective surgery in KNH is 79 percent.

The patients underwent the planned procedure which are categories by prevalence of PSAP as shown in Table 4.

Table 4: Surgical procedure and prevalence of extended surgical antibiotic prophylaxis.

	Total (N)	Total (%)	PSAP (No)	PSAP (Yes)
Internal Fixation of Large Bones	99	61%	22%	78%
Closed internal fixation of small bones	13	8%	31%	69%
Clean Procedure not Involving Implants	21	13%	10%	90%
Arthroscopic Procedures	3	2%	67%	33%
Spinal Procedures	11	7%	27%	73%
Primary TKR / Primary THR	12	7%	8%	92%
THR/TKR Revision	2	1%	0%	100%

The results indicates that three in every five patients were planned for internal fixation of large bones, 13 percent for clean procedure and on in every twelve (8 percent) were planned for closed internal fixation of small bones. For each of the planned procedure, Table further

indicates the prevalence of PSAP, such that 78 percent of internal fixation of large bones had PSAP and likewise all the revision for total hip or knee replacement had PSAP.

4.3 Patient related factors associated with PSAP

The prevalence of PSAP was evaluated on a number of factors related to patient attributes such as presence of comorbidities, type of comorbidity, allergies to antibiotics, smoking history, alcohol consumption and American Society of Anesthesiology (ASA) score and the results are shown in table below.

Table 5: Patient characteristics in relation to PSAP

	Total (Count)	Total (Percent)	PSAP (No)	PSAP (Yes)	χ -Square	P-value
Does the patient have any comorbidities?						
No	145	90%	21%	79%	0.161	0.688
Yes	16	10%	25%	75%		
Type of comorbidities						
Hypertension	11	69%	27%	73%		
Diabetes	4	25%	25%	75%	NA	NA
Several	1	6%	0	100%		
Does the patient have any allergic reaction to Antibiotics?						
No	160	99%	21%	79%	0.269	0.604
Yes	1	1%	0%	100%		
Does the patient smoke?						
No	155	96%	21%	79%	0.558	0.455
Yes	6	4%	33%	67%		
Does the patient have a history of taking alcohol?						
No	156	97%	21%	79%	1.104	0.293
Yes	5	3%	40%	60%		
American Society of Anesthesiologist (ASA) score (N=143)						
Normal healthy patient	92	64%	22%	78%		1.00

	Total (Count)	Total (Percent)	PSAP (No)	PSAP (Yes)	χ -Square	P-value
A patient with mild systemic disease	41	29%	20%	80%	Fishers exact =0.565	
A patient with severe systemic disease	10	7%	20%	80%		

The results above indicate that 10 percent of the patients have comorbidities and amongst them 75 percent were classified as having PSAP. Further analysis indicates that there is no significant association between having comorbidities and being PSAP (p-value>0.05). The reported comorbidities include hypertension (11), diabetes (4) and one patient had combination. The patients who had hypertension and diabetes, 73 and 75 percent were classified as having PSAP, respectively.

Further investigation including deviant behavior indicate that only four (4) percent of the patients smoke and among them 67 percent (4 patients) are classified as PSAP. Analysis on the association between smoking status and PSAP categorization indicates that the difference occurs by chance (p-value>0.05). Additionally, three percent of the patients consume alcohol and three in every five (60 percent) are classified as having PSAP. The difference in the categories occur by chance (p-value>0.05) and cannot be attributed to the PSAP categorization or alcohol consumption. Finally, the patients were aggregated by ASA scores and over half (64 percent) of the patients planned for elective surgery depicted a normal and healthy appearance, 29 percent had mild systemic disease while seven percent had severe systemic disease. Amongst the ASA scoring, 78 percent of patient who were normal had PSAP and 80 percent those who had mild and sever systemic diseases, respectively were PSAP. The analysis of the differences in the categorization occurred by chance (p-value>0.05).

4.4 Antibiotics prescribed during the entire surgical procedure

4.4.1 Preoperative prescription

The study sought to evaluate the practice of prescribing antibiotics during the entire process of surgery inclusive of SAP given preoperatively, intraoperatively and post-operatively. Further

documentation involves cadre of prescriber, type of antibiotic, dosage, duration, time before incision, blood loss, application of tourniquet, and blood transfusion.

Table 6: pre-operative procedures in relation to PSAP

	Total (Count)	Total (percent)	PSAP (No)	PSAP (Yes)
Cadre of prescriber before incision (N=136)				
Anesthesiologist	19	14%	26%	74%
Registered Clinical Officer	61	45%	18%	82%
Registrar	53	39%	17%	83%
Clinical officer in training	3	2%	33%	67%
Type of pre-operative antibiotics used				
Cefazolin	160	99%	21%	79%
Amoxicillin/clavulanic acid	1	1%	100%	0%
Time given before incision (N=155)				
Less than an hour	135	87%	21%	79%
More than an hour	20	13%	25%	75%
Application of tourniquet (N=159)				
Yes	48	30%	29%	71%
No	111	70%	18%	82%
Time antibiotic was given before tourniquet application (N=45)				
Less than an hour	38	81%	34%	66%
More than an hour	7	19%	14%	86%

The results indicate that, during the pre-operative prescription of antibiotics, majority (45 percent) of prescriber were the registered clinical officers, followed by registrars at 39 percent, 14 percent by anesthesiologist and 2 percent were done by clinical officer in training. For the patients whose pre-operative antibiotics was prescribed by Anesthesiologist, Registered Clinical Officer, Registrar and Clinical officer in training those who had PSAP include 74%, 82%, 83% and 67%, respectively. Out of the 161 patients, 99 percent received the cefazolin antibiotic prior to the planned surgery and amongst them, 79 percent were classified as PSAP unlike the one patient who was prescribed amoxicillin/clavulanic acid and was not classified as PSAP. On the recommended time of prescription prior to surgery, 87 percent were within

one hour (recommended) while 13 percent received the antibiotic past the recommended 1 hour. On the other hand, the difference between those who received at recommend timeframe against those who did not receive and their categorization for PSAP does not have any statistical significance (χ=0.126, p-value=0.723).

The pre-operative dosage by the age of the patient is shown in Table 7.

Table 7: Preoperative antibiotic dosages of cefazolin with comparison to age

	Total (count)	Total (percent)	0 to 18 years	19 to 59 years	60 years and above
2g	110	69%	4%	81%	15%
1g	34	21%	12%	82%	6%
Less than 1g	7	4%	100%	0%	0%
450g	4	3%	100%	0%	0%
175mg	1	1%	100%	0%	0%
3g	1	1%	0%	100%	0%
330mg	1	1%	100%	0%	0%
500g	1	1%	0%	100%	0%
750mg	1	1%	0%	100%	0%

4.4.2 Intraoperative prescription

This study sought to investigate intraoperative procedure which include duration of surgery, prescription of antibiotics, intraoperative challenges, blood loss and whether transfusion was done. The results are presented both in prose form and in a tabular format for ease of understanding. During the surgical procedure, 23 patients (14 percent) had their procedure taking longer than 4 hours, while the rest, 86 percent had their procedure take less than four hours.

The prescription of antibiotics intraoperatively by length of surgery is shown in Figure 6.

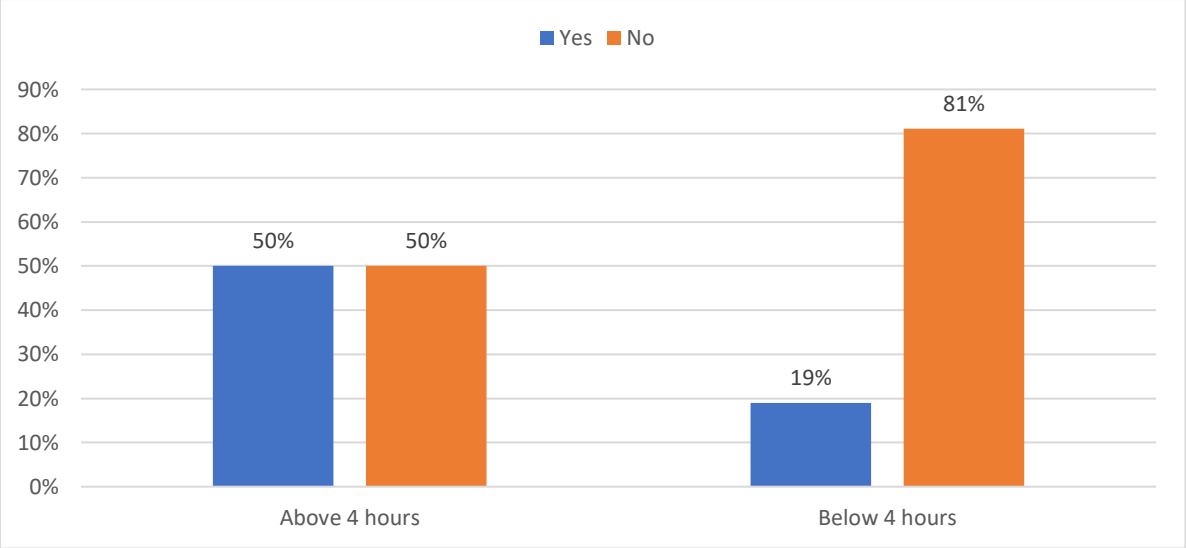

Figure 6: Intraoperative antibiotic prescription

It is recommended that surgeries that take longer than 4 hours, should be accompanied with a re-dose of antibiotics. The results indicate that half of the patients whose surgery took more than 4 hours received an intraoperative antibiotic whereas eight in every ten (81 percent) patients whose operation took less than 4 hours received an intraoperative antibiotic. This disparity in practice is an indication of a significant departure from the recommendations (χ=9.45, p-value=0.002).

Amongst those who were given an intraoperative antibiotic, 26 patients of the total received vancomycin (16%) and 5 cases (3%) received cefazolin. Of the total who received intraoperative antibiotics, 84 percent received Vancomycin while 16 percent received Cefazolin as shown in Figure below.

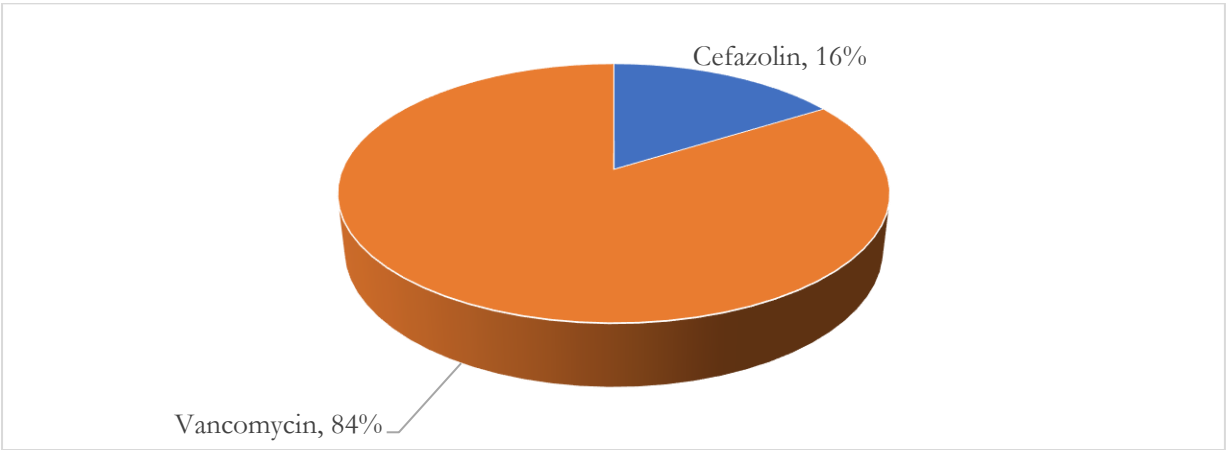

Figure 7: type of Intraoperative antibiotic prescribed

For those who received Cefazolin 25 percent presented multiple procedures and case complexity in each and half of them had no complexities. Amongst those who received Vancomycin, 8 percent had multiple procedures, 42 percent had case complexity and none had surgical issues. Further on matters dosage, for those who received Cefazolin, 20percent received 1 g, 60 percent received 2 g and 20 percent received 500g. Similarly, amongst the patients who received Vancomycin, 8 percent received 1 g, 88 percent received 2g and 4 percent received 1.5 g.

The prescription of intraoperative antibiotics was investigated across the surgical procedures and the results are shown in Figure below.

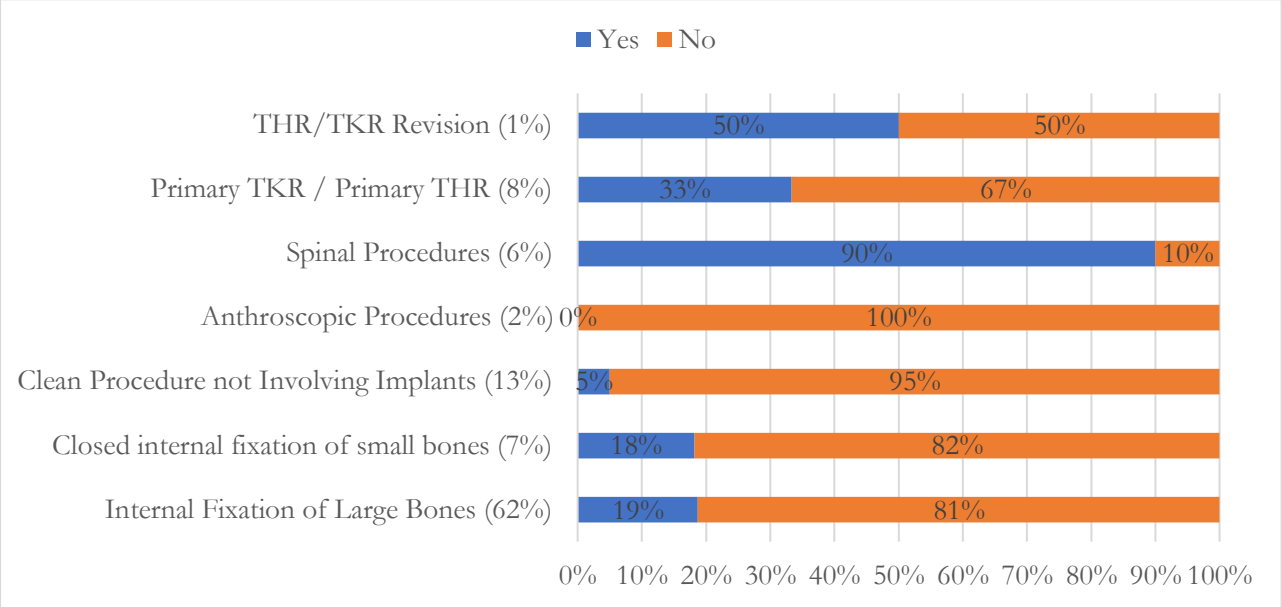

Figure 8: Planned surgery and intraoperative antibiotic use

The results indicate the 90 percent of spinal procedures received an intraoperative antibiotic while none of the arthroscopic procedures received intraoperative antibiotic.

Out of the 35 surgical cases that took more than 4 hours, 4 patients (3%) had patient bleed more than 1000mls while 97 percent bled less than 1000mls. A good clinical practice requires that patient who bleed above 1000mls of blood during the procedure should be transfused. Further investigation indicates that half of patients who bled past 1000mls were transfused while the rest were not. The difference between those who lost blood and being transfused indicates as strong statistical significance and implication that there is departure from quality clinical practices (χ=12.002, p-value=0.001).

4.4.3 Postoperative prescription

After the surgical procedure is completed, the medical practitioner should prescribe antibiotics according to the guidelines. The antibiotics that were prescribed postoperative are shown in Table below.

Table 8: post-operative antibiotics by duration

	1 Day	2 Days	3 Days	5 Days	7 Days	Start
	32	14	62	61	9	2
Cefazolin	88%	79%	87%	87%	78%	100%
Amoxicillin/clavulanic acid	22%	36%	13%	20%	22%	50%
Cefuroxime	3%	0%	8%	11%	0%	0%
Gentamicin	0%	14%	0%	0%	0%	0%
Ceftriaxone	19%	0%	6%	7%	22%	50%
Flucloxacillin	3%	7%	3%	8%	22%	0%
Clindamycin	3%	7%	5%	3%	0%	0%
Tazobactam	0%	7%	0%	3%	0%	0%
Metronidazole	0%	7%	3%	7%	22%	0%
Ceftazidime	0%	0%	3%	0%	11%	0%

Table 9: Postoperative prescription by age

	Total		Age category of the patient		
	Count	Percent	0 to 18 yrs	19 to 59 yrs	60 yrs +
Cefazolin	134	86%	86%	86%	94%
Amoxicillin/clavulanic acid	25	16%	19%	15%	19%
Cefuroxime	9	6%	10%	6%	0%
Ceftriaxone	8	5%	19%	3%	0%
Flucloxacillin	5	3%	5%	3%	6%
Metronidazole	4	3%	5%	3%	0%
Clindamycin	3	2%	0%	3%	0%
Gentamicin	1	1%	0%	1%	0%
Tazobactam	1	1%	5%	0%	0%
Ceftazidime	1	1%	5%	0%	0%

The postoperative antibiotic prescription by age of the patient is shown in the table above. The results indicate that Cefazolin is the most prescribed antibiotic across the ages followed by Amoxicillin/clavulanic acid and Cefuroxime.

Table 10: Postoperative antibiotic by prescriber

	Total		Cadre of the prescriber		
	Count	Percent	Consultant orthopedic	Resident orthopedics	SHO Anesthesia
Cefazolin	134	86%	43%	88%	100%
Amoxicillin/clavulanic acid	25	16%	86%	13%	0%
Cefuroxime	9	6%	14%	6%	0%
Ceftriaxone	8	5%	0%	6%	0%
Flucloxacillin	5	3%	14%	3%	0%
Metronidazole	4	3%	0%	3%	0%
Clindamycin	3	2%	14%	1%	0%
Gentamicin	1	1%	0%	1%	0%
Tazobactam	1	1%	0%	1%	0%
Ceftazidime	1	1%	0%	1%	0%

The results indicate that all the Cefazolin is prescribed by all SHO Anesthesia, 88 percent of Resident orthopedics and 43 percent of consultant orthopedic.

The analysis on type of procedure and postoperative antibiotic prescription indicates that one in every three of patients with arthroscopic procedures were not prescribed with post-operative antibiotics as shown in Figure below.

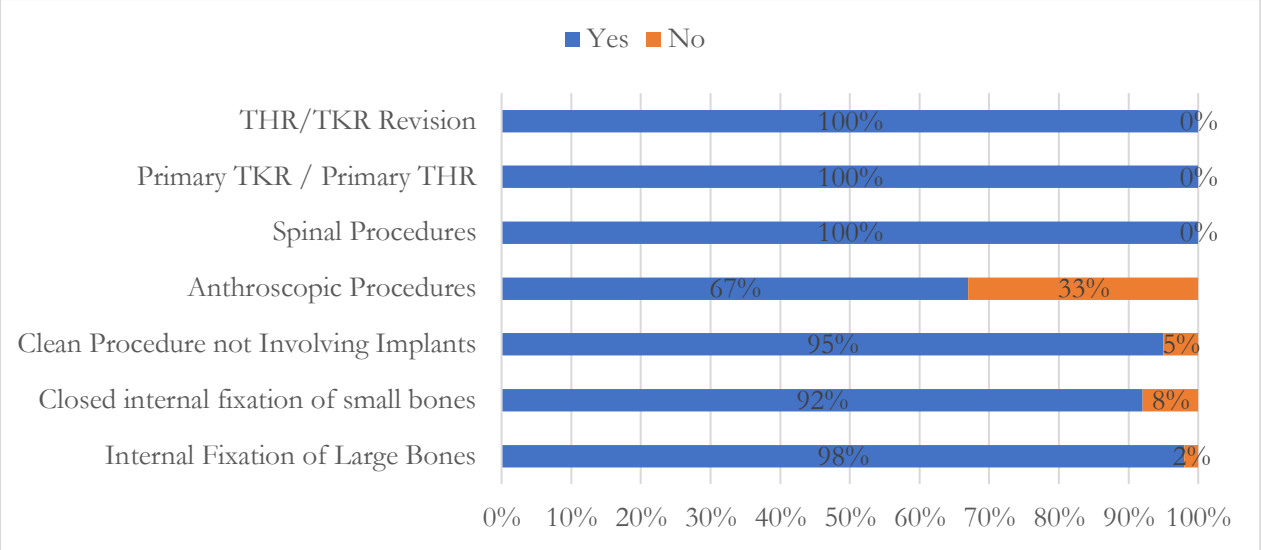

Figure 9: Postoperative prescription by type of procedure

4.5 Factors leading to prolonged SAP

Table 11: Awareness of guidelines among the antibiotic prescribers

	Total respondents	
	Count	Percent
Awareness of KNH guidelines	124	77
Unaware of KNH guidelines	30	19
No response	7	4

The results indicate that knowledge of guidelines among health care prescribers was 77%, and 19% of prescribers did not have a knowledge of local surgical antibiotic prophylaxis.

Each of the prescribers that did have knowledge of SAP, were asked on their reasons for use of the antibiotic given and this is summarized in the table below.

Table 12: Factors associated with the choice of antibiotics.

	Total respondents		PSAP	
	Count	Percent	No	Yes
Case complexity	22	18%	5%	95%
Cefazolin not available	10	8%	30%	70%
Surgeon Preference	13	10%	15%	85%
Prevent surgical site infection control	33	27%	12%	88%
Long duration in surgery	10	8%	20%	80%
Multiple procedures	7	6%	29%	71%
No response	29	23%	52%	48%

The results indicate that the choice of antibiotic is driven by the need to prevent surgical site infection (27%), case complexity (18%), surgeons' preference (10%), unavailability of Cefazolin and long duration in surgery at 8% each and multiple procedures at 6%.

CHAPTER 5: DISCUSSION

The objective of this study was to assess the practice of prophylactic antibiotics use in elective orthopedic procedures at Kenyatta National Hospital.

The choice of surgical antibiotic prophylaxis

According to the findings of the study, 99% of patients received cefazolin in the preoperative stage of prophylactic antibiotic use which is in keeping with the KNH guidelines. In contrast to a previous local study done in KNH that showed cefazolin was given in 28.6% of patients despite it being the antibiotic of choice. (6) This shows cefazolin is currently used widely as prophylactic antibiotic which is ideal due to its narrow spectrum and effective against the common organisms that cause SSI. However, in the two cases for total hip replacement/ total knee replacement revisions, it is recommended to use a single vancomycin dose of 1gm IV infusion in addition to the cefazolin. This was not done. For arthroscopic procedures no prophylaxis is recommended but in this study three arthroscopic procedures were carried out and all these patients were given cefazolin antibiotics preoperatively which again is not in keeping with the guidelines.

Intraoperative five patients were readministered intravenous cefazolin and of these cases, only two cases were found where the procedure exceeded above 4hours. Hence it was justified since due to the half-life of antibiotic, maintain the concentration of antibiotic at the surgical site tissue, cefazolin is re-dosed and twenty-six patients received intrawound vancomycin powder. According to research there is controversy in the use of vancomycin at the surgical site. Despite lack of high evidence orthopedic surgeons use vancomycin local application especially in arthroplasty and spine instrumentation cases. The U.S Preventive Services Task Force advocates its use on the basis that it does reduce risk of surgical wound infection. (73) The pharmaceutical companies and the food and drug administration body do not advocate for its use. (72) We also found use of vancomycin most commonly used among spine (90% of cases) and arthroplasty TKR/THR procedure (67%) of cases followed by internal fixation of large bones.

Postoperative 97% of patients operated were put on antibiotics, out of this 86% of patients were given cefazolin and this is in keeping with the guidelines. and this is the most commonly used across all boards as choice of surgical antibiotic prophylaxis. (31) This is slightly lower rate but in keeping with another study where cefazolin was the most preferred first-line antibiotic favored by 96% of surgeons. (4)

Amoxicillin/clavulanic acid was prescribed post operatively in 16 % of patients followed by cefuroxime 6% and due to its extended spectrum, it is not routinely used as prophylaxis. (31) This is much lower in contrast to local study where post operatively amoxicillin/clavulanic acid was at 41%. (6) This could be due to follow of guidelines and availability of cefazolin.

Based on the study, Ceftriaxone was used in 8% and gentamycin 1% of the cases. Antibiotics like gentamycin and ceftriaxone are not advocated as they do not cover for the most common organism and because of their wide coverage this can lead to AMR. (53) however, this is a much lower percentage compared to previous local study showing use of ceftriaxone is 40.8% as antibiotic prophylaxis. (6) This shows declining use of ceftriaxone. One of the reasons as to the declining use could be due to resistance patterns and also following the KNH guidelines.

Other antibiotics used but infrequent were flucloxacillin, clindamycin, tazobactam, metronidazole and ceftazidime. Penicillin such as flucloxacillin, tazobactam and Amoxicillin/clavulanic acid are recommended in some countries like Malaysia as SAP. (54) The use of clindamycin is advocated in cases of allergy which our study only one patient had allergy to sulfur-based drugs. (51) ceftazidime is a third-generation cephalosporin hence more gram-negative coverage hence not advocated as a prophylactic antibiotic same as metronidazole which has anaerobic coverage and most common organisms causing SSIs are gram positive organism hence not effective. (15) Hence in terms of post operative use despite the high percentage of use of cefazolin inappropriate antibiotic types, 18% of patients had inappropriate antibiotic type prescribed in our study.

Dosage of surgical antibiotic prophylaxis

The antibiotic's concentration must be kept above the minimal inhibitory concentration of the infectious organisms until skin closure, (31) hence dosage and duration are key to achieving this.

As per this study, 68% of patients received 2grams of cefazolin preoperative, 21% received 1 gram and only one case received 3grams. Less than 10% received less than 1 gram. According to guidelines the dose of initial preoperative dose of cefazolin is 2g and child less than 12 years receives 30mg/kg dosage and patients above 120kilograms receive 3grams of cefazolin. Hence 21% of patients have received lower dose. Those that received less than 1gram, 100% were below 18 years age group indicating use based on age/weight of patient but a limitation was the study was not able to get the weights of the patients.

Intraoperative cefazolin given in 5 patients, mostly 1gram intravenous single dose and vancomycin 2grams most commonly (88%) was used in all cases for local wound site application. Due to controversy of vancomycin use, appropriate dosages of vancomycin at wound site are not available but studies have shown use safely without adverse events anywhere between 1 to 2 grams depending on surgical wound size, but in some studies 0.5 to 6 grams have been used. We did not collect data on the wound size but in general use of 2 grams can be considered safe according to previous studies. (72) No intravenous vancomycin was being used despite being advocated in revision THR/TKR procedures. As in most studies of use of vancomycin in spine procedures, we found vancomycin use in 90% of spine procedure followed by every 2 in 3 cases of arthroplasty uses vancomycin at local surgical site. (73)

In the post operative period cefazolin as the most commonly prescribed as discussed above, 74% of patients were given 1gram of cefazolin and only 7% given 2 grams and the rest were given less than 1 gram. The discrepancy seen in this dosing between preoperative and post operative could be attributed to the cadre of prescriber of the antibiotics. For the post operative antibiotics 91% were resident orthopedics and for the preoperative antibiotics it was divided among clinical officer (38%) anesthesia residents (33%) and anesthesiologists (12%).

The duration of surgical antibiotic prophylaxis

Preoperative antibiotics should be given 30- 60 minutes before surgery and 10 minutes before torniquet inflation. (46) we found in this study that preoperative antibiotic was given within 60minutes from incision in 84% of cases. This is similar to local study that showed 84.6%. (6) In 12% antibiotics were prescribed more than 60 minutes from incision time. In some studies SAP given after 120minutes period are at risk of 6 times higher of SSI compared to within 120minutes. (45) The accepted duration among several bodies including WHO (18) is usually within 60 minutes from incision time.

30% of the total cases, a tourniquet was used and in 100% antibiotic was given before torniquet application ideally 10 minutes which is recommended according to the KNH guidelines, of note however is 7 cases where the tourniquet was used, the antibiotic was given 1 hour after the application of tourniquet. Torniquet application and time of incision is usually minimal and not significant during these cases so as to limit tourniquet time hence in these 7 cases it was not ideal and hence the total cases that prophylaxis was given more than 60 mins are more.

According to KNH guidelines for long procedures, the prophylactic dose of cefazolin should be repeated after 4 hours due to half-life of 1.1-2.2 hrs. since our patients all were elective cases with normal renal function levels then we found that 23 cases (14%) the duration of operation exceeded 4 hours

In the postoperative period, it is universally accepted that in general regardless of procedure SAP should not extend beyond 24-hour duration. (56) the risks outweigh the benefit of PSAP. In the post operative period SAP can be categorized according to the specific procedure as we will discuss below

Procedures like internal fixation of large bones require 2 further doses 8hourly and maximum 3 doses irrespective of surgical drain. We found that this was the most common procedure with 61% of total cases which includes but not limited to fixation of long bones like tibia, femur and humerus with tibial nailing, femur nailing and humerus plating respectively among others. Out of these cases 78 % cases had prolonged SAP meaning antibiotics were given more than a day from time of closure.

In arthroplasty cases which includes primary TKR/THR and revision arthroplasty cases ideally requires only 2 further doses of prophylactic antibiotic cefazolin 8 hourly, we found in this study revision cases despite being only 2 cases both cases SAP was prolonged and 92% cases for the primary, PSAP was given. There are studies that show extended use of SAP reducing rate of SSI especially in arthroplasty cases (11) but other studies show conflicting results and show no added advantage of PSAP PJI agreement report proceedings advocate heavily that SAP should not exceed 24 hours from first antibiotic given. (5). Hence this could be a cause of high prevalence of PSAP especially in the arthroplasty group

Other cases like closed internal fixation (small bones), arthroscopic procedures, clean procedures not involving implant fixation and spine procedures do not require any further antibiotics after closure of the skin. We found that there was a remarkably high use of antibiotic prophylaxis in these procedures

Prevalence of extended SAP

The prevalence of prolonged surgical antibiotic prophylaxis is 79 %. This is slightly higher to the descriptive cross-sectional study carried out at KNH on SAP for all surgical patients, including emergencies that found PSAP of 76.9%. (6) compared to one point prevalence study across Europe, PSAP was 25 %. (7) in another cross-sectional study prevalence of

PSAP was 12%. (12) In comparison to these studies our PSAP rates are high which is unacceptable.

The factors associated with prescribing practices of SAP

The high prevalence rate of PSAP can be related to number of factors that have been well described in previous studies, our aim of this study was to identify the factors that predispose health cadres giving PSAP despite clear recommendation that follow evidence-based medicine practices.

There are number of patient factors that were related to PSAP such as age, BMI, ASA score, diabetes, alcohol and smoking history in previous studies (65) however we found no significant association of diabetes and hypertension, ASA scoring and alcohol and smoking history with the use of PSAP. However, the numbers of the same in our population were limited. In separate studies despite comorbidities like diabetes, PSAP has no added advantage. (31)

In terms of surgical factors, it is recommended that operations greater than 4 hours and excessive bleeding of 1500mls or greater requires re-dosing of antibiotics intra-operatively. (33) but this does not justify use of prolonged PSAP. In view of this factors some of the factors we found in the study that were of note include case complexity, long duration of surgery, multiple procedures which were in keeping with previous studies. (66) In terms of the type of surgery, the highest rate of PSAP were in revision and primary TKR/THR operations, this can be explained due to the fears of infections by surgeon that leads to PJI that is usually devastating with high morbidity and cost implications (17). However, interestingly clean procedures not involving implant fixation was the third highest in terms of rates of PSAP which is quite astonishing as this usually have the lowest risk compared to all other procedures. There are studies that indicate presence of drain as a factor of PSAP (67) but in this study did not find drain use as a factor for prolonged SAP.

We found the Surgeon factors that lead to PSAP could be due to the lack knowledge of guidelines. The knowledge of the local guidelines was unknown to 19% of prescribers. despite this low percentage there is still a high rate of PSAP of 79% meaning despite knowledge of this guidelines, most subscribers still do not follow these guidelines. these could be attributed to other factors like surgeons' preference and fear of SSIs

5.1 CONCLUSION

Most of the patients in the study were scheduled for elective surgery following trauma and cefazolin was the most common drug for SAP. Cefazolin is the drug of choice in local and many international guidelines hence this is impressive. The dosage used is also in line with the guidelines and was appropriate for a particular age. Vancomycin was used intraoperatively in many cases in spite of worries on its use and effect on AMR. This could be attributed to the many controversies and lack of strong evidence.

The rate of prolonged use of prophylactic antibiotic is extremely high and despite having guidelines. A significant number of prescribers did not have knowledge of guidelines on SAP hence in order to reduce rate of PSAP, more awareness of the KNH guidelines need to be established among the antibiotic prescribers. The other factors that were found to lead to inappropriate antibiotic use was lack of cefazolin in hospital, complexity of procedures and long duration of surgery.

5.2 RECOMMENDATIONS

Follow-up should be carried out on these patients and outcome such as prevalence of SSI among the PSAP vs recommended SAP will enable physicians make informed decisions.

In the operating rooms and in the surgical wards, carry out the prescribed antibiotics in accordance with the established dosage schedule making copies of these guidelines available at these places and pinned on notice boards for access to health care professional prescribing SAP.

More investigations on prescriber's knowledge, attitude and practices in order to determine the key elements that govern antibiotic prescribing practices.

SAP education for surgeons and anesthesia professionals through training workshops and regular medical education

AMS programs can play a key role in ensuring adequate use of SAP. Collaboration with a multi-disciplinary team including the surgeons, infectious disease specialists and pharmacist that play a key role in implementing and monitoring the use of SAP. Especially on the use of local intra-operative vancomycin.

Conducting routine audits, usually quarterly or half yearly, to determine whether policies are being followed

5.3 LIMITATIONS

There were challenges in obtaining weight and height for the patients as most are trauma patients for elective fixation with difficulties in getting weight as this could be a one of the areas since the antibiotic dosages are given based on estimates from age.

Looking at prophylactic antibiotic use there is the aspect of the use of antibiotic-loaded cement in joint arthroplasties which was not picked in this study.

Kenyatta national hospital has majority trauma orthopedic cases, in consecutive sampling, the trauma elective orthopedic cases were more than other cases hence unequal distribution. This limitation, however, was tackled by the current division of the orthopedics into the thematic unit with equal representation in terms of theatre and ward allocation**.**

This was a descriptive cross-sectional study; the entire population group needed to be studied hence large sample size was required to increase accuracy. The formula used to get the current sample size ensured the results obtained were true representation and maintained credibility of this study.

The purpose of SAP is to prevent SSI. This study was not looking at the outcomes of SAP and PSAP.

The blood loss during the procedure was difficult to be calculated accurately and estimated blood loss was the anesthetic assessment of blood loss at the end of procedure, this however, did not affect the study results as the estimated blood loss was reliable enough to access as a moderating factor in the use of antibiotics.

REFERENCES

1. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, Reinke CE, Morgan S, Solomkin JS, Mazuski JE, Dellinger EP. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA surgery. 2017 Aug 1;152(8):784-91.
2. Ligogo BL. Rational Use of Antibiotics Among Patients Admitted To Critical Care Units At Kenyatta National Hospital And Its Impact On Clinical Outcomes (Doctoral dissertation, University of Nairobi),2020.
3. Crader MF, Varacallo M. Preoperative antibiotic prophylaxis.
4. Gans I, Jain A, Sirisreetreerux N, Haut ER, Hasenboehler EA. Current practice of antibiotic prophylaxis for surgical fixation of closed long bone fractures: a survey of 297 members of the Orthopaedic Trauma Association. Patient safety in surgery. 2017 Dec;11(1):1-6.
5. Parvizi J, Gehrke T, Chen AF. Proceedings of the international consensus on periprosthetic joint infection. The bone & joint journal. 2013 Nov;95(11):1450-2.
6. Gitau SN. Patterns of Perioperative Antibiotic Surgical Prophylaxis Among Surgical Patients Undergoing Surgery in Knh Theatres (Doctoral dissertation, University of Nairobi)2020.
7. Plachourasi D, Karki T, Hansen S, Hopkins S, Lyytikainen O, Moro ML, Rellly J, Zarb P, Zingg W, Kinross P, Weistl K. Antimicrobial use in European acute care hospitals: results from the second point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use, 2016 to 2017. EUROSURVEILLANCE. 2018 Nov 15;23(46):15-28.
8. Versporten A, Zarb P, Caniaux I, Gros MF, Drapier N, Miller M, Jarlier V, Nathwani D, Goossens H, Koraqi A, Hoxha I. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. The Lancet Global Health. 2018 Jun 1;6(6):e619-29.
9. Nagata K, Yamada K, Shinozaki T, Miyazaki T, Tokimura F, Oka H, Tajiri Y, Tanaka S, Okazaki H. Non-inferior comparative study comparing one or two day antimicrobial prophylaxis after clean orthopaedic surgery (NOCOTA study): a study protocol for a cluster pseudo-randomized controlled trial comparing duration of antibiotic prophylaxis. BMC Musculoskeletal Disorders. 2019 Dec;20(1):1-9

10. Inabathula A, Dilley JE, Ziemba-Davis M, Warth LC, Azzam KA, Ireland PH, Meneghini RM. Extended oral antibiotic prophylaxis in high-risk patients substantially reduces primary total hip and knee arthroplasty 90-day infection rate. JBJS. 2018 Dec 19;100(24):2103-9.
11. Siddiqi A, Forte SA, Docter S, Bryant D, Sheth NP, Chen AF. Perioperative antibiotic prophylaxis in total joint arthroplasty: a systematic review and meta-analysis. JBJS. 2019 May 1;101(9):828-42.
12. Rohrer F, Maurer A, Noetzli H, Gahl B, Limacher A, Hermann T, Bruegger J. Prolonged antibiotic prophylaxis use in elective orthopaedic surgery–a cross-sectional analysis. BMC musculoskeletal disorders. 2021 Dec;22(1):1-1.
13. Infectious Diseases Society of America (IDSA). Combating antimicrobial resistance: policy recommendations to save lives. Clinical Infectious Diseases. 2011 May 1;52(suppl_5): S397-428.
14. Hilal-Dandan R, Brunton L. Goodman and Gilman Manual of Pharmacology and Therapeutics, 2. McGraw Hill Professional, Philadelphia; 2013.
15. Kamere N, Garwe ST, Akinwotu OO, Tuck C, Krockow EM, Yadav S, Olawale AG, Diyaolu AH, Munkombwe D, Muringu E, Muro EP. Scoping Review of National Antimicrobial Stewardship Activities in Eight African Countries and Adaptable Recommendations. Antibiotics. 2022 Aug 25;11(9):1149.
16. Polk Jr HC, Christmas AB. Prophylactic antibiotics in surgery and surgical wound infections. The American Surgeon. 2000 Feb 1;66(2):105.
17. Al-Mulhim FA, Baragbah MA, Sadat-Ali M, Alomran AS, Azam MQ. Prevalence of surgical site infection in orthopedic surgery: a 5-year analysis. International surgery. 2014;99(3):264-8
18. World Health Organization. Global guidelines for the prevention of surgical site infection. World Health Organization; 2016.
19. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surgical infections. 2013 Feb 1;14(1):73-156.
20. Kates SL, Borens O. systemic antibiotics. In: Principles of Orthopedic Infection Management. Stuttgart: Georg Thieme Verlag; 2016. p. 71–3.
21. Cohen ML. Changing patterns of infectious disease. Nature. 2000;406(6797):762–7.

22. Taneja N, Sharma M. Antimicrobial resistance in the environment: The Indian scenario. Indian Journal of Medical Research. 2019;149(2):119.
23. Maina M, Mwaniki P, Odira E, Kiko N, McKnight J, Schultsz C, English M, Tosas-Auguet O. Antibiotic use in Kenyan public hospitals: Prevalence, appropriateness and link to guideline availability. International Journal of Infectious Diseases. 2020 Oct 1;99:10-8.
24. Sharma KD, Saini RP, Karthik L. Current trends of antibiotic resistance in clinical isolates of Staphylococcus aureus. Frontiers in biology. 2014 Aug;9(4):287-90.
25. Taitt CR, Leski TA, Erwin DP, Odundo EA, Kipkemoi NC, Ndonye JN, Kirera RK, Ombogo AN, Walson JL, Pavlinac PB, Hulseberg C. Antimicrobial resistance of Klebsiella pneumoniae stool isolates circulating in Kenya. Plos one. 2017 Jun 2;12(6):e0178880.
26. Ratemo NK. Antimicrobial susceptibility pattern of bacterial isolates from pus samples at Kenyatta National Hospital, Kenya (Doctoral dissertation, University of Nairobi).
27. The Journal of Global Antimicrobial Resistance Meets the World Health Organization (WHO). Journal of Global Antimicrobial Resistance. 2019;18:305–8.
28. Nyabanda J. The value of single dose flucloxacillin in clean major surgical operations (Doctoral dissertation, University of Nairobi.).
29. Dhammi IK, Haq RU, Kumar S. Prophylactic antibiotics in orthopedic surgery: Controversial issues in its use. Indian journal of orthopaedics. 2015 Jul;49(4):373.
30. AlBuhairan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. The Journal of bone and joint surgery. British volume. 2008 Jul;90(7):915-9.
31. Bryson DJ, Morris DL, Shivji FS, Rollins KR, Snape S, Ollivere BJ. Antibiotic prophylaxis in orthopaedic surgery: difficult decisions in an era of evolving antibiotic resistance. The bone & joint journal. 2016 Aug;98(8):1014-9.
32. Cooke FJ, Holmes AH. The missing care bundle: antibiotic prescribing in hospitals. International journal of antimicrobial agents. 2007 Jul 1;30(1):25-9.
33. Dehne MG, Mühling J, Sablotzki A, Nopens H, Hempelmann G. Pharmacokinetics of antibiotic prophylaxis in major orthopedic surgery and blood-saving techniques. Orthopedics. 2001 Jul 1;24(7):665-9.

34. Abildgaard JT, Backes J, Hawkins RJ. Preventing infection in shoulder surgery. Journal of Shoulder and Elbow Surgery. 2018 Jul 1;27(7):1333-41.
35. Zeiler HJ, Busse WD. Antibacterial Therapy: Achievements, Problems, and Future Perspectives. Springer-Verlag; 1997.
36. van den Broek AK, Prins JM, Visser CE, van Hest RM. Systematic review: the bioavailability of orally administered antibiotics during the initial phase of a systemic infection in non-ICU patients. BMC infectious diseases. 2021 Dec;21(1):1-1.
37. Zurbuchen U, Ritz JP, Lehmann KS, Groene J, Heidari M, Buhr HJ, Germer CT. Oral vs intravenous antibiotic prophylaxis in elective laparoscopic cholecystectomy—an exploratory trial. Langenbeck's Archives of Surgery. 2008 Jul;393(4):479-85.
38. M Roberts D. The relevance of drug clearance to antibiotic dosing in critically ill patients. Current pharmaceutical biotechnology. 2011 Dec 1;12(12):2002-14.
39. Mansoor A, Mahabadi N. Volume of distribution. InStatPearls [Internet] 2021 Jul 26. StatPearls Publishing.
40. Ulldemolins M, Rello J. The relevance of drug volume of distribution in antibiotic dosing. Current Pharmaceutical Biotechnology. 2011 Dec 1;12(12):1996-2001.
41. Himebauch AS, Sankar WN, Flynn JM, Sisko MT, Moorthy GS, Gerber JS, Zuppa AF, Fox E, Dormans JP, Kilbaugh TJ. Skeletal muscle and plasma concentrations of cefazolin during complex paediatric spinal surgery. BJA: British Journal of Anaesthesia. 2016 Jul 1;117(1):87-94.
42. Zamoner W, de Freitas FM, Garms DS, de Oliveira MG, Balbi AL, Ponce D. Pharmacokinetics and pharmacodynamics of antibiotics in critically ill acute kidney injury patients. Pharmacology Research & Perspectives. 2016 Dec;4(6):e00280.
43. Gunderson BW, Ross GH, Ibrahim KH, Rotschafer JC. What do we really know about antibiotic pharmacodynamics?. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2001 Nov;21(11P2):302S-18S.
44. Lorkowski J, Maciejowska-Wilcock I. Surgical Safety Checklist: Polychromatic or Achromatic Design. Invasive Diagnostics and Therapy. 2021 Dec 31:11-6.
45. Burke JP. Maximizing appropriate antibiotic prophylaxis for surgical patients: an update from LDS Hospital, Salt Lake City. Clinical Infectious Diseases. 2001 Sep 1;33(Supplement_2):S78-83.

46. Yeap JS, Lim JW, Vergis M, Yeung PA, Chiu CK, Singh H. Prophylactic antibiotics in orthopaedic surgery: guidelines and practice. Medical Journal of Malaysia. 2006 Jun 1;61(2):181.
47. Niimi R, Hasegawa M, Kawamura G, Sudo A. One-day antibiotic infusion for the prevention of postoperative infection following arthroplasty: A case control study. International Scholarly Research Notices. 2011;2011.
48. Thonse R, Sreenivas M, Sherman KP. Timing of antibiotic prophylaxis in surgery for adult hip fracture. Annals of the Royal College of Surgeons of England. 2004 Jul;86(4):263.
49. Burger JR, Hansen BJ, Leary EV, Aggarwal A, Keeney JA. Dual-agent antibiotic prophylaxis using a single preoperative vancomycin dose effectively reduces prosthetic joint infection rates with minimal renal toxicity risk. The Journal of arthroplasty. 2018 Jul 1;33(7):S213-8.
50. Sewick A, Makani A, Wu C, O'Donnell J, Baldwin KD, Lee GC. Does dual antibiotic prophylaxis better prevent surgical site infections in total joint arthroplasty?. Clinical Orthopaedics and Related Research®. 2012 Oct;470(10):2702-7.
51. French GL. Enterococci and vancomycin resistance. Clinical Infectious Diseases. 1998 Aug 1;27(Supplement_1):S75-83.
52. Macharia JT. Determination of bacterial isolate profiles, their antimicrobial susceptibility patterns and trends of antibiotic use in patients with open fractures (Masters dissertation, University of Nairobi). 2020.
53. Rafati M, Shiva A, Ahmadi A, Habibi O. Adherence to American society of health-system pharmacists surgical antibiotic prophylaxis guidelines in a teaching hospital. Journal of research in pharmacy practice. 2014 Apr;3(2):62.
54. Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. The application of evidence-based measures to reduce surgical site infections during orthopedic surgery-report of a single-center experience in Sweden. Patient safety in surgery. 2012 Dec;6(1):1-8.
55. Liu Y, Ryan ME, Lee HM, Simon S, Tortora G, Lauzon C, Leung MK, Golub LM. A chemically modified tetracycline (CMT-3) is a new antifungal agent. Antimicrobial agents and chemotherapy. 2002 May;46(5):1447-54.

56. Stefánsdóttir A, Robertsson O, W-Dahl A, Kiernan S, Gustafson P, Lidgren L. Inadequate timing of prophylactic antibiotics in orthopedic surgery. We can do better. Acta orthopaedica. 2009 Dec 1;80(6):633-8.
57. Ondari JN. Comparative study of 24-hour versus five-day prophylactic antibiotic use in gustilo ii open tibia fractures at Kenyatta National Hospital (Doctoral dissertation, University of Nairobi).
58. Loo LW, Liew YX, Lee W, Lee LW, Chlebicki P, Kwa AL. Discontinuation of antibiotic therapy within 24 hours of treatment initiation for patients with no clinical evidence of bacterial infection: a 5-year safety and outcome study from Singapore General Hospital Antimicrobial Stewardship Program. International journal of antimicrobial agents. 2019 May 1;53(5):606-11.
59. Graham SM, Lubega N, Mkandawire N, Harrison WJ. Total hip replacement in HIV-positive patients. The Bone & Joint Journal. 2014 Apr;96(4):462-6.
60. Bates J, Mkandawire N, Harrison WJ. The incidence and consequences of early wound infection after internal fixation for trauma in HIV-positive patients. The Journal of Bone and Joint Surgery. British volume. 2012 Sep;94(9):1265-70.
61. Sousa R, Muñoz-Mahamud E, Quayle J, Dias da Costa L, Casals C, Scott P, Leite P, Vilanova P, Garcia S, Ramos MH, Dias J. Is asymptomatic bacteriuria a risk factor for prosthetic joint infection?. Clinical infectious diseases. 2014 Jul 1;59(1):41-7.
62. Cumming D, Parker MJ. Urinary catheterisation and deep wound infection after hip fracture surgery. International orthopaedics. 2007 Aug;31(4):483-5.
63. Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, Abbas M, Atema JJ, Gans S, van Rijen M, Boermeester MA. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. The Lancet Infectious Diseases. 2016 Dec 1;16(12):e276-87.
64. Branch-Elliman W, O'Brien W, Strymish J, Itani K, Wyatt C, Gupta K. Association of duration and type of surgical prophylaxis with antimicrobial-associated adverse events. JAMA surgery. 2019 Jul 1;154(7):590-8.
65. Ridgeway S, Wilson J, Charlet A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. The Journal of bone and joint surgery. British volume. 2005 Jun;87(6):844-50.
66. Abbas M, Aghayev E, Troillet N, Eisenring MC, Kuster SP, Widmer AF, Harbarth S, Balmelli C, Eisenring MC, Harbarth S, Kuster SP. Temporal trends and epidemiology

of Staphylococcus aureus surgical site infection in the Swiss surveillance network: a cohort study. Journal of Hospital Infection. 2018 Feb 1;98(2):118-26.

67. Olsen MA, Nepple JJ, Riew KD, Lenke LG, Bridwell KH, Mayfield J, Fraser VJ. Risk factors for surgical site infection following orthopaedic spinal operations. JBJS. 2008 Jan 1;90(1):62-9.
68. Abdul-Jabbar A, Takemoto S, Weber MH, Hu SS, Mummaneni PV, Deviren V, Ames CP, Chou D, Weinstein PR, Burch S, Berven SH. Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data. Spine. 2012 Jul 1;37(15):1340-5.
69. Kallen AJ, Wilson CT, Larson RJ. Perioperative intranasal mupirocin for the prevention of surgical-site infections: systematic review of the literature and meta-analysis. Infection Control & Hospital Epidemiology. 2005 Dec;26(12):916-22.
70. Engesæter L, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty Effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register. Acta Orthopaedica Scandinavica. 2003 Jan 1;74(6):644-51.
71. Singh G, Passi D, Daga D, Manas A, Vignesh U, Bhave SM. Study of antibiotic efficacy of topical vancomycin powder in treatment of infected mandibular fractures and soft tissue surgical site infections. Journal of Family Medicine and Primary Care. 2019 Oct;8(10):3340.
72. Takahashi H, Iida Y, Yokoyama Y, Hasegawa K, Tsuge S, Fukutake K, Nakamura K, Wada A. Use of intrawound vancomycin powder against postoperative infection after spine surgery. Spine Surgery and Related Research. 2018 Jan 20;2(1):18-22.
73. Kanj WW, Flynn JM, Spiegel DA, Dormans JP, Baldwin KD. Vancomycin prophylaxis of surgical site infection in clean orthopedic surgery. Orthopedics. 2013 Feb 1;36(2):138-46.
74. Espinosa MM, Bieski IG, Martins DT. Probability sampling design in ethnobotanical surveys of medicinal plants. Revista Brasileira de Farmacognosia. 2012;22:1362-7.

BUDGET BREAKDOWN

The budget was as follows

ITEMS	**COST (kshs)**
Research fees for KNH-UON ERC	2,000
NACOSTI	1,000
Stationery and printing	20,000
Research assistant fee (3 research assistants each 20,000)	60,000
Health information system – KNH statistics department	500
Statistician fee	35,000
Miscellaneous	10,000
Total	**128,500**

APPENDIX I:

PARTICIPANT INFORMATION AND CONSENT FORM

FOR EROLLMENT IN THE STUDY

Title of Study: PRACTICE OF PROPHYLACTIC ANTIBIOTIC USE IN ELECTIVE ORTHOPEDIC PROCEDURES AT THE KENYATTA NATIONAL HOSPITAL

Principal Investigator: Dr. Shabir Adamjee

Research assistant:

I would like to talk to you about my study. The purpose of this consent is to give information you will need to help you decide whether or not to be a participant in the study. Please feel free to ask any questions you may want to ask **regarding the aim of this research and the role you play by enrolling in this study, and any other clarifications that you may have before** signing this consent. **After answering all your questions to your contentment, you may decide to be in this study or not. Once you agree to participate in the study, your name and signature will be required.** By signing this consent, you do agree that personal information will be taken regarding your diagnosis and relevant operation details.

The decision you take is entirely voluntary and anytime you feel to withdraw, you may do so without any hesitation or consequences. you may wish to exit at any time and withdraw without any victimization. **Refusal to participate will not affect the services you are entitled in this or any other health facilities.**

May I continue? YES/NO

This study has approval by the KNH-UoN Ethics and Research Committee protocol No…….

‘

WHAT IS THIS STUDY ABOUT?

The investigator and the research assistant listed above will interview patients who are undergoing elective orthopedic operation. The purpose of the interview is to get data like age, weight, height, history of any chronic disease, allergies to medication and smoking and alcohol history. Then once this data is collected the investigator will monitor and interview the health professional regarding antibiotic usage preoperatively until you stop taking antibiotics. You will not have to undergo any tests and during this study the treatment course will not be altered or changed as this will be observation and interviews only.

The main aim of this study is to find the prevalence of inappropriate prophylactic antibiotic practices and determine the factors associated with them, this may benefit in standardization of antibiotic use hence tackling antimicrobial resistance which is a big crisis in today's world.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THE RESEARCH STUDY

If you agree to participate in this study then you will be interviewed by a trained research assistant in an area where you feel comfortable. This may last approximately two to five minutes. This interview will cover topics such as age, weight, height, history of any chronic disease, allergies to medication and smoking and alcohol history. No further tests or participation will be required by you.

ARE THERE ANY RISKS ASSOCIATED WITH THIS STUDY?

One potential risk is loss of privacy; however, we use a code number for each patient and all your information is kept confidential as possible. Any question during the interview that may be uncomfortable then those will be skipped. Otherwise in this study no harms or complication can arise.

ANY QUESTION/CLARIFICATION SO FAR? YES/NO

ARE THERE BENEFITS BEING IN THIS STUDY?

This may not benefit you directly but will provide us with information that can be used in policies and guidelines for the improvement of health care delivery.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

NO, there is no cost implication in enrolling in this study due to fact that data obtained will be from interview and observations with no cost to the participant.

WHAT IF YOU HAVE QUESTIONS IN THE FUTURE?

In case you need to contact the principal investigator or research assistant for any inquiries please feel free to do so on

Telephone: 0722207529 email: sadamjee15@gmail.com

Primary supervisor contacts:

1. Fred Sitati Consultant Orthopedic and Trauma Surgeon,
Department of Orthopedic Surgery, University of Nairobi
Email: fredsitati@yahoo.com TEL: 0722607220
2. Edward Gakuya Consultant Orthopedic and Trauma Surgeon,
Lecturer, Department of Orthopedic Surgery, University of Nairobi
Email: kibaka62@gmail.com TEL: 0721932799

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

Participant's statement

I have read this consent form. I have had my questions answered in a language that I understand. I freely agree to participate in this research study

Participant printed name:

_____

Participant signature / Thumb stamp _____ Date _____

Parent statement

For children below 18 years

As a parent/legal guardian I have read and understood the consent form and freely agree for my child to participate in this study

Participant printed name:

_____

Parent signature / Thumb stamp _____ Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher 's Name: _____ **Date**: _____

Signature

_____

APPENDIX II:

FOMU YA TAARIFA NA RIDHAA YA MSHIRIKI

KWA KUJIANDIKISHA KATIKA SOMO

Kichwa cha utafiti: MAZOEZI YA MATUMIZI YA KUKUA VINJA VYA PROPHYLACTIC KATIKA TARATIBU ZILIZOCHAGUA ZA MIFUPA KATIKA HOSPITALI YA TAIFA YA KENYATTA

Mpelelezi mkuu: Dr shabir adamjee

Msaidizi wa utafiti:

Ningependa kuzungumza nawe kuhusu masomo yangu. Madhumuni ya ridhaa hii ni kutua taarifa utakazohitaji ili kukusaidia kuamua kama kuwa mshiriki au la. Tafadhali jisikie huru kuuliza maswali yoyote ambayo unaweza kutaka kuuliza kuhusu lengo la utafiti huu na jukumu lako kwa kujiandikisha katika utafiti huu, na ufafanuzi mwingine wowote ambao unaweza kuwa nao kabla ya kusaini kibali hiki. Baada ya kujibu maswali yako yote kwa kutosheka kwako, unaweza kuamua kuwa katika utafiti huu au la. Ukishakubali kushiriki katika utafiti, jina na saini yako zitahitajika. Kwa kutia saini idhini hii, unakubali kwamba taarifa za kibinafsi zitachukuliwa kuhusu utambuzi wako na maelezo muhimu ya operesheni.

Uamuzi unaochukua ni wa hiari kabisa na wakati wowote unahisi kujiondoa, unaweza kufanya hivyo bila kusita au matokeo yoyote. unaweza kutaka kuondoka wakati wowote na kujiondoa bila dhuluma yoyote. Kukataa kushiriki hakutaathiri huduma unazostahiki katika kituo hiki au kingine chochote cha afya.

Naweza kuendelea? NDIO LA

Utafiti huu umeidhinishwa na itifaki ya kamati ya maadili na utafiti ya KNH-UoN Nambari ……..

SOMO HILI LINAHUSU NINI?

Mchunguzi na msaidizi wa utafiti walioorodheshwa hapo juu watawahoji wagonjwa wanaofanyiwa upasuaji wa kuchaguliwa wa mifupa. Madhumuni ya mahojiano ni kupata data kama umri, uzito, urefu, historia ya ugonjwa wowote sugu, mizio ya dawa na uvutaji sigara na historia ya pombe. Kisha data hii inapokusanywa mchunguzi atafuatilia na kumhoji mtaalamu wa afya kuhusu utumiaji wa viuavijasumu kabla ya upasuaji hadi utakapoacha kutumia viuavijasumu. Hutalazimika kufanyiwa majaribio yoyote na wakati wa utafiti huu kozi ya matibabu haitabadilishwa au kubadilishwa kwani hii itakuwa uchunguzi na mahojiano pekee.

Lengo kuu la utafiti huu ni kupata kuenea kwa mazoea yasiyofaa ya kuzuia viuavijasumu na kuamua sababu zinazohusiana nayo, hii inaweza kufaidika katika kusanifisha matumizi ya viuavijasumu hivyo basi kukabiliana na ukinzani wa viuavijasumu ambalo ni janga kubwa katika ulimwengu wa leo.

NINI KITAENDELEA UKIAMUA KUWA KWENYE UTAFITI?

Ukikubali kushiriki katika utafiti huu basi utahojiwa na msaidizi wa utafiti aliyefunzwa katika eneo ambalo unahisi vizuri. Hii inaweza kudumu takriban dakika mbili hadi tano. Mahojiano haya yatashughulikia mada kama vile umri, uzito, urefu, historia ya ugonjwa wowote sugu, mizio ya dawa na uvutaji sigara na historia ya pombe. Hakuna majaribio zaidi au ushiriki utahitajika na wewe.

JE, KUNA HATARI YOYOTE INAYOHUSISHWA NA UTAFITI HUU?

Hatari moja inayoweza kutokea ni kupoteza faragha; hata hivyo, tunatumia nambari ya msimbo kwa kila mgonjwa na maelezo yako yote yanawekwa siri iwezekanavyo. Swali lolote wakati wa mahojiano ambalo linaweza kuwa na wasiwasi basi hayo yatarukwa. Vinginevyo katika utafiti huu hakuna madhara au matatizo yanaweza kutokea.

SWALI/UFAFANUZI WOWOTE HADI SASA? NDIO LA

JE, KUNA FAIDA KUWA KATIKA UTAFITI HUU?

Huenda hili lisikufaidishe moja kwa moja lakini litatupatia taarifa zinazoweza kutumika katika sera na miongozo ya uboreshaji wa utoaji wa huduma za afya.

JE, KUWA KWENYE SOMO HILI LITAKUGHARIMU LOLOTE?

HAPANA, hakuna maana ya gharama katika kujiandikisha katika utafiti huu kutokana na ukweli kwamba data iliyopatikana itatoka kwa mahojiano na uchunguzi bila gharama kwa mshiriki.

VIPI IKIWA UNA MASWALI BAADAYE?
Ikiwa utahitaji kuwasiliana na mtafiti kwa maswali yoyote tafadhali jisikie huru kufanya hivyo kwa
simu 0722207529 barua pepe sadamjee15@gmail.com

Anwani za msimamizi mkuu:
1. Fred Sitati Mshauri wa Upasuaji wa Mifupa na Kiwewe,
Idara ya Upasuaji wa Mifupa, Chuo Kikuu cha Nairobi
Barua pepe: fredsitati@yahoo.com TEL: 0722607220
2. Edward Gakuya Mshauri Daktari wa Mifupa na Kiwewe,
Mhadhiri, Idara ya Upasuaji wa Mifupa, Chuo Kikuu cha Nairobi
Barua Pepe: kibaka62@gmail.com TEL: 0721932799

Kwa maelezo zaidi kuhusu haki zako kama mshiriki wa utafiti unaweza kuwasiliana na Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi Nambari 2726300 Ext. 44102 barua pepe uonknh_erc@uonbi.ac.ke.

Taarifa ya mshiriki

Nimesoma fomu hii ya idhini. Nimejibiwa maswali yangu kwa lugha ambayo ninaelewa. Ninakubali kwa uhuru kushiriki katika utafiti huu wa utafiti kushiriki katika utafiti huu

Mshiriki aliyechapishwa jina_____

Saini ya mshiriki / muhuri wa kidole_____ Tarehe_____

taarifa ya mzazi

Kwa watoto chini ya miaka 18

Kama mzazi/mlezi wa kisheria nimesoma na kuelewa fomu ya idhini na ninakubali kwa uhuru mtoto wangu kushiriki katika utafiti huu

saini ya mzazi / stempu ya kidole_____ Tarehe_____

Taarifa ya mtafiti

i, aliyewekwa chini, nimeelezea kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyetajwa hapo juu na kuamini kwamba mshiriki ameelewa na kwa hiari ametoa idhini yake.

Jina la mtafiti _____

Saini ya mtafiti _____ Tarehe _____

APPENDIX III: KNH guidelines on surgical antibiotic prophylaxis

TABLE 13: 2021 KNH guidelines on surgical antibiotic prophylaxis

PROCEDURE	**COMMON ORGANISMS**	**RECOMMENDED PROPHYLAXIS**
Internal fixation of large bones	Skin commensals e.g., S aureus, Coagulase negative staphylococci, Coliforms	**Cefazolin 2g** IV initiated 30 to 60 minutes before the skin incision (child <12 years: 30mg/kg up to 2g) THEN Repeat 8-hourly for 2 further doses. (**Max 3 doses** irrespective of the presence of surgical drains)
Other (closed) internal fixation		**Cefazolin 2g** IV (child <12 years: 30mg/kg up to 2g)
Arthroscopic and other clean procedures not involving foreign material (e.g., pins, plates)		Prophylaxis **NOT** required
Spinal procedures	Skin commensals e.g., S aureus, Coagulase negative staphylococci, Coliforms	**Cefazolin 2g** IV initiated 30 to 60 minutes before the skin incision (child <12 years: 30mg/kg up to 2g)
Primary Total Hip Replacement (THR) OR Total Knee Replacement (TKR)	Skin commensals e.g., S aureus, Coagulase negative staphylococci, Coliforms	**Cefazolin 2g** IV initiated 30 to 60 minutes before the skin incision (child <12 years: 30mg/kg up to 2g) then repeat 8-hourly for 2 further doses.
THR/TKR Patients requiring revision/ re-operation without any Pre-existing infections	Skin commensals e.g., S aureus, Coagulase negative staphylococci, Coliforms	**Cefazolin 2g** IV initiated 30 to 60 minutes before the skin incision (child <12 years: 30mg/kg up to 2g) then repeat 8-hourly for 2 further doses. **PLUS** **Vancomycin 1gm** IV infusion (1.5g for patients >80kg actual body weight)

If tourniquet is to be used, the full dose of the antibiotic should be infused prior to application of the tourniquet.

TABLE 14: 2021 KNH guidelines on surgical antibiotic prophylaxis and redosing for normal and reduced kidney function

Antimicrobial	Pre-op Dose	Half-life, h	Half-life in ESRD	Normal Renal function Re-dose after (hours)[1]	Reduced renal function Re-dose based on CrCl after (hours)[2]	Administration
Cefazolin	2g, 3g if >120kg	1.1-2.2	40-70	4 6 8	CrCl>35:4 CrCl 10-35:6 CrCl <10:8	IV push over 3-5 min
Ceftriaxone	2g	5.4-10.9		12	N/A	IV push over 3-5 min
Clindamycin	900mg	2.0-4.0	3.0-5.0	6	6	Infusion
Gentamicin	5mg/kg, max 400mg	2.0-3.0	50-70	No re-dose	No re-dose	Infusion
Metronidazole	500mg	6.0-8.0	7.0-21	8	8	Infusion
Vancomycin	15mg/kg	4.0-8.0	44.1-406.4	12	N/A	Infusion should not exceed 1g in 60min
Cefuroxime	1.5g	1.0-2.0	3.5	8	24	IV push over 3-5 min

1. For long procedures, the prophylactic dose should be repeated after the number of hours indicated on the table.
2. For long procedures in patients with renal insufficiency, the dose should be repeated after the duration indicated.

Creatinine Clearance = [[140 - age (yr)]*weight (kg)]/ [72*serum Cr (mg/dL)] (multiply by 0.85 for women)**.**

TABLE 15: 2021 KNH guidelines Recommended doses and re-dosing intervals for commonly used antimicrobials for surgical prophylaxis.

Antimicrobial	Recommended doses		$T_{1/2}$ in adults with normal renal function	Recommended re-dosing interval(from initiation of preoperative dose)
	Adults	Pediatrics		
Ampicillin–sulbactam	3g (ampicillin 2g/sulbactam 1g)	50 mg/kg of the ampicillin component	0.8–1.3	2
Ampicillin	2g	50mg/kg	1–1.9	2
Aztreonam	2g	30 mg/kg	1.3–2.4	4
Cefazolin	2g, 3g for patients weighing ≥120kg	30 mg/kg	1.2–2.2	4
Cefuroxime	1.5g	50 mg/kg	1–2	4
Cefoxitin	2g	40 mg/kg	0.7–1.1	2
Cefotetan	2g	40 mg/kg	2.8–4.6	6
Ceftriaxone	2g	50–75 mg/kg	5.4–10.9	NA
Ciprofloxacin	400mg	10 mg/kg	3–7	NA
Clindamycin	900mg	10 mg/kg	2–4	6
Ertapenem	1g	15 mg/kg	3–5	NA
Fluconazole	400mg	6 mg/kg	30	NA
Gentamicin	5 mg/kg based on dosing weight (single dose)	2.5 mg/kg based on dosing weight	2–3	NA
Levofloxacin	500mg	10 mg/kg	6–8	NA
Metronidazole	500mg	15 mg/kg Neonates weighing <1200 g should receive a single 7.5-mg/kg dose	6–8	NA
Moxifloxacin	400mg	10 mg/kg	8–15	NA
Piperacillin-tazobactam	3.375g	Infants 2–9 mo: 80 mg/kg of the piperacillin component Children >9 mo and 100mg/kg of the piperacillin component	0.7–1.2	2
Vancomycin	15 mg/kg	15 mg/kg	4–8	NA

APPENDIX IV: DATA COLLECTION FORM

1. PATIENT BIODATA

Serial No.

Age ……. years ……. Months

Sex (male/female) ….....

2. PREOPERATIVE ASSESSMENT

THEMATIC UNIT (spine/trauma/foot and ankle/ pediatric/oncology/hand/arthroplasty or sports medicine): choose one

Diagnosis:

……

……

Type of surgery planned:

……

……

Comorbidities:

……. Hypertension ……HIV

……. Diabetes ……Rheumatoid arthritis

……. Asthma ….....Hypercholesteremia

……. kidney disease ….……. COPD

Others ……

Drug history –

Allergy to Antibiotics

……

……

……

History of smoking …… pack years

Alcohol intake …… units per day

ASA – score …….

3. IN THEATRE ASSESSMENT

3.1 CADRE OF HEALTH CARE PRESCRIBING ANTIBIOTICS

……. Anesthesiologist

……. Registered clinical officer

……. Registrar

……. Clinical officer in training

3.2 SURGICAL PROPHYLACTIC ANTIBIOTIC USAGE

Were any antibiotics prescribed for this patient? (Yes/no)

If yes

Antibiotic type	Dose	Duration
1.		
2.		
3.		

Time given before incision? ……. minutes

Tourniquet application? (Yes/no)

If yes then the time of antibiotic given before tourniquet application? .....minutes

Is this as per the guidelines of the hospital? Yes/no

If not appropriate as per guidelines, then ask the following questions to the prescriber

Are you aware of the guidelines for surgical antibiotic prophylactic antibiotic use? (Yes/no)

What are the factors that determine your choice of surgical antibiotic prophylaxis?

……
……
……
……

3.3 OPERATIVE DETAILS

Duration of operation ……HOURS …… MINUTES

Any intraoperative challenges?

……Contamination of instrument

……Multiple procedures

……Case complexity

Others

……
……
……

Estimated blood loss ……. MLS

Transfusion given?

Any intraoperative antibiotic used? If yes

The antibiotic used ……

Dosage …….

3.4 POST-OPERATIVE PERIOD

Are any antibiotics prescribed on the treatment sheet? (Yes/no)

Antibiotic type	Dose	Duration
1.		
2.		
3.		
4.		
5.		

The cadre of health personnel prescribing antibiotics

……Consultant orthopedic

……Resident orthopedics

……Medical officer

……Medical officer intern

Are you aware of the Kenyatta national guidelines on the use of surgical antibiotic prophylaxis? (Yes /no)

If yes then indication according to the prescriber for prolonged surgical antibiotic prophylactic use

……

……

……

……

APPENDIX V

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/135

28th March, 2023

Dr. Shabir Adamjee Najmudin
Reg.No.H58/11429/2018
Dept. of Orthopaedic Surgery
Faculty of Health Sciences
University of Nairobi

28 MAR 2023
KNH/UoN-ERC

Dear Dr. Najmudin,

RESEARCH PROPOSAL: PRACTICE OF PROPHYLACTIC USE IN ELECTIVE ORTHOPAEDIC PROCEDURES AT THE KENYATTA NATIONAL HOSPITAL (P897/12/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P897/12/2022.**The approval period is 28th March 2023 – 27th March 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Assistant Director, Health Information Dept., KNH
The Chairperson, KNH- UoN ERC
The Chair, Dept. of Orthopaedic Surgery, UoN
Supervisors: Dr. Fred Sitati Dept. of Orthopaedic Surgery, UoN
Dr. Edward Gakuya , Dept. of Orthopaedic Surgery, UoN

APPENDIX VI

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **206151**

Date of Issue: **29/April/2023**

RESEARCH LICENSE

This is to Certify that Dr.. SHABIR NAJMUDIN ADAMJEE of University of Nairobi, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Nairobi on the topic: PRACTICE OF PROPHYLACTIC ANTIBIOTIC USE IN ELECTIVE ORTHOPEDIC PROCEDURES AT THE KENYATTA NATIONAL HOSPITAL for the period ending : 29/April/2024.

License No: **NACOSTI/P/23/25409**

206151

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

See overleaf for conditions

THE SCIENCE, TECHNOLOGY AND INNOVATION ACT, 2013 (Rev. 2014)

Legal Notice No. 108: The Science, Technology and Innovation (Research Licensing) Regulations, 2014

The National Commission for Science, Technology and Innovation, hereafter referred to as the Commission, was the established under the Science, Technology and Innovation Act 2013 (Revised 2014) herein after referred to as the Act. The objective of the Commission shall be to regulate and assure quality in the science, technology and innovation sector and advise the Government in matters related thereto.

CONDITIONS OF THE RESEARCH LICENSE

1. The License is granted subject to provisions of the Constitution of Kenya, the Science, Technology and Innovation Act, and other relevant laws, policies and regulations. Accordingly, the licensee shall adhere to such procedures, standards, code of ethics and guidelines as may be prescribed by regulations made under the Act, or prescribed by provisions of International treaties of which Kenya is a signatory to
2. The research and its related activities as well as outcomes shall be beneficial to the country and shall not in any way;
    i. Endanger national security
    ii. Adversely affect the lives of Kenyans
    iii. Be in contravention of Kenya's international obligations including Biological Weapons Convention (BWC), Comprehensive Nuclear-Test-Ban Treaty Organization (CTBTO), Chemical, Biological, Radiological and Nuclear (CBRN).
    iv. Result in exploitation of intellectual property rights of communities in Kenya
    v. Adversely affect the environment
    vi. Adversely affect the rights of communities
    vii. Endanger public safety and national cohesion
    viii. Plagiarize someone else's work
3. The License is valid for the proposed research, location and specified period.
4. The license any rights thereunder are non-transferable
5. The Commission reserves the right to cancel the research at any time during the research period if in the opinion of the Commission the research is not implemented in conformity with the provisions of the Act or any other written law.
6. The Licensee shall inform the relevant County Director of Education, County Commissioner and County Governor before commencement of the research.
7. Excavation, filming, movement, and collection of specimens are subject to further necessary clearance from relevant Government Agencies.
8. The License does not give authority to transfer research materials.
9. The Commission may monitor and evaluate the licensed research project for the purpose of assessing and evaluating compliance with the conditions of the License.
10. The Licensee shall submit one hard copy, and upload a soft copy of their final report (thesis) onto a platform designated by the Commission within one year of completion of the research.
11. The Commission reserves the right to modify the conditions of the License including cancellation without prior notice.
12. Research, findings and information regarding research systems shall be stored or disseminated, utilized or applied in such a manner as may be prescribed by the Commission from time to time.
13. The Licensee shall disclose to the Commission, the relevant Institutional Scientific and Ethical Review Committee, and the relevant national agencies any inventions and discoveries that are of National strategic importance.
14. The Commission shall have powers to acquire from any person the right in, or to, any scientific innovation, invention or patent of strategic importance to the country.
15. Relevant Institutional Scientific and Ethical Review Committee shall monitor and evaluate the research periodically, and make a report of its findings to the Commission for necessary action.

National Commission for Science, Technology and Innovation(NACOSTI),
Off Waiyaki Way, Upper Kabete,
P. O. Box 30623 - 00100 Nairobi, KENYA
Telephone: 020 4007000, 0713788787, 0735404245
E-mail: dg@nacosti.go.ke
Website: www.nacosti.go.ke