SINGLE DOSE VERSUS EXTENDED DOSE ANTIBIOTICS IN PREVENTION OF SURGICAL SITE INFECTION IN ELECTIVE CAESAREAN SECTION AT A TERTIARY HOSPITAL IN KISUMU-KENYA:

A RANDOMIZED CONTROLLED TRIAL

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS AND GYNECOLOGY

SCHOOL OF MEDICINE

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DECLARATION

This thesis is my original work and has not been presented for the award of any other degree or to any other University.

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ACKNOWLEDGMENT

I would wish to thank my supervisors Dr. Kays Muruka and Dr. Walter Otieno alongside Dr. Maricianah Onono for their guidance from proposal conceptualization and development of the proposal, during the entire period of data collection and in the final thesis write-up.

I would also wish to thank my colleagues in the Department of Reproductive Health, Jaramogi Oginga Odinga Teaching and Referral Hospital and Dr. Neto Oballa for their input towards the development of this thesis.

DEDICATION

This study is dedicated to all Obstetricians and Gynaecologists who work during the day and night to ensure safety of women giving birth via caesarean section.

ABSTRACT

When compared to other surgical procedures overall, Caesarean section (CS) accounts for the most recorded cases of surgical site infection (SSI). Following CS, antibiotic prophylaxis usage has been proven to lower incidence of SSI in both high risk and low risk individuals. However, it is not obvious if either single dose (SD) or extended dose (ED) antibiotic prophylaxis make much difference in SSI prevention despite previous research emphasizing the importance of antibiotic prophylaxis in surgical procedures The main objective of this study was to compare the effectiveness of SD, and ED antibiotics in elective CS in prevention of SSI. This was an open label randomized control study carried out in 9 months period beginning March 2022 to December 2022 at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH). 150 consenting patients were randomly distributed into control and intervention arms. Subjects in booth groups received intravenous (IV) ceftriaxone one gram 30 minutes before operation; subjects in control arm received additional IV ceftriaxone and metronidazole for 48 hours then amoxicillin 500mg every 8 hours and metronidazole 500mg tablets for 5 days. The participants were followed up for evidence of SSIs for 4 weeks. Data was collected and recorded into an abstraction form during the period of follow up by the investigator and research assistant. The completed forms were received, checked for completeness, and keyed into the computer. The data was analyzed using Statistical Package for Social Sciences (SPSS) Version 25. Rate of SSI was assessed and compared across study arms. Patients 'factors associated with infection rate were analyzed at bivariate levels using Chi square and Fisher's exact test. Multivariate logistic regression test was further done to determine factors associated with SSI. All covariates with p-value <=0.05 at bivariate analysis were included in multivariate logistic regression with 95% confidence intervals were reported. Out of the 75 on SD arm, 2 (2.6%) developed SSI, whereas of the 75 on ED arm, 1 (1.3%) developed SSI. Patient factors such as age, income status, parity, level of education, indication for CS, type of incision, amount of blood loss, random blood sugar level prior to operation, white blood cell level, type of anesthesia did not have significant influence in development of SSI in both the trial arms during the twenty-eight days of follow up. The findings showed that there was no statistically significant difference in occurrence of post elective caesarian SSI between the SD and ED groups with a p value of 0.567 at 1 degree of freedom (df) with a 95% confidence interval (CI) of 0.533044 – 5.559 with relative risk (RR) of 0.493. In conclusion, SD prophylaxis is equally effective as ED prophylaxis in prevention of SSI in elective CS. This study recommends that in the absence of evidence of SSI, there is no justification for ED of antibiotics as SD is sufficient.

TABLE OF CONTENTS

ABBREVIATIONS

ACOG	American College of Obstetrics and Gynecology
AMR	Antimicrobial resistance.
ASA	American Society of Anesthesiologists.
BMI	Body Mass Index
CD	Caesarean Delivery.
CDC	Centers for Disease Control and Prevention.
CS	Caesarean Section
HAIs	Health Care-Associated Infections.
ID	Identification.
IV	Intravenous.
JOOTRH	Jaramogi Oginga Odinga Teaching and Referral Hospital.
MRSA	Methicillin-resistant S. aureus
MUERC	Maseno University Ethical Review Committee.
NICE	National Institute for Health and Care Excellence.
OPD	Outpatient department
OR	Relative risk
NNIS	National Nosocomial Infections Surveillance.
RCT	Randomized Controlled Trial
SSI	Surgical Site infection.
WHO	World Health Organization.
HCUP NIS	Healthcare Cost and Utilization Project National Inpatient Sample
SD	Single dose
ED	Extended dose

OPERATION DEFINATION OF TERMS

Caesarean Section - Defines the birth of a foetus via laparotomy and then hysterotomy.

Elective Caesarean Section –Refers to planned caesarean section due to prior existing obstetric indication.

Endometritis -Endometritis is inflammation of the endometrial lining of the uterus characterized by the presence of marked uterine tenderness and or malodorous discharge and fever.

Extended Antibiotics Dose - Refers to prophylactic administration of ceftriaxone before skin incision and further administration of ceftriaxone and metronidazole doses till day two before discharge. This is followed by a five-day course of oral amoxicillin and metronidazole.

Single Antibiotic Dose – Refers to prophylactic administration of one dose of Ceftriaxone before skin incision with no administration of additional doses of antibiotics to the patient.

Febrile morbidity was defined as the presence of a temperature higher than or equal to 38°C on two occasions at least 4 hours apart during the postoperative period, excluding the first 24 hours after surgery.

Fever - the temporary increase in the body's temperature in response to a disease or illness. that exceeds 38°C.

Prophylactic Antibiotics- Preoperative antibiotic prophylaxis defined as administering antibiotics prior to performing surgery to help decrease the risk of postoperative infections.

Surgical Site Infection - A surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place within the first twenty-eight (28) days.

Symphysis-fundal height - It is the distance from the pubic bone to the top of the uterus.

Urinary tract infection - defined as positive urine culture, with or without dysuria and fever.

Wound Infection- Presence of local induration and tenderness associated with purulent discharge from the wound.

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

One of the main challenges for the surgeon in sub-Saharan Africa is the high risk of SSI. In two recent WHO-led review papers, the risk of SSI in developing countries was strikingly higher than in equivalent surgical procedures in high-income countries and the problem was found to be particularly acute in sub-Saharan Africa (Aiken et al., 2012)**.** In Kenya , Surgical site infection is a significant contributor to maternal morbidity and is among the leading cause of maternal deaths (Dare, 2019).

Recent research comparing the rates of surgical site infections (SSIs) among surgical procedures revealed that caesarean deliveries have higher rates of SSIs than other surgical procedures by 9%, which calls for a reconsideration of infection control in this patient population (Lijaemiro et al., 2020) **.**

Despite being a life-saving procedure, CS is , with a 20-fold increase in frequency, the most important risk factor SSI and the best predictor of puerperal sepsis (Conroy et al., 2012) .As one of the frequent procedures in hospitals around the world, CS averages about 22.9 million operations annually (Aulakh et al., 2018). SSIs are seen in between 1.2% and 5.2% of CS in industrialized nations and between 2.5% and 30.9% in low-income nations, despite being one of the most avoidable consequences of surgery (Aulakh et al., 2018)**.** Risk factors for SSI include obesity, smoking, blood transfusion, age, malnutrition, immune incompetence, immunosuppressive therapy, longer pre-operative hospitalization, and diabetes mellitus. Factors specifically related to C-sections include lack of prenatal care, multiple pregnancies, history of

previous C- section, chorioamnionitis, pre-labor rupture of the fetal membranes, labor dystocia, emergency/labored delivery, and obstetrical service performed in the teaching hospitals (Zejnullahu et al., 2019).

The most common strategy used internationally to reduce morbidity due to SSI is antibiotic prophylaxis preferably by cephalosporins (Pooja et al., 2021). In actual practice, antibiotics are mostly used inappropriately for procedures deemed to pose risk of infection. This misuse of antibiotics impacts efforts made worldwide to stop the spread of bacterial resistance to antibiotics. The WHO strategy for antibiotic resistance containment highlights the importance of effective use of antibiotics at all levels of the health system to reduce the effects of resistance while ensuring access to the best treatment feasible (Alemkere, 2018). Prophylactic antibiotics reduce SSIs but injudicious use increases resistance (Nitrushwa et al., 2019).

Appropriate use of antibiotics minimizes sepsis, reduces healthcare costs, saves nursing time, and minimizes antibiotic drug resistance (Pooja et al., 2021). Instead of sterilizing tissues, antibiotic prophylaxis is used during surgery to lower the colonization pressures of bacteria introduced during surgery to a level that the patient 's immune system can handle (Mugisa et al., 2018).

Following CS, antibiotic prophylaxis has been proven to lower incidence of SSI in both high risk and low risk individuals. It is not obvious if either SD or ED antibiotic prophylaxis make much difference in SSI prevention despite previous research emphasizing the importance of antibiotic prophylaxis in surgical procedures (Pinto-Lopes et al., 2017).

Previous research on current use of antibiotic prophylaxis for CS demonstrate that ED of antibiotics minimize infectious morbidity post CS and this has created a split within the present

practice despite evidence suggesting that SD is just as beneficial as extended regimen.(Lamont et al., 2011)**.**

Even though there exist recommendation by clinical guidelines and there is enough literature proving the efficacy of SD of antibiotic prophylaxis being as effective as prolonged use of combination of antibiotics, it is not universally accepted and adopted amongst surgeons especially in CS (Pooja et al., 2021).

Concerns about adverse effects of antibiotics and rising cases of antibiotic resistance worldwide has led to the increased scrutiny on the use of antibiotics especially in hospital setting and the introduction of antibiotic surveillance in some facilities (Pinto-Lopes et al., 2017)**.**

In Kenya , a previous research in 2014 noted the tendency of over-prescription of antibiotics especially in patients who have undergone surgery is a concern and the need to regulate antibiotic prescriptions is raised (Charles, 2014)**.** In 2018 a survey found that sixty seven percent of all patients who were treated in JOOTRH in 2018 were found to be on antibiotics further pointing to the high rate of antibiotics use in the facility (Okoth et al., 2018).

1.2 Statement of problem

Antibiotics are an essential component of modern medicine and, as such, the cornerstone of bacterial infection prevention and treatment in the healthcare sector. The selection, timing and duration of antibiotics have been demonstrated to vary widely in previous investigations on antibiotic prophylaxis. Factors including variance in published recommendations, the dearth of acceptance of the standards among surgeons and lack of accessibility of guidelines by health care workers have all contributed to this variation in practice across different settings.

The necessity to avoid SSIs should not be viewed as a reason to order antibiotics indiscriminately, as this is also hazardous as antibiotics misuse leads to antibiotic resistance. Concerns about antibiotic use in JOOTRH especially among patients undergoing surgical treatments, include misuse, rising resistance rates, increased morbidity, mortality, and rising cost of treatment. There is inadequate data to ascertain whether ED regimens or SD regimens are more effective at lowering the incidence of SSIs following elective CS in JOOTRH and Western Kenya region at large. This gap in knowledge and varied practice in antibiotic use pose a challenge at a time where antibiotic resistance is on the rise worldwide.

1.3 Hypotheses

Ho_1: There was no statistically significant influence of patient factors on SSI between SD, and ED antibiotic used as a prophylaxis among women undergoing elective CS.

Ho_2: There was no significant difference in occurrence of SSI between SD, and ED used as a prophylaxis among women undergoing elective CS.

1.4 Objectives of the study

1.4.1 BROAD OBJECTIVE

To assess the effectiveness of single versus ED antibiotics in elective CS in prevention of surgical site infection at a tertiary hospital Kisumu- western Kenya.

1.4.2 Specific objective

1. To determine patient factors associated with SSI when using SD, and ED antibiotics as prophylaxis among women undergoing CS section at a tertiary hospital in Kisumu.

2. To compare the occurrence of SSI when using SD, and ED antibiotics as prophylaxis among women undergoing elective CS at a tertiary hospital in Kisumu

1.5 Justification of the study

Previous studies show that ED of antibiotics minimize infection post CS despite evidence that SD is just as effective and this has posed an equipoise in the current practice(Lamont et al., 2011)**.** There is no national consensus on antibiotic use in elective CS from the Ministry of Health (MOH) and every institution is expected to have its own antibiotic protocol. Both SD and ED regimens are employed at JOOTRH with great interpersonal variability.

Concerns about adverse effects of antibiotics alongside rising cases of antibiotic resistance worldwide has caused antibiotic use to be more closely monitored especially in hospital settings and antibiotic surveillance to be initiated in some hospitals **(**MacHowska et al., 2020; Pinto-Lopes et al., 2017)**.** The results of this study will be used by clinicians to formulate policies on the use of SD antibiotics in elective CS.

1.6 Significance of the study

Rational use of antibiotics not only provides an opportunity to reduce widespread antibiotic resistance that is currently a global threat to the existing antibiotics but also will reduce the cost of surgical procedures. This study provided data to support whether SD antibiotic use is effective in preventing SSI compared to ED antibiotics in elective CS. The results will be used to influence policy formulation on SSI prevention both at the hospital level, county, and nation level. The data can also be used for audit purposes whether there is rational use of antibiotics among women undergoing elective CS.

CHAPTER TWO

LITERATURE REVIEW

2.1 History of surgical site infection post caesarean delivery

Surgical procedures were routinely associated with SSIs until the1860s, when Joseph Lister prop osed antisepsis protocol, which reduced sepsis and death from 50% to 15%. (Lamont et al., 2011).

2.2 Caesarean section

Cesarean delivery is defined as operative procedure used to extract the fetus through incisions on the abdominal wall and uterus. Elective Cesarean delivery is the planned extraction of a fetus that is performed before the onset of labor or before the appearance of any indication that might constitute urgent indication (Sung et al.,2022).

Indications for elective CS include; repeat cesarean section, pathologies likely to cause obstruction of the lower genital tract, obstructive Condyloma, vaginal septa, and fibroids , pelvic abnormalities and breech presentation (Hannah et al., 2000)**.** Due to its consistently rising numbers in both developed and developing countries, CS is one of the most performed surgery globally in recent decades (Nitrushwa et al., 2019).

2.3 Antibiotics use in Caesarean Delivery

Wound infection occurs in 1.4 percent of patients who receive antibiotics prophylaxis within 3 hours of skin incision after elective surgery, compared to 0.6 percent of patients who get it within 2 hours of skin incision. Antibiotic prophylaxis given within sixty minutes of skin incision is more effective in reducing sepsis when compared to administration of the same drugs after cord clamping and has no effect on maternal and neonatal infection (Rubin et al., 2021) .

Prophylactic antibiotics reduce the incidence of SSI especially when used before incision for either elective or emergency CS by two thirds to three quarters respectively (Allegranzi et al., 2011).

In surgical procedures, the goal of antibiotic prophylaxis is not to sterilize tissues but rather to lo wer the colonization pressure of microorganisms introduced during surgery to a level that the patient's immune system can overcome (Peitsidis, 2012).

Rational use of prophylactic antibiotics prevents post-operative infections, reduces costs, saves nursing time, and development of antibiotic drug resistance. SD pre-operative antibiotic prophylaxis has been demonstrated to be as effective as multiple antibiotic treatments in prevention of post-operative infections (van Buul et al., 2012).

SD reduces cost of treatment , doesn't overburden nurses and increases on availability of supplies to use in low income settings without exposing patients who have undergone elective CS to a risk of surgical site infection (van Buul et al., 2012).

In a systematic review and metanalysis in 2017 comparing single versus multiple dose antibiotic prophylaxis there was inconclusive evidence to ascertain if there is a difference between single and multiple dose regimens in reducing the incidence SSI after CS The quality of evidence was very low and well-designed RCTs are needed (Pinto-Lopes et al., 2017).

Inappropriate antibiotic selection, prolonged prophylactic antibiotic use, and timing of delivery may result in complications, raise therapy costs, and promote bacterial strain resistance (MacHowska et al., 2020) .

2.4 Antibiotic Use in Kenya and JOOTRH

In a point prevalence survey of antibiotic use at JOOTRH in 2018 , findings revealed that sixty seven percent of patients received antibiotics in both outpatient and in patient visits (Okoth et al., 2018).

While antibiotic dosing appeared to be acceptable in JOOTRH, this institution has no available antibiotic protocol and antibiotic use was found to be high in surgical cases. This has necessitated the need for educational intervention to encourage rational use of antibiotics (Charles, 2014; Okoth et al., 2018).

2.5 Risk factors and Burden of SSIs

Despite the introduction of World Health Organization (WHO) surgical checklist in a bid to improve surgical outcomes, rate of surgical site infection has only decreased by 50 %. among surgical patients. SSI accounts for 36% of nosocomial infections. SSIs are associated with significant morbidity, mortality, and increased costs in health care. SSIs significantly increase the postoperative length of the hospital stay, hospital charges, and risk of death(World Alliance for patient safety, 2008). A study in United States of America in 2009 analyzing the incidence and impact of SSIs on hospital utilization and treatment found that SSIs extended the length of stay by 9.7 days, while increasing costs by $20.842 per admission (Lissovoy et al., 2009).

There are factors associated with an increased risk of SSI among women who have CS and they include emergency cesarean section, prolonged labor , prolonged ruptured membranes, frequent vaginal examinations during labor and internal fetal monitoring, urinary tract infection, low hemoglobin , obesity, uncontrolled sugar levels, unskilled operator and lack of operative technique, prolonged duration of surgery and type of incision (Liabsuetrakul et al., 2002).

The epidemiology of SSIs is complicated by the heterogeneous nature of these infections and varies widely between surgeons, patients, hospitals, procedures, and methods of surveillance. Large (> 500 beds) teaching hospitals have the highest risk for SSIs, followed by small teaching hospitals (< 500 beds), followed by nonteaching hospitals, which have the lowest rates (8.2 vs. 6.4 vs. 4.6%) (Poggio, 2013)**.**

2.6 Common causes of SSIs

Table 2.1: Common causative agents of SSIs (Singhal, 2023)

Pathogen	**Percentage Of Infection**
Staphylococcus aureus	20
Coagulase-negative staphylococci	14
Enterococci	12
Pseudomonas aeruginosa	8
Escherichia coli	8
Enterobacter species	7
Proteus mirabilis	3
Klebsiella pneumoniae	3
Streptococci	3
Candida albicans	2

2.7 Classification of SSIs and surgical wounds

According to the Center for Disease Control, SSI is categorized into three different types namely:

1. Superficial infection involves only the skin and subcutaneous tissue.
2. Deep infection penetrates deep tissue, such as facial and layer of muscles.
3. Organ/space infection involve any organ or space other than the incision site (Aulakh et al., 2018)

Infectious complications following cesarean delivery include fever, wound infection, endometritis, bacteremia, other serious infection (including pelvic abscess, septic shock, necrotizing fasciitis and

septic pelvic vein thrombophlebitis) and urinary tract infections (Liabsuetrakul et al., 2002)**.** The patients who develop SSIs have 2-11 times greater risk of death as compared to the patients having no SSI (Birhanu et al., 2022).

A greater challenge has been faced by the surgeons while handling SSI especially selection of appropriate antibiotics. This challenge is evidenced by increasing drug resistance as reported in several literatures such as in the journal of antimicrobial resistance (Llor & Bjerrum, 2014).

2.8 Conceptual Framework

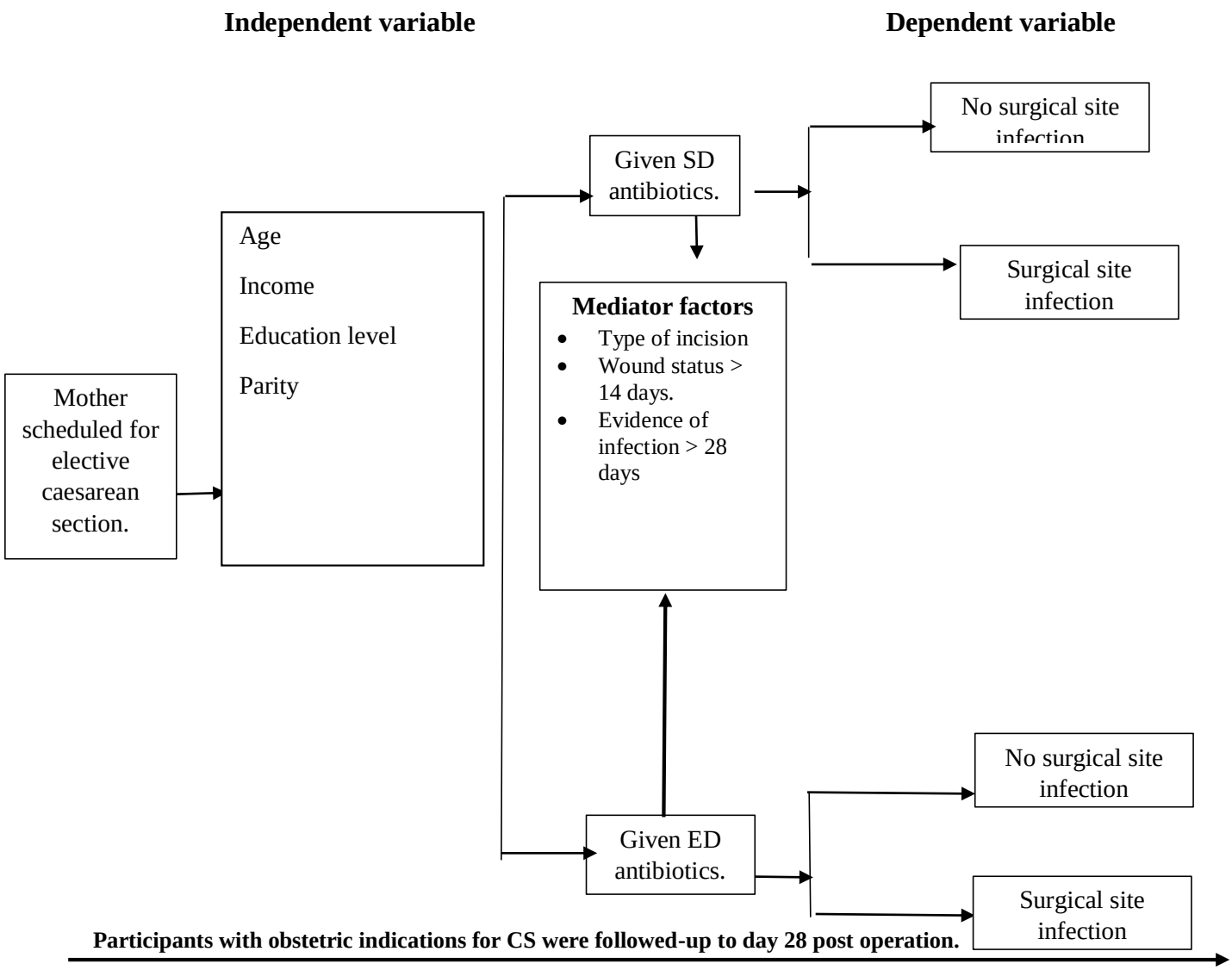

Figure 2.1: Conceptual framework of the study

CHAPTER THREE

METHODOLOGY

3.1 Overview

This was an open label randomized control study to compare effectiveness of SD, and ED antibiotic prophylaxis in prevention of SSIs in elective CS.

3.2 Study Design

This was an open label randomized control trial conducted at JOOTRH in Kisumu County. Eligible participants were randomized in a 1:1 fashion to SD prophylactic antibiotic (intervention) or ED prophylactic antibiotics (control) after elective CS. This study was not pegged on to a bigger clinical trial and has provided data to inform the need for a bigger study covering a bigger region. The aim to treat model was applied in the study and the researcher was a licensed and practicing medical practitioner. This study was prospective in nature since patients were enrolled before surgery was carried out.

It was not practical to blind the study since the patients needed to be aware of what they were receiving, and nurses needed to know what medication they were administering. The data collected was quantitative in nature and was filled in standardized forms.

3.3 Study site

The study was conducted at JOOTRH in Kisumu City, Kisumu County. Kisumu County is in the western part of Kenya near Lake Victoria. It borders Kericho County on the eastern side and Vihiga County to the north (see appendix I). It covers an area of approximately 2,085 square kilometers. It comprises 7 constituencies, Nyakach, Kisumu Town East, Muhoroni, Seme, Nyando Kisumu

Town West and Kisumu Central. Economic activities in Kisumu involves fishing, farming sugar, farming rice and trading. Kisumu County hosts Kisumu City, which is the third largest City in Kenya and has a population of approximately 1,155,574 (national census 2019).

This study was done at the Department of Obstetrics and Gynaecology in JOOTRH. JOOTRH is located about 2 kilometers from the Kisumu City Center. JOOTRH serves as the main referral Hospital to County, Sub-County and Private Hospitals in more than 10 counties in the Western Kenya Region with a population of more than 5 million. Medical records indicated that approximately 5000 deliveries are conducted within the hospital every year with about 24% being through CS over the last 3 years. The number of elective CS averages six every week. JOOTRH, also being a public health facility, serves clients from both low and middle socio-economic status and this diversity was necessary to make objective analysis on matters related to determinants of postpartum complications. JOOTRH has an outpatient department, maternity (Ante natal care, post-natal care) and gynecology departments all receiving female patients. The main mandate of JOOTRH is to provide curative, preventive, promotive and rehabilitative health services. It offers specialized clinical services in various disciplines. It serves as a center for research activities, training for medical students and health workers. The hospital has a total of 880 staff: consisting of 492 regular staff, 107 from partners, 140 casuals/contract, 141 outsourced services (JOOTRH, 2016).

This study was carried out at JOOTRH because: unlike other regional referral hospitals like Kenyatta National Hospital and Moi Teaching and Referral Hospital, JOOTRH has no existing antibiotic protocol guiding surgical procedures , it has 600 bed capacity making it fall among facilities with projected higher rates of SSIs based on the bed capacity(Poggio, 2013).Approximately 300 CS (emergency and elective) are carried out quarter yearly. Overall

antibiotic use in surgical patients is high in JOOTRH according to previous study carried out in the hospital (Okoth et al., 2018).

3.4 Target Population / Study Population

The target population included women seeking to deliver at JOOTRH.

The study population comprised of women aged 18 – 49 years admitted for elective CS at the facility during the period between March 2022 to December 2022 and were willing to take part in the study.

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion Criteria

- Women aged 18 and above.
- Women admitted at JOOTRH for elective CS.
- Indication for elective CS at term.
- Patients who consented to participate in the study.

3.5.2 Exclusion Criteria

- Recent antibiotic use within two weeks
- Immunosuppressive condition / therapy.
- Allergy to Ceftriaxone (antibiotic prophylaxis)
- Indication for emergency CS.
- Signs and symptoms of active systemic infection.

3.6 Sample Size determination

Sample size was calculated using a formula derived from the article of Sample Size and Power determination from Boston University School of Public Health indicated in the link below.

https://sphweb.bumc.bu.edu/otlt/mph-modules/bs/bs704_power/bs704_power_print.html (Lisa Sullivan, 2018)

The study hypothesized that SD prophylactic antibiotic use is as effective as extended prophylactic antibiotic course in SSI prevention. Patients admitted for elective CS at the facility were randomly assigned to the intervention or control arm of the study.

The test of the hypothesis was conducted to compare patients in the SD arm , with those in ED arm. Previous research in Tanzania showed that surgical site infection rate without antibiotic prophylaxis was about 25% (Mawalla et al., 2011). This study postulated that 15% decrease in surgical site infection among those on single and extended antibiotic would have been clinically meaningful.

Thus, this study sought to detect this difference in infection rate by calculating a sample size to ensure that the power of the test is 80% using a two-sided test and a 5% level of significance.

It first computed the effect size by substituting the proportions of patients in each study arm who were expected to develop infection:

P_1=0.21 (i.e., 0.25 X 0.85=0.2125) and P_2=0.25

Overall proportion, p=0.23 (i.e., (0.21+0.25)/2)

$$\text{Effect size (ES)} = \frac{|P1-P2|}{\text{SQR}(P(1-P))} = \frac{0.02}{0.421} = 0.047506$$

Therefore, the study sample size was.

$$\text{Sample size (SS)} = 2 * \left(\frac{Z1-\beta + Z_{\frac{\alpha}{2}}}{ES}\right)\text{^}2 = \frac{1.96+0.84}{0.047506} = 58.9$$

Factoring in 20% attrition & refusal rate

$$\text{Minimum sample size required for each arm} = \frac{58.94}{(1-(\frac{20}{100}))} = 75$$

Total number of participants recruited = 75 X 2 =150

3.7 Sampling techniques

3.7.1 Randomization

Simple randomization was used to allocate study participants. A total of 150 opaque envelopes of the same size were prepared for this study; 75 envelopes containing papers marked "Intervention," and the remaining envelopes containing papers marked "control." Before picking, all envelopes were thoroughly mixed in a box to allow equal chance of random selection and eliminate selection bias. Each study participant selected one sealed envelope and then gave it to the research assistant to open.

SD antibiotic prophylaxis was prescribed to the intervention arm, this comprised of ceftriaxone 2 grams given intravenously 15-45 min before skin incision. The anesthetist as part of preoperative surgical checklist before incision gave the prophylactic antibiotic. Ceftriaxone 2 grams was given in 500mls of normal saline as a slow infusion during preloading with fluids before anesthesia is administered.

Postoperative monitoring in the wards for any signs and symptoms of surgical site infection was done before discharge on the third post-operative day. This group was reviewed after 2 weeks in the outpatient clinic and were assessed for any signs of surgical site infection.

In the control group, once 2 grams of Ceftriaxone was given by the anesthetist, the participants received an additional 2 days of Ceftriaxone 2gm once a day and Metronidazole 500mg three times a day in the ward by nurses. Finally, oral amoxicillin 500 milligrams three times a day and metronidazole 500mg three times a day to complete 7 days at home were given. The participants were reviewed after 2 weeks in the outpatient clinic and assessed for signs of surgical site infection.

All participants regardless of randomization allocation were monitored in the postnatal ward on each of the two postoperative days and assessed for signs and symptoms of infection using a standardized tool. Their temperature was taken using non- contact infrared thermometer to avoid unnecessary contact with skin surface.

Blood pressures were taken using Omron digital blood pressure machine (available in the wards) rather than manual blood pressure measurement to avoid user bias.

Pulse and blood oxygen saturation were measured using EDAN digital machine to avoid provider bias in counting the pulse.

In both groups, the bladder catheter was removed after 12 hours from the time start of surgery. The occlusive dressing applied in theatre was removed after 48 hours and the wound left open. All participants were followed up on day 14 and day 28 after CS and wound examined for any signs of SSI.

3.8 Recruitment

3.8.1 Strategies for recruitment

This was an interventional, open label, two-armed, randomized, single-center, equivalence study conducted at JOOTRH, Kisumu County, Kenya.

From the hospital records, in the year 2021, 6012 women were admitted to the maternity unit and 4200 deliveries were conducted. Of these deliveries, 1040 are caesarean deliveries. The target population is women admitted at JOOTRH caesarean delivery. The patients for elective cesarean section were booked from the antenatal clinic a day prior to operation. Eligible patients were recruited into the study before surgery after they were admitted in the wards once they consented (Figure 3.1).

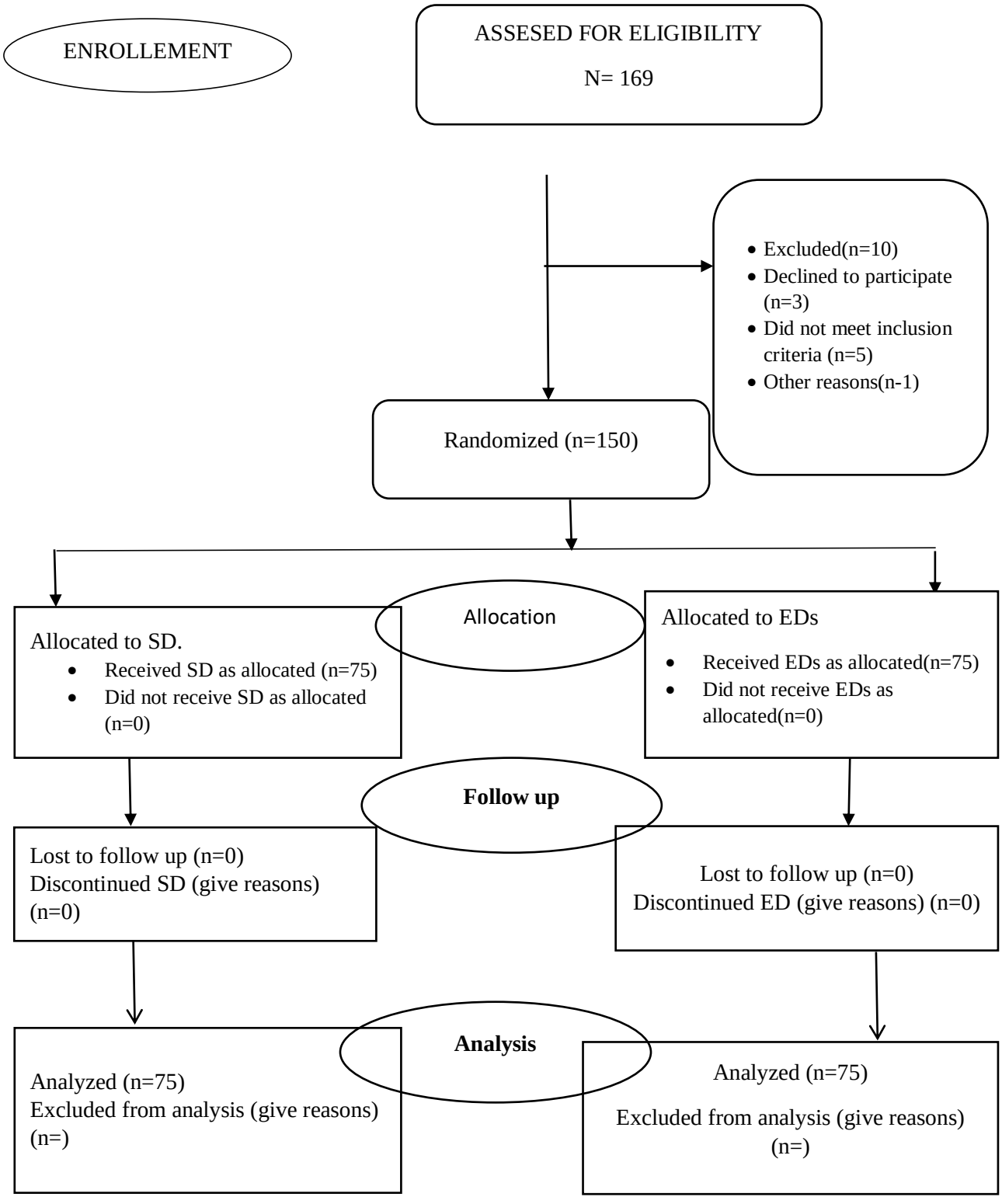

Figure 3.1: Recruitment strategy borrowed from Igwemadu (2018)

3.9 Data collection technique and instrument

Data was collected by a research assistant who was trained. Initial data was collected and recorded abstraction form during admission for elective CS by the investigator and research assistant.

The investigator and the research assistant checked on administration of antibiotics as per randomization up to the time of discharge of participants. The participant's examination findings including vital signs, and surgical site state were documented in the abstraction form at the time of discharge and at two weeks postpartum during a physical review visit at the hospital. A follow up phone call was made at day 28 postpartum to enquire about the surgical site.

Pulse and oxygen saturation levels were obtained uniformly from an EDAN digital machine while in the wards prior to discharge and at two weeks postpartum. Blood pressure was measured using Omron digital blood pressure monitoring machine from the left upper arm while in the wards prior to discharge and at two weeks postpartum. Temperature was measured using non-contact infrared thermometer at the forehead while in the wards before discharge and at 14 days' post-partum.

CDC criteria was used to diagnose surgical site infection i.e.

Patient who had at least one of the following:

a) Purulent drainage from the superficial incision
b) Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
c) At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, and superficial incision is deliberately opened by surgeon and culture positive or not cultured.
d) Diagnosis of superficial incision SSI by the surgeon or attending physician.

3.10 Pre-testing of data collection tools for Validity and Reliability

Pre-testing of abstraction form was carried out at Kisumu County hospital three weeks before the actual data collection began.

To establish the number to be pretested, Conrad and Blair equation was employed to compute the power to detect a problem in at least one interview and a prevalence of the problem *p*.(Perneger et al., 2015).

$$n = \frac{\ln(1 - \text{Power})}{\ln(1 - p)}$$

With the Power of 90% and a prevalence of SSIs being at 15 % of all CS, and expected occurrence >1, the pretesting sample size was 15 from the table derived from Conrad and Blair equation.

Table 2 Required sample size to detect with high probability (80 or 90 %) a problem with a questionnaire, by problem prevalence, for at least one or two occurrences of the problem in the sample

Prevalence	Power >80 %		Power >90 %	
	≥1 occurrence	≥2 occurrences	≥1 occurrence	≥2 occurrences
0.01	161	299	230	388
0.02	80	149	114	194
0.03	53	99	76	129
0.04	40	74	57	96
0.05	32	59	45	77
0.06	27	49	38	64
0.07	23	42	32	55
0.08	20	37	28	48
0.09	18	33	25	42
0.10	16	29	22	38
0.11	14	27	20	34
0.12	13	24	19	31
0.13	12	23	17	29
0.14	11	21	16	27
0.15	10	19	15	25
0.20	8	14	11	18
0.25	6	11	9	15
0.30	5	9	7	12

During pretesting of the abstraction form, a sample of sixteen (16) eligible women were randomized to balance for both controls and intervention groups to get equal presentation during pretesting. The pretesting procedure was carried out in a two-week period in a similar manner to the research process. These participants were not part of the study thereafter. During pretesting, the researcher evaluated the explicitness and analyzability of the research questions and terminology deemed difficult were simplified.

3.11 Quality assurance and Quality control

In terms of quality assurance, the study adhered to the WHO surgical safety check list (World Health Organization, 2009). All participants were assigned a non-identifiable study ID number upon enrolment. All data records were identified by study ID only. The link between identifiable participant information and study IDs was locked in a secure location.

3.12 Data management and analysis

The completed abstraction form was received, checked for completeness, and entered into the computer. The data was analyzed using Statistical Package for Social Sciences (SPSS) Version 25. The study summarized the categorical variables using frequency counts and percentages. For the socio-demographic variables, analysis by the outcome of interest was whether there was an infection. Chi-square test of independence was used to assess the association categories of explanatory variables and the infection, frequencies and percentages were reported for each factor.

The surgical site infection rate was assessed and compared across study arms. Patients 'factors associated with infection rate were analyzed at bivariate levels using Chi square test. Multivariate logistic regression test was further done to determine factors associated with SSI.

All covariates with p-value <=0.05 at bivariate analysis were included in multivariate logistic regression. Relative risk (RR) with 95% confidence intervals were reported. All estimates were reported at a 95% confidence interval, and all the comparisons done at 5% level of significance.

3.13 Initial Screening Procedures

3.13.1 INFORMED CONSENT

The consenting process was done at the point of admission at the ward one to two days prior to elective CS. Informed consent to participate in the study and for the elective CS were taken by the researcher and research assistant in the ward. The consent included purpose of the research, the process of participant selection, and duration of the study, risks, and benefits of the study. The consent form highlighted to the patients their rights to refuse to participate in the study and that their confidentiality was safeguarded.

3.13.2 Consenting process

The consenting process included the following:

Introduction; stated the researcher's name and the title of the study being undertaken. It informed the participants that their sociodemographic characteristics, clinical characteristics, and laboratory results were accessed during the study.

Purpose of the research: The purpose was explained to the participants as one that aimed to assess the ceftriaxone use in prevention of surgical site infection when administered as a single prophylaxis dose versus when used as an ED. The findings of this study would help formulate antibiotic protocol to be used for patients undergoing elective CS at JOOTRH.

Participant Selection: This study involved expectant women admitted to JOOTRH with indication for elective CS.

Duration of the study: It was explained to the participants how long they were expected to be part of the study. During follow up, the participants were informed that they would be reviewed after surgery on days three, day fourteen and day twenty-eight. This study took place from the time of admission for elective CS and subsequent enrollment to 28 days after operation.

Risks and benefits: The possible risks and benefits that may have been encountered by the participants were explained to the participants in an open manner. The participants benefited from close follow and immediate intervention in case of SSIs. The results of this study would be used to formulate a protocol on antibiotic use in CS.

Minimal risks of infection were anticipated and the close follow up during the study duration enabled me to pick any potential signs of infection and appropriate treatment was given immediately.

Right to refusal: Participants were explained to about their right to decline to participate in the study. They were accorded the best available care in the hospital regardless of their choice.

Remuneration: The researcher explained to the participants that no monetary gains would be achieved during their participation in the research and that their participation was purely voluntary.

Confidentiality: Each participant was accorded a unique identifier number that was under custody of the researcher who kept their information under lock and key. This safeguarded the participants' confidential information**.**

Certificate of consent: After ascertaining that the participants had fully understood all that the study entailed, they were given time to ask questions and their concerns responded to satisfactorily before they were allowed to sign the consent form voluntarily.

3.13.3 Determination of study eligibility following screening

All women who were scheduled for elective CS and had consented for the study were eligible for inclusion.

3.13.4 Enrolment

Those who were recruited picked an opaque sealed envelope from a concealed box and open it under the direct supervision of a research assistant just before surgery. Each participant was enrolled to the arm of the study indicated on the card in the envelope she had picked. This eliminated provider bias.

3.14 Randomization

Simple randomization was used to allocate study participants. A total of 150 sealed envelopes were prepared for this study; 75 envelopes containing papers marked "Intervention," and the remaining envelopes containing papers marked "control." Before picking, all envelopes were mixed in a box to allow equal chance of random selection and eliminate selection bias. Each study participant selected one sealed envelope and then opened it in the presence of the research assistant just before the operation.

3.15 Intervention

Intervention started after eligible participants were divided into two study arms namely, Intervention and Control. Intervention arm included those who received a single intravenous dose of ceftriaxone (2g) 30 to 60 minutes before operation, and control arm included those who received multiple doses of ceftriaxone (2g) both 30 to 60 minutes before operation and additional doses for 48 hours after surgery.

CDC criteria was used to diagnose surgical site infection i.e.

Patient has at least one of the following:

e) Purulent drainage from the superficial incision.
f) An organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
g) At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, and superficial incision is deliberately opened by surgeon and is culture positive or not cultured.
h) Diagnosis of superficial incisional SSI by the surgeon or attending physician.

3.16 Follow-up timeline

All participants were reviewed on day three before discharge, and day 14 at the postnatal outpatient clinic as per JOOTRH protocol. They were further followed up on day 28 via a phone call to ask for any signs and symptoms that may suggest surgical site infection. Patients of concern on day 28 after the phone call were reviewed physically in the hospital as part of outpatient visit before exiting the study.

Otherwise, well healed participants were exited from the study on day 28.

Follow-up procedures: In each visit temperature, pulse, inspection of incision site and serial fundal heights measurement were recorded in a tool.

Patient's records were checked if pus swab for microscopy, culture and sensitivity was taken from wounds with surgical site infection for both groups and in case antibiotic change was instituted.

3.17 Ethical Considerations

Approval for this study was obtained from Maseno University School of Graduate Studies while ethical approval was obtained from both Maseno University Ethical Review Committee (MUERC) and JOOTRH ISERC and NACOSTI. Authorization to access patients in the hospital was sought from the hospital administration. Written consent from the study participants was sought and signed at the beginning of the study. In addition, every respondent was assured of confidentiality of the shared information and was made aware of the freedom to withdraw from the study if she so wished. For the respondents found to have special needs, immediate assistance was provided by the researcher or by research assistants. The rights and welfare of the vulnerable study participants was assured and respected during the study period as only those who willingly and voluntarily agreed to participate in the study were included. The entire study was guided by all ethical procedures and protocols involving human participants aimed at upholding beneficence.

3.18 Limitations of the study

Small sample size of 150 which affected the power of the study hence the results cannot be generalized to the general populations.

CHAPTER FOUR

RESULTS

4.1 Introduction

Influence of patient factors among pregnant women who used SD and ED on surgical site infection was evaluated. The study recorded age, income status, parity status, and education level as patient factors that might influence SSI. Mediator factors such as indication for elective CS, type of incision, skin closure technique, lochia smell on day 14, wound status on day 14, type of anesthesia and white cell count were also evaluated if they influenced development of SSI.

	Single dose					**Extended dose**				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**Infection**	**Total**	**RR**	**P value**
Age										
18-29	26	1	27			36	0	36		
30-39	43	0	43	0.973	0.529	35	1	36	0.968	0.638
40-49	4	1	5			3	0	3		
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**Infection**	**Total**	**RR**	**P value**
Income										
<10,000	27	2	29			23	1	24		
10000-30000	31	0	31	0.892	0.9357	33	0	33	0.8124	0.9214
>30,000	15	0	15			18	0	18		
	Single dose					**Extended dose**				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**Infection**	**Total**	**RR**	**P value**
Education level										
Primary	19	1	20			20	1	21		
Secondary	22	1	23	0.934	0.291	30	0	30	0.795	0.597
Tertiary	32	0	32			24	0	24		
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**Infection**	**Total**	**RR**	**P value**
Indication for CS										
Breech	9	0	9			12	0	12		

Placenta previa	5	0	3	1.041	0.491	1	0	1	0.917	0.439
1 previous scar	17	1	18			21	1	22		
Oblique lie	13	0	13			14	0	14		
Vaginal Warts	1	0	1			1	0	1		
2 previous scars	19	1	20			18	0	18		
3 previous scars	9	0	9			7	0	7		
	Single dose					**Extended dose**				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**infection**	**Total**	**RR**	**P value**
Type of Incision										
SUMI	19	1	20	0.851	0.067	19	0	19	0.743	0.373
Low transverse incision	54	1	55			55	1	56		
Blood Loss										
<500mls	39	0	39	0.466	0.136	0	0	0	0.514	0.333
500- 1000mls	34	2	36			36	1	37		
>100mls	0	0	0			38	0	38		
WBC count										
Within normal limits	71	2	73	0.973	0.812	71	1	72	0.959	0.837
Deranged	2	0	2			3	0	3		
	Single dose					**Extended dose**				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**infection**	**Total**	**RR**	**P value**
Skin closure										
Non-absorbable suture	5	0	5	0.902	0.571	2	0	2	0.929	0.868
Absorbable suture	68	2	70			72	1	73		
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**infection**	**Total**	**RR**	**P value**
Parity										
Nulliparous	7	1	8	0.8	0.737	7	0	7	0.7824	0.812
Para 1	21	0	21			21	1	22		
Para 2	31	1	32			29	0	29		
Para 3	9	0	9			11	0	11		
Para 4	5	0	5			6	0	6		

	Single dose					Extended dose				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**infection**	**Total**	**RR**	**P value**
Type of anesthesia										
Spinal anesthesia	69	1	70	0.879	0.413	65	1	66	0.858	0.710
General anesthesia	4	1	5			9	0	9		
Wound status on day 14										
Clean	61	0	61	1.032	0.0915	73	1	74	0.926	0.453
Indurated	10	1	11			1	0	1		
Minimal pus	2	1	3			0	0	0		
Deep tissue involvement	0	0	0			0	0	0		
Organ space involvement	0	0	0			0	0	0		

	Single dose					Extended dose				
Factor	**No infection**	**Infection**	**Total**	**RR**	**P value**	**No infection**	**infection**	**Total**	**RR**	**P value**
RBS										
<11 mmol/l (normal)	62	2	64	0.849	0.552	62	1	63	0.838	0.660
>11 mmol/l (high)	11	0	11			12	0	12		
Lochia Smell on day 14										
Non foul smelling	68	1	69	0.782	0.068	74	0	74	0.536	0.4967
Foul smelling	5	1	7			0	1	1		

Figure 4.1 Socio-demographic and obstetric characteristics of the patients in the SD and ED groups.

4.1.1. Influence of age as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

During the study period, 169 women were assessed for eligibility ,150 eligible women were recruited. Ten were excluded, three declined to participate in the trial, five did not meet inclusion criteria and one was not included for other reasons. The overall mean age (± standard deviation) of the participants in the SD arm was 31.32 ± 7.69 years and 30.4 ± 6.51 years in the ED arm. There was not a significant difference in the mean ages of the two groups. The study observed that the age as a patient factor did not statistically have an influence on surgical site infection with p-value of 0.529 with RR of 0.9724 in SD and a p-value of 0.638 with RR of 0.9892 in ED arms respectively.

4.1.2 Influence of income status as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

The level of household income did not have statistically significant influence on surgical site infection in both study arms with p-value of 0.9357 with relative risk of 0.8920 in the SD group p-value of 0.9214 and a relative risk of 0.8124 in the ED group.

4.1.3 Influence of parity as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Parity was evaluated in both study arms and was found not to significantly have influence on surgical site infection with a p- value of 0.737 with RR of 0.8 in SD arm and a p-value of 0.812 with RR of 0.7824 in the ED arm of the trial.

4.1.4 Influence of level of education as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Level of education was evaluated in both study arms and was found to have no statistically significant influence on surgical site infection with a p- value of 0.291 with RR of 0.934 in the SD arm and a p-value of 0.597 with RR of 0.795 in the ED arm.

4.1.5 Influence of indication for CS as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Indication for CS was found to have no statistically significant influence on surgical site infection in both study arms with a p-value of 0.491 with RR of 1.041 in the SD arm and a p-value of 0.439 with RR of 0.917 in the ED arm.

4.1.6 Influence of type of incision as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Type of incision was evaluated in both study arms and was found to have no significant statistical influence on surgical site infection with a p-value of 0.067 RR of 0.751 in the SD trial arm and a p-value of 0.373 and RR of 0.743 in the ED trial arm.

4.1.7 Influence of blood loss as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

The study revealed that blood loss did not have statistically significant influence on surgical site infection in both study arms with a p-value of 0.136 with RR of 0.466 in the SD trial arm and a p-value of 0.333 and RR of 0.514 in the ED trial arm.

4.1.8 Influence of random blood sugar as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

The study showed that random blood sugar did not have significant influence on surgical site infection in both study arms with a p- value of 0.552 with RR of 0.849 in the SD trial arm and a p-value of 0.660 with RR of 0.838 in the ED arm.

4.1.9 Influence of white blood cell count a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

White blood cell count was evaluated in both study arms and had no significant influence on surgical site infection with a p-value of 0.812 with RR of 0.973 in the SD arm and a p-value of 0.837 with RR of 0.959 in the ED arm.

4.1.10 Influence of type of anesthesia as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Type of anesthesia was found to have no significant influence on surgical site infection in both study arms with a p value of 0.413 with RR of 0.879 in the SD arm and a p-value of 0.710 with RR of 0.858 in the ED arm.

4.1.11 Influence of type of skin closure as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Type of skin closure was found to have no statistically significant influence on surgical site infection in both study arms with a p-value of 0.571 with RR of 0.902 in the SD arm and a p-value of 0.868 with RR of 0.929 in the ED arm.

4.1.12 Influence of wound status on day 14 as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Wound status on day 14 was evaluated and found to have no statistically significant influence on surgical site infection in both study arms with a p- value of 0.0915 with RR of 1.032 in the SD arm and a p-value of 0.453 with RR of 0.926 in the SD arm of the trial.

4.1.3 Influence of lochia smell on day 14 as a patient factor among pregnant women who used SD, and ED antibiotics on surgical site infection.

Lochia smell on day 14 did not significantly influence surgical site infection in both study arms with a p-value of 0.068 with RR of 0.782 in the SD arm and a p-value of 0.4967 with RR of 0.536 in the ED arm.

Table 4.2 Comparison between SD & ED antibiotic used as a prophylaxis to establish evidence of infection during twenty-eight days of follow up.

Exposure	Infected	Non-Infected	Total
SD	2 (2.6%)	73 (97.4%)	75
ED	1 (1.3%)	74 (98.7%)	75
P-value	0.567		
Risk ratio	0.493		

The occurrence of SSI was compared in both SD and ED study arms and no statistically significant difference was gotten with p- value of 0.567 and RR of 0.493.

CHAPTER FIVE

DISCUSSION

5.1 Introduction

In Sub-Saharan Africa, economic and social factors are thought to constitute major barriers to the prevention of SSI because of the high incidence of SSI. The incidence of post-cesarean SSI ranges from 3 to 24% (Cyriaque Dégbey, 2021). In this current study, patient factors such as age, income status, parity of the patient, education level, random blood sugar levels of the patient, and lochia smell were investigated for their influence on surgical site infection in both SD antibiotic group and ED antibiotic group among women undergoing elective CS. This study revealed that among women undergoing elective CS, these patient factors did not statistically have influence on surgical site infection during the twenty-eight days of follow up. Mediator factors such as indication for CS, type of incision, amount of blood loss during operation, type of skin closure, and form of anesthesia were analyzed if they influenced surgical site outcome among those randomized to SD antibiotics compared with those randomized to ED antibiotics among women undergoing elective CS. The mediator factors did not statistically have significant influence on SSI among SD and ED groups of women undergoing elective CS. The findings of this study was consistent with the (David Nitrushwa, 2021) that also found that observed that patient factors had insignificant impact on SSI among women randomized for CS. The hypothetic reason why there was no significant impact of patient factors and mediator factors on surgical site outcome in this study could be that our inclusion criteria targeted patients in good health status who were scheduled for elective CS and used ceftriaxone and metronidazole unlike higher incidence of SSI in a similar study by (Shakya, 2010) who used Cephalexin and metronidazole. In another study done in Tanzania by (Fadhili, 2013), higher incidence of SSI was found of 4.8% and this difference could be attributed

to inclusion of both emergency CS and elective CS unlike in our study that only analyzed elective cesarean section cases.

Surgical site infection prevention remains a big concern for the surgeon and appropriate prophylactic antibiotics can reduce the potential infections among women undergoing elective CS. Apart from prophylaxis, good surgical skills, good hemostasis, less tissue trauma, and aseptic technique are important factors in minimizing surgical site infections among women scheduled for elective CS. (Landy, 2017). In this current study, prophylactic SD of antibiotics (ceftriaxone) was compared with EDs of antibiotics (ceftriaxone and flagyl plus additional doses of amoxicillin and flagyl). This present study observed that there was no statistically significant difference in the occurrence of SSI between the patients who received SD as compared to ED antibiotics for elective CS. The hypothetical reason why there was no significant difference between the single and the ED of prophylactic antibiotics groups could be that both regimens were equally effective in prevention of surgical site infection. The results of this study were consistent with Igwemadu et al., (2022), who reported that single-dose ceftriaxone and metronidazole is as effective as multiple doses for antibiotic prophylaxis to prevent post-CS infections. Other related study by Kalaranjini., Veena, and Rani, (2013) observed that usage of SD Ceftriaxone for elective CS before skin incision and after cord clamping did not have significant difference in the occurrence of post-operative infectious morbidity as no adverse outcome was recorded.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

1. The patient factors namely age, income, parity, education level, indication for elective CS, type of incision, random glucose levels, and type of anesthesia did not have any statistically significant effect on development of SSI in both SD and ED trial arms.
2. There was no significant difference in surgical site infection between SD, and ED antibiotics use as prophylaxis among women who underwent elective caesarean section

6.2 Recommendations

1. There is need to use SD antibiotic to prevent SSIs post elective CS and patients followed up to day 28 for any signs of SSI.
2. We recommend an appropriately powered trial that will capture SD versus ED antibiotic use both in elective and emergency CS.

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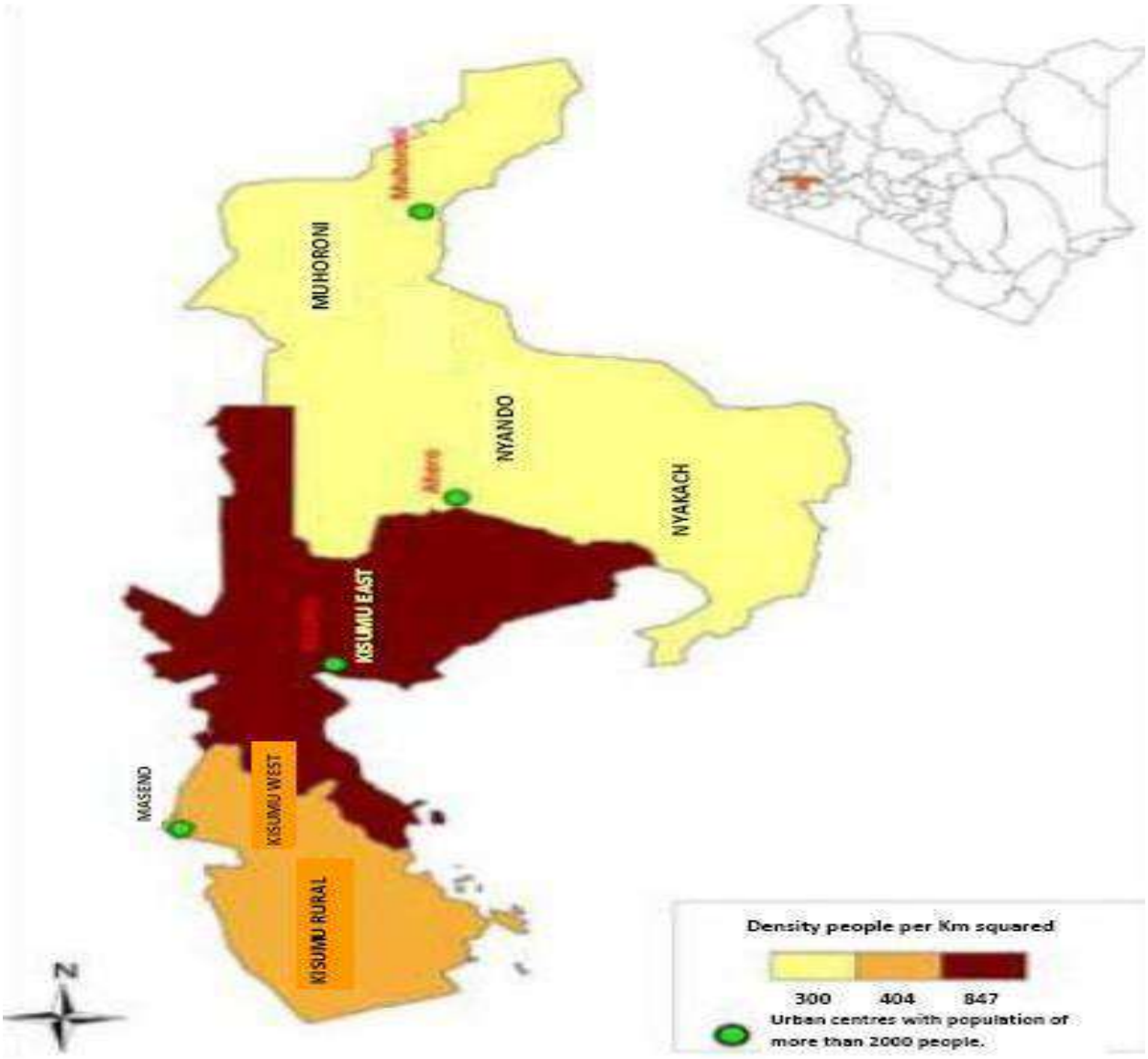
APPENDICES

APPENDIX I: A MAP OF KISUMU COUNTY



APPENDIX II: CONSENT FORM

Introduction: My name is Dr. Juma Steven, a postgraduate student in Reproductive Health at Maseno University. I am conducting research on effectiveness of single-dose antibiotic use in elective caesarean section in prevention of surgical site infection at JOOTRH, Kisumu, Kenya. I am inviting you to be part of this research to which I will be asking you questions regarding possible surgical site complications after elective caesarean section which will include your sociodemographic characteristics and clinical characteristics. I will further obtain your laboratory parameters from your hospital records.

Purpose of the research: This study will assess the antibiotic use in prevention of surgical site infection when administered as a single prophylaxis dose versus when used as an ED. The findings of this study help formulate antibiotic protocol to be used for patients undergoing elective caesarean section at JOOTRH.

Participant Selection: This study will involve expectant women admitted to JOOTRH with indication for elective caesarean section.

Duration of the study: This study will take place from the time of your admission for elective caesarean section and subsequent enrollment to 28 days after operation.

Risks and benefits: The participants will benefit from close follow and immediate intervention in case of SSIs, the results of this study will be used to formulate a protocol on antibiotic use in caesarean section.

Minimal risks of infection are anticipated and your close follow up during the study duration will enable me to pick any potential signs of infection and appropriate treatment be given immediately.

Right to refusal: I would bring it to your attention that you as a patient have the right to decline to be a participant. You will still be accorded the best available care in the hospital.

Remuneration: No monetary gains will be achieved during your participation in the research Your participation should be purely voluntary.

Confidentiality: You as a participant will have a unique number code as your reference and this will be under the custody of the researcher who will keep them under lock and key during the study period before later filling it with your hospital documents.

Certificate of consent: Having read (been read to) the consent and having had the opportunity to ask questions, I voluntarily consent to be a participant in this research.

Name of participant ……

Signature ……...

Date ……

Name of Principal investigator …….

Signature …….

Date …….

APPENDIX III : FOMU YA IDHINI

Fomu ya Idhini

Utangulizi: Naitwa Dk. Juma Steven, mwanafunzi wa shahada ya uzamili katika Afya ya Uzazi katika Chuo Kikuu cha Maseno. Ninafanya utafiti kuhusu ufanisi wa matumizi ya dozi moja ya viuavijasumu katika sehemu ya upasuaji iliyochaguliwa ili kuzuia maambukizo ya tovuti ya upasuaji huko JOOTRH, Kisumu, Kenya. Ninakualika kuwa sehemu ya utafiti huu ambao nitakuwa nikikuuliza maswali kuhusu matatizo yanayoweza kutokea kwenye tovuti ya upasuaji baada ya upasuaji wa pekee ambao utajumuisha sifa zako za demokrasia ya kijamii na sifa za kiafya. Nitapata zaidi vigezo vya maabara yako kutoka kwa rekodi zako za hospitali.

Madhumuni ya utafiti: Utafiti huu utatathmini matumizi ya viuavijasumu katika kuzuia maambukizi ya tovuti ya upasuaji wakati unasimamiwa kama kipimo kimoja cha kuzuia dhidi ya wakati unatumiwa kama dozi iliyopanuliwa. Matokeo ya utafiti huu yanasaidia kuunda itifaki ya viuavijasumu itakayotumika kwa wagonjwa wanaojichagulia kwa njia ya upasuaji katika JOOTRH.

Uteuzi wa Mshiriki: Utafiti huu utahusisha wanawake wajawazito waliolazwa JOOTRH na dalili ya sehemu ya upasuaji ya kuchagua.

Muda wa utafiti; Utafiti huu utafanyika kuanzia wakati wa kulazwa kwako kwa upasuaji wa kuchagua na uandikishaji unaofuata hadi siku 28 baada ya upasuaji.

Hatari na manufaa: Washiriki watafaidika kutokana na ufuatiliaji wa karibu na uingiliaji kati wa haraka katika kesi ya SSIs, matokeo ya utafiti huu yatatumika kuunda itifaki ya matumizi ya antibiotiki katika sehemu ya upasuaji.

Hatari ndogo za kuambukizwa zinatarajiwa na ufuatiliaji wako wa karibu wakati wa muda wa utafiti utaniwezesha kuchagua dalili zozote zinazowezekana za kuambukizwa na matibabu ifaayo nipewe mara moja.

Cheti cha ridhaa: Baada ya kusoma (kusomwa hadi) ridhaa na kupata fursa ya kuuliza maswali, ninakubali kwa hiari kuwa mshiriki katika utafiti huu.

Jina la mshiriki ……

Sahihi ……...

Tarehe ……

Jina la Mchunguzi…….

Sahihi …….

Tarehe …….

APPENDIX IV: DATA ABSTRACTION SHEET

Participant's unique number: _____.

Date of surgery : _____

Age: : Weight

Parity:

Level of education: Primary Secondary College

Household Income per month: < 10000 10000- 30000 > 30000

Indication for caesarean section: _____

Allergy to Drugs: YES NO

Full Hemogram: WBW_____ : Hb_____ : Platelets_____

UEC: Urea_____: Creatinine_____

Random blood sugar level (done a day before surgery): _____ mmol/l

Skin incision SUMI Low Transverse.

Estimated blood loss <500mls 500mls – 1000mls >1500mls

Type of suture for Skin Closure Absorbable Non-Absorbable

Duration of Caesarean Section (From skin incision to skin closure) _____ minutes.

Type of Anesthesia: Spinal Anesthesia General Anesthesia

Vital Signs on Day 1	Morning	Afternoon	Evening
Pulse			
Temperature (Celsius)			

Respiratory Rate

Blood Pressure

Uterine Involution; Well contracted Boggy Uterus

Fundal height

Wound examination

Clean

Indurated

Discharging Pus

Wound Dehiscence

Burst Abdomen

Lochia Evaluation

Amount mild moderate Excessive

Color Rubra Alba Serosa Other_____

Smell Non foul smelling Foul smelling

Vital Signs on Day 2 Morning Afternoon Evening

Pulse

Temperature (Celsius)

Respiratory Rate

Blood Pressure

Uterine Involution Well Contracted Boggy Uterus Tender Non Tender

Fundal height

Wound examination

Clean

Indurated

Discharging Pus

Wound Dehiscence

Burst Abdomen

Lochia Evaluation

Amount mild moderate Excessive

color Rubra Alba Serosa Other_____

Smell Non foul smelling Foul smelling

Discharged On :

Vital Signs on Day 14

Pulse

Temperature (Celsius)

Respiratory Rate

Blood Pressure

Uterine Involution Well Contracted Boggy Uterus Tender Non Tender

Fundal height

Wound examination Clean Indurated Discharging Pus Wound Dehiscence Burst Abdomen

Lochia Evaluation

Amount mild moderate Excessive

color Rubra Alba Serosa Other_____

Smell Non foul-smelling Foul smelling

Results of other investigation

Use of antibiotics based on Culture and Sensitivity of Pus swab Yes No

Follow up call On Day 28 Via Phone

Any evidence of wound infection (discharge , open wound) Yes No

APPENDIX IV: APPROVAL LETTER FROM SCHOOL OF GRADUATE STUDIES, MASENO UNIVERSITY

MASENO UNIVERSITY ETHICS REVIEW COMMITTEE

Tel: +254 057 351 622 Ext: 3050
Fax: +254 057 351 221

Private Bag – 40105, Maseno, Kenya
Email: muerc-secretariate@maseno.ac.ke

REF: MSU/DRPI/MUERC/01044/22 **Date:** 1st March, 2022

TO: Dr. Juma Steven Odhiambo
MMED/SM/00006/019
Department of Obstetrics and Gynecology
School Of Medicine, Maseno University
P. O. Box, Private Bag, Maseno, Kenya

Dear Sir,

RE: Effectiveness of Single-Dose Antibiotic use in Elective Caesarean Section in Prevention of Surgical Site Infection at Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu County, Kenya: A Randomized Control Trial

This is to inform you that **Maseno University Ethics Review Committee (MUERC)** has reviewed and approved your above research proposal. Your application approval number is MUERC/01044/22.The approval period is 1st March, 2022 – 28th February, 2023.
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 Maseno University Ethics Review Committee (MUERC).
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 Maseno University Ethics Review Committee (MUERC) within 24 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 Maseno University Ethics Review Committee (MUERC) within 24 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 Maseno University Ethics Review Committee (MUERC).

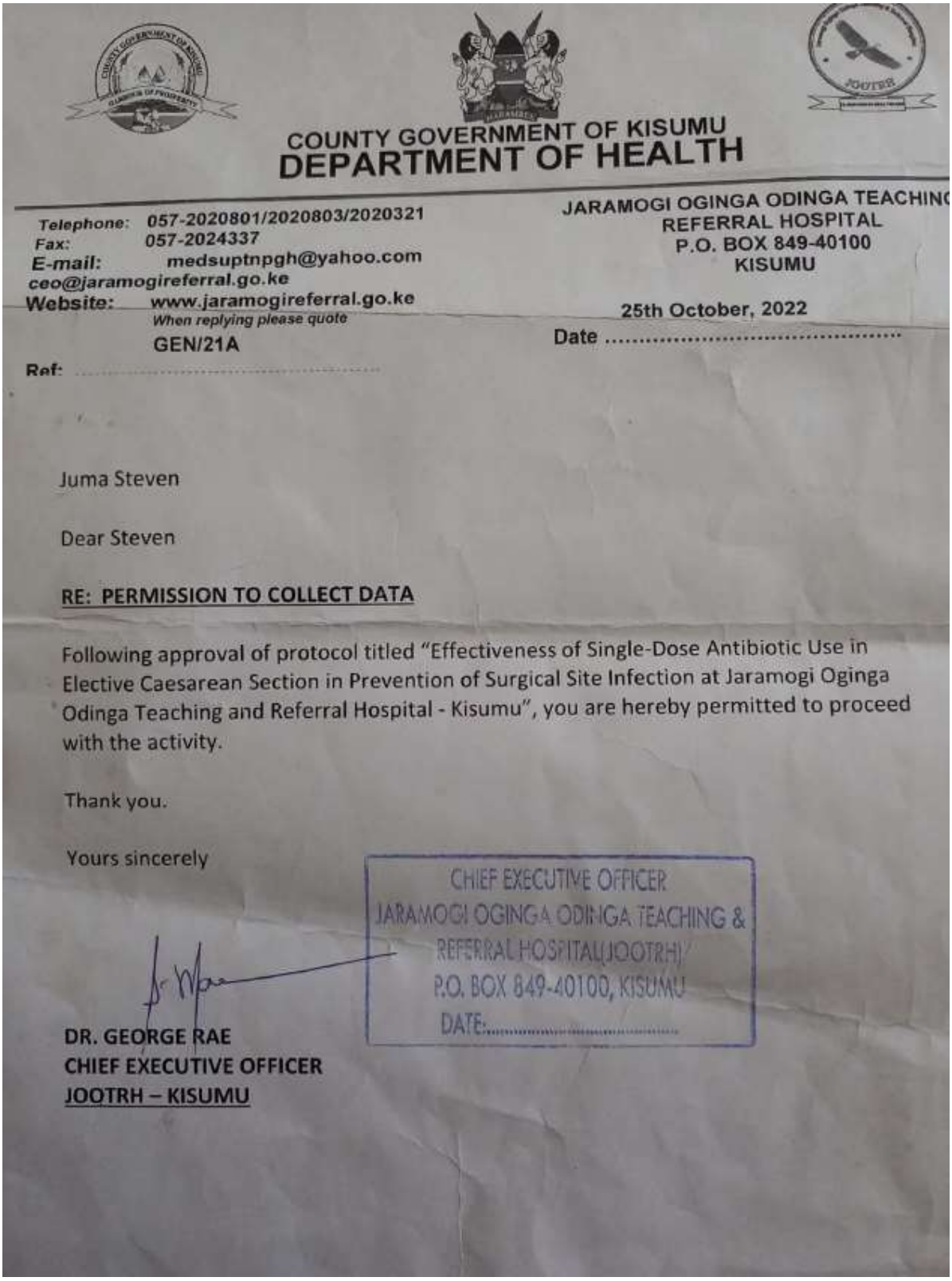
Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely

Prof. Philip O. Owuor, PhD, FAAS, FKNAS
Chairman, MUERC

MASENO UNIVERSITY ETHICS REVIEW COMMITTEE 01 MAR 2022

APPENDIX V: APPROVAL FROM JOOTRH



COUNTY GOVERNMENT OF KISUMU
DEPARTMENT OF HEALTH

Telephone: 057-2020801/2020803/2020321
Fax: 057-2024337
E-mail: medsuptnpgh@yahoo.com
ceo@jaramogireferral.go.ke
Website: www.jaramogireferral.go.ke
When replying please quote
GEN/21A

JARAMOGI OGINGA ODINGA TEACHING
REFERRAL HOSPITAL
P.O. BOX 849-40100
KISUMU

25th October, 2022

Date .....

Ref: .....

Juma Steven

Dear Steven

RE: PERMISSION TO COLLECT DATA

Following approval of protocol titled "Effectiveness of Single-Dose Antibiotic Use in Elective Caesarean Section in Prevention of Surgical Site Infection at Jaramogi Oginga Odinga Teaching and Referral Hospital - Kisumu", you are hereby permitted to proceed with the activity.

Thank you.

Yours sincerely

CHIEF EXECUTIVE OFFICER
JARAMOGI OGINGA ODINGA TEACHING &
REFERRAL HOSPITAL(JOOTRH)
P.O. BOX 849-40100, KISUMU
DATE:.....

DR. GEORGE RAE
CHIEF EXECUTIVE OFFICER
JOOTRH – KISUMU

APPENDIX VI: PERMIT FROM NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY, AND INNOVATION (NACOSTI)

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: 736057

Date of Issue: 25/March/2022

RESEARCH LICENSE

This is to Certify that Dr., STEVEN nthandu JUMA of Maseno University, has been licensed to conduct research in Kisumu on the topic: EFFECTIVENESS OFSINGLE-DOSE ANTIBIOTIC USE IN ELECTIVE CAESAREAN SECTION IN PREVENTION OF SURGICAL SITE INFECTION AT JARAMOGI OGINGA ODINGA TEACHING AND REFERRAL HOSPITAL, KISUMU COUNTY, KENYA: A RANDOMIZED CONTROL TRIAL. for the period ending : 25/March/2023.

License No: NACOSTI/P/22/16507

736057

Application 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.

APPENDIX VII: PHARAMACY AND POISONS BOARD APPROVAL

MINISTRY OF HEALTH

PHARMACY AND POISONS BOARD

Telegrams: "MINIHEALTH", Nairobi
Telephone: Nairobi 020 2716905/6 , 3562107
Cellphone: 0733 – 884411/0720608811 P.O. BOX 27663-00506
Fax: 2713409

LENANA ROAD

PHARMACY AND POISONS BOARD
HOUSE

NAIROBI

When replying please quote

Ref. No. PPB/ECCT/22/09/03/2022(279) **26th September 2022**

DR. STEVEN ODHIAMBO JUMA,

Principal Investigator ECCT/22/09/03,

REGISTRAR OBSTETRICS AND

GYNECOLOGY MASENO UNIVERSITY,

0727535519.

Dear Sir/Madam,

RE: ECCT/22/09/03: INITIAL APPROVAL; FFECTIVENESS OF SINGLE-DOSE ANTIBIOTIC USE IN ELECTIVE CAESAREAN SECTION IN PREVENTION OF SURGICAL SITE INFECTION AT JARAMOGI OGINGA ODINGA TEACHING ANS REFERRAL HOSPITAL (SINGLE DOSE VERSUS EXTENDED DO).

Reference is made to the above study.

We acknowledge receipt of the following documents;

1. Copy of favorable opinion letter from the local Ethics Review Committee (ERC).
1044_22_new_dr_juma_steven_1_03_22.pdf dated 9th September 2022 Version 1
1044_22_new_dr_juma_steven_1_03_22_2.pdf dated 9th September 2022 Version 1
1044_22_new_dr_juma_steven_1_03_22_4.pdf dated 24th September 2022 Version 1
1044_22_new_dr_juma_steven_1_03_22_5.pdf dated 24th September 2022 Version 1
1044_22_new_dr_juma_steven_1_03_22_6.pdf dated 24th September 2022 Version 1
2. Copy of current Practice Licenses for the investigators and study Pharmacist
steven_practice_licence_osp76590_7.pdf dated 9th September 2022 Version 1
neto_retention_licence3289521.pdf dated 24th September 2022 Version 1
steven_practice_licence_osp76590_7_2.pdf dated 24th September 2022 Version 1
neto_retention_licence3289521_1.pdf dated 24th September 2022 Version 1
steven_practice_licence_osp76590_7_3.pdf dated 24th September 2022 Version 1
neto_retention_licence3289521_1_2.pdf dated 24th September 2022 Version 1
steven_practice_licence_osp76590_7_4.pdf dated 24th September 2022 Version 1
neto_retention_licence3289521_1_3.pdf dated 24th September 2022 Version 1
3. Copy of approval letter(s) from collaborating institutions or other regulatory authorities, if applicable
research_permit_nacosti_p_22_16507.pdf dated 9th September 2022 Version 1
1044_22_new_dr_juma_steven_1_03_22_3.pdf dated 9th September 2022 Version 1
research_permit_nacosti_p_22_16507_2.pdf dated 24th September 2022 Version 1
research_permit_nacosti_p_22_16507_3.pdf dated 24th September 2022 Version 1
research_permit_nacosti_p_22_16507_4.pdf dated 24th September 2022 Version 1
4. Indemnity cover for PI, investigators and study Pharmacist.
indemnity_certificate_dr_steven_odhiambo_juma.pdf dated 9th September 2022 Version 1
lesly_neto_1.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_2.pdf dated 24th September 2022 Version 1
lesly_neto_1_2.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_4.pdf dated 24th September 2022 Version 1
lesly_neto_1_3.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_6.pdf dated 24th September 2022 Version 1
lesly_neto_1_4.pdf dated 24th September 2022 Version 1
5. Signed Investigator(s) CV(s) including that of study Pharmacist (NB: The CV should include the current workload of the Principal Investigator)
cv_22_11_2021_dr_kays_muruka_maseno_univ.pdf dated 9th September 2022 Version 1
steven_odhiambo_juma_1.pdf dated 9th September 2022 Version 1
dr_w_otieno_nov_2021.pdf dated 9th September 2022 Version 1
steven_odhiambo_juma_1_2.pdf dated 9th September 2022 Version 1
dr_w_otieno_nov_2021_2.pdf dated 9th September 2022 Version 1
cv_22_11_2021_dr_kays_muruka_maseno_univ_2.pdf dated 9th September 2022 Version 1
cv_22_11_2021_dr_kays_muruka_maseno_univ_3.pdf dated 24th September 2022 Version 1
dr_w_otieno_nov_2021_3.pdf dated 24th September 2022 Version 1
steven_odhiambo_juma_1_3.pdf dated 24th September 2022 Version 1
dr_w_otieno_nov_2021_4.pdf dated 24th September 2022 Version 1
steven_odhiambo_juma_1_4.pdf dated 24th September 2022 Version 1
steven_odhiambo_juma_1_5.pdf dated 24th September 2022 Version 1
6. Evidence of recent GCP training of the core study staff
cert2.docx dated 9th September 2022 Version 1
cert1.docx dated 9th September 2022 Version 1
cert2_2.docx dated 9th September 2022 Version 1
cert1_2.docx dated 9th September 2022 Version 1
cert1_3.docx dated 24th September 2022 Version 1
cert2_3.docx dated 24th September 2022 Version 1
cert1_4.docx dated 24th September 2022 Version 1
cert2_4.docx dated 24th September 2022 Version 1
declaraion_of_waiver_57.pdf dated 24th September 2022 Version 1
7. Detailed budget of the study
pharmacy_and_poisons_board_applications.html dated 9th September 2022 Version 1
declaraion_of_waiver_25.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_41.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_59.pdf dated 24th September 2022 Version 1
8. Stability data of the investigational product
declaration_and_waiver_16.docx dated 9th September 2022 Version 1
declaraion_of_waiver_20.pdf dated 24th September 2022 Version 1

declaraion_of_waiver_37.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_53.pdf dated 24th September 2022 Version 1
9. Adequate data and information from previous studies and Phases to support carrying out of the current study
declaration_and_waiver_17.docx dated 9th September 2022 Version 1
declaraion_of_waiver_19.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_36.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_52.pdf dated 24th September 2022 Version 1
10. Cover Letter (Should list all the submitted documents, their version numbers and dates)
dr_juma.pdf dated 24th September 2022 Version 1
cover_letter_54.pdf dated 24th September 2022 Version 1
cover_letter_55.pdf dated 24th September 2022 Version 1
sakuh_kisii220922201301_1.pdf dated 24th September 2022 Version 1
11. The Study Protocol
research_proposal_dr_juma.docx dated 24th September 2022 Version 1
research_proposal_dr_juma_3.docx dated 24th September 2022 Version 1
research_proposal_dr_juma_4.docx dated 24th September 2022 Version 1
research_proposal_dr_juma_5.docx dated 24th September 2022 Version 1
12. Patient Information leaflet and Informed consent form
consent_to_participate_in_research.docx dated 24th September 2022 Version 1
declaraion_of_waiver_16.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_33.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_49.pdf dated 24th September 2022 Version 1
13. Investigators Brochure/Package inserts
declaraion_of_waiver.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_17.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_34.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_50.pdf dated 24th September 2022 Version 1
14. Registration of the study at Pan African Clinical Trials Registry https://pactr.samrc.ac.za
declaraion_of_waiver_2.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_15.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_32.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_48.pdf dated 24th September 2022 Version 1
15. Investigational Medicinal Product Dossier (IMPD)
declaraion_of_waiver_3.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_18.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_35.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_51.pdf dated 24th September 2022 Version 1
16. GMP certificate of the investigational product from the site of manufacture
declaraion_of_waiver_4.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_21.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_38.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_54.pdf dated 24th September 2022 Version 1
17. Certificate of Analysis of the investigational product
declaraion_of_waiver_5.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_22.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_39.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_55.pdf dated 24th September 2022 Version 1
18. Pictorial Sample of the investigational products. This sample should include the text of the labeling to be used
metronidazole_0.pdf dated 24th September 2022 Version 1
amoxil.pdf dated 24th September 2022 Version 1
ceftriaxone.pdf dated 24th September 2022 Version 1
metronidazole_0_2.pdf dated 24th September 2022 Version 1
ceftriaxone_2.pdf dated 24th September 2022 Version 1
metronidazole_0_3.pdf dated 24th September 2022 Version 1
amoxil_2.pdf dated 24th September 2022 Version 1
amoxil_3.pdf dated 24th September 2022 Version 1
ceftriaxone_3.pdf dated 24th September 2022 Version 1
metronidazole_0_4.pdf dated 24th September 2022 Version 1
19. Evidence of contractual agreement between sponsor and Principal Investigator.
declaraion_of_waiver_6.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_23.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_40.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_56.pdf dated 24th September 2022 Version 1
20. DSMB Charter including the composition and meeting schedule
declaraion_of_waiver_7.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_24.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_3_2.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_58.pdf dated 24th September 2022 Version 1
21. Financial declaration by Sponsor and/or PI
declaraion_of_waiver_8.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_26.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_42.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_60.pdf dated 24th September 2022 Version 1
22. Clinical Trials Insurance cover for study participants
declaraion_of_waiver_9.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_3.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_5.pdf dated 24th September 2022 Version 1
indemnity_certificate_dr_steven_odhiambo_juma_7.pdf dated 24th September 2022 Version 1
23. For multicentre/multi-site studies, a site specific addendum for each of the proposed sites including among other things the sites' capacity to carry out the study i.e personnel, equipment, laboratory etc
declaraion_of_waiver_10.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_27.pdf dated 24th September 2022 Version 1
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declaraion_of_waiver_61.pdf dated 24th September 2022 Version 1
24. Payment of fees
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declaraion_of_waiver_29.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_45.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_62.pdf dated 24th September 2022 Version 1
25. Statistical Analysis Plan
declaraion_of_waiver_12.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_30.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_46.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_63.pdf dated 24th September 2022 Version 1
26. Signed Checklist
declaraion_of_waiver_13.pdf dated 9th September 2022 Version 1
declaraion_of_waiver_31.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_47.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_3_3.pdf dated 24th September 2022 Version 1
27. A signed statement by the applicant indicating that all information contained in, or referenced by, the application is complete and accurate and is not false or

misleading.
declaraion_of_waiver_14.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_28.pdf dated 24th September 2022 Version 1
declaraion_of_waiver_44.pdf dated 24th September 2022 Version 1
sakuh_kisii22092220130_1_2.pdf dated 24th September 2022 Version 1
28. Signed Declaration by Sponsor or Principal investigator that the study will be carried out according to the protocol and applicable laws, regulations and GCP requirements.
declaraion_to_abideb_law.pdf dated 24th September 2022 Version 1
dr_juma_2.pdf dated 24th September 2022 Version 1
declaraion_to_abideb_law_2.pdf dated 24th September 2022 Version 1
declaraion_to_abideb_law_3.pdf dated 24th September 2022 Version 1

After review of the documents, the Pharmacy and Poisons Board Expert Committee on Clinical Trials grants approval to the study **SINGLE DOSE VERSUS EXTENDED DO. (ECCT/22/09/03).**

This approval is **valid for one year** and in case the study extends beyond one year from the date of this letter, you are required to seek approval before proceeding with the study. The expiry date is 26th September 2023.

1. All safety reports should be submitted to ECCT as per the current PPB clinical trials guidelines.
2. Take note that it is your responsibility to inform the PPB of any changes to the protocol, research design and procedures that could introduce new or more than minimum risk to human subjects.
3. The Pharmacy and Poisons Board requires you to **provide regular updates and half yearly reports**, especially on Suspected Unexpected Serious Adverse Reactions (SUSARS) from the study, for monitoring purposes and involve the PPB where necessary.
4. You are also reminded that upon conclusion of the study, you shall be required to submit the executive summary report of the study **within 30 days** while a copy of the clinical study report **in ICH E3 format** should be submitted to us **within 180 days** of the study closure.

Yours Sincerely,

Dr. Samuel Kerama

For Chief Executive Officer