UNIVERSITY of RWANDA

COLLEGE OF MEDICINE & HEALTH SCIENCES

SCHOOL OF MEDICINE & PHARMACY

# PREOPERATIVE ANTIBIOTIC PROPHYLAXIS VERSUS PLACEBO IN CLEAN, NON-PROSTHETIC SURGERY AT CHUK. IMPACT ON SURGICAL SITE INFECTIONS AND COST OF CARE.

Dissertation submitted in partial fulfillment of the requirements for the award of the degree of Master of Medicine in General Surgery, University of Rwanda

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**DECLARATION**

**Researcher:**

I, **Dr Sibomana Isaie**, declare that this research ‘’**Preoperative antibiotic prophylaxis versus placebo in clean, non-prosthetic surgery at CHUK**. **Impact on surgical site infections and cost of care’’** is my own work and has never been submitted to any University for any professional or academic award.

Signed date: May 2019

Sibomana Isaie/Resident in General Surgery/UR

**Supervisor:**

I hereby declare that this research: **“Preoperative antibiotic prophylaxis versus placebo in clean, non-prosthetic surgery at CHUK**. **Impact on surgical site infections and cost of care’’** was submitted by Dr Sibomana Isaie with my approval.

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I also thank all surgeons, nurses and anesthetists who contributed much to my surgical training. You helped me to achieve my dream.

**Dr Sibomana Isaie**

**DEDICATION**

To God the Almighty for whom I owe my existence, for his love and blessings

To my beloved parents who did everything so that I become who I am today

To my brothers and sisters

To all my teachers and patients who participated in my training

To my Classmates and all my friends.

I dedicate this work

## LIST OF ABREVIATIONS

**ASA** : American society of anesthesiology

**CC** : Cubic centimeter

**CHUK** : Centre hospitalier Universitaire de Kigali (Kigali University Teaching Hospital)

**HOD** : Head of Department

**DVT** : Deep venous thrombosis

**ENT** : Ear-Nose-Throat

**GI** : gastrointestinal

**HAI** : Healthcare associated infections

**HIV** : Human immunodeficiency virus

**IRB** : Institutional review board

**LMIC** : Low and middle income country

**LOHS** : Length of hospital stay

**MIC** : Minimum inhibitory concentration

**MODS** : Multiple organ dysfunction syndrome

**NNIS** : National nosocomial infections surveillance

**PE** : Pulmonary embolism

**PMH** : Past medical history

**SIRS** : systemic inflammatory response syndrome

**SSI** : surgical site infection

**UDT** : Undescended testis

**UR** : University of Rwanda

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## ABSTRACT

**Introduction:** surgical site infections represent the most frequent adverse event affecting the safety of surgical patient worldwide. Several preventive measures have been put in place including preoperative antibiotic prophylaxis. Their benefits are proved for clean-contaminated and contaminated wounds. However, there is lack of consensus on the use of antibiotic prophylaxis in clean surgery especially in area with high rate of surgical site infections.

**Objectives:** this study aimed to determine the impact of preoperative antibiotic prophylaxis on SSI rate and cost of care in clean non-prophylactic surgeries at CHUK

**Methods:** a double blind randomized controlled trial of patients undergoing clean, non-prosthetic elective surgical procedures at CHUK. With 1:1 allocation, one group was assigned for preoperative intravenous cefazolin (intervention group) within an hour of skin incision and the other group was assigned for a similar looking preparation of water for injection (control group). The primary outcome was the rate of surgical site infection at discharge and after 30 postoperative days.

**Results:** 142 patients were recruited, 72 in intervention group and 70 in control group. The age range between 4 months to 85 years (mean age of 25.4; IQR: 39.75), and 65 (47.8 %) were pediatric (15 years and below); 97 were male and 44 female. 121 (85%) patients were ASA score 1 and 21 (15%) patients were ASA score 2. Thyroid, hernias and hydrocele accounted almost 2/3 of the procedures. The overall SSI rate within 30 postoperative days was 2.2% (3 patients) in which 2 patients were from control group and one from intervention group and the difference was not significant (P=0.559). Postoperative hypoxia was associated with increased risk of SSI (P<0.05) and being an adult patient was an independent factor for SSI in clean surgery. There was a total increment of hospital cost of 285,600 RFW (321USD) in intervention group compared to the control one.

**Conclusion:** routine use of preoperative antibiotics should be discouraged as they do increase cost of care without an impact on SSI rate in patients undergoing with clean non-prosthetic surgeries.

# CHAPTER 1: INTRODUCTION

## 1.1. Background

Surgical site infections are the most common health care-associated infections (HAI) that surgeons encounter and represent the most frequent adverse event affecting patient safety worldwide.[1]Thus, prevention of SSIs is a key issue to patient safety and maintained success of surgical interventions.[2]Risk factors for SSI are multi-factorial and prevention is a standard practice in surgery. Among preventive measures include antibiotic prophylaxis prior to surgery.

The goals of prophylactic administration of antibiotics to surgical patients are to reduce the incidence of SSI and to use antibiotics in a manner that is supported by evidence of effectiveness. Antibiotic prophylaxis should be regarded as one component of an effective policy for the control of HAI.[3]

The use of antibiotics prophylaxis in the prevention and reduction of the incidence of SSIs is widespread and evidence has demonstrated the importance of timing of administration, selection of the agent, and duration of the prophylaxis. Despite this evidence, the recommendations are not routinely followed.[4]Inappropriate prescribing and excessive use of antimicrobials may increase antibiotic resistance, adverse drug events, and costs.[5]

There is a wide gap between international standards and local practices on antibiotic prophylaxis.[5]For instance, most of hospitals in China are using prophylactic antibiotic during thyroid surgery, which is a clean procedure. In China, the decision of the use of antibacterial regimens is left solely to treating surgeon's discretion and, therefore, some will choose to prescribe antibacterial regimens for pre-, intra-, and postoperative periods up until sutures are removed.[6]Some recent work indicates an absence of any benefit from antibiotic prophylaxis in clean non-prosthetic surgery[7].

### 1.2. Problem statement

There is a general lack of consensus whether antibiotic prophylaxis should or not be given in clean surgeries especially in Africa where the rate of SSI represents a significant surgical burden[8]. Giving preoperative antibiotics is considered as one of the preventive measures for SSI, thus reduction of morbidity and mortality in surgical patients.
Surgical wounds are classified into four classes and prophylactic antibiotics are given based on the type of the wound.

At CHUK preoperative antibiotic prophylaxis are usually given by anesthetists prior to surgery within 30 to 60 min of skin incision. There are routinely administered to all patients without clear local guidelines. However, some studies have proved no benefit of giving antibiotic prophylaxis in some clean non- prosthetic surgical procedures such as elective hernia repair without mesh, hydrocelectomy, orchidopexy, thyroid surgery, removal of prosthetic implant and ankle surgeries.
This practice not only increases cost to patients, but also increases risk of developing antibiotic resistance.

### 1.3. Justification of the study

CHUK is one of the major teaching hospitals of Rwanda. It is located in the city center of Kigali and receives referred patients from all of the corners of the country[9]. Its services are organized into departments. The surgical department has 8 units based on specialties: general surgery, orthopedics, neurosurgery, urology, plastic surgery, pediatric surgery, ENT and ophthalmology.
Like in other LMIC, most of surgical procedures performed at CHUK are emergencies[10].

All surgical procedures require some measures to decrease the incidence of HAIs and among them there is preoperative antibiotic prophylaxis. Traditional thinking was that all patients need preoperative prophylactic antibiotics but the benefits of them are proved mainly for clean-contaminated and contaminated wounds; for dirty ones, therapeutic instead of prophylactic antibiotics are prescribed. On the other hand, the evidence has showed that preoperative antibiotics have no proven benefits in clean surgeries for some selected patients.
Having most of the studies on prophylactic antibiotics in clean surgery conducted from developed countries, it is difficult to change the practice in Africa based on their results. Some

health care providers are still thinking that the environment where the studies were conducted is quite different from the African one to allow any single surgical procedure to be performed without giving antibiotics.

In addition to this, lack of local guidelines lead to poor antibiotics prescription with even adding some postoperative doses of antibiotics in patients who really do not need them. The consequences are increment in drug resistance bacteria and patient cost.
We expect that this study will provide the evidence on prophylactic antibiotics in clean surgeries performed in African settings and that will also generate local guideline based on its results. Patients and hospitals will benefit from this study as the quality of care will improved based on generated evidence.

### 1.4. Hypothesis:

There is no difference in SSI rates when preoperative prophylactic antibiotics are used or not used for clean non-prosthetic surgery at CHUK. However their use may be associated with increased cost of care.

### 1.5. Research questions:

- Do prophylactic antibiotics decrease surgical site infections in clean procedures at CHUK?
- Do antibioprophylaxis increase the overall cost of care?

### 1.6. Objectives

#### 1.6.1. General objectives

- To determine the impact of preoperative antibiotic prophylaxis on SSI rate and cost of care in clean non-prophylactic surgeries at CHUK

#### 1.6.2. Specific objectives

- To determine the rate of SSI in clean, non-prosthetic surgery in a tertiary referral hospital in Rwanda
- To compare the rate of SSI in antibiotic and placebo groups
- To compare the adverse events and cost of care between the 2 groups

# CHAPTER 2: LITERATURE REVIEW

## 2.1. Surgical site infection (SSI)

The term surgical site infection is used to encompass the surgical wound and infections involving the body cavity, bones, joints, meninges and other tissues involved in the operation.[3]

The United States Centers for Disease Control and Prevention (US CDC) has developed criteria which define SSI as infection related to an operative procedure that occurs at or near the surgical incision (incisional or organ/space) within 30 days of the procedure or within 90 days if prosthetic material is implanted at surgery.[11]

SSIs are one of the most important causes of healthcare-associated infections (HAIs). They are associated with considerable morbidity and it has been reported that over one-third of postoperative deaths are related, at least in part, to SSI. In addition, SSI can double the length of time a patient stays in hospital and increase the costs of health care.[12]

CDC criteria for defining surgical site infection include one or more of the following:[13,14]

- A purulent exudate from a surgical wound
- Obtainig a positive fluid culture from a surgical wound that was closed primarily
- Opened surgical site having at least one clinical sign of infection (pain, swelling, erythema, warmth) in which culture is positive or not cultured
- Clinical diagnosis of infection by the surgeon.

### 2.1.1. Types of SSI

There are 3 types of surgical site infection depending of anatomical level of the infection:

- Superficial SSI which are infections involving only the skin or subcutaneous tissue of the incision
- Deep SSI: include infections involving the deep soft tissues (e.g., fascia and muscle layers) of the incision.
- Organ-space SSI: are the infections involving any part of the anatomy that was opened or manipulated during an operation (other than the incision)

The US Center for Disease Control's (CDC) NNIS (National Nosocomial Infections Surveillance) divide the risk factors for surgical site infection into 3 main cathegories[3]:

- The American Society of Anesthesiologists (ASA) score, which is linked with the status of the patient before surgery
- Wound class, reflects the state of contamination of the wound
- Duration of operation which reflect the complexity of the surgery.

### 2.1.2. Classification of surgical wounds:[3]

Surgical wounds are classified into four different classes based on operative features. The class of the wound is used to estimate risk for SSI.

- Clean surgery refers to operations in which no inflammation is encountered and the respiratory, alimentary or genitourinary tracts are not entered. There is no break in aseptic operating theatre technique.
- Clean contaminated wounds refer to operations in which the respiratory, alimentary or genitourinary tracts are entered but without significant spillage.
- Contaminated wounds refer to operations in known area of acute inflammation. These also include wounds with visible contamination.
- Dirty wounds include operations in the presence of pus, where there is a previously perforated hollow viscus, or compound/open injuries more than four hours old.

### 2.1.3. SSI rates according to wound class[15]

| Type of surgery | Infection rate with antibiotic prophylaxis (%) | Infection rate without antibiotic prophylaxis (%) |
|---|---|---|
| Clean | 1-2 | The same |
| Clean-contaminated | <10 | Gastric surgery up to 30%<br>Biliary surgery up to 20% |
| Contaminated | 15–20 | Variable but up to 60% |
| Dirty | < 40 | Up to 60% or more |

While widely used, this classification scheme is not the only factor for predicting risk of SSI. Other factors, such as the operative technique, length of surgery, and health of the surgical patient, are also important in predicting infectious risks for SSI.[12,16]

At present, four preventive measures are considered as having a high level of evidence for reduction of surgical site infection: surgical hand preparation; appropriate antibiotic prophylaxis; postponing of an elective operation in the case of active remote infection; and surgeon expertise and good surgical technique[17]

### 2.1.4. Treatment of established SSI

Essential to treating surgical infection is dependent on the type of SSI. In general, drainage and debridement are the cornerstones of management.

With deep SSI, this may require opening and draining the entire incision, while superficial SSI may only require a limited area of drainage. Fibrinous debris is removed and any remaining sutures or staples in the area of infection should also be removed.

The open wound commonly needs specific wound care to allow healing by secondary intention, although delayed primary or secondary closure may be feasible in selected cases. The open

wound is managed with interactive moist dressings and wound desiccation should be avoided. Most superficial and deep SSIs do not require antibiotics when drainage and debridement is prompt.[18]

Some SSI will also require specific antibiotics for the putative pathogen. Indications for antibiotics in surgical practice for treating surgical site infection include:[18]

- Cellulitis
- Lymphangitis
- Bacteremia
- Systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS)
- Definite pathogens (e.g., beta-hemolytic streptococcus)
- Large numbers of organisms (e.g., critical-colonization local infection)
- Poor host defenses (e.g., immunosuppression, diabetes)

### 2.2. Preoperative antibiotic prophylaxis

To prevent SSI, patients are given antibiotic prophylaxis prior to operation. Antibiotic prophylaxis is defined as the use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications.[3]

The goals of prophylactic administration of antibiotics to surgical patients are to:

- Reduce the incidence of surgical site infection
- Use antibiotics in a manner that is supported by evidence of effectiveness
- Minimize the effect of antibiotics on the patient's normal bacterial flora
- Minimize adverse effects
- Cause minimal change to the patient's host defenses.

It is important to emphasize that surgical antibiotic prophylaxis is an adjunct to, not a substitute for, good surgical technique.

Prophylactic administration of antibiotics inhibits growth of contaminating bacteria, and their adherence to prosthetic implants, thus reducing the risk of infection.[3]
The need for prophylactic antibiotics is dependent on the operation and wound classification.

The value of perioperative prophylaxis is established for clean-contaminated procedures[7].
For clean surgery, prophylaxis has been recommended for prosthetic device implantation procedures. Generally, clean procedures do not require antibacterial prophylaxis unless a prosthetic implant is involved.
However, evidence of post-operative infections from other clean procedures is under-reported and antibacterial prophylaxis is advisable for some procedures (e.g., breast surgery).[19]

### 2.2.1. Antibiotic administration

The effectiveness of the administration of preoperative antibiotic agents has been shown for certain surgical interventions.[17]However, there are other operations where the data does not support routine use of prophylactic antibiotics. Exceptions for routine use of prophylactic antibiotics include clean elective surgery without foreign material, for example, hernia repair, thyroid surgery, removal of implant material, dermatologic surgery and some foot and ankle surgery.[17]

Like other clean non-prosthetic surgical procedures, prophylactic systemic antibiotics are not indicated for patients undergoing thyroidectomy. However, many surgeons worldwide still use prophylactic antibiotics in this clean procedure because of undue fear of infection. Increasing clinical evidence suggests that antibiotics are not necessary to prevent incision infection in these surgeries.[20]In addition to that, a randomized study of prophylaxis antibiotic in open inguinal hernia surgery revealed no significant benefit over placebo.[21]An other study done in Nigeria randomized pediatric patients undergoing clean surgery into 2 groups. One to receive preoperative antibiotics other to receive placebo. They have found that prophylactic antibiotics make no difference to infection rate, which is already low. Moreover, the prescription of antibiotics in these cases increases the cost of surgery approximately by 27%[22].

Four components are important to appropriate administration of perioperative
antimicrobial prophylaxis and include appropriate antibiotic selection, timing, redosing, and discontinuation.[23]

### 2.2.2. Antibiotic selection

#### 2.2.2.1. Spectrum

The antibiotic used for prophylaxis needs to cover the common organisms that would most likely cause SSI. In other words, specific types of procedures are known to be associated with specific microorganisms, and antibiotics have clear profiles of the organisms they will effectively cover Staphylococci and Streptococci are the most common organisms of concern for most procedures, whereas anaerobes and Enterobacteriaceae are common for GI cases.

#### 2.2.2.2. Activity

An ideal prophylactic antibiotic is bactericidal rather than bacteriostatic. Bactericidal agents imply bacterial killing and subsequent reduction in potential inoculum size at the surgical site. Bacteriostatic agents inhibit cell growth but do not produce cell death or a reduction in bacterial population

### 2.2.3. Timing and dosing of antibiotic prophylaxis

The goal of appropriately timed prophylactic antibiotic is to achieve adequate serum and tissue levels of antibiotic before incision and to maintain these throughout the procedure.

An adequate antibiotic level is defined as a concentration higher than the minimum inhibitory concentration (MIC) of the suspected pathogens in the surgical wound at the time of incision. Multiple studies support administration of antimicrobial prophylaxis close to the time of incision, and prior to it, to achieve the desired protective benefit[24,25].

The goal of administering antibiotics intraoperatively is to maintain adequate serum and tissue levels during the highest risk period, which is while the incision is open. Observational studies have shown that repeated intraoperative dosing of an antibiotic with a short half-life is associated with a decreased risk of SSI. Redosing of antibiotics should be based on the specific antibiotic's half-life and the patient's creatinine clearance, but also intraoperative bleeding of more than 1500 cc.

### 2.2.4. Discontinuation of prophylactic antibiotic

Antibiotic prophylaxis should be discontinued within 24 h after surgery end time, except for cardiac surgery, which has been approved for up to 48 h of coverage, although no strong data support this extension.

There are no data to support a prolonged course of prophylactic antibiotics. In fact, many studies show no added benefits of postoperative doses, possibly because the highest risk period is while the incision is open. Furthermore, there are risks of prolonged antibiotic usage such as the development of drug resistant pathogens.

## CHAPTER 3: METHODOLOGY

### 3.1. Study design

From September 2017 till August 2018, we conducted a double blind randomized controlled trial where one group of patients undergoing clean, elective surgical procedures at CHUK was assigned for preoperative antibiotic (intervention) while the other one was assigned for placebo (control). Antibiotic used was cefazolin and the placebo was a similar looking preparation of water for injection given within 30-60 minutes of skin incision.

### 3.2. Study description and randomization process

We randomized patients in a 1:1 allocation ratio using a simple randomization. Using a sealed envelope containing numbers for placebo or antibiotics, anesthetists randomly allocated each patient for antibiotic prophylaxis or placebo before starting surgery and administered the chosen drug. Patients, investigator and surgeons were all blinded to the intervention.

All patients were not operated by the same surgeon; however, preventive measures for SSIs such as effective surgical hand scrub, proper skin preparation and sterility of materials and instrument were applied systematically in all groups. Dressing of the wound was removed 48 hours after operation and no further dressing was applied. There was one blinded outcome assessor to document the status of surgical wound at discharge and after 30 postoperative days.

### 3.3. Study setting

CHUK is the largest referral and teaching hospital of Rwanda serving about 75% of Rwandan population. It has 650 beds distributed for all departments[26]. The study was conducted in the department of surgery which has 120 bed and 8 operating theaters shared among all surgical subspecialties. In 2010, there were 4164 operations performed and only a third was electives[9].

### 3.4. Study population

This study included all adults and pediatric patients who were operated at CHUK for clean surgeries without use of prosthesis. Clean surgeries were classified based on CDC criteria as operations in which no inflammation is encountered and the respiratory, alimentary or genitourinary tracts are not entered (Appendix A).[3,27]

### 3.5. Inclusion and exclusion criteria

We included:

- All elective non-prosthetic surgical procedures classified as clean surgeries based on CDC criteria mainly from general surgery, pediatric surgery, ENT and plastic surgery.

The following were the exclusion criteria:

- Emergency cases
- Any patient with ASA >2
- Procedures lasting more than 2 hours
- Patients who were taking antibiotics within 2 days prior to operation for other reasons

### 3.6. Sample size

Sample size was calculated using the following formula:

$$N = \frac{Z^2(P1Q1 + P2Q2)}{D^2}$$

- N = Sample size
- Z = the unit deviate for type 1 error rate (95% confidence interval) =1.96
- Baseline risk of SSI is 5% ($P_1$=0.05)
- This study has 80.0% power to detect a P2 = 0.010
- Q1 = 1-P1
  Q2 = 1-P2
  D = P1-P2
- Therefore, we found 69 patients in each group.

### 3.7. Data collection, entry and analysis

Data was collected using a questionnaire (Appendix B) and included as variables; demographic data, type of surgery, ASA score, type and dose of antibiotic used, time between prophylaxis and skin incision, duration of surgery, patient's coomorbidities such as diabetes, steroids use, HIV status, intraoperative complications (bleeding requiring transfusion), postoperative complications

(need for reoperation, hypotension, hypoxia, postoperative mechanical ventilation), skin closure (continuous vs interrupted, type of suture material) and use of drains.

We used SPSS-23 for data entry and analysis. Pearson Chi-Square test was used to test categorical variables and binary as well as multivariate regression analysis were used when necessary to test the relationship between the intervention and the outcome (SSI)

### 3.8. Outcome measures

- The primary outcome was SSI at discharge and at 30 days after surgery.
- Secondary outcomes were adverse events, hospital cost, in-hospital and 30 day mortality, major complications (unplanned reoperation, cardiac arrest, ventilator greater than 48 hours, DVT/PE, stroke, pneumonia) and length of hospital stay.

### 3.9. Ethical considerations

Patents were explained the intervention before being recruited those accepting to be included in the study were requested to provide a written consent and assent (Appendix C).

Approval for the study was obtained from the Department of surgery Ethics and Research committee, and from the University of Rwanda IRB committee (Appendix D).

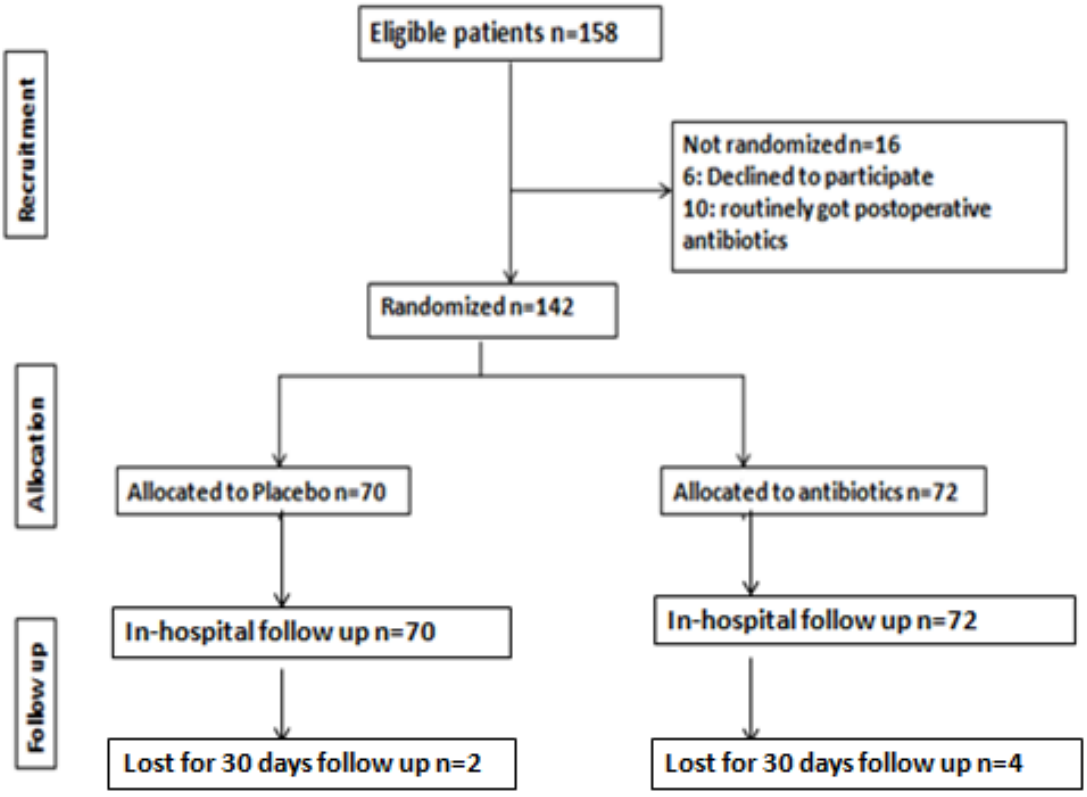
This study followed CONSORT protocol and was registered as RCT in PROSPERO database under record number: NCT03595852

## CHAPTER 4. RESULTS

### 4.1. Descriptive data characteristics

The trial recruited 142 patients with clean surgeries. They were randomized into 2 groups; 72 patients in intervention group and 70 in placebo group. The former received preoperative antibiotic (cefazolin iv 2 gr single dose in adults or 30 mg/kg in pediatrics within 30 to 60 minutes of skin incision) and the later received similar looking preparation with placebo (water for injection). Both patient and surgeon were blinded for intervention. In-hospital follow up was 100%; however 2 patients in placebo group and 4 in intervention group were lost for follow up after discharge (figure 1)

Figure 1: Flow diagram of the trial



The age range between 4 months to 85 years (mean age of 25.4; IQR: 39.75), and 65 (47.8 %) were pediatric (15 years and below) (figure 2); 97 were male and 44 female with M: F ratio of 3:1 (figure 3). In this study, 121 (85%) patients were ASA score 1 and 21 (15%) patients were ASA score 2.

Patient characteristics and variables were almost equally controlled between the 2 groups as showed in table 1.

Table 1: Patient characteristics

| | | Intervention Number (%) | Control/placebo Number (%) |
|---|---|---|---|
| Age | Pediatrics (≤15 years) | 35(24.64) | 30(21.12) |
| | Adults (>15 years) | 37(26.05) | 40(29.16) |
| Sex | Female | 18(12.67) | 26(18.30) |
| | Male | 53(37.32) | 44(30.98) |
| Past medical history | None | 59(41.54) | 59(41.54) |
| | Diabetes | 3(2.11) | 2(1.40) |
| | hypertension | 8(5.63) | 8(5.63) |
| | Smoking | 2(1.40) | 0 |
| | Immunosupression | 0 | 1(0.70) |
| ASA score | 1 | 62(43.66) | 59(41.54) |
| | 2 | 10(7.04) | 11(7.74) |
| Type of surgery | Thyroid | 9(6.33) | 19(13.38) |
| | Hernia | 17(11.97) | 16(11.26) |
| | Hydrocele | 19(13.38) | 13(9.15) |
| | Undescended testis | 7(4.92) | 5(3.52) |
| | Varicose veins | 6(4.22) | 6(4.22) |
| | Others | 14(9.85) | 11(7.74) |
| Antiseptic | Povidone | 35(24.64) | 38(26.76) |
| | Chlorhexidine | 37(26.05) | 32(22.53) |
| Time before skin incision | ≤30 minutes | 43(30.28) | 35(24.64) |
| | >30 minutes | 29(20.42) | 35(24.64) |

| | | | |
|---|---|---|---|
| Duration of surgery | ≤60 minutes | 56(39.43) | 44(30.98) |
| | >60 minutes | 16(11.26) | 26(18.30) |
| Blood loss | ≤25 cc | 53(37.32) | 47(33.09) |
| | >25 cc | 19(13.38) | 23(16.19) |
| Skin closure | Interrupted | 26(18.30) | 17(11.97) |
| | Continuous | 46(32.39) | 53(37.32) |
| Suture type | Monofilament | 46(32.39) | 52(36.61) |
| | Braided | 26(18.30) | 18(12.67) |
| Dain use | Yes | 11(7.74) | 16(11.26) |
| | No | 61(42.95) | 54(38.02) |
| Adverse drug reaction | Yes | 0 | 0 |
| | No | 72(50.70) | 70(49.30) |

Figure 2: age of patient population studied

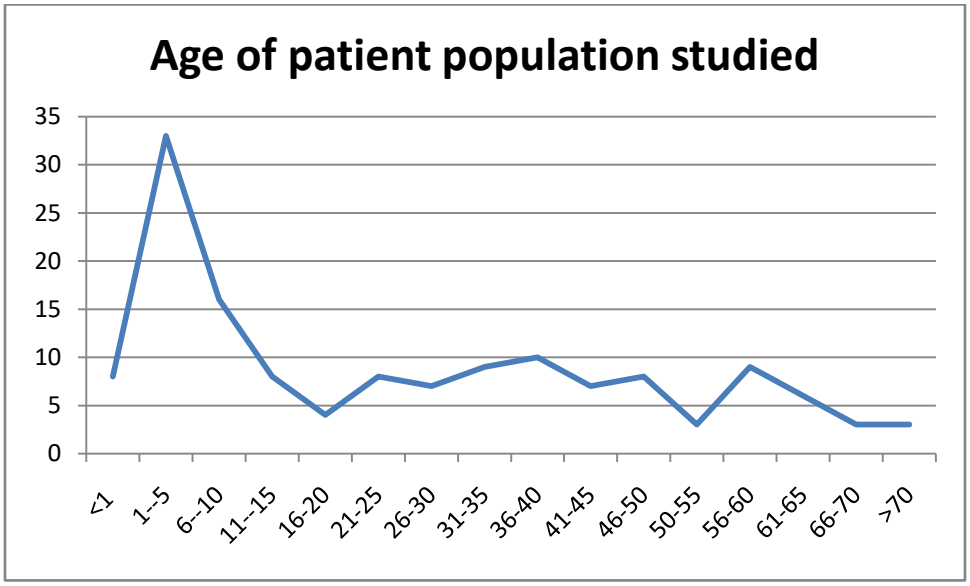
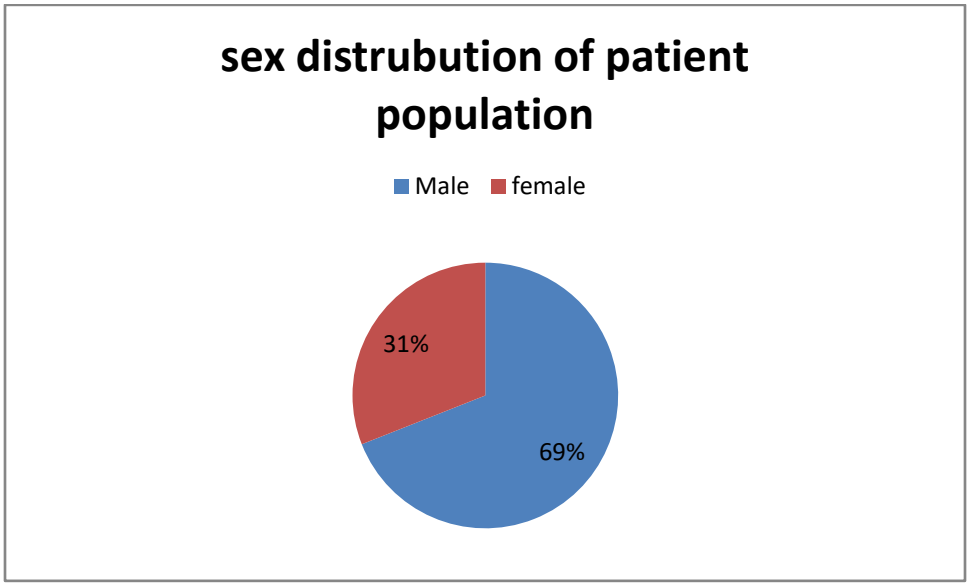


Figure 3: sex distribution of the patient population




Important past medical history was hypertension in 11.3% of patients, diabetes in 3.5% and HIV in 0.7% (table2)

Table 2: Past medical history of patient population studied

| PMH | frequency | percent | cumulative percent |
|---|---|---|---|
| None | 118 | 83.1 | 83.1 |
| Diabetes | 5 | 3.5 | 86.6 |
| Hypertension | 16 | 11.3 | 97.9 |
| smoking | 2 | 1.4 | 99.3 |
| HIV | 1 | 0.7 | 100 |
| total | 142 | 100 | |

Most of clean surgeries recruited were hernias, hydroceles, undescended testis and varicose veins. Among them, hernias and hydrocele accounted 45.7% of study population as indicated in table 3.

Table 3: type of procedures included in the trial

| type of procedure | Frequency | Percent | Cumulative Percent |
|---|---|---|---|
| thyroid | 28 | 19.7 | 19.7 |
| hernia | 33 | 23.2 | 43 |
| hydrocele | 32 | 22.5 | 65.5 |
| undescended testis | 12 | 8.5 | 73.9 |
| varicose vein | 12 | 8.5 | 82.4 |
| *others | 25 | 17.6 | 100 |
| Total | 142 | 100 | 100 |

*Others operations include: lipomas 7, parathyroid mass 5, varicocele 5, HPS (hypertrophic pyloric stenosis) 2, syndactily release 2, TGD (thyroglossal duct) cysts 2, breast lumpectomy 1, abdominal rectopexy 1.

Skin preparation was done using 2 types of antiseptic solutions depending on which preparation was available at the time of surgery. Povidone was used in 73 (51%) patients while chlorhexidine was used in 69 (49%) patients.

After randomization, patients underwent operation and apart for antibioprophylaxis, everything else was done according to local protocols and guidelines.
Surgical wounds were closed primarily using either monofilament sutures (nylon or monocryl) in 69% of patients or braided (polyglactin) in 31% and technique of wound suturing was either continuous (subcuticular) in 70% or simple interrupted in 30% of patients. Surgical drains (mainly closed system drains) were used in 27 (19%) of patients.

**4.2. Primary outcome**

The primary outcome was the SSI at discharge from the hospital and within 30 postoperative days. There was no SSI documented at discharge in all patients. However, 3 patients (2 in placebo group and 1 in antibiotic group) developed SSI within 30 postoperative days. All were superficial SSI and were managed at health center. The overall SSI rate at 30 days in clean surgery was 2.2%. (Table 4)

Table 4: SSI rate after 30 postoperative days comparing intervention and placebo groups

| | | Intervention | | | Percentage | P value |
|---|---|---|---|---|---|---|
| | | Placebo | Antibiotic | Total | | |
| SSI after 30 days | no | 66 | 67 | 133 | 97.78 | |
| | yes | 2 | 1 | 3 | 2.2 | **0.559** |
| *Total | | 68 | 68 | 136 | 100 | |

*Patients followed after 30 postoperative days excluding 6 patients who were lost for follow up

Table 5: Univariate analysis with with Pearson Chi-Square test of other variables tested and suspected to influence SSI:

| **Variables** | | **SSI after 30 days** | | **P value** |
|---|---|---|---|---|
| | | No (%) N=133(97.79) | Yes (%) N=3(2.20) | |
| **Patient characteristics** | | | | |
| Age | Pediatric(≤15 years) | 62 (47) | 2 (67) | 0.491 |
| | Adults (>15 years) | 71 (53) | 1 (33) | |
| Sex | Female | 41 (31) | 0 | 0.250 |
| | Male | 92 (69) | 3 (100) | |
| Past medical history | None | 110 (83) | 3 (100) | 0.960 |
| | Diabetes | 4 (3) | 0 | |
| | Hypertension | 16 (12) | 0 | |
| | smoking | 2 (2) | 0 | |
| | HIV | 1 (1) | 0 | |
| ASA score | I | 113(85) | 3(100) | 0.467 |
| | II | 20(15) | 0 | |
| Type of surgery | Thyroid | 26 (20) | 0 | 0.471 |
| | Hernia | 31 (23) | 2 (67) | |
| | Hydrocele | 32 (24) | 0 | |
| | UDT | 11 (8) | 0 | |
| | Varicose veins | 11 (8) | 0 | |
| | Others | 22 (17) | 1 (33) | |

| | | | | |
|---|---|---|---|---|
| **Intraoperative factors** | | | | |
| **Antiseptic** | **Chlorhexidine** | 69 (52) | 0 | **0.099** |
| | **Povidone** | 64 (48) | 3 (100) | |
| Time before skin incision | <=30 min | 72 (54) | 2 (67) | 0.666 |
| | >30 min | 61 (46) | 1 (33) | |
| Duration of surgery | <=60min | 96 (72) | 1 (33) | 0.141 |
| | >60 min | 37 (28) | 2 (67) | |
| Estimated blood loss | <=25ml | 94 (71) | 2 (67) | 0.880 |
| | >25ml | 39 (29) | 1 (33) | |
| Use of drain | No | 110 (83) | 3 (100) | 0.429 |
| | Yes | 23 (17) | 0 | |
| Skin closure technique | Interrupted | 40(30) | 2(67) | 0.175 |
| | Continuous | 93(70) | 1(33) | |
| Suture type | Monofilament | 92(69) | 2(67) | 0.926 |
| | braided | 41(31) | 1(33) | |
| **Postoperative factors** | | | | |
| Hypotension | No | 130 (98) | 3 (100) | 0.793 |
| | Yes | 3 (2) | 0 | |
| **Hypoxia** | No | 131 (99) | 0 | **<0.001**** |
| | Yes | 2 (1) | 3 (100) | |
| Post op mechanical vent | No | 132 (99) | 3 (100) | 0.880 |
| | Yes | 1(1) | 0 | |
| Hospital stay | <=1 day | 61 (46) | 1 (33) | 0.666 |
| | >1 day | 72 (54) | 2 (67) | |

**p-value <0.05 (statistically significant)

Important variables were put into multivariate model to study their relationship towards the development of SSI at 30 postoperative days. Variables with zero frequencies were excluded from the model [Table 6].

Table 6: Multivariate analysis of factors associated with surgical site infection at 30 days

| Variables | Odds ratio | 95% confidence interval | P value |
|---|---|---|---|
| Prophylactic antibiotic | 0.33 | 0.02, 5.09 | 0.427 |
| Adult | 57.08 | 1.23, 2649.31 | **0.039**** |
| Incision time >30 min | 0.42 | 0.03, 6.80 | 0.545 |
| Surgery time >60 min | 26.78 | 0.41, 1744.9 | 0.123 |
| Continuous skin closure | 0.13 | 0.01, 2.11 | 0.15 |
| Braided suture | 0.37 | 0.01, 9.07 | 0.541 |
| LOHS >1 day | 0.29 | 0.01, 15 | 0.54 |

**p-value <0.05 (statistically significant)

## CHAPTER 5: DISCUSSION

### 5.1. General data overview

The trial was conducted after obtaining approval from UR/CMHS/IRB and CHUK ethical committee and was registered in clinical trials under record number NCT03595852. All eligible patients were 158 and among them 142 fulfilled the inclusion criteria.

Patients were allocated into 2 groups; the intervention group received single dose of intravenous cefazolin within 60 minutes of skin incision while the control (placebo) group received similar looking preparation of water for injection.
Second generation cephalosporin (cefazolin) was used in all patients in intervention group and the dose of 2 gr was given as single dose in adults or 30mg/kg in children under 30 Kg. This is the same recommended prophylactic antibiotic in clean surgery by most of the guidelines as it cover most likely organisms to cause SSI.[1, 3,7,25,24]

The study recruited all age group and the range was 4 months to 85 years where pediatric population (under 15 years) was 47.8%. This is different from other studies which only studied each age group separately.[6,22]Male to female ratio was 3:1 reflecting the study population in which 47.8% were having inguinal hernias and hydroceles which are predominant in male[28].

Clean surgeries recruited were based on CDC criteria for surgical wounds classification [Appendix A] and included mainly thyroid, hernias and hydrocele which accounted almost 2/3 of the procedures. This is different from most of the same studies done on preoperative antibiotic prophylaxis in clean surgeries which were considering only procedure by procedure type[6,20,21].

### 5.2. Surgical site infection rate in clean surgery

Our patients were followed for SSI occurrence at discharge and at 30 postoperative days as recommended by The US CDC guidelines on postoperative follow up for SSI in clean surgeries without prosthesis use[11].

48 hours post-operatively, dressings were removed in all wounds and were inspected by resident for signs of SSI. This same practice of early dressing removal (within first 48 hours) is also supported by many guidelines with no detrimental effect on outcome[29]. Occasionally the

principal investigator (PI) was the one to document the status of the wound at discharge. Where hospital stay was less than 48 hours, the wounds were not inspected at discharge; however, the patients were instructed to consult the nearest health center for dressing removal and were advised to document any abnormal wound status to be communicated to the attending.

In overall, there was no in-hospital SSI observed in all clean surgeries performed.
However, three patients developed SSI (2 in placebo group and 1 in antibiotic group) within 30 post operative days. The infections were superficial based on CDC definitions of SSI[12]. Therefore, the rate of SSI was 2.2% which is comparable to the findings from other studies where Sweta Shah et al[30] found the rate of 1.57%, while in a large Cochrane review of antibiotic prophylaxis in hernia repair the rate was 3.5-4.9%[31]. Almost similar designed study done in Nigeria for patients undergoing thyroid surgery found SSI rate of 2.5% which is comparable to our findings[32].

Although 2 patients versus 1 got SSI in placebo and antibiotic group respectively, it was not statistically different (P=0.559). The same was observed in most of the studies done in clean surgeries especially on thyroid and hernias which failed to prove any decrease in SSI with use of prophylactic antibiotics in clean surgeries[20,21,22]. In contrast to these studies, a Cochrane meta-analysis of 17 randomized trials (11 hernioplasty and 6 herniorrhaphy trials) came out with different conclusion supporting preoperative antibiotics not only in hernioplasty but also in herniorrhaphy procedures. However, it recommend to take into consideration other different factors which are patient and hospital related as well as the settings in which the studies are being conducted.[13,31]

### 5.3. Univariate analysis of other factors associated with SSI

Univariate analysis using Pearson $\chi^2$ test was done to determine the factors likely to influence SSI. P-value of <0.05 was considered as significant [Table5]. Only postoperative hypoxia was found to carry a significant risk for SSI (P<0.001).
Considering postoperative hypoxia, the benefits of perioperative oxygen supplementation on reduction of SSI rate were proved from several studies. There are based on the rationale that hyperoxygenation in perioperative period increases partial pressure of oxygen at the wound site which increases neutrophil activity with ultimate decrease in SSIs.[33,34]

Like the findings from other studies, postoperative hypoxia is strongly associated with increase of SSI rate, however there is still fluctuating evidence regarding supplemental oxygen delivery in reduction of SSI rate.[35,36]

Comparing the types of antiseptic skin preparation used, there was a trend towards increase of SSI when povidone was used as antiseptic compared to chlorhexidine (P= 0.099). Though the results are not significant, Rabih et al have found significant reduction of SSI rate by using chlorhexidine-alcohol than povidone-iodine solution for skin preparation.[37] Similar results were also found in a systematic review and meta-analysis by Gaetano et al who reported a moderate-quality evidence supporting the use of chlorhexidine over povidone for preoperative skin preparation to prevent SSI.[38]

### 5.4. Multivariate analysis of predictive variables for SSI

Variables with distributed outcome were analysed with multivariate model to determine the one that can be used to predict patients with a higher risk of SSI before the operation [Table 6].

Being an adult patient (above 15 years) was an independent predictor of SSI (OR 57.08; 95% C.I of 1.23, 2649.31). Based on different changes in physiology, it is known that older adults are at increased risk of SSI compared to children due to an increased risk of comorbid conditions as well as age-related immune system changes in phagocytosis, cellular migration, and antibody production[39], however none of our patient with SSI had comorbidities and as the confidence interval is very wide, this results cannot be used to represent the entire population, therefore further studies are needed to determine the difference in SSI rate in pediatric and adult population undergoing clean procedures.

The other variables such as length of hospital stay, skin incision before 30 or 60 min of antibiotics, suture type and skin closure techniques were not independent predictors of SSI.

### 5.5. Adverse drug reaction in patient population studied

Based on the definition of adverse drug reaction[40], none of our patient developed adverse reaction to the antibiotic used. Although antibiotics carry important risk of adverse reaction to patients, its incidence rate remains unknown in patients undergoing clean surgeries[12].

### 5.6. Patient and hospital cost related to the antibiotic use

Patient cost is expected to increase when additional intervention is added on surgical procedure. For this study it was difficult to estimate the increase in individual patient cost with use of antibiotic due to mixture of operations and additional intraoperative details (e.g: 2 same procedures may have different cost depending on different materials used such as type and number of sutures, duration of oxygen and different analgesia received). However, considering the cost of cefazolin of 2400 RFW/ 1gr vial, patients in intervention group total cost increment was 285,600 RFW* (25X2,400 +47X4,800) based on that adults patients got 2gr of cefazolin while pediatric patients under 30Kg got 30mg/kg.

This amount of money constitute a significant economic burden and additional health care cost not only to the hospital but also to the patient. Therefore it can be saved as long as antibiotics will not add any benefits in terms of SSI control in clean non-prosthetic surgery.

Many studies have focused on the hospital burden of SSIs which are estimated to be around billon of US dollars[1]. SSI basically increase hospital stay and cost related to their treatment.[6] On the other side the cost related to inappropriate use of antibiotics has not been estimated, however, few studies have proved that unnecessary antibiotic prophylaxis in clean surgery do increase patient cost and antibiotic resistant[16,30]. The same findings were observed by Abubaker et al in their audit on antibiotic prophylaxis in a Sudanese teaching hospital which found that irrational use of antibiotic was caused by absence of clinical guidelines with consequence of development of bacteria resistance and higher costs.[5]

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***285,600 RFW = 321USD**

## CHAPTER 6: CONCLUSION

Antibiotic prophylaxis in surgery constitutes one of the measures to decrease SSI which carry a significant burden to surgical patients. However, not all patients undergoing surgery need antibiotics and appropriate use should be encouraged as overuse of antibiotics is associated with increased cost of care and antibiotic resistance.

This study has proved that clean surgeries can safely be performed in African settings without the use of preoperative antibiotic prophylaxis with no increase in SSI rate.

## RECOMMENDATIONS

- Based on the findings, we recommend no antibioprophyalaxis in clean non-prosthetic wounds.
- We also recommend to develop local guideline on antibiotic prophylaxis in clean surgery at CHUK based on results of this study

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**Appendix A: CDC SURGICAL WOUND CLASSIFICATION DEFINITIONS**

**Surgical Wound Classification Grades (I–IV) as Defined by the CDC**

| CDC Surgical Wound Classification Definitions |
|---|
| *Class I/Clean:* An uninfected operative wound in which no inflammation is encountered, and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow no penetrating (blunt) trauma should be included in this category if they meet the criteria. |
| *Class II/Clean-Contaminated:* An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in a sterile technique is encountered. |
| *Class III/Contaminated:* Open, fresh, accidental wounds. In addition, operations with major breaks in a sterile technique (eg, open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute or no purulent inflammation is encountered are included in this category. |
| *Class IV/Dirty-Infected:* Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation. |

CDC = Centers for Disease Control and Prevention.

## Appendix B: STUDY QUESTIONNAIRE

**PREOPERATIVE ANTIBIOTIC PROPHYLAXIS VERSUS PLACEBO IN CLEAN, NON-PROSTHETIC SURGERY AT CHUK. IMPACT ON SURGICAL SITE INFECTIONS AND PATIENT COST. DATA COLLECTION TOOL**

**Demographic data**

Patient initials: .....
Age: .....
Sex: .....
Hospital IP: .....
Phone number: .....or .....

**Past medical history**

Diabetes ☐
Hypertension ☐
Cancer ☐
Smoking ☐
Immunosuppression: Cancer treatment, HIV infection, Steroid use: Yes ☐ No ☐ Which one: .....
ASA score: .....

**Type of clean surgery to be done**

Thyroid ☐
Hernia without mesh ☐
Hydrocele ☐
Undescended testis ☐
Others: .....

**Perioperative**

Antibiotic prophylaxis given Yes ☐ No ☐
If yes: type of antibiotic: ..... Dosage: .....
Time between antibiotic and skin incision: ..... Minutes
Need of second dose of antibiotic Yes ☐ No ☐
Estimated blood loss: ..... mls
Need of transfusion Yes ☐ No ☐ If yes, how many units of PRBCs used: .....
Duration of surgery (between skin incision and closure): ..... Minutes

**Skin closure**

Technique: continuous vs. interrupted, or others (specify): .....
Type of suture material: .....
Use of drain Yes ☐ No ☐
If yes. Duration of drains: .....Hours Duration of dressing: ..... Hours

**Postoperative complications:**

Need for reoperation Yes ☐ No ☐
Hypotension Yes ☐ No ☐
Hypoxia Yes ☐ No ☐
Postoperative mechanical ventilation Yes ☐ No ☐
Others: .....

**Outcome**

SSI documented before discharge Yes ☐ No ☐
Length of hospital stay: .....(in days)
Death Yes ☐ No ☐
Major complications:
Unplanned reoperation Yes ☐ No ☐
Cardiac arrest yes ☐ No ☐
Ventilator greater than 48 hours Yes ☐ No ☐
DVT/PE Yes ☐ No ☐
Pneumonia Yes ☐ No ☐
SSI after 30 days Yes NO

**Appendix C: CONSENT AND ASSENT FORMS IN ENGLISH AND KINYARWANDA**

**ASSSENT FORM**

Project title: "**PREOPERATIVE ANTIBIOTIC PROPHYLAXIS VERSUS PLACEBO IN CLEAN, NON-PROSTHETIC SURGERY AT CHUK. IMPACT ON SURGICAL SITE INFECTIONS AND PATIENT COST".**

Investigators: Dr SIBOMANA ISAIE, MD
Tel: 0788558658
Email: siibomana@gmail.com

We are doing a research study on antibiotic prophylaxis versus placebo in clean non prosthetic surgery. If you decide that you want to be part of this study, you may receive antibiotic prophylaxis or placebo prior to surgery.

You can ask questions any time, now or later. You can talk to the doctors, your family or someone else. You do not have to be in this study, no one will be mad at you if you don't want to do this. We will also ask your parents if they would like you to be in the study. Even if you say yes now, you can change your mind later.

When we are finished with this study, we will write a report about what was learnt. This report will not include your name or that you were in the study.

**ASSENT**

I want to take part in this study. I know I can change my mind at any time.
**Name of the child**: …….
**Verbal assent given**: yes **Date**: …/…/……

I confirm that I have explained the study to the participant to the extent compatible with the participant understands, and that the participant has agreed to be in the study.

Name of person obtaining the assent and

Signature: …… Date: …/…/……

ICYEMEZO CYUBURENGANZIRA BWO KWINJIRA MUBUSHAKASHATSI (munsi y imyaka 18)

**UMUTWE WI BYIGWA**: **“Guhabwa cyangwa kudahabwa umuti wica tumwe mu dukoko twa mikorobe mbere yo kubagwa zimwe mu ndwara zisa neza kandi zidakenera insimburangingo muri CHUK**”.

Abashakashatsi: Dr SIBOMANA Isaie

Telefoni: 0788558658

Turakora ubushakashatsi kubijyanye n’indwara zisa neza zibagwa zidakeneye insimburangingo. Niwemera kwitabira ubu bushakashatsi, uzashyirwa mu cyikiro cy’abashobora kubagwa babonye cyangwa batabonye umwe mu miti yica tumwe mu dukoko two mu bwoko bwa mikorobe mbere yo kubagwa. Ushobora kubaza abaganga cyangwa umuryango wawe, cyangwa undi muntu uwo ariwe wese, igihe icyo aricyo cyose .

Ntabwo ari itegeko kwitabira ubu bushakashatsi. Ntawe uzakurakarira nuba utabyitabiriye. Tuzabaza n’ababyeyi bawe niba bemera ko witabira ubu bushakashatsi. Nubwo wakwemera ubu ,wemerewe kuva muri ubu bushakashatsi igihe cyose ushakiye.

Niturangiza ubu bushakashatsi, tuzandika amakuru y’ ibyo twabonye ariko izina ryawe ntaho rizagaragara.

Icyemezo: Nemeye kwitabira ubu bushakashatsi

Izinary’umwana……..

Itariki …… / ……. /……

Ndemeza ko nsobanuriye uwitabiriye ubu bushakashatsi ku rwego abisobanukirwa bituma yemera kwitabira.

Amazina n’umukono by’ uwasobanuriye umwana:

……

Itariki: ……/…...../……

**INFORMATION SHEET & CONSENT/ IBISOBANURO NO KWEMERA KUJYA MUBUSHAKASHATSI**

Please read carefully before before deciding on research participation/ Soma neza mbere yo kwemeza niba ujya mubushakashatsi

**Purpose of the research study/ Icyo ubushakashatsi bugamije:** To provide evidence regarding antibiotic prophylaxis prior to surgery in clean non prosthetic procedures. /Kugaragaza ubumenyi nyabwo burebana no gutanga umwe mu miti yica tumwe mu dukoko two mu bwoko bwa mikorobe mbere yo kubagwa zimwe mu ndwara zisa neza kandi zidakenera insimburangingo

**What you will do in the study/ Icyo usabwa muri ubu bushakashatsi:** You will be asked about you're your identification and past medical history. Then after you will be asked to participate in this study by deciding to receive antibiotic prophylaxis or no prophylaxis prior to surgery; after your decision you will not be aware of whether you have or not received prophylaxis antibiotic. 30 days from discharge to the hospital you will be called and asked questions regarding your wound for present or absent of signs of surgical site infection. You may skip any questions that make you uncomfortable. You may also elect to discontinue your participation in this study at any time without any negative impact on your expected treatment / uzabazwa ibijyanye n'umwirondoro wawe ndetse n'ubundi burwayi ufite cyangwa waba warigeze kugira. Nguma uzasabwa kujya murubu bushakashatsi uhitamo guhabwa cyangwa kudahabwa umuti wica tumwe mu dukoko two mu bwoko bwa mikorobe mbere yo kubagwa; nyuma y'icyemezo cyawe ntuzamenya niba wahawe cyangwa utahawe uwo muti. Nyuma y'iminsi 30 warasezerewe mu bitaro tuzaguhamagara tukubaza ibijyanye n'igisebe niba harigeze kuba cyangwa kutaba ibimenyetso bijyanye no kwinjirirwa kwa mikorobe. Ushobora gutaruka ikibazo wumva ko kikubangamiye. Ndetse ushobora no guhitamo guhagarika gukomeza kuba murubu bushakashatsi igihe icyo aricyo cyose ntazindi ngaruka kubuvuzi ugomba guhabwa

**Time required/Igihe usabwa:** The time you will be in hospital and 30 days after hospital disharge/ igihe uzaba uri mu bitaro nu mu minsi 30 nyuma yo gutaha.

**Risks/ ingaruka mbi :** There is small risk of surgical site infection or allergy to antibiotic/Hari ingaruka nke cyane zuko igisebe gishobora kwinjirirwa na mikorobe cyangwa umubiri ukivurumbatanya ku muti wica udukoko.

**Benefits/ Ingaruka nziza:** You will not be compensated for your participation. The study will provide evidence of antibiotic prophylaxis in clean non prosthetic surgery at CHUK. This will reduce misuse of antibiotics but also may contribute to reduction of bacterial resistance and patient cost. Ntabihembo bigenewe uzitabira ubu bushakashatsi. Ubu bushakashatsi buzatanga ubumenyi nyabwo burebana no gutanga umwe mu miti yica tumwe mu dukoko two mu bwoko bwa mikorobe mbere yo kubagwa zimwe mu ndwara zisa neza kandi zidakenera insimburangingo mu bitaro bya CHUK. Ubu bushakashatsi buzagabanya ikoreshanabi ry'imito yica udukoko ariko nanone bushobora kuzafasha kugabanya za mikorobe zidakangwa n'imiti ndetse bukagabanya n'amafaranga umurwayi yishyura.

**Confidentiality/Kugirirwa ibanga:** The information that you give in the study will be handled confidentially. Your information will be assigned a code number. The list connecting your name to this code will be kept in a locked file. When the study is completed and the data have been analyzed, this list will be destroyed. Your name will not be used in any report/Amakuru uzaduha azakoreshwa muburyo bw' ibanga. Uzahabwa umubare w'ibanga kandi impapuro zihuza amazina n'umubare w'ibanga zizabikwa mukabati gafungwa, zizanatwikwe ubushakashatsi burangiye. Ntahantu nahamwe havugwa ubu bushakashatsi hazagaragara amazina yawe.

**Right to withdraw from the study/Uburenganzira bwo kwikura mubushakashatsi:** You have the right to withdraw from the study at any time without penalty/ wemerewe kwivana mubushakashatsi igihe cyose wabishakira ntazindi nkurikizi cg ingaruka mu kuvurwa kwawe.

**If you have questions about the study, contact/Ukeneye ibindi bisobanuro wabaza:**

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**If you have questions about your rights in the study, contact/ Mugihe uburenganzira bwawe butakubahirizwa wabaza:**

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**Agreement:**

I agree to participate in the research study described above/Nemeye kujya mubushakashatsi nasobanuriwe haruguru.

**Signature: _____ Date: _____**