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Comparative And Cost Benefit Analysis: Vancomycin Versus Ancef In Total Knee Arthroplasties

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COMPARATIVE AND COST BENEFIT ANALYSIS: VANCOMYCIN VERSUS ANCEF IN TOTAL KNEE ARTHROPLASTIES

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Abstract

Background: Total knee arthroplasty (TKA) is the definitive treatment for degenerative joint disease of the knee. Total joint infections, although low, are a complication that can be a massive expenditure on health care systems and patients. Economic costs have the potential of being high for this procedure. It is estimated to treat these TKA infections, primarily methicillin-resistant Staphylococcus aureus (MRSA) to be between $68,000 and $107,000.

Purpose: The purpose of this retrospective study is to determine whether vancomycin has greater cost benefits and efficacy in reducing post-operative infection rate of total knee arthroplasties than does cefazolin.

Methods: A retrospective chart review of 1661 total knee arthroplasty charts was completed. A random sample of 313 charts was obtained and data extracted. A two tailed t-test analyzed comorbidities with readmission related to total knee arthroplasty infection, and the Wilcoxon signed rank test was used to determine if smoking, BMI >40kg/m2, diabetes >200mg/dL, history of MRSA, and recent hospitalization variables had a relationship by chance.

Results: The two-tailed t-test showed a significant correlation between the variables and readmission related to total knee arthroplasty infection. The null hypothesis was rejected for each variable except readmission related to TKA infection and recent hospitalization, which was an expected finding.

Conclusion: Total Knee Arthroplasty infections can be a massive expenditure on healthcare. Further studies are needed to determine vancomycin's efficacy over cefazolin and/or the efficacy of adding vancomycin to cefazolin as a preoperative combination.

Keywords: total knee arthroplasty infections, vancomycin, cefazolin

Chapter 1

Introduction

Background

Total knee arthroplasty (TKA) is the definitive treatment for degenerative joint disease of the knee (Shahi & Parvizi, 2015). Total knee arthroplasty is widely used to relieve the pain of end stage primary osteoarthritis and improve activities of daily living (Weinstein et al., 2013). The frequency of TKA procedures has been increasing over the years as the population ages. Patel, Guild, and Kumar (2018) reported a projected increase in total knee replacements of approximately 3.4 million by 2030. The younger population may potentially experience longer lives while living with degenerative joint disease. This increased longevity will increase the need for total joint replacement in the future (Nwachukwu et al., 2015).

Despite the advances in total knee arthroscopic procedures, complication rates in the postoperative short- and long-term still exist (Sadigursky, Pires, Rios, Filho, Castro de Queiroz, & Azi, 2017). Infections can be one of the most challenging complications due to potential difficulties with treatments. Prophylaxis protocols have been created along with antibiotic regimens to assist with decreasing the incidence of these infections.

Total joint infections can result in total joint revisions and potentially increase the cost of health care exponentially. Total joint infections are preventable if the new prophylaxis measures are followed including MRSA screening, MRSA decolonization, preoperative skin preparation with hibiclens, perioperative glycemic control, modification of venous thromboembolism protocols, operative environment controls, and antibiotic selection (Burger et al., 2018).

As with all medical procedures, there are risks involved when consenting to medical interventions such as total knee arthroplasty. Current literature supports the use of first or

second-generation cephalosporin or penicillin for primary total knee arthroplasty (Kheir, Tan, L., Azboy, Tan, D., & Parvizi, 2017). Total joint infections, although low, are a complication that can be a massive expenditure for health care systems and patients (Shahi & Parvizi, 2015).). The International Concensus Meeting (ICM) workgroup, a group of worldwide professionals on postoperative joint infections, stated that certain conditions can increase the risk of developing postoperative joint infections (Shahi & Parvizi, 2015).

Total joint infections may be complicated by patient comorbidities such as smoking, BMI >40kg/m2, diabetes 200mg/dL, history of methicillin resistant Staphylococcus aureus, and recent hospitalization (Shahi & Parvizi, 2015). Patients with infected joint prosthesis can require multiple surgical procedures and hospital admissions (Burger, Hansen, Leary, Aggarwal, & Keeney, 2018). Economic costs can potentially be high for additional surgical procedures with estimates of $68,000 and $107,000 to treat susceptible and resistant infectious organisms (Burger et al., 2018).

Prophylaxis Antibiotics

There are many different antibiotics available for infection prevention. Bacteriostatic antibiotics limit the growth of bacteria predominately by disrupting the protein and folic acid synthesis along with DNA replication within the bacteria (Meehan, Jamali, & Nguyen, 2009). However, bacteriostatic agents only disrupt the growth and reproduction of the bacteria but do not kill the bacteria. Beta-lactam antibiotics kill the bacteria by inhibiting the cell wall synthesis and inducing cytolysis, or the disruption of the cell (Meehan et al., 2009). The majority of antibiotic prophylactic agents used in total joint arthroplasty such as penicillin, cephalosporins, vancomycin, and aminoglycosides are considered bactericidal, meaning they kill the bacteria (Meehan et al., 2009).

An important consideration in antibiotic usage is the spectrum of action. While not all antibiotics cover all organisms, the chosen antibiotic must cover the organism most common to the procedure's cause of postoperative infection. In addition to this, the antibiotic's half-life that covers the decisive portion of surgery (the first two hours after incision) must be adequate with therapeutic concentrations lasting until wound closure (Meehan et al., 2009). Depending on the antibiotic the surgeon chooses, additional dosing may be necessary if surgical procedures last longer than the minimum inhibitory concentration of the drug.

Lastly, the cost of the antibiotic should be considered as well. Costs of the drug are more than the cost to the hospital. It also includes monitoring, administration, repeat doses, adverse effects, and infection if the antibiotic fails to adequately cover the organisms involved (Meehan et al., 2009). According to Meehan (2009), "the Surgical Care Improvement Project (SCIP) Advisory Committee, part of a national initiative to reduce surgical morbidity and mortality by 25% by 2010, and the American Academy of Orthopaedic Surgeons (AAOS), the preferred antimicrobial for patients undergoing total hip or knee arthroplasty is cefazolin and cefuroxime". Although these drugs are relatively cheap, and have been studied extensively, if an infection occurs, treatment must begin with an additional antibiotic such as vancomycin and can become quite expensive to treat (Meehan et al., 2009).

Problem

Although cephalosporins and penicillin cover a broader range of microbials, vancomycin has traditionally been ordered for patients with allergies to penicillin or in patients with positive methicillin-resistant Staphylococcus aureus (MRSA) (Kheir et al., 2017). Methicillin-resistant staphylococcus aureus has given pause to many providers whom may consistently order cephalosporins for total joint arthroplasty. In a randomized control trial by Young, Zhang,

Freeman, Mutu-Grigg, Pavlou, and Moore (2014), "data from the National Nosocomial Infection Surveillance System reported, between 1992 and 2003, the rate of methicillin resistance in S aureus infections rose from 35.9% to 64.4%, an increase of 3.1% per year" (p. 58). Vancomycin is not only recommended in patients with beta lactam allergies and MRSA infections but also in facilities where increased cases of MRSA have been documented (Liu, Kakis, Nichols, Ries, Vail, & Bozic, 2014). Providing the correct antibiotics preoperatively to patients can potentially save the healthcare systems thousands of dollars annually by reducing infection rates in total knee arthroplasty procedures. Decreasing the cost to patients as well as time spent in the hospital saves thousands of dollars for the healthcare facility and the patient. The comorbidities listed as smoking, BMI >40kg/m2, diabetes >200mg/dL, or HbA1c >7, recent hospitalization, or history of MRSA may increase the risk associated with a postoperative total knee arthroplasty infection. Vancomycin is the usual drug administered when a readmission related to a total knee arthroplasty infection has occurred.

Research Question

In total knee arthroplasty procedures can the addition of prophylactic vancomycin to the cefazolin regimen or use alone, in patients with smoking, BMI >40 kg/m2, diabetes >200mg/dL or HbA1c>7, history of MRSA, or recent hospitalization decrease postoperative total knee arthroplasty infections and associated costs?

The purpose of this research study is to determine whether vancomycin has greater cost benefits and efficacy in reducing the incidence of postoperative total knee arthroplasty infection rates than does cefazolin in patients with smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c, history of MRSA, or recent hospitalization.

P: Patients having total knee arthroplasty procedures in two hospitals in Mississippi River Delta

I: Reduction in infections related to antibiotics and associated risk factors

C: Vancomycin or Ancef antibiotic usage comparison

O: A decrease in infection rate with a comparable decrease in cost in patients with associated risk factors such as smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c, history of MRSA, or recent hospitalization.

The aims of the study were: 1) determine whether cefazolin or vancomycin was used preoperatively in the patient population having undergone a total knee arthroplasty from January 2013 to December 2018 in the hospitals studied; 2) perform a cost benefit analysis to determine the feasibility potential savings using vancomycin preoperatively in the patient population having undergone a total knee arthroplasty; and 3) to determine the feasibility of a policy change based on cost saving analysis from using vancomycin alone or with cefazolin for the preoperative antibiotic cost in patients with associated risk factors such as smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c, history of MRSA, or recent hospitalization.

H_1Readmission related to total knee arthroplasty infections are directly related to associated co-morbidities in patients with associated risk factor of smoking.

H_0 Readmission related to total knee arthroplasty infections are not directly related to associated co-morbidities in patients with associated risk factor of smoking.

H_1Readmission related to total knee arthroplasty infections are directly related to associated co-morbidities in patients with associated risk factor of BMI >40kg/m2.

H_0 Readmission related to total knee arthroplasty infections are not directly related to associated co-morbidities in patients with associated risk factor of BMI >40kg/m2.

H_1Readmission related to total knee arthroplasty infections are directly related to associated co-morbidities in patients with associated risk factor of diabetes >200mg/dL or HbA1c.

H_0 Readmission related to total knee arthroplasty infections are not directly related to associated co-morbidities in patients with associated risk factor of diabetes >200mg/dL or HbA1c.

H_1Readmission related to total knee arthroplasty infections are directly related to associated co-morbidities in patients with associated risk factor of history of MRSA.

H_0 Readmission related to total knee arthroplasty infections are not directly related to associated co-morbidities in patients with associated risk factor of history of MRSA.

H_1Readmission related to total knee arthroplasty infections are directly related to associated co-morbidities in patients with associated risk factor of recent hospitalization.

H_0 Readmission related to total knee arthroplasty infections are not directly related to associated co-morbidities in patients with associated risk factor of recent hospitalization.

Cost Benefit Analysis

Cost Benefit Analysis (CBA) is the process used to gauge the benefits of a decision or taking action minus the cost associated with taking that action (Kenton, 2019). According to Yu, Garvin, Healy, Pellegrini, and Iorio (2015), "the rising volume of joint arthroplasties in this country generates significant expenditures to the American healthcare system and healthcare payers are currently targeting Total Joint Arthroplasty for healthcare cost-savings initiatives" (p. e60).

The analysis of Medicare claims data from 2003 to 2004 has resulted in a total of 11,855,702 beneficiaries, of which, 19.6% were 30-day readmissions (Yu et al., 2015). The cost of readmissions, based on the data, was approximately $17.4 billion (Yu et al., 2015). Similarly, in another analysis of over 300 hundred hospitals participating in the American College of Surgeons National Surgical Quality Improvement Program, data showed one of the top three reasons for readmission after total joint arthroplasty (18.8%) were surgical site infections (Nichols & Vose, 2016). Containing costs is critical to maintaining a hospital's sustainability; however, it cannot come at the expense of patient outcomes (Nichols & Vose, 2016).

The Knee Society developed a standardized list (Appendix A**)** of possible complications after total knee arthroplasty for a commonly accepted approach to readmission (Yu et al., 2015). While this list includes readmission causes, this study will focus on readmissions related to infections within postoperative total knee arthroplasties, specifically the patient population with smoking, diabetes >200mg/dL or Hb/A1c>7, BMI >40kg/m2, recent hospitalization, and history of MRSA. There is a consensus among experts in the Knee Society stating "deep infection" is a legitimate description of an infected total joint (Healy et al., 2013). In an observational study by Zawadzki et al. (2017), an exploratory analysis was completed to include California, Massachusetts, and Florida Medicare population data from 2009 to 2013 to determine primary readmission causes in each state specifically chosen for geographically area and population. Specifically, readmissions for THA and TKA were evaluated due to the associated high penalty costs (Zawadzki et al., 2017). The average Medicare costs associated with a primary total knee arthroplasty without complications or comorbidities from the west, the east and the coastal states are as follows: CA = $14,337.00, FL =$10,387.00, and MA = $14,488.00 (Zawadzki et al.,

2017). With the involvement of MRSA, readmission length of stay (LOS) was increased by 2-3 days respectively (Zawadzki et al., 2017). "Preventing surgical site infections due to MRSA can potentially save hospitals up to $60,000 per patient", according to Zawadzki et al (2017, p. 4).

A possible option for total joint infection prevention is the dual administration of antibiotics should a patient exhibit any risk factors for a potential joint infection. Possible risk factors for total joint infections include BMI >40kg/m2, history of MRSA, smoking, recent hospitalization, and diabetes >200mg/dL or HbA1c >7 (Burger et al., 2018). Although controversial, the addition of a second antibiotic may be effective to address institutional or regional patterns of infections (Burger et al., 2018). The Center for Disease Control and Prevention (CDC) compiles data on the incidence of MRSA infections that occur within hospitals on a state by state basis ("National action plan", 2013). Determining the areas in each state with a higher incidence reporting of MRSA can be difficult and inaccurate if hospitals do not report in a timely manner ("National action plan", 2013).

Chapter 2

Review of Literature

A review of literature was conducted using the search terms *vancomycin, total joint arthroplasty, cost analysis, antibiotics, post-operative joint infections, and antibiotic therapy*. This search included articles assembled from Pubmed, CINAHL, Google Scholar, and Medline (OVID) databases. Twenty articles were found in reviewing the literature with dates between 2011 and 2019. The review of literature contained articles with subject material on total knee arthroplasty infections, dosing of vancomycin and cefazolin, and cost and burden associated with treatment and revision of total knee arthroplasty.

Total Knee Arthroplasty Infection

The prevention of surgical site infections in total joint arthroplasty remains a major focus of health care attention due to the increased costs associated with revision surgery and the possible additional procedures to treat the infection (Shahi & Parvizi, 2015). A *revision knee replacement surgery* can be performed to replace a surgical knee implant that is no longer functioning properly. This malfunctioning device can cause scar tissue, bone loss, and instability in the knee and make a revision much more difficult to perform (Liu et al., 2014). According to Shahi and Parvizi (2015), a definite periprosthetic joint infection (PJI) is present when:

1. there is a sinus tract communicating with the prosthesis, or
2. a phenotypically identical pathogen is isolated by culture from 2 or more separate tissue or fluid samples obtained from the affected prosthetic joint, or
3. when three of the following five criteria exist:

1) Elevated serum erythrocyte sedimentation rate and serum C-reactive protein concentration,
2) Elevated synovial white blood cell count, or change on leukocyte esterase test strip
3) Elevated synovial polymorphonuclear percentage
4) Positive histological analysis of periprosthetic tissue
5) A single positive culture

Currently, the recommendation for surgical prophylaxis in routine total joint arthroplasty is a second generation cephalosporin (Lee, 2016). However, over the last several years, the changes in resistant organisms in total joint arthroplasty infections have raised questions as to whether the current antibiotic recommendations remain adequate for prophylaxis. In a study conducted by Shahi and Parvizi (2015), the use of vancomycin was considered to be appropriate in patients who are carriers of MRSA, patients from dialysis units or centers with an outbreak of MRSA, healthcare workers, and patients who are allergic to penicillin (p.74).

In a retrospective study, authors reviewed infection control surveillance data on 1446 TKAs of which 31 infections were documented between June 2008 and June 2012 (Liu et al., 2014). Review of the data indicated a predominantly high rate of infections associated with TKA revision. During the time period, the infection rate of TKA revisions was 8.79%, of which 5.49% was due to MRSA (Liu et al., 2014). The overall infection rate on primary, first time, TKA was 0.86% respectively with the MRSA infection rates of 0.43% (Liu et al., 2014). Based on the results of study, a

recommendation of the addition of vancomycin was added for surgical prophylaxis (Liu et al., 2014). After vancomycin was added to the surgical prophylaxis routine, a significant decline in periprosthetic joint infection (PJI) resulted among patients undergoing TKA revision from 7.89% to 3.13% (p=0.046) (Liu et al., 2014).

According to Shahi and Parvizi (2015), PJI can occur with exogenous or hematogenous pathogenesis at the timing of clinical manifestation. "Based on the time interval between surgery and the clinical manifestations, PJI can be divided into four different stages" (Shahi & Parvizi, 2015).

1. Stage one/early: symptoms start within the first 4 to 8 weeks postoperatively.
2. Stage two/delayed: presents 3 to 24 months after the surgery.
3. Stage three/late onset: usually occurs after 2 years postoperatively.
4. 4.Stage four/silent PJI: a condition in which a positive culture is captured at the time of revision in a patient with no symptom of infection

The International Concensus Meeting (ICM) workgroup, a group of worldwide professionals on PJI, stated that certain conditions can increase the risk of developing PJI (Shahi & Parvizi, 2015).

1.In the presence of uncontrolled diabetes (glucose levels >200 mg/L/ HbA1C>7

2. morbid obesity (body mass index >40 kg/m2)

3. excessive smoking (> one pack per day)

4. recent hospitalization

5. history of staphylococcus or MRSA infection

In addition to the review of risk factors, vancomycin administration as primary antibiotic prophylaxis does not appear to have been adequately studied in the last two decades since the increase of MRSA and community acquired (CA) MRSA (Crawford et al., 2012). "The

appropriate use of perioperative antibiotic prophylaxis is a key intervention for preventing surgical site infections (SSI) in clean and clean contaminated surgery" (Crawford et al., 2012, p. 1474). "Vancomycin has been clinically available for over fifty years and has been recommended as either a primary or adjuvant agent in those patients with high S. aureus colonization, in institutions where a "high" prevalence of MRSA exists, *and* when a surgical procedure (orthopaedic, sternotomy, vascular graft) involves an implant" ((Crawford et al., 2012, p. 1474).

Crawford et al. (2012) cited two systematic reviews that were conducted to compare the rate of SSIs in patients receiving antibiotic prophylaxis with either a glycopeptide (vancomycin or teicoplanin) or B-lactam agent. According to a meta-analysis conducted by Crawford et al. (2012), outcomes from 5,761 cardiothoracic patients from 7 randomized, controlled studies between 1988 and 2002 were examined. B-lactam and glycopeptides were shown to be equally effective for prevention of SSIs with a 95% confidence interval (Crawford et al., 2012). However, a subset analysis suggested that B-lactam antibiotics were more effective than glycopeptides for prevention of deep chest SSIs while glycopeptides were shown to be more effective for the prevention of SSIs caused by methicillin-resistant gram-positive bacteria (CI, .330-.895) (Crawford et al., 2012).

In the second systematic review of randomized controlled studies, the authors found that glycopeptides and B-lactam antibiotics demonstrated similar outcomes for the prevention of SSIs. A total of 14 studies were identified between 1990 and May 2008 including several studies used in the first mentioned meta-analysis. Only one study within the meta-analysis exhibited a statistically significant disparity in infection rates

between antibiotic prophylaxis with vancomycin (3.7%) and cefazolin or cefamandole (12.8%; RR, 0.29; 95% CI, .11-.81) (Crawford et al., 2012). The review remained inconclusive to determine what level of MRSA prevalence was required to justify the clinical or economical use of a glycopeptide (Crawford et al., 2012). The authors did comment that although both meta analyses provided insight into the randomized clinical trials, the studies were performed over a decade ago and do not account for the increasing prevalence of MRSA and community acquired (CA) MRSA.

Cost Analysis of Total Knee Arthroplasty Revision and Infection

The considerable increase in total knee arthroplasty performed and the increase in younger and more active populations appear to indicate a significant increase in total knee arthroplasty procedures in the near future (Rodriguez-Merchan, 2011). The authors also identified the major challenges associated with additional surgery with the possibility of additional surgical postoperative infections. This increase in infection may lead to decreased functional capacity for patients and huge economic impact for health care institutions (Rodriguez-Merchan, 2011).

Weber et al., (2018) analyzed clinical outcome, complication rates, and cost effectiveness of revision arthroplasty. This retrospective review analyzed 162 hip and knee arthroplasties from the institutional joint registry. Responder rate, patient reported outcome measures, complication rates, and patient individual charges in relation to reimbursement, were compared with a matched control group of primary total joint replacements (Weber et al., 2018). Although improvement in total joint arthroplasty is continuing, total joint revision surgery has also increased, and the increased numbers of revisions represent a financial drain on health care systems (Weber et al., 2018). Despite all surgical efforts, revision surgery has not decreased and has been termed the arthroplasty burden (Weber et al., 2018). Weber et al., (2018) reported in outcome measures one

year postoperatively, Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores showed a lower improvement for revision arthroplasty (24.3± 30.3) compared with primary total joint arthroplasty (41.2 +/-21.3, $p<0.001$). Mean operating time was 52 minutes longer for revision surgery compared to primary joint replacement. In addition to longer operating times, patients with revisions had an increase in total hospital stays compared to the control group. The authors found an increase in financial expenses of revision surgery, compared to primary total knee arthroplasty; revision surgery is associated with considerable financial expense, (Weber et al., 2018).

An additional study considered the rates and causes of hospital readmissions after total knee arthroplasty. This retrospective cohort study included 1408 patients, of which 262 patients were revision TKAs and 113 patients were revision infection TKAs (Schairer, Vail, & Bozic, 2014). All readmission dates were within the 90-day window after discharge and were evaluated for timing and cause. Readmission criteria were labeled surgical or medical. The results indicated: unplanned readmission rate for the entire cohort was 4% at 30 days and 8% at 90 days (Schairer et al., 2014). According to Schairer et al., (2014), "revision of an infected TKA had the highest readmission rate after 90 days postoperatively, followed by revision TKA, with primary TKA having the lowest rate", (p. 181). Unplanned readmissions required a surgical follow up procedure in 42% of the cases (Schairer et al., 2014). Surgical causes of readmission were 77.1% within the 90-day timeframe and 60.3 % within the 0-30-day timeframe. Of the 91 readmissions in the 90-day timeframe, 17 (18.7%) were admitted for surgical site infection (Schairer et al., 2014). In summary, risk of readmission and associated cost is higher among patients undergoing revision TKA when compared to patients undergoing primary TKA.

Lastly, in a study by Nichols and Vose (2016) the factors and costs associated with discharge and readmission within 90 days of surgery for primary hip and knee arthroplasty was assessed. This study was a retrospective analysis of a large database used for health care claims from the Truven MarketScan Database (2009-2013). Patients were selected if aged > 18 years, with continuous health plan coverage from 3-month baseline through 3-month follow-up. Postoperative infection was the most frequent listed complication for readmissions in all cohorts; primary TKA (7%), THA readmissions (8.5%), TKA revision (35.6%) and THA revision (22.4%) (Nichols & Vose, 2016). The highest costs included patients who either had a complication or blood transfusion during the hospital stay, and who were discharged to a skilled nursing facility (SNF) with a readmission within 90 days (Nichols and Vose, 2016). The average total 90-day costs related to readmission ranged from $31,558 to $37,370 for each cohort, while average total 90-day costs ranged from $48,995 to $80,491 (Nichols and Vose, 2016). In all, patients who experienced a complication or received a blood transfusion subsequently experienced much greater incremental costs for a 90-day episode of care with a significantly higher risk of readmission after total joint arthroplasty (Nichols and Vose, 2016).

The majority of the literature focused on infection rates with cefazolin vs vancomycin when used as a primary preoperative antibiotic without considering all risk factors such as obesity, smoking, diabetes, recent hospitalization, and previous history of MRSA infection. Geographical areas may present with larger than normal occurrences of MRSA prevalence, however this data can be difficult to gather. Current randomized controlled trials were limited within this topic and, more research is needed to determine the effectiveness of vancomycin versus cefazolin for a preoperative antibiotic in total knee arthroplasty. The possibility of decreased costs associated with primary total knee arthroplasty and vancomycin use will be discussed further in this paper.

Vancomycin and Cefazolin Dosing and Administration

Kheir et al. (2017) performed a single-institution, retrospective study on 1,828 patients who underwent primary total joint arthroplasty and received vancomycin prophylaxis between 2008 and 2014. Throughout this time period, 5,810 additional patients underwent primary total joint arthroplasty and received cefazolin as the preoperative antibiotic (Kheir et al., 2017). Kheir et al., (2017) postulated vancomycin was routinely administered incorrectly as a one-gram standard dosage although it should be administered as a weight based (15 mg/kg) protocol. The authors discovered that of the 1828 procedures in which vancomycin monotherapy was used, 1,130 (62%) were under dosed, 518 (28%) were adequately dosed, and 180 (10%) were overdosed according to the weight-based dosage guidelines from recent clinical studies (Kheir et al., 2017). The results of this study did not recommend monotherapy vancomycin use for total joint arthroplasty based on 94% of patients receiving a fixed dose of vancomycin for choice of prophylactic antibiotic (Kheir et al., 2017).

In a similar study, the indications for vancomycin prophylaxis to prevent MRSA have been increasing (Catanzano, Phillips, Dubrovskaya, Hutzler, & Bosco, 2014). Throughout the guidelines, the recommended dosage for vancomycin traditionally has been one gram delivered intravenously (Catanzano et al., 2014). This retrospective chart review by Catanzano et al. (2014) was based on 216 patients who screened positive for MRSA prior to undergoing elective total joint or spine surgeries between January 2009 to January 2012. This cohort of patients was given 1 gram of vancomycin within one hour of surgical incision for antibiotic prophylaxis. The study initiated by revising the dosing schedule to include vancomycin 15 mg/kg per, correctly calculating the dosage for each

included patient, and comparing the values to the traditional dosage of 1 gram per patient dosing (Catanzano et al., 2014). This calculation was used to determine whether the patient was under dosed or overdosed per the recommended dosage of 15 mg/kg. Also considered was surgical time accompanied by pharmacokinetic vancomycin (VAN) levels at the end of procedures (Catanzano et al., 2014). The author's results ensued, out of 216 patients who tested positive for MRSA, 149 patients (69%) were found to be underdosed while 22 patients (10%) were determined to be overdosed. The calculated VAN level at the end of procedure was < 15 mg/L in 60% of patients with the one-gram dose compared with 12% (p=0.0005) with weight-based dosing (Catanzano et al., 2014). The conclusion highlighted the importance of providing weight-based dosing per health care providers to provide accurate coverage for vancomycin in surgical prophylaxis (Catanzano et al., 2014).

Additionally, Burger et al., (2018), compared total joint infections and renal toxicity rates when a first-generation cephalosporin was used as primary antibiotic or used in conjunction with vancomycin. This retrospective study consisted of 1,997 primary TJAs treated with cefazolin alone (1044 TJA) or cefazolin with single dose vancomycin (953 TJA) (Burger et al., 2018). The vancomycin group included 477 TJAs with infusion started at least 45 minutes or more before incision and 477 TJAs with the infusion started at less than 45 minutes before skin incision (Burger et al., 2018). After reviewing the results of the study, the additional dose of vancomycin did not significantly lower PJI rates when compared with cefazolin administration alone (1.6% vs 2.1%, P=.32). However, when vancomycin was infused at least 45 minutes before surgical incision, the rates for PJI were significantly lower (0.2%) when compared with other TJA procedures performed using vancomycin and cefazolin (2.9%, P <.01) or with cefazolin alone (2.1%, P <.01). In addition, the renal toxicity rates observed were no different between the

compared groups (Burger et al., 2018). In short, the authors found that the addition of vancomycin to cefazolin at least 45 minutes before skin incision reduced the overall rate of PJIs with low renal toxicity involvement.

Translation Framework

This study was based on Andrew Pettigrew and Richard Whipp's (1991) Model of Strategic Management of Change (White et al., 2016). This model is a strategic model of change that includes the interaction of three dimensions of strategic change: context, content, and process (Figure 1). The *context*, or the "why" of change, consists of both internal and external factors that may have initiated the change, such as the organizational culture, leadership, type of clinical setting, and characteristics of the organization (White et al., 2016). The content, the *what* of change, describes the actions to be changed or altered. In translation of research, according to White et al., (2016), "these are the key organizational elements in the system focused on to enhance or to support the use of evidence", (p. 54). The last dimension, the *process* or *how* of change, includes the methods, actions, strategies, and interactions that will be used in order to make the change happen to facilitate usage of the new evidence (White et al., 2016).

Figure: 1

Pettigrew and Whipp's Framework of Change

Process: (how)

- Implementation of data collection
- Review of current model
- patterns of Infection related to MRSA

Content: (what)

- Potential change in preoperative prophylaxis antibiotic
- Current readmission status of infected total knee

Context: (why)

(Internal)

- Strategic policy adjustments
- Internal data collection
- Restructuring of current process

Context: (why)

(External)

- Current literature
- Reported incidence of MRSA to CDC
- Legislative requirements on mandatory healthcare reporting

Source: Pettigrew and Whipp's (1991) Context-Content- Process framework

(image altered by author)

Based on Pettigrew and Whipp's widespread research, the authors maintain that there are *five* relating factors that are critical to the effective management of strategic change:

1). *Environmental assessment*: The continuous monitoring of both the internal and external environment through open learning systems.

2). *Human resources:* as assets and liabilities. Employees should feel trusted and valued.

3). *Linking strategic and operational change*. Bundling of operational activities can lead to new strategic changes.

4). *Leading the change.* Direction, vision, values, coordination and creation of a climate for change.

5). *Overall coherence.* Consistent with clear goals, consonant with the environment, and creation of competitive edge that is feasible.

Attempting to align the context of primary preoperative antibiotic for total joint arthroplasty with new standards can be challenging as surgeons generally adhere to guidelines established based on decades old research. Based on Pettigrew and Whipp's framework, the goal of changing thinking, or implementing a change, related to administration of antibiotic can be a daunting task. Attempting to gather evidence based on internal and external factors associated with postoperative total knee infections will be the process or the "how" in guiding practice. The process, or the "how", is to implement the evidence from the methods, strategies, or interventions used to determine if the cost can be reduced (Stetler, Ritchie, Rycroft-Malone, Schultz, & Charns, 2007). By using this guiding framework, changes could potentially happen within institutional antibiotic policies for total knee arthroplasty if given the correct data to focus the evidence on change (Stetler et al., 2007). In this project, the *context*, is the incidence of

postoperative joint infection rates and the cost efficacy of vancomycin versus the currently used cefazolin. Attempting to decrease the cost related to postoperative total knee infection rate and to decrease the infection rate for the patient is the "why" of the framework. The *content,* or the "what", is the change or addition to of preoperative antibiotic prophylaxis before total knee arthroplasty surgery is performed. This content can include patient risk factors, microbial documentation, co-morbidities, timing of antibiotic administration, and known risk factors.

Chapter 3

Methodology and Analysis

Taking clinical pathways into consideration, a retrospective chart review was chosen for this study. Project site requirements and demographics were gathered, analyzed, and determined to be appropriate for the project review. The project was included patients who have undergone a total knee arthroplasty from January 2013 to December 2018 at two rural hospitals in the Mississippi River Delta. Data was collected from January 2020 to February 2020 from the electronic medical record (EMR) computer database with February 28, 2020 being the last data collection.

A total of 1661 charts were collected for review. A random sample number generator was used to generate a random list of integers as a comprehensive version (www.calculator.net, n.d.). The sample size calculator was utilized to obtain a needed sample of 313 based on a 95% confidence level with a margin error of 5%. This random number generator endured was measurements are needed to have a confidence level of 95% that the real value is within ± of the measured value ("Random number generator", n.d.). The aims of the study were:

1. determine whether cefazolin or vancomycin were used preoperatively in the patient population having undergone a Total Knee Arthroplasty from January 2013 to December 2018 in the studied hospitals
2. To perform a cost benefit analysis to determine the feasibility of savings using vancomycin preoperatively in the patient population having undergone a Total Knee Arthroplasty. Documented risk factors such as smoking, diabetes (>200mg/dL; HbA1c >7%), previous staphylococcus infection, history of Methicillin Resistant

Staphylococcus Aureus infection, previous hospital admission, male gender, and Body Mass Index (BMI > 40kg/M2 were the variables used.

3. Lastly, to determine the feasibility of a policy change based on cost saving analysis from using vancomycin alone or with cefazolin for the preoperative antibiotic.

Research Sample

The sample was chosen based on the diagnosis of osteoarthritis (CPT code 716.9) and total knee arthroplasty (CPT code 27447) as the primary procedure; including data on readmissions to the hospital due to an infected total knee joint (Devay, 2019). The population utilized is based on a sample of patients:

1. having undergone a total joint arthroplasty procedure
2. microbiology of infection material
3. preoperative MRSA screening,
4. preoperative antibiotic ordered
5. readmissions related to post-operative infection after TKA
6. length of stay (LOS) associated with readmission
7. gender
8. associated risk factors (see Table 2) for total knee arthroplasty postoperative infection.

Data on length of stay during readmission and total number of surgical interventions was also gathered and analyzed. The population consisted of 1661 total knee arthroplasty procedures from two hospitals in one health system within rural Mississippi River Delta. A random sample of 313 charts was reviewed based on the inclusion and exclusion criteria listed. Table 1 lists the inclusion criteria and associated risk factors for total knee arthroscopy procedure.

Table 1. Total knee arthroplasty description criteria with associated risk factors

• Readmission related to TKA infection
• Body Mass Index/Obesity (BMI >40kg/m2)
• Diabetes >200mg/L or HbA1c >7
• History of MRSA/Staphylococcus aureus infection
• Smoker
• Recent hospitalization

Only non-identifiable demographic data was gathered. Inclusion criteria were based on patients having a total knee arthroplasty procedure between January 2013 and December 2018. Informed consent had been obtained on each patient prior to this study with the surgical consent which consents to possible research using unidentifiable information. Patient records were excluded if a readmission occurred based on a medical diagnosis unrelated to total knee arthroplasty procedures or infection from total knee arthroplasty. No readmissions were found based on medical diagnosis related to this study criterion. All data was securely locked when not in use under a secure passcode only known by the primary researcher.

Approval

Internal review board approval from the participating health care centers (See Appendix B) with informed consent and from Arkansas State University (see Appendix C) was obtained. Each informed consent was obtained from each patient by admission staff as they consented for surgical procedures at the participating facilities.

Data Collection Tool

The data collection tool is Surgical Site Infection (SSI) (see Appendix D) form and was downloaded from the Centers for Disease Control. The expiration date on the data collection form is 12/31/2022 and has been validated by the Centers for Disease Control and the National Healthcare Safety Network. The SSI form used for this study was modified to remove patient demographic data for the included population. A random sample of 313 charts were collected from January 15th, 2020 through February 28th ,2020. There was gathered data that would lead to the identity of subject's information collected. All data was kept secure under passcode protection, and all statistical data was stored on computers with access only to the primary investigator.

Protection of Human Subjects

"Human subjects research must be guided by a statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution", (Health & Human Services, 2017). Being a retrospective study, no consents were obtained from any individuals during this data collection. The risk was considered minimal to human subjects. The collected data was stored on a password protected thumb drive maintained in a locked file cabinet with access by the primary investigator. All information obtained and statistical data was stored on a computer with a secure passcode only known by the primary investigator.

Data Collection

Operative records for patients having undergone total knee arthroplasty from January 2013 to December 2018 were analyzed from two hospitals within the rural Mississippi River Delta area and included surgical cases from five orthopedic surgeons. The infection control

director and medical records executive assistant director assisted with gathering data within the designated time period. The reports were free from any patient identifying information. The data was downloaded into a Microsoft Excel format spreadsheet without patient identifiers and delivered via secure hospital protected password protected email server. Data was then disseminated on additional excel spreadsheet by individual cells using the validated SSI data collection tool. All statistical data was analyzed by the primary investigator and kept secure with secure pass coded protection.

Bias

There are several ways bias may present in a study and attempting to alleviate all bias would be difficult. However, an effort to decrease potential bias is essential to any research project or study. This study may not be able to be generalized or representative of the population at large. The main bias possibility for this study was selection bias.

Selection bias can be caused by the type of sample selected. Although cohort studies have high accuracy and efficiency as advantages, they may also suffer from selection bias (Easer, Zoccali, Jager & Dekker, 2009). According to Panacci and Wilkins (2010), “When a study population is identified, selection bias occurs when the criteria used to recruit and enroll patients into separate study cohorts are inherently different”. This can be a much larger issue in retrospective and case-control studies where exposure and outcome may have already occurred at individual selection for study inclusion (Panacci & Wilkins, 2010). This study did not include patients that may have become infected and shipped to other facilities for treatment. Since this study cannot be generalized, it may not be representative of all of the population to which the findings may be applied (Malone, Nicholl & Tracey, 2014). With randomized controlled studies which contain rigorous concealment blinding, selection bias may be greatly reduced (Malone,

Nicholl & Tracey, 2014). For the purposes of this study, selection was focused solely on total knee arthroplasty procedures from two rural hospitals located in the Mississippi River Delta.

Statistical Analysis

Pearson Correlation

The Pearson correlation is one of the most common methods used in statistical analysis when assigning numerical values (Nettleton, 2014). This method assigns a value between -1 and 1, where 0 is no correlation, 1 is total positive correlation, and -1 is total negative correlation (Nettleton, 2014). The Pearson's correlation method in this study represents several relationships between the associated risks factors for infected postoperative total knee arthroplasties as well as relationships with readmissions related to antibiotic usage and infected total knee arthroplasties. For example, a correlation value of 0.7 between two variables would indicate that a significantly positive relationship exists between the two variables (Nettleton, 2014). If the value of the correlation is negative then as the value of A increases, the value of B would decrease.

Paired t-Test

Paired t-tests are conducted to examine if mean differences exist between variables. The dependent sample t-test for paired means is an appropriate test if each of the two samples can be matched on a particular characteristic or to examine the effects over time (Razali, N. & Wah, Y, 2011). The assumptions of normality and homogeneity of variance will also be assessed. One can use the paired t-test when there is one measurement variable and two nominal variables. One of the nominal variables has only two values, so that you have multiple pairs of observations. The most common thing is that one nominal variable represents an individual, or a before and after. The null hypothesis is that the mean difference between paired observations is

zero. When the mean difference is zero, the means of the two groups must also be equal. Because of the paired design of the data, the null hypothesis of a paired t-test is usually expressed in terms of the mean difference (McDonald, J., 2014). The paired t-test assumes that the differences between pairs are normally distributed; you can use the histogram to describe this. If the differences between pairs are severely non normal, it would be better to use the Wilcoxon signed-rank test (McDonald, J., 2014).

Wilcoxon Signed Rank Test

The Wilcoxon Signed Rank Test is the equivalent to the non-parametric equivalent paired t-test. This statistical test is used for continuous scale or ordinal data for the dependent variables and time or condition for independent variables (Conover, W. & Iman, R., 1981). When using a non-parametric test, it is better to summarize using medians rather than means. SPSS will only allow variables categorized as *scale* to be analyzed using this statistical method. The Wilcoxon Signed Rank test is the appropriate test to compare differences derived from the same population when the dependent variable is ordinal or continuous. It is used to assess differences from matched pair designs or repeated measures (Conover, W. & Iman, R., 1981). Given that this statistical analysis does not follow the normal distribution, the non-parametric nature of this test is conducted as there are no assumptions due to the normality being violated.

Chapter 4

Results and Discussion

Cost Benefit Analysis

The sequela of total knee arthroplasty infections can be a significant burden on any hospital system. The correct preoperative antibiotic prophylaxis is the first line defense in the prevention of a potential infection. Cost benefits of using vancomycin instead of cefazolin in patients with certain comorbidities are a controversial topic. The American College of Surgeons National Surgical Quality Improvement Program recommends first generation cephalosporins as the first line preoperative antibiotic for total knee arthroplasty procedures (Nichols & Vose, 2016). The price for cefazolin and vancomycin are listed below at the two hospitals within this study (Table 2).

Table 2: Antibiotic Charges

Antibiotic Cost for Hospital *	**Antibiotic Cost Patient Charge**
Cefazolin 1 gram= $3.31	Pt Charge= $136.75
Cefazolin 2 gram= $6.01	Pt Charge= $152.50
Vancomycin 1 gram= $15.01	Pt Charge= $152.50

*Information obtained from Director of Pharmacy, Purchasing Officer

In the two hospitals, the estimated initial cost of a Total Knee Arthroplasty procedure is $7,000. The average post-operative total knee arthroplasty infection readmission cost is $19,000. The two hospitals had a total of five of 313 infections from the random sample. The postoperative costs of the readmissions for postoperative joint infections from 2013-2018. These

costs reflect multiple days of treatment care from $30,000 to approximately $68,000 after multiple days both in-patient and outpatient with vancomycin treatment for infection into the joint prosthesis. All postoperative total knee arthroplasty infections from the two hospitals reviewed were readmitted. Daily administration of vancomycin usage, daily care, and additional surgical procedures to remove or treat existing infection is included in the cost of infected knee. See Table 3 for a description of costs.

Table 3. ***Total Knee Postoperative Infections and Associated Costs***

Year	***Initial Cost***	***Cost of Infected Total Knee Procedure***	***Antibiotic Treatment/ Vancomycin daily***	***LOS Charges *$677/day***	***Total Estimated Cost of Readmission of TKA Infection***
2013	$0**	$0	$0	$0	$0
2014	$7,000	$19,000	$152.50 x 19 days=$2897.50	19 days LOS x $677/day=$12,863	$41,760.50
2015	$7000 x 2 procedures= $14,000	$19,000 x 2 procedures= $38,000	14 days x 152.20 (1st TKA) = $2,135; 36 weeks (252 days) x 152.50 (2nd TKA) = $38, 430	14 days LOS x $677/day =$9,478; 21 days LOS x $677/day =$14,217	$116, 260 (2 TKA infections with readmission)
2016	$0**	$0	$0	$0	$0
2017	$7,000	$19,000	29 days x $152.50 = $4,422.50	29 days LOS x $677/day =$19,633	$50,055.50
	$7,000	$19,000	6 days x $152.50 =$915	6 days LOS x $677/day = $4,062	$30,977
2018	$0**	$0	$0	$0	$0
Total					$239,053

*All information obtained from infection control department within project site**No infection this year.

Total estimated cost of infected total knee arthroplasties range from $30,000 to $68,000 at the two hospitals per the years the infections were documented. The average cost of the procedure with no infection was $7,000 with no complications. The average cost of one gram of ancef for the hospitals in this study is $3.31 and two gram is $6.01. The average cost for the hospitals of one gram of vancomycin: $15.01. The addition of vancomycin to each additional postoperative total knee infection cost the two hospitals an estimated $48,000 in antibiotic. The addition of vancomycin to ancef regimen as a combination prophylactic preoperative treatment would cost an additional $3,662.10 in cost (see Table 4).

Table 4. Ancef Cost vs. Vancomycin Cost x Cohort

Ancef 1 gram	Ancef 2 grams	Vancomycin 1 gram	Total Hospital infection cost – Additional Antibiotic Cost = Savings
313 sample x $3.31 =$ 1,036.03	**313 sample x $6.01 = $ 1,881.13**	**313 sample x $15.01= $ 4,698.13 (vancomycin given alone to all participants) ($4698.13-$1,036.03=$3,662.10) ($3662.10 would be the addition of vancomycin added to ancef protocol)**	**$239,053 (total cost of infections x 5 years) - $3,662.10 (additional cost of vancomycin added) = $235,390.90 potential savings**

The vancomycin column (Table 4) shows the cost of vancomycin given exclusively preoperatively for each total knee arthroplasty. The last column in Table 4 shows a potential cost saving analysis if one gram of vancomycin were added to the ancef protocol. The $235, 390.90 divided by the five years of reviewed charts on total knee arthroplasty procedures from the two hospitals would potentially save $47,078.18 annually. Each of the postoperative documented infections were given ancef preoperatively, became infected, were readmitted to the hospital for subsequent care, and then given repeated doses of vancomycin on scheduled intervals. The cost savings for patients with comorbidities of smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c, history of MRSA, and recent hospitalization provide the basis for a new policy (See appendix F). If a patient has the existing comorbidities before the primary total knee arthroplasty, vancomycin can be given per the new policy. Vancomycin shows a return on investment in Table 5 as being given as the primary preoperative antibiotic based on the comorbidities of smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c, history of MRSA, and recent hospitalization.

Table 5. Return on Investment

	Hospital Cost	**Patient Cost**	**Return on Investment**
Ancef	**$3.31**	**$136.75**	**$133.44**
Vancomycin	**$15.01**	**$152.50**	**$137.49**

Demographics

Data was gathered and analyzed for postoperative infections in total knee arthroplasty procedures between two hospitals in the Mississippi River Delta. Demographics of the subjects included age and gender. Three hundred thirteen charts were gathered with 164 females (52.4 %) and 149 males (47.9 %). Age of subjects ranged from 43 to 83 (see Table 6) with a mean age of 65.61 (see Figure 2). The bell curve shown in Figure 2 shows a normal distribution. One outlier, age 43, is outside of the normal distribution, while 61 years of age is the most frequently observed age for total knee arthroplasty procedure. The observations for age had an average of 65.61 (SD = 8.30, SE_M = 0.47, Min = 43.00, Max = 83.00, Skewness = -0.00, Kurtosis = -0.85, Mdn = 65.00). When the skewness is greater than 2 in absolute value, the variable is considered to be asymmetrical about its mean (Westfall & Henning, 2013). When the kurtosis is greater than or equal to 3, then the variable's distribution is distinctly different than a normal distribution in its trend to produce outliers (Westfall & Henning, 2013). The summary statistics can be found in Table 6.

Table 6.

Summary Statistics Table for Interval and Ratio Variables

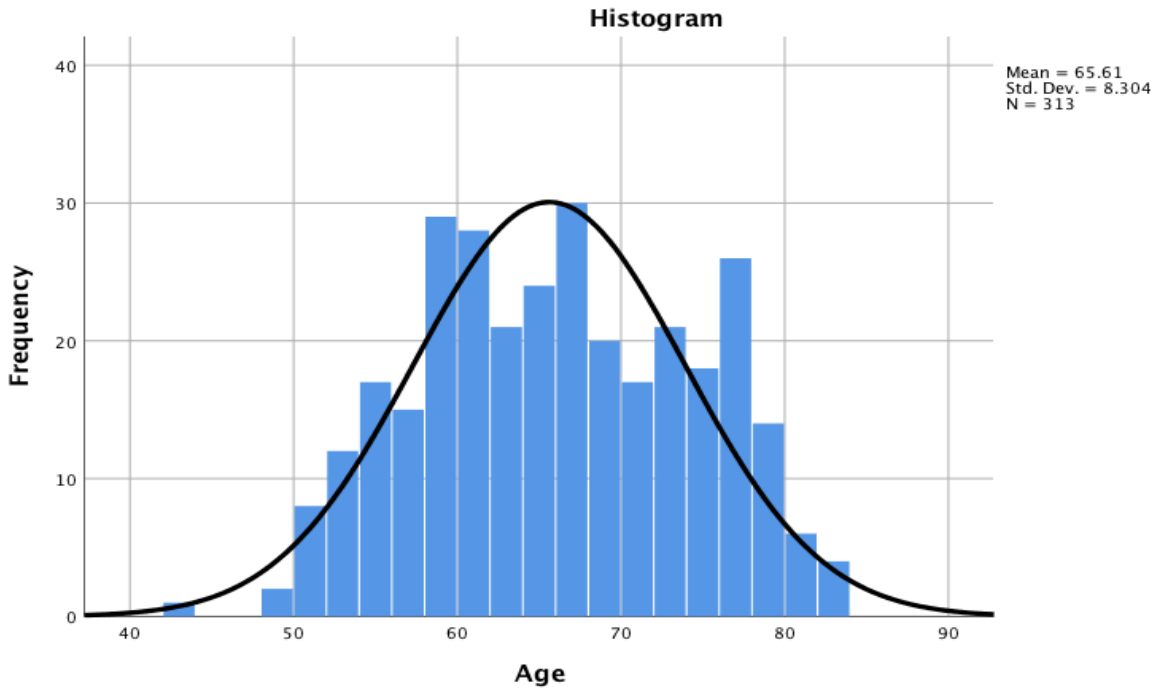
Variable	*M*	*SD*	*n*	SE_M	Min	Max	Skewness	Kurtosis	*Mdn*
Age	65.61	8.30	313	0.47	43.00	83.00	-0.00	-0.85	65.00

Quantiles:

	Age
10%	54.200
20%	58.000
25%	59.000
30%	61.000
40%	63.000
50%	65.000
60%	68.000
70%	71.000
75%	72.000
80%	74.000
90%	77.000

Note. '-' denotes the sample size is too small to calculate statistic

Figure 2.



Summary statistics were calculated for each interval and ratio variable. Frequencies and percentages were calculated for each nominal variable. Several patients had various underlying disease processes. In the group of observed patients, 22 (7.03%) had diabetes blood glucose > 200mg/dL with an HbA1c 7, 48 (15.34%) patients had a BMI >40kg/M2. Forty-eight (15.34%) patients were smokers in this study and 14 (4.47%) were diagnosed with a history of MRSA. Frequencies and percentages are presented in Table 7.

Table 7.

Frequency Table for Nominal Variables

Variable	*n*	*%*
Diabetes_blood_glucose_200mg_dl_or_HbA1c_7		
1	22	7.03
2	291	92.97
Missing	0	0
BMI_40kg_M2		
1	48	15.34
2	265	84.66
Missing	0	0
smoker		
1	48	15.34
2	264	84.35
Missing	1	0.32
History_of_MRSA		
1	14	4.47
2	299	95.53
Missing	0	0

1=yes; 2=no; MRSA=Methicillin Resistant Staphylococcus Aureus; Note. Due to rounding errors, percentages may not equal 100%.

Analysis

Pearson's Correlation with Vancomycin

A Pearson's correlation was assessed to determine the relationship between readmissions of total knee arthroplasty with infections and the variables: smoking, BMI > 40kg/m2, diabetes blood glucose > 200 mg/dL, recent hospitalization, and history of MRSA infection. Vancomycin was used as the dependent variable: smoking, BMI >40 kg/M2, diabetes >200 or HbA1c >7, history of MRSA, and history of recent hospitalization was used as independent variables.

Cohen's standard (Table 8) was used to evaluate the strength of the relationships between the independent and dependent variables, where coefficients between .10 and .29 represent a small effect size, coefficients between .30 and .49 represent a moderate effects size, and coefficients above .50 indicate a large effect size (Cohen, 1988). This number indicates the p-value. If the p-value or coefficient is 0.10 to .29 then the strength of the association has a small correlation. If the p-value or coefficient has a value of .30 to .49, then the strength of the association has a moderate correlation or relationship. Lastly, if the p-value or coefficient is greater than .50, then the association has a large association or relationship (Cohen, 1988).

Table 8. ***Cohen's Standard***

Coefficient Value	Strength of Association
0.1 < | r | < 0.29	Small correlation
0.3 < | r | < 0.49	Medium moderate correlation
| r | > 0.5	Large, strong correlation

Results

The statistical analysis from the Pearson's correlation was run as independent paired tests. The independent variables: smoker, diabetes >200mg/dL or HbA1c >7, BMI >40 kg/M2, recent hospitalization, and previous MRSA infection were paired with vancomycin to determine

statistical significance. A significant positive correlation was observed between Vancomycin ordered and history of MRSA (r_p = 0.16, p = .004) (Table 5). This correlation suggests a relationship that indicates when vancomycin ordered increases, higher levels of MRSA increases as well as Vancomycin is the antibiotic typically ordered to treat MRSA (0.16) This positive correlation is a finding that was to be expected during this analysis. While being paired individually with vancomycin, the remaining co-morbidities did not show to have a statistically significant relationship (Table 9).

Table 9.

Pearson Correlation Results Between Vancomycin Ordered and Risk Factors

Combination	r_p	**Lower**	**Upper**	p
Vancomycin Ordered- History of MRSA	0.16	0.05	0.27	.004
Vancomycin ordered- BMI >40kg/m2	0.10	-0.01	0.21	.088
Vancomycin ordered-Recent Hospitalization	0.04	0.15	0.07	.470
Vancomycin ordered- Smoker	0.10	-0.01	0.21	.090
Vancomycin ordered- Diabetes >200mg/dL or HbA1c>7	0.06	-0.05	0.17	.310
Note: the confidence intervals were computed using a = 0.05; n = 313				

A Pearson's correlation was also run with ancef and the independent variables to determine statistical significance. A significant negative correlation was observed between Ancef ordered and history of MRSA (r_p = -0.16, p = .005). This negative correlation is also an expected finding during this analysis that suggests a relationship between ancef and MRSA (-0.16) (Table 10).

Table 10.

Pearson Correlation Results Between Ancef Ordered and Risk Factors

Combination	r_p	**Lower**	**Upper**	***p***
Ancef Ordered- History of MRSA	*-0.16*	-0.27	-0.05	*.005*
Ancef_Ordered-Diabetes_blood_glucose_200mg_dl_or_HbA1c_7	-0.05	-0.16	0.06	.339
Ancef Ordered- Smoker	-0.09	-0.20	0.20	.109
Ancef Ordered- BMI > 40 kg/m2	-0.09	-0.20	0.02	.107
Ancef Ordered- Recent Hospitalization	0.04	-0.07	0.15	.463

Note. The confidence intervals were computed using α = 0.05; n = 313

Two-Tailed Paired Samples *t*-Test

(Readmission related to TKA infection and Diabetes)

In addition to the Pearson correlation that individually compared co-morbidities to Vancomycin and Ancef usage, a Two-Tailed Paired Samples t-Test was performed along with a Shapiro- Wilk test to determine normal distribution. A Wilcoxon Signed rank test is used in the place of the Shapiro-Wilk test in this study for a nonparametric alternative statistical test (Conover & Iman, 1981).

A *Shapiro-Wilk test* was conducted to determine whether the differences in readmission related to TKA infection and diabetes blood glucose >200mg/dL or HbA1c >7 could have been produced by a normal distribution (Razali & Wah, 2011). A Shapiro-Wilk test tests the null hypothesis that a given sample came from a normally distributed population. Therefore, if the p value is less than the selected alpha level, then the null hypothesis is rejected and there is evidence that the data tested are not normally distributed (Razali & Wah, 2011). The results of this test were significant based on an alpha value of 0.05, $W = 0.37$, $p < 0.01$. This suggests readmission related to TKA infection and diabetes blood glucose are unlikely to have been produced from a normal distribution, meaning normality was violated in this test.

Results.

The result of the *two-tailed paired samples t-test* was significant based on an alpha value of 0.05, $t(312) = 3.32$, $p < .001$, indicating the null hypothesis can be rejected. This finding suggests the mean of readmission related to TKA infection and the mean of diabetes blood glucose >200mg/dL or HbA1c >7 was significantly different from zero. The mean of readmission related to TKA infection was significantly higher. The results can be observed in Table 11.

The two tailed Wilcoxon signed rank test is a non-parametric test that does not share distributional assumptions with the paired samples *t*-test. This test result between readmission related to TKA infection and diabetes blood glucose >200mg/dL or HbA1c >7 was significant based on an alpha value of 0.05, $V = 308.00$, $z = -3.27$, $p = .001$ which means the differences are not likely due to random variation. The median of readmission related to TKA infection (Mdn = 2.00) was significantly lower than the median of diabetes blood glucose >200mg/dL or HbA1c

>7 (Mdn =2.00) which means that diabetes blood glucose >200mg/dL or HbA1c >7 does have an effect on readmissions related to TKA infections.

Readmission related to TKA infection and smoker

A two-tailed paired samples t-test was conducted to examine whether the mean difference of readmission related to TKA infection and smoker was significantly different from zero. A normal distribution was not produced as evidenced by the results from the Shapiro-Wilk test (Razali & Wah, 2011). The result from this test were significant based on an alpha value of 0.05, $W = 0.48$, $p < 0.001$ which suggests the normality assumption was violated.

The results of the two-tailed paired samples t-test was significant based on an alpha value of 0.05, $t(311) = 6.54$, $p < .001$, indicating the null hypothesis can be rejected. This suggests the mean between the two variables was significantly different from zero, but the mean of readmission related to TKA infection was significantly higher than the mean of smoker. Table 11 shows the results from the test.

The two-tailed Wilcoxon signed rank test was conducted to determine if any differences existed between readmission related to TKA infection and smoker. The results were significant based on an alpha value of 0.05, $V = 1150.00$, $z = -6.14$, $p < .001$. This result indicated that the differences was not likely due to chance. The median of readmission related to TKA infection (Mdn = 2.00) was significantly lower than the median of smoker (Mdn = 2.00). Readmissions related to TKA infections are directly related to smokers which means as the rate of infections increase, the rate of smokers increase as well, and this is less likely due to chance.

Readmission related to TKA infection and BMI

Readmissions related to TKA infection and BMI >40kg/M2 were significantly different from zero based on the two-tailed paired samples t-test. A normal distribution was not found based on the Shapiro-Wilk test with a significant alpha value of 0.05, $W = 0.48$; $p < .001$, which suggests the normality was violated. The null hypothesis can be rejected based on the significant result from the two-tailed paired samples t-test 0.05, $t(312) = 6.54$, $p < .001$. This suggests the differences in mean of readmission related to TKA infection and BMI were significantly different from zero (Table 11).

The two-tailed Wilcoxon sign rank test showed significance based on readmission related to TKA infection and BMI of 0.05, $V = 1150.00$, $z = -6.14$, $p < .001$, indicating these differences are not due to random chance. The median associated with readmission related to TKA infection (Mdn =2.00) was significantly lower than the median of BMI >40kg/M2 (Mdn = 2.00).

Readmission related to TKA infection and history of MRSA

The results from the two-tailed paired samples t-test was significantly different from zero. Normality was assessed by the Shapiro-Wilk test and the results suggested an unlikely normal distribution based on an alpha value of 0.05, $W = 0.25$, $p < .001$ when comparing readmission related to TKA infection and history of MRSA. The null hypothesis was rejected based on the significant alpha value of 0.05, t (degrees of freedom-312) = 2.34, $p = .020$. This finding suggests that the mean of history of MRSA and the mean of readmission related to TKA infection was significantly different from zero with readmission related to TKA infection showing a significantly higher mean.

The differences in readmission related to TKA infection and history of MRSA were not due to random chance based on the significant results from two-tailed Wilcoxon signed rank test value 0.05, $v = 96.00$, $z = -2.32$, $p = .020$. The median results of history of MRSA (Mdn = 2.00)

were significantly higher than those of readmission related to TKA infection (Mdn = 2.00). The following table presents the results (Table 11).

Readmission related to TKA infection and Recent hospitalization

The mean difference of readmission related to TKA infection and recent hospitalization was significantly different from zero. Normality was tested with the Shapiro-Wilk which was found to be significant based on an alpha value of 0.05, W = 0.12, p <.001. The results indicated the normality assumption was violated and a normal distribution was unlikely between readmission related to TKA infection and recent hospitalization.

The null hypothesis cannot be rejected based on the significant alpha value of 0.05, t (312) = -0.45, p = .655 (Table 11).

Table 11. Readmission Related to TKA infection and associated risk factors Combinations

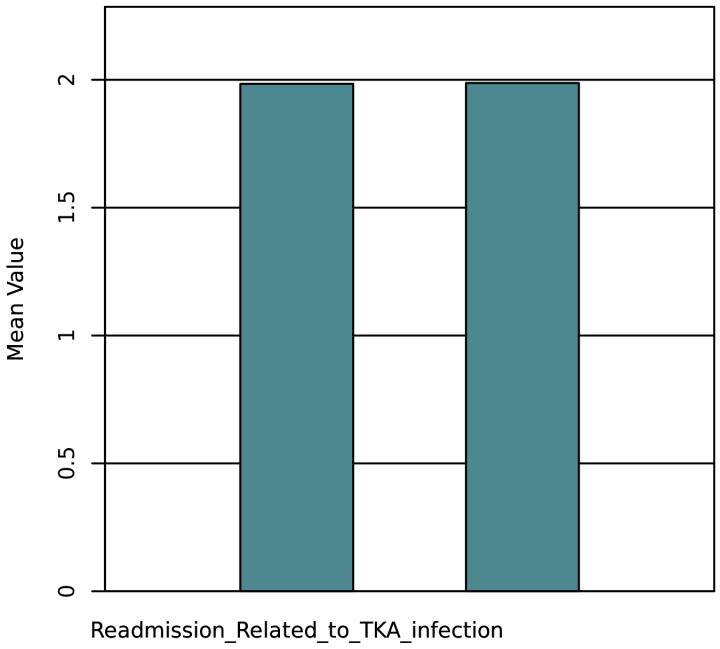
Combinations	**M/M**	**SD/SD**	***t***	***p***	**d**
Readmission related to TKA/Diabetes blood glucose >200mg/dL	1.98/1.93	0.13/0.26	3.32	<.001	0.19
Readmission related to TKA infection/smoking	1.98/1.85	0.13/0.36	6.54	<.001	0.37
Readmission related to TKA infection/BMI >40kg/m2	1.98/1.85	0.13/0.36	6.54	<.001	0.37
Readmission related to TKA infection/Recent hospitalization	1.98/1.99	0.13/0.11	-0.45	.655	0.03
Readmission related to TKA infection/History of MRSA infection	1.98/1.96	0.13/0.21	2.34	.020	0.13

Note: The confidence intervals were computed using a=0.05; n=313;M/M=Combinations; SD/SD=combinations; *Degrees of Freedom for the t-statistic = 312. d represents Cohen's d.*

These findings were not significantly different from zero. This finding suggests that recent hospitalizations and readmissions related to TKA infections are not dependent on one another, and any significance would be a chance finding. The following bar chart (Figure 3) displays the findings.

Figure 3.

The means of readmission related to TKA infection and recent hospitalization



The results from the two tailed Wilcoxon signed rank test were not significant and are explainable by random chance based on an alpha value of 0.05, V=6.00, z = -0.45, p = .655. This

suggests readmission related to TKA infection has no direct relationship with recent hospitalization.

Policy

The two hospitals studied do not have an existing policy for antibiotic prophylaxis for total joint arthroplasty procedures. Each of the orthopaedic surgeons chooses ancef 1 gram if preoperative weight is less than 80 kg and ancef 2 grams if weight is over 80 kg. If the patient has an existing allergy to penicillin, each surgeon consistently orders one gram of vancomycin as the preoperative antibiotic. However, should an infection arise, the current hospital policy states that vancomycin will be administered as the antibiotic to treat the existing postoperative joint infection (See appendix E).

As an approach to a new policy implementation, guidelines can be set forth to implement vancomycin as the preoperative antibiotic prophylactic chosen by the hospital based on the following criteria:

a) BMI > 40 kg/m2
b) Smoker
c) Diabetes >200 mg/dL or HbA1c >7
d) Recent hospitalization
e) History of MRSA infection

Each patient is screened through preoperative anesthesia testing (PAT) before any surgical procedure and all comorbidities can be addressed at this time. A checklist of the criteria for total knee arthroplasty antibiotic policy guidelines (see appendix F) will be created and distributed to the PAT nurses to determine if a patient qualifies for the vancomycin regimen of antibiotic in place of cefazolin. This information from the PAT interview will be placed in this patient's chart and the appropriate antibiotic will be pulled for surgery. The surgeon's orders can

be updated to include vancomycin to be administered if the risk factors are present in the patient history. Each surgeon will also be made aware of the cost benefit analysis associated with the use of vancomycin over cefazolin in the presence of the existing comorbidities.

Chapter 5

Discussion

This cost benefit analysis and policy implementation of this retrospective chart review was to determine whether vancomycin has greater cost benefits and efficacy in reducing the incidence of postoperative total knee arthroplasty infection rates than does cefazolin in two hospitals in the Mississippi River Delta. The associated total knee arthroplasty infections revealed no correlations with vancomycin. The possibility of adding vancomycin to the existing procedure of ordering ancef for preoperative antibiotics could decrease the chance for postoperative infections.

The results of this study support vancomycin could have cost benefits and efficacy in reducing postoperative total knee arthroplasty infections. Correlations were analyzed between hospital readmissions and its relationship to total knee arthroplasty infections and the patient co-morbidity variables of smoking, BMI, diabetes, history of MRSA, and recent hospitalizations. This study demonstrated no associated significant correlations between any of the comorbidities *individually* and readmissions related to TKA infections. However, as the number of comorbidities increase, the chance for infection increases. The two tailed paired samples t-test was conducted which led to the Wilcoxon signed rank test. This test allowed the rejection of the null hypothesis and revealed that the associations between the hospital readmissions related to the TKA infections and the comorbidity variables were not just by random chance based on the p value.

In summary, based on this analysis, the null hypotheses were rejected based on readmission related to total knee arthroplasty infections are not directly related to associated co-

morbidities in patients with associated risk factor of smoking, BMI >40kg/m2, diabetes >200mg/dL, and history of MRSA. The null hypothesis was accepted for readmission related to total knee arthroplasty infection is not directly related to the associated comorbidity recent hospitalization based on the analysis.

The cost benefit analysis of choosing vancomycin over ancef shows a difference in pricing based on what the hospital is charged, and what the patient is charged for each antibiotic. The return on investment table shows vancomycin as being the more profitable of the two antibiotics based on cost analysis. The hospital pays $3.31 for each gram of ancef and $15.01 for each gram of vancomycin. The patient is charged $136.75 for each gram of ancef and $152.50 for each gram of vancomycin for a difference of $4.05 more for each gram of vancomycin that is infused in the place of ancef. Creating a policy to change the practice within the hospital can potentiate the savings associated with this antibiotic cost saving analysis. The current practice from the orthopaedic surgeons is to use ancef as the prophylactic preoperative antibiotic for total joint knee arthroplasty procedures. A new policy would take into account patient comorbidities such as smoking, BMI > 40 kg/m2, diabetes .200 mg/dL or HbA1c >7, recent hospitalization, and history of MRSA infection before issuing a preoperative antibiotic which could potentially decrease infection rates and save the hospital and patient thousands of dollars.

Limitations of Study

There are several limitations to this study focused on total knee arthroplasty infections with comorbidities of smoking, BMI >40kg/m2, diabetes >200mg/dL or HbA1c>7, history of MRSA, or recent hospitalization. The hospital's infection control departments only tracked the deep tissue infection (into the mechanical prosthesis) and therefore, any additional superficial infections that may have occurred were not listed as infection in the database. Secondly, due to a

lack of manpower, the ability to capture and track all infections was limited. The inability to determine whether or not patients sought treatment at a different facility also demonstrated a limitation. If a patient had an infection but chose to seek treatment within another health care system, this infection would not have been traceable.

This study was not generalizable to the population due to the demographics of the rural area and the small sample size. This lack of generalizability affects the external validity of the study. In order for this study to be generalizable to the population, a correct proportion of each population would need to have been represented in this sample which is not true of this study.

Implications for Practice

White, Dudley-Brown, and Terhaar (2016) define stakeholders are those individuals directly impacted by the outcomes of proposed projects. This DNP project directly impacts many stakeholders within the hospital and the community. These include patients, healthcare workers, administrators, and insurance providers. The current guidelines for prophylactic antibiotic usage before a total knee arthroplasty are based on information from studies more than a decade old. Over the last ten years, MRSA has purportedly become a larger concern for infection and may be concentrated in certain geographical areas (Kourtis et al., 2019). Despite the decline over the last decade of recorded MRSA bloodstream infections, *S. aureus* continues to cause significant morbidity and mortality across the United States (Kourtis et al., 2019).

According to Kourtis et al. (2019), "in 2017, an estimated 119,247 S. aureus bloodstream infections with 19,832 associated deaths occurred". However, during 2005-2012 rates of hospital-onset MRSA bloodstream infection decreased by 17.1% annually, but the decline slowed during 2013-2016" (p.215). Although a decline in MRSA infections has been documented, the United States is still behind on the 2020 goal of the Healthcare-Associated

Infection National Action Plan of a 50% reduction in hospital onset MRSA infections (Kourtis et al., 2019, p. 214). As the incidence appears to be declining in the rates of MRSA, the patient population continues to face higher health costs and treatment failure (Labreche et al., 2013). A possible policy change in the hospitals could facilitate a healthier patient population and save both the patient and healthcare system thousands of dollars.

The provider must be willing to use every available tool to combat the infections including adjustments to preoperative antibiotic usage as guided by literature evidence. Attempting to follow guidelines set forth by The Infectious Diseases Society of America (IDSA) related to MRSA infections have resulted in shorter times to resolution than MRSA infections treated without the recommendations (Labreche et al., 2013). Treating patients preoperatively with the right antibiotic before an infection occurs could be the credible first line defense in preventing readmissions and systemic antibiotic infusions.

Many authors agree cefazolin single preoperative dose before total joint arthroplasty is the best choice. However, studies have shown in the presence of revision surgery, targeted use of cefazolin and vancomycin significantly reduced the incidence of infections such as MRSA (Ratto, Arrigoni, Rosso, Bruzzone, Dettoni, Bonasia, & Rossi, 2016). Although there are many other proven preventative strategies to decreasing post-operative joint infections such as decreasing operating room traffic, glove changes during procedure, pulsed lavage, and control of glucose levels before and after surgery, preoperative antibiotic use one hour before incision remains the most definitive measure utilized (Ratto et al., 2016).

Recommendations for Future Studies

Continuing research will be paramount to ensure continued success of a change. Additional studies with a larger population would-be beneficial in obtaining a better understanding of comorbidities and antibiotic selection.

A short-term goal to prevent infections could be a publication of findings related to the changes in medication administration, timing, and selection. Collaboration between orthopaedic surgeons, pharmacy, and anesthesia may promote patient satisfaction with retention of the initial hardware placed in the total knee joint and decreased infection. Continued surveillance of potential microbes within the hospital setting may also increase awareness of risk factors and antibiotic administration. Documenting and preventing microbiology infectious material such as MRSA and MSSA is part of the *5 Million Lives Campaign* (Institute of Healthcare Improvement, 2014). This campaign focuses on basic changes in infection control processes within the hospital setting (IHI, 2014). Continued studies on MRSA and contact precautions are still a major concern in the hospital setting. Handwashing is an age old process that has been replaced by the alcohol rub/scrub. Many nurses and doctors forget to don the appropriate attire before entering a patient's room and transfer microbes from one patient to the next. Continued surveillance on contact issues should remain a source of study.

Conclusion

Total knee arthroplasty (TKA) is the definitive treatment for degenerative joint disease of the knee (Shahi & Parvizi, 2015). Total knee arthroplasty is widely used to relieve the pain of end stage primary osteoarthritis and improve activities of daily living (Weinstein et al., 2013). The frequency of total knee arthroplasty has been increasing over the last two decades with the aging population. Patel, Guild, and Kumar (2018) reported a projected increase in total knee replacements of approximately 3.4 million by 2030. As the number of elderly patients continues

to grow in the United States, the younger population is potentially experiencing longer lives while living with degenerative joint disease. The need for total joint replacement will continue to show increased growth in the future (Nwachukwu et al., 2015).

In order to continue to provide patient care with high standards, preoperative prophylactic antibiotics must be continually updated to ensure post-operative infections remain relatively muted. A current review of the literature shows a gap in current guidelines related to microbial involvement and antibiotic usage in total knee arthroplasty. In order to bridge this gap, a proposed change in antibiotic prophylaxis was analyzed to determine if the current guidelines are adequate to combat the rate of total knee arthroplasty joint infections. Along with the gap in antibiotic usage, the comorbidities among patients have also become an issue when choosing an antibiotic. Smoking, BMI >40kg/m2, diabetes 200mg/dL, history of MRSA, and recent hospitalization play a major role in determining the possibility of a postoperative total knee arthroplasty infection.

Ancef has been the gold standard antibiotic for the last twenty to thirty years for a total knee arthroplasty procedure. However, as the patient presents with the risk factor comorbidities, vancomycin may prove to be the better choice to prevent a postoperative infection. The cost associated with a post-operative total knee arthroplasty infection can be anywhere from $68,000-$107,000. Attempting to close the gap and save a hospital and patient thousands of dollars along with a patient's time and health is a vast achievement.

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Appendix A.

Knee Society

Responses of members of The Knee Society regarding TKA complications and adverse events and their definitions*

Complication/Adverse event	ICD-9 code	% agree with complication	Definition	% agree with definition
1. Bleeding	998.11	99.0	Postoperative bleeding requiring surgical treatment	75.8
2. Wound complication	998.32	99.0	Failure of wound healing requiring reoperation or a change in TKA protocol	77.8
3. Thromboembolic disease	453.40	97.0	Symptomatic thromboembolic event requiring more intensive,	87.9

			nonprophylactic anticoagulant or antithrombotic treatment during the first 3 months after index TKA	
4. Neural deficit	997.09	94.9	Postoperative neural deficit (sensory or motor) related to the index TKA	90.9
5. Vascular injury	997.20	96.0	Intraoperative vascular injury requiring surgical repair, bypass grafting, or stenting (compartment syndrome or amputation should be reported)	97.0
6. Medial collateral ligament injury	844.10	92.9	Intraoperative or early postoperative medial collateral ligament injury requiring repair,	93.9

			reconstruction, a change in prosthetic constraint, revision surgery, or TKA protocol	
7. Instability	996.42	92.8	Symptomatic instability reported by the patient and confirmed by laxity on physical examination as defined by The Knee Society Knee Score	74.2
8. Malalignment		88.4	Symptomatic malalignment reported by the patient and confirmed radiographically with angular deformity in the coronal plane > 10° from the mechanical axis	82.1
9. Stiffness [8]	719.56	92.9	Limited ROM as reported by the patient and	81.8

			demonstrated in a physical examination with extension limited to 15° short of full extension or flexion < 90° (not applicable if preoperative arc of motion < 75°)	
10. Deep periprosthetic joint infection	996.66	99.0	A deep periprosthetic joint infection can be diagnosed when there is a sinus tract communicating with the prosthesis; or a pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or 4 of the following 6 criteria exist: elevated ESR and serum CRP concentration; elevated synovial WBC count;	88.9

			elevated synovial PMN; presence of purulence in the affected joint; isolation of a microorganism in one culture of periprosthetic tissue or fluid; or > 5 neutrophils/high-power field in 5 high-power fields observed from histologic analysis of periprosthetic tissue at ×400 magnification [22]	
11. Periprosthetic fracture	996.44	96.0	Periprosthetic fracture of the distal femur, proximal tibia, or patella (operative or nonoperative treatment should be recorded)	93.9
12. Extensor mechanism disruption	729.65 727.66	95.9	Disruption of the extensor mechanism (surgical repair	94.9

			and/or extensor lag should be recorded)	
13. Patellofemoral dislocation	996.42	95.9	Dislocation of the patella from the femoral trochlea (direction of instability should be recorded)	92.8
14. Tibiofemoral dislocation	996.42	94.9	Dislocation of the tibiofemoral joint (direction of instability should be recorded)	95.9
15. Bearing surface wear	996.46	95.8	Wear of the bearing surface symptomatic or requiring reoperation	81.3
16. Osteolysis	996.45	94.8	Expansile lytic lesion adjacent to one of the implants ≥ 1 cm in any one	91.7

			dimension or increasing in size on serial radiographs/CT scans	
17. Implant loosening	996.41	99.0	Implant loosening confirmed intraoperatively or identified radiographically as a change in implant position or a progressive, radiolucent line at the bone-cement or bone-implant interface	91.7
18. Implant fracture or tibial insert dissociation	996.43	97.9	Implant fracture or dissociation of the tibial insert from the tibial implant	91.6
19. Reoperation		96.0	Return to the operating room related to the index	84.8

		TKA (reasons for reoperation should be recorded)	
20. Revision	97.9	Revision of one or more of the TKA implants (femur, tibia, tibial insert, patella)	92.6
21. Readmission	84.8	Admission to the hospital for any reason during the first 90 days after TKA (reasons for admission and relation to index TKA should be recorded)	79.8
22. Death	95.9	Death occurring for any reason during the first 90 days after TKA (cause of death and relation to	89.8

index TKA should be recorded)
* All of the proposed TKA complications and adverse events and their definitions were endorsed by the members of The Knee Society ($p < 0.001$); ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; WBC = white blood cell; PMN = neutrophil percentage.
(Reproduced from:
Healy, W. L., Della Valle, C. J., Iorio, R., Berend, K. R., Cushner, F. D., Dalury, D. F., & Lonner, J. H. (2013). Complications of total knee arthroplasty: standardized list and definitions of the Knee Society. *Clinical orthopaedics and related research*, *471*(1), 215–220. doi:10.1007/s11999-012-2489-y)

Appendix B:

10 11 19

Zelda Epperson
School of Nursing
P.O. Box 910
State University AR, 72467

Dear Ms. Epperson:

The White River Medical Center Institutional Review Board (IRB) reviewed your request for approval of a retrospective chart review for The Cost Benefit and Efficacy of Vancomycin over Ce azolin in Reducing Post-operative Infection rate in Total Knee Arthroplasties.

We are pleased to let you know we approved the research study using the "Expedited Approval" process. As per IRB policy, this request is approved for the data review, based on the following criteria:

1. No risk to patients.
2. No cost to WRMC.
3. All data is collected using WV numbers and data will be kept locked inside a secure area.

Respectfully,

Anil Kumar, M.D.
White River Medical Center
IRB Chair

WHITE RIVER HEALTH SYSTEM
www.WhiteRiverHealthSystem.com

1710 Harrison Street • P.O. Box 2197 • Batesville, AR 72503-2197
(870) 262-1200 • Fax (870) 262-1458

October 4, 2019

Arkansas State University-Jonesboro
Institutional Review Board
c/o Research and Technology Transfer
Post Office Box 2760
State University, Arkansas 72467

To Whom It May Concern:

A graduate student at the Arkansas State University-Jonesboro Department of Nursing has requested permission to conduct the Research Project named below at White River Health Systems during the period of January 2020-April 2020.

This letter notifies you that I/we grant permission to Zelda Epperson, a student of Arkansas State University-Jonesboro Doctor of Nursing Practice program to collect data at the location listed below.

Project Title: The cost benefit and efficacy of vancomycin over cefazolin in reducing post-operative infection rate in total knee arthroplasties.

Principal Investigator: Zelda Epperson

Study Site Location: White River Health Systems
1710 Harrison Street, Batesville, Arkansas 72501

Permission granted by:

ANIL KUMAR, IRB CHAIR at WRMC
Print Name and Title:

Anil Kumar
Signature:

10/11/2019
Date:

Appendix C.

RESEARCH AND TECHNOLOGY TRANSFER

P.O. Box 2760, State University, AR 72467 | o: 870-972-2694 | f: 870-972-2336

November 15, 2019

Principal Investigator: Zelda Epperson

Board: Institutional Review Board (IRB)

Study: FY19-20-84 The cost benefit and efficacy of vancomycin over cefazolin in reducing post-operative infection rate in total knee arthroplasties.

Submission Type: Initial

Board Decision: Exempt

Approval Date: November 15, 2019

Thank you for your submission of New Project materials for this research study. The Arkansas State University IRB has determined this research qualifies for exemption under 45 CFR 46.104(d) under:

Category 4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

- Changes to the protocol must be submitted to the IRB for approval as they may alter exempt-eligible status.
- Continuing IRB review is not required if there are no changes to the protocol.
- When the research is complete, please log in to Cayuse to submit a closure report.

- Investigators are also asked to promptly report any unanticipated problems or complaints to the Committee.

Please retain a copy of this correspondence for your records. If you have any questions, please contact the Director of Research Compliance at (870) 972-2694 or IRB@astate.edu. Please include your study title and study label.

Sincerely,

Amy R. Pearce, Ph.D.

Chair, Institutional Review Board

Appendix D.

Data Tool

Surgical Site Infection (SSI)

Form Approved OMB No. 0920-0666 Exp. Date: 12/31/2022 www.cdc.gov/nhsn

Event #:	
*Subject ID:	
Secondary ID:	
*Gender: F M Other	:
Ethnicity (Specify):	Race (Specify):
*Event Type: SSI	*Date of Event:
*NHSN Procedure Code:	ICD-10-PCS or CPT Procedure Code:
*Date of Procedure: .*Outpatient Procedure: Yes No	
*MDRO Infection Surveillance: □ Yes, this infection's pathogen & location are in-plan for Infection Surveillance in the MDRO/CDI Module □ No, this infection's pathogen & location are **not** in-plan for Infection Surveillance in the MDRO/CDI Module	
*Date Admitted to Facility:	Location:
Event Details	
*Specific Event: □ Superficial Incisional Primary (SIP) □ Deep Incisional Primary (DIP) □ Superficial Incisional Secondary (SIS) □ Deep Incisional Secondary (DIS) □ Organ/Space (specify site): _____	
*Infection present at the time of surgery (PATOS): □ Yes □ No	

*Specify Criteria Used (check all that apply):

Signs & Symptoms □ Drainage or material†

□ Pain or tenderness

□ Swelling or inflammation

□ Erythema or redness

□ Heat

□ Fever

□ Incision deliberately opened/drained

□ Wound spontaneously dehisces □ Abscess

□ Sinus tract □ Hypothermia □ Apnea
□ Bradycardia □ Lethargy
□ Cough

□ Nausea

□ Vomiting □ Dysuria

Laboratory

□ Organism(s) identified

□ Culture or non-culture-based testing not performed

□ Organism(s) identified from blood specimen

□ Organism(s) identified from ≥ 2 periprosthetic specimens

□ Other positive laboratory tests†
□ Imaging test evidence of infection

Clinical Diagnosis
□ Physician diagnosis of this event type

□ Physician institutes appropriate antimicrobial therapy†

□ Other evidence of infection found on invasive procedure, gross anatomic exam, or histopathologic exam †

□ Other signs & symptoms† †per specific site criteria

*Detected: □ A (During admission) □ P (Post-discharge surveillance) □ RF (Readmission to facility where procedure performed) □ RO (Readmission to facility other than where procedure was performed)	
*Secondary Bloodstream Infection: Yes No	**Died: Yes No .SSI Contributed to Death: Yes No
Discharge Date:	*Pathogens Identified: Yes No *If Yes, specify on pages 2-3.
Assurance of Confidentiality: The voluntarily provided information obtained in this surveillance system that would permit identification of any individual or institution is collected with a guarantee that it will be held in strict confidence, will be used only for the purposes stated, and will not otherwise be disclosed or released without the consent of the individual, or the institution in accordance with Sections 304, 306 and 308(d) of the Public Health Service Act (42 USC 242b, 242k, and 242m(d)). Public reporting burden of this collection of information is estimated to average 35 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC, Reports Clearance Officer, 1600 Clifton Rd., MS D-74, Atlanta, GA 30333, ATTN: PRA (0920-0666). CDC 57.120 (Front) Rev 7, v8.6	

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Pathogen #	**Gram-positive Organisms**
	Staphylococcus coagulase-negative **VANC** SIRN (specify species if available): _____
	____*Enterococcus faecium* ____*Enterococcus faecalis* ____*Enterococcus* spp.
	(Only those not identified to the species level) **DAPTO** S NS N **GENTHL§** S R N **LNZ** S I R N **V ANC** S I R N
	Staphylococcus aureus **CIPRO/LEVO/MOXI** S I R N **OX/CEFOX/METH** S I R N
	CLIND S I R N **RIF** S I R N **DAPTO** S NS N **TETRA** S I R N **DOXY/MINO** S I R N **TIG** S NS N **ERYTH** S I R N **TMZ** S I R N **GENT**

	S I R N **V ANC** S I R N **LNZ** S R N
Pathogen #	**Gram-negative Organisms** _____ _____
	Acinetobacter (specify species) _____ **AMK AMPSUL** **AZT CEFEP** **CEFTAZ** **CIPRO/LEVO** SIRN SIRN SIRN SIRN SIRN SIRN

	COL/PB SIRN **TETRA/DOXY/MINO** SIRN **GENT IMI** **MERO/DORI** SIRN SIRN SIRN **TMZ TOBRA** SIRN SIRN **PIP/PIPTAZ** SIRN
	Escherichia coli **AMK** S I R N

	CEFTAZ **AMP** S I R N **CEFUR** **AMPSUL/AMXCLV** S I R N **CEFOX/CTET** **AZT CEFAZ** S I R N S I R N **CIPRO/LEVO/MOXI** **CEFEP** **CEFOT/CEFTRX** S I/S-DD R N S I R N **COL/PB†** SRN

	TETRA/DOXY/MIN O SIRN SIRN SIRN SIRN **ERTA GENT IMI MERO/DORI** SIRN SIRN SIRN SIRN **TIG TMZ TOBRA** SIRN SIRN SIRN **PIPTAZ** SIRN SIRN
	Enterobacter

	(specify species) _____ **AMK** S I R N **CEFTAZ** **AMP** S I R N **CEFUR** **AMPSUL/AMXCLV** S I R N **CEFOX/CTET** **AZT CEFAZ** S I R N S I R N **CIPRO/LEVO/MOX I** **CEFEP** S I/S-DD R N

	COL/PB† SRN **CEFOT/CEFTRX** S I R N SIRN SIRN SIRN SIRN **ERTA GENT IMI MERO/DORI** SIRN SIRN SIRN SIRN **TIG TMZ TOBRA** SIRN SIRN SIRN **PIPTAZ** **TETRA/DOXY/MIN O**

	SIRN SIRN
	____*Klebsiella pneumonia* ____*Klebsiella oxytoca* ____*Klebsiella aerogenes* **AMK** S I R N **CEFTAZ** **AMP** S I R N **CEFUR** **AMPSUL/AMXCLV** S I R N **CEFOX/CTET** **AZT CEFAZ**

	S I R N S I R N **CIPRO/LEVO/MOXI** **CEFEP** S I/S-DD R N **COL/PB†** SRN **CEFOT/CEFTRX** S I R N SIRN SIRN SIRN SIRN **ERTA GENT IMI MERO/DORI** SIRN SIRN SIRN SIRN **TIG TMZ TOBRA**

	SIRN SIRN SIRN **PIPTAZ** **TETRA/DOXY/MINO** SIRN SIRN

Drug Codes:

AMK = amikacin

AMP = ampicillin

AMPSUL = ampicillin/sulbactam AMXCLV = amoxicillin/clavulanic acid

ANID = anidulafungin

AZT = aztreonam

CASPO = caspofungin

CEFAZ= cefazolin

CEFEP = cefepime

CEFOT = cefotaxime

CEFOX= cefoxitin

CEFTAZ = ceftazidime

CEFTRX = ceftriaxone

CEFUR= cefuroxime CTET= cefotetan CIPRO = ciprofloxacin CLIND = clindamycin COL = colistin

DAPTO = daptomycin DORI = doripenem DOXY = doxycycline ERTA = ertapenem

ERYTH = erythromycin

FLUCO = fluconazole

FLUCY = flucytosine

GENT = gentamicin

GENTHL = gentamicin –high level test

IMI = imipenem ITRA = itraconazole LEVO = levofloxacin LNZ = linezolid

MERO = meropenem METH = methicillin MICA = micafungin MINO = minocycline MOXI = moxifloxacin

OX = oxacillin PB = polymyxin

PIP = piperacillin

PIPTAZ = piperacillin/tazobactam

RIF = rifampin

TETRA = tetracycline

TIG = tigecycline

TMZ = trimethoprim/sulfamethoxazole

TOBRA = tobramycin VANC = vancomycin VORI = voriconazole

I = Intermediate

R = Resistant NS = Non-susceptible S-DD = Susceptible-dose dependent N = Not

Surgical Site Infection (SSI)

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Appendix E

Preoperative MRSA Surveillance Culture Protocol for Elective Total Joint Replacement

1. At least 2 weeks prior to surgery, the patient will go to paranesthesia testing (PAT) for bilateral nares PCR

2. The Infection Preventionist will review positive culture reports daily

3. All growth is reported to the Orthopaedic liaison who will coordinate treatment with the assistance of the Infection Preventionist and the Infection Prevention Advisor

4. If nares are positive for MRSA:

    a) The patient will be decolonized by applying mupirocin ointment 2% intranasal (both nares) twice daily x 5 days

    b) The patient will be given vancomycin for prophylaxis in the place of ancef

5. If the nares are positive for MSSA (oxacillin sensitive Staph aureus):

    a) The patient will receive decolonization with mupirocin ointment as outlined above

    b) The patient will receive ancef prophylaxis

6. All elective total joint replacement patients will wash with 4% chlorhexidine gluconate (CHG)

7. The Infection Prevention physician advisor will assist with ordering the decolonization therapy and CHG if needed.

Appendix F

Total Knee Arthroplasty Antibiotic Policy Procedure

I. Policy:

Based on evidenced based practice all patients with the co-morbidities listed in this policy are having a Total Knee Arthroplasty, will be administered Vancomycin based on weight at 15mg/kg.

II. Purpose:

The purpose of the procedure is to establish guidelines for antibiotic use based on patient comorbidities.

III. Procedure:

1) Unless otherwise ordered, **Ancef** will be administered:
2) 1-gram Ancef if patient weighs < 80 kg
3) Unless otherwise ordered, For the following risk factors, **Vancomycin** will be administered at 15mg/kg**
    1) Diabetes >200 mg/dL or HbA1c >7
    2) Smoking
    3) History of MRSA
    4) Recent hospitalization
    5) BMI >40kg/m2

***Note: If patient meets two or more of the qualifying risk factors, vancomycin will be initiated, and surgeon will be notified of change of order.*