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Surgical site infections after total knee arthroplasty - an audit from ‘catch up arthroplasty’ weeks at Helen Joseph Hospital

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Surgical site infections after total knee arthroplasty - an audit from ‘catch up arthroplasty’ weeks at Helen Joseph Hospital



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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine

Johannesburg, 2021

Declaration

I, Warren Meier, declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Orthopaedic Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

.....

(Signature of candidate)

26TH day of MAY 2021 in RIVONIA

Dedication

To those who mean the most to me: my wife Nicole, my parents Robbie and Manuela and my sister Jaqui

Thank you for helping me attain my life's achievements!
May I forever make you proud.

Presentations arising from research project

- Poster presentation at the Wits Faculty of Health Sciences Virtual Research Day & Post-graduate Expo, Thursday 15 October 2020.

- Poster presentation at the South African Orthopaedic Association Congress, November 2020.

Abstract

Introduction: There is a paucity of literature on lower limb arthroplasty from local South African and Sub-Saharan African populations. South African State hospitals have demonstrated long elective lower limb arthroplasty waiting lists. To decrease these waiting times, Helen Joseph Hospital, a South African State hospital, has initiated ‘catch up arthroplasty’ weeks.

Aim: To perform an audit of the epidemiology and determine the prosthetic joint infection and superficial sepsis incidence rates in patients undergoing total knee arthroplasty during ‘catch up arthroplasty’ weeks at Helen Joseph Hospital.

Methodology: One hundred and seventeen (117) patients’ files from ‘catch up arthroplasty’ weeks at Helen Joseph Hospital were retrospectively reviewed. Biochemical, histological and microbiological results were retrieved via the National Health Laboratory Service database. Analysis was performed between patient variables (demographics, comorbid diseases etc.) and three outcome measures: prosthetic joint infection, superficial surgical site infection and overall post-operative surgical site infection. Prosthetic joint infection was defined using the 2018 revised Musculoskeletal Infection Society criteria.

Results: The average waiting time for total knee arthroplasty was 19.9 months. The average age was 64.4 years. Eighty three percent (83%) of the total knee arthroplasty procedures were performed on females. Osteoarthritis was the underlying diagnosis in 96.9% of cases. Type I obesity was the most common World Health Organisation body mass index category and 80% of the population was overweight. The average operative time was 106.4 minutes. The prosthetic joint infection incidence was 0.85%, and the superficial surgical infection incidence was 9.40%.

Conclusion: This was the first study to objectively determine a prosthetic joint infection incidence in Sub-Saharan Africa using validated criteria. The paucity of data from South Africa and Sub-Saharan Africa on audits of this kind demonstrates that more studies of this nature are needed to understand the differences in demographics and epidemiology of total joint arthroplasty populations and how these differences translate into risks for post-operative infective outcomes in our region.

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Nomenclature

AIDS	Acquired Immunodeficiency Syndrome
BMI	Body mass index
CRP	C-reactive protein
DMARDs	Disease modifying anti-rheumatic drugs
ESR	Erythrocyte sedimentation rate
HbA1c	Haemoglobin A1c
HIV	Human Immunodeficiency Virus
HJH	Helen Joseph Hospital
ICD	International Classification of Diseases
MSIS	Musculoskeletal Infection Society
NHLS	National Health Laboratory Service
OA	Osteoarthritis
OPS	Overall post-operative sepsis
OT	Operative (skin to skin) time
PJI	Prosthetic joint infection
SSA	Sub-Saharan Africa
SSI	Superficial surgical site infection
THA	Total hip arthroplasty
THR	Total hip replacement
TKA	Total knee arthroplasty
TKR	Total knee replacement

WCC White cell count

WHO World Health Organisation

1. Introduction

1.1 Background and literature review

Joint arthroplasty has improved the quality of life of many patients worldwide with debilitating pain and limited function as a result of degenerative joint conditions that are refractory to medical therapy (1). Globally, approximately two million total hip (THA) and total knee arthroplasties (TKA) are performed annually (2). With an ageing population, epidemiological studies expect these numbers to increase further, raising the demand for these procedures (3).

TKA is an effective means of eliminating pain and improving functional outcomes in patients requiring the procedure, however it is not without its complications (4). The longevity and durability of these prostheses are ever improving, however being synthetic, the components do eventually fail (5). Common reasons for TKA failure include: aseptic loosening, infection, instability and arthrofibrosis (stiffness) (5, 6). With the improvements in surgical technique, prosthetic component composition design and perioperative care, the aetiology of failure of TKA is evolving, however, overwhelmingly the two most common reasons for failure are infection and aseptic loosening (5-7). Consequently, these are the two most common reasons for revision TKA (7). Results vary as to which of these two complications is the most frequent reason for revision TKA. Universally, infection predominates as the most common reason for revision TKA within two years after primary TKA (5-7). Although prosthetic joint infection (PJI) is the most common reason for early revision TKA, its overall incidence is low making it a fairly uncommon complication after TKA (2, 5, 8). Overall, PJI incidence rates are typically around 1-2% with rates following TKA slightly higher than those following THA (2, 8). For these reasons, the core focus of this study will focus on PJI in patients following TKA.

Surgical site infections following TKA may be superficial or deep. Superficial surgical site infections (SSIs) involve the skin and subcutaneous tissue, but do not communicate with the knee joint (9). These infections often resolve with a course of antibiotics and local wound care (9). Deep surgical site infections that involve the

joint prosthesis and adjacent tissues are defined as PJI (8). PJI is a severe, dreaded complication that may occur after TKA (4, 8). The occurrence of PJI has a huge impact on the life of patients, including multiple readmissions, prolonged antibiotic therapy, potential loss of function of the knee, and it can also have a psychological impact (2, 10). The ultimate goal following a PJI diagnosis is to eradicate the infection and return the knee to an acceptable, pain free range of motion and function. The results may vary in patients as the final outcome depends on a multitude of patient and infection characteristic variables (8, 10). Occasionally, the only realistic outcome may be to remain with a chronic infected prosthesis, while on the other extreme the infection may be eradicated at the expense of joint function resulting in pseudoarthrosis, arthrodesis or amputation (10).

Commonly quoted risk factors for SSI and PJI prior to TKA include: prolonged surgical time, prior knee infection or surgery, diabetes, obesity, malnutrition, smoking, compromised immune status, immunosuppressive therapy, inflammatory arthropathies as well as a host of environmental and procedure related factors (pre-operative patient preparation, prophylactic antibiotic use, operative room environment, and post-operative anticoagulation) (8, 10-12). These risk factors can be divided into intrinsic and extrinsic factors and further subdivided into modifiable and non-modifiable risk factors (8). Among the most important modifiable intrinsic risk factors are glycemic control, body mass index (BMI) adjustment, inflammatory arthropathy control and medication adjustment, as well as smoking cessation (8, 12). Human Immunodeficiency Virus (HIV) positive status regardless of CD4 count is an important independent non-modifiable risk factor for post-operative septic complications including PJI (13).

Diabetics have a two to four times increased risk of developing SSI and PJI (8, 12). The risk is worse if the diabetes is poorly controlled, but more importantly if the peri-operative glycemic control is poor (11, 12, 14). Many guidelines advise a pre-operative HbA1c level below 8-9% to minimise the risk of post-operative sepsis, however no evidence based guidelines are published that preclude elective joint arthroplasty above any single pre-operative HbA1c level (14). BMIs $\geq$ 40 have been associated with an increased risk of PJI (11, 15, 16). In some studies, a BMI of < 25 has been shown to be a risk factor for PJI (8). Higher BMIs are associated with longer operative times, concomitant metabolic syndrome and paradoxical

malnutrition, while lower BMIs are associated with poor nutritional reserve, inflammatory arthropathies and immune suppression (8, 12). Recommendations suggest that patients with a BMI > 40 should have their TKA postponed, especially if associated with poor glycemic control (11, 12). PJI risk in patients with inflammatory arthropathies is related to both the severity of the disease and the immune modifying drugs taken to control the disease (8, 12). PJI rates increase in patients with chronic, poorly controlled inflammatory arthropaties and patients using corticosteroids or biologic disease modifying anti-rheumatic drugs (DMARDs) (8, 12). Corticosteroids should be weaned to low doses and biologic DMARDs should be stopped one dosing cycle prior to TKA (8, 12). Methotrexate does not need to be stopped as it is not associated with increased PJI risk (8, 12). A positive smoking status increases the risk of PJI, with current smokers at a higher risk than prior smokers (12). Smoking cessation up to one month prior to surgery is recommended (12).

PJI is a dreaded complication for both the patient and orthopaedic surgeon, and may possibly be the most challenging complication to manage following TKA (8, 17). One of the most challenging aspects stems from the difficulty in making a diagnosis of PJI (8, 17, 18). A reason for this is due to the lack of a single clinical or laboratory test which can accurately be used to diagnose PJI (8, 18). In 2011, the Musculoskeletal Infection Society (MSIS) proposed criteria to attempt to standardise the diagnosis of PJI. These criteria comprise a combination of physical examination findings, microbiological data, laboratory inflammatory markers, intra-operative findings and synovial fluid analysis (17). In 2018 this definition was revised to criteria that were more evidence based, as opposed to the 2011 criteria which were largely based on expert opinion (19). The revision was also developed amidst concerns of the sensitivity of the 2011 definition, and incorporated newer, validated, diagnostic tests (19). In 2012, the Infectious Diseases Society of America also published diagnostic criteria, however, no definition for PJI has been universally adopted (18, 20, 21). A delay in the recognition of PJI may risk failure of revision surgery, so a prompt diagnosis is crucial (18, 21). This may be one factor that results in some patients being diagnosed and treated for PJI without meeting the MSIS or any other standardised diagnostic criteria (21). In 2015, Koh et al. performed a multi-centre study in Korean hospitals and found that only 65% of all the patients treated with two stage revision for PJI after TKA met the MSIS criteria (21). The tables shown below indicate the 2011 and 2018 revised MSIS criteria for the diagnosis of PJI (17, 19).

Table 1.1: 2011 MSIS criteria for the diagnosis of PJI (17).

TABLE I MSIS Criteria for the Diagnosis of PJI and Thresholds for the Minor Diagnostic Criteria[3]*		
		Recommended Threshold
Major criteria	(1) Two positive periprosthetic cultures with phenotypically identical microorganisms or (2) A sinus tract communicating with the joint	
Minor criteria		
	(1) Elevated serum CRP and ESR	10 mg/L, 30 mm/hr
	(2) Elevated SF WBC count or changes in the leukocyte esterase strip	3,000 cells/μL, + or ++
	(3) Elevated SF PMN%	80%
	(4) Positive histological analysis of the periprosthetic tissue	>5 neutrophils per high-power field in 5 high-power fields (×400)
	(5) A single positive culture	

*PJI is present when 1 of the major criteria, or 3 of 5 of the minor criteria, are met. CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, SF = synovial fluid, WBC = white blood cell, and PMN% = polymorphonuclear neutrophil percentage.

Table 1.2 : Revised 2018 MSIS criteria for the diagnosis of PJI (19).

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

		Minor Criteria	Score	Decision
Preoperative Diagnosis	Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
		Elevated ESR	1	
	Synovial	Elevated synovial *WBC count or LE*	3	2-5 Possibly Infected [a]
		Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	0-1 Not Infected
		Elevated synovial CRP	1	

	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
Intraoperative Diagnosis	Preoperative score	-	≥6 Infected
	Positive histology	3	4-5 Inconclusive [b]
	Positive purulence	3	
	Single positive culture	2	≤3 Not Infected

Key: CRP: C-reactive protein (>1mg/dL), D-Dimer (> 860ng/ml), ESR: erythrocyte sedimentation rate (> 30 mm/h), Synovial WBC (white blood cell) count (> 3000 cells/μl), LE: Leucocyte esterase (+ + positive), Synovial PNM (polymorphonuclear) % (>80%), Synovial CRP (> 6.9 mg/L), Histology (greater than 5 neutrophils per high-power field in 5 high power fields observed from histologic analysis of peri-prosthetic tissue at 400x magnification) [a]For patients with inconclusive minor criteria, operative criteria can also be used to fulfil definition for PJI [b]Consider further molecular diagnostics such as next-generation sequencing.

The classification of PJI with regard to the timing of onset is important to distinguish for the following two main reasons: the likelihood of the causative organism, and possible options for eradication and treatment. The first useful classification system describes the occurrence of PJI from onset post-operatively. Early onset PJI occurs within 3 months following surgical prosthetic implantation, delayed onset PJI occurs between 3 and 12-24 months, and late onset PJI occurs after 12-24 months (11, 22). It should be noted that the time at which delayed and late onset PJI occur differs among authors (18, 22-24). Early and delayed onset PJI usually represent infections that were introduced in the patients at the time of surgery (22-24). Early onset PJIs are usually caused by relatively virulent organisms that are numerous, and are in the planktonic phase, such as *Staphylococcus aureus* and gram negative bacilli (22-24). In contrast, delayed onset PJIs are usually caused by less virulent organisms that are more likely to be in a sessile state in biofilms such as coagulase negative *staphylococci* (22-24). Late onset PJIs occur most frequently due to haematogenous spread from a distant body site (22-24).

A second useful classification system was described by Tsukayama et al. in 2003 which divided PJI into four categories with a proposed mode of management for each type (10). The first category is an infection in which a positive intra-operative specimen is found. The scenario is usually a patient undergoing revision TKA for presumed aseptic loosening and a routine intraoperative specimen is subsequently found to be positive. The suggestion from Tsukayama et al. is that these infections be treated with antibiotics alone with curative rates in excess of 90% (10). The second category consists of early post-operative infections defined as occurring within one month after surgery, and is subdivided into superficial and deep infections. The third category includes infections resulting from haematogenous spread, but no time frame is described. Both second and third category infections present with acute inflammation and systemic toxicity, and the suggestion by Tsukayama et al. is that an attempt can be made to salvage these prostheses (10). Treatment with a prompt, thorough debridement and antibiotics is reported to have a cure rate of 60-80% (10). The fourth category includes late post-operative infections that present indolently after a month post-surgery. The suggested management of these infections involves implant removal, thorough debridement, antibiotic cement spacer placement and intravenous antibiotics for a minimum of six weeks (10). Reimplantation of a new prosthesis can be considered as a secondary management procedure that can be

implemented at a later stage once the infection has been eradicated (10). The below tables display a summary of the classification system, as well as the likely organism and suggested management strategies per infection, adopted from Tsukayama et al.'s original text in 2003 (10).

Table 1.3: Classification of PJI according to Tsukayama et al. (10).

TABLE II Classification of Infection on the Basis of Clinical Presentation

I. Positive intraoperative culture

II. Early postoperative infection
   A. Superficial
   B. Deep

III. Acute hematogenous

IV. Late chronic

Table 1.4: Likely causative organism and proposed treatment per infection according to Tsukayama et al. (10).

TABLE III Early Superficial Infection

Diagnosis	Treatment	Usual Bacterial Source	Results of Authors' Clinical Experience
· <4 weeks · Fever · Inflammation · Fluid/pus · No sinus · No extension through capsule	· Gram stain/culture · Débridement/irrigation · Closure/antibiotic beads · Intravenous antibiotics × 6 weeks	· Coagulase-negative staphylococcus · Coagulase-positive staphylococcus	· 13/13 resolved

TABLE IV Early Deep Infection

Diagnosis	Treatment	Usual Bacterial Source	Results of Authors' Clinical Experience
· <4 weeks · Fever · Inflammation · Fluid/pus · No sinus · Extension through capsule	· Gram stain/culture · Polyethylene insert removed · Débridement/irrigation · Closure/antibiotic beads · Intravenous antibiotics × 6 weeks	· Coagulase-positive staphylococcus · Coagulase-negative staphylococcus · Gram-negative bacillus	· Prosthesis salvaged in 5/10. After repeat débridement, infection eradicated in 9/10.

TABLE V Acute Hematogenous Infection

Diagnosis	Treatment	Usual Bacterial Source	Results of Authors' Clinical Experience
· >4 weeks · Fever · Inflammation · Fluid/pus · No sinus · Extension through capsule	· Gram stain/culture · Polyethylene insert removed · Débridement/irrigation · Closure/antibiotic beads · Intravenous antibiotics × 6 weeks	· Coagulase-positive staphylococcus · Streptococcus	· 5/7 resolved

TABLE VI Late Chronic Infection

Diagnosis	Treatment	Usual Bacterial Source	Results of Authors' Clinical Experience
· >4 weeks · Fever · Induration · Fluid/pus · Sinus · Extension through capsule	· Gram stain/culture · All components removed · Débridement/irrigation · Closure/antibiotic articulators · Intravenous antibiotics × 6 weeks	· Coagulase-positive staphylococcus · Coagulase-negative staphylococcus · Gram-negative bacillus	· 24/29 resolved

The above mentioned classification system, and proposed management of PJI, may seem outdated. The considerations of surgical management of patients with PJI is multifactorial and current practice on what surgery to perform is based on patient preference, implant and soft tissue condition, host factors and pathogen characteristics (8). Surgical options for revision after PJI include debridement and retention of the prosthesis, debridement and polyethylene exchange, one stage exchange (more frequently performed in Europe), two stage exchange (more frequently performed in the United States of America), resection arthroplasty, arthrodesis and amputation (8, 22, 25). In 2018, Abad and Haleem proposed treatment algorithms that were adopted from original texts sourced from the Infectious Diseases Society of America. Zimmerli et al. summarised these algorithms as shown in the figures below (8, 20, 22).

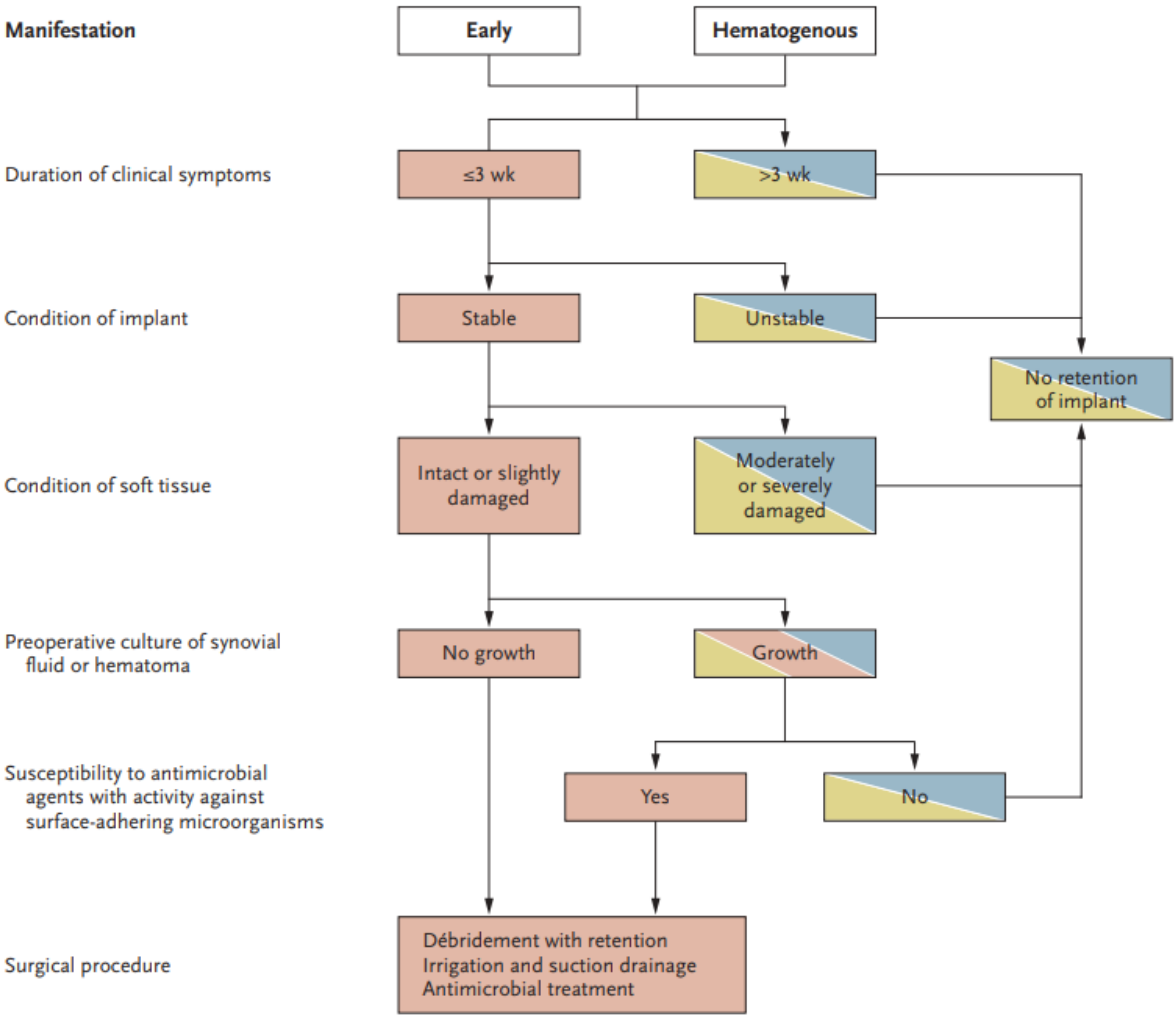

Figure 1.1: Algorithm for the management of early and haematogenous PJIs (8, 20, 22).

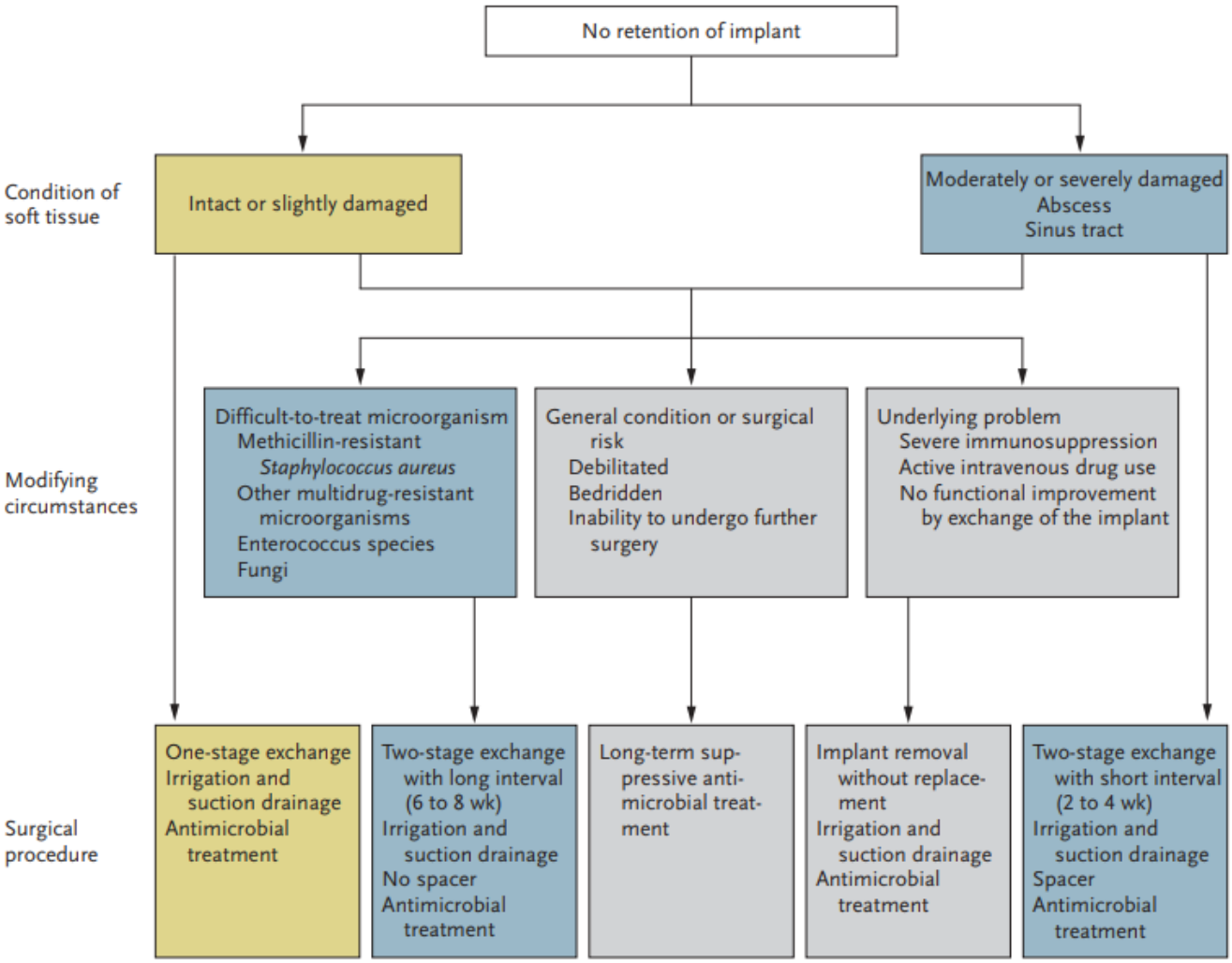

Figure 1.2: Algorithm for the management of patients with PJI not qualifying for retention of implants (8, 20, 22).

Another major concern and challenge in the management of PJI after TKA is related to the use of antibiotics. In principle, the antibiotics used for PJI need to attain therapeutic drug levels within bone over a prolonged period, as well as have activity against microorganisms that are biofilm producing and slow growing (8, 22). In many cases, the best way to attain this goal is to use long courses of combination drugs through various routes (8, 20, 22). Rifampicin is indicated in most cases of *Staphylococcal* infections as a combination regimen with another sensitive drug when the intention is to retain or exchange the implant (8, 20, 22, 26). The concern of using such protocols is the prolonged toxic effects of the drugs in patients resulting in poor compliance and the emergence of resistant microorganisms (22, 26). In all cases, the offending pathogen needs to be determined in order to direct antimicrobial therapy (20, 22, 24). The optimal duration for antimicrobial therapy depends on the

clinical scenario and offending pathogen, however global standards have not been defined and no consensus has been met (8). Current guidelines by experts suggest four to six weeks of antibiotic use for any resection arthroplasty cases, and between three months (hip prostheses) and six months (knee prostheses) of antibiotic use for patients with PJIs treated with implant retaining or exchange protocols (8, 20, 22). These guidelines have recently been questioned by Lora-Tamayo et al. in 2016 who suggested that shorter durations (eight weeks) may be as effective as longer protocols in acute *Staphylococcal* PJI although some doubt remained with regard to the benefit in infected knee prostheses (26).

South African State hospitals have demonstrated very long waiting lists for THA and TKA, sometimes in excess of five years (27). In an effort to attempt to curb this demand, and decrease waiting times, a number of Johannesburg State hospitals, including Helen Joseph Hospital (HJH), have initiated ‘catch up arthroplasty’ weeks. At HJH, during these weeks, as many as possible pre-determined patients awaiting THRs and TKRs are operated on. Qualified orthopaedic surgeons, with varying levels of arthroplasty experience, are assigned to theatre lists filled with patients requiring these procedures. Qualified orthopaedic surgeons are assisted by orthopaedic registrars and medical officers during these procedures. Some of these surgeons do not work exclusively at HJH, but are called in for the week to help with the load. HJH initiated a ‘catch up arthroplasty’ ‘move and walk’ week in October 2015. Initially, three ‘move and walk’ weeks were held per year, and in 2017 it became a quarterly event. This is a fairly new concept in South African State hospitals and therefore there is no literature defining the parameters, epidemiology and complications of this unique patient population.

The ever increasing number of TKAs raises a concern on the social and economic burden that these procedures will place on hospitals and the national health system (28). An even greater concern is related to treating PJI after TKA (29). Globally there has been an increasing trend to publish statistical data on lower limb arthroplasty cases in order to improve patient outcomes (6). There is a paucity of literature published about the outcomes of total joint arthroplasties in Sub-Saharan Africa (SSA). In 2019 Davies et al. published the first systematic review about the outcomes of total joint arthroplasty in SSA but did not include any data from South Africa (30). To the best of my knowledge no local data from South Africa has been published that

relates to post-operative SSI and PJI rates following TKA. For this reason, it is important to investigate and understand the South African population demographics of total joint arthroplasty patients managed at an institution, and it is prudent to include SSI and PJI rates when describing these audit statistics.

1.2 Study Aim and Objectives

Aim:

To determine the superficial surgical site infection (SSI) and prosthetic joint infection (PJI) incidence rates in patients undergoing total knee arthroplasty (TKA) during 'catch up arthroplasty' weeks at Helen Joseph Hospital.

Objectives:

1. To describe the demographics and epidemiology of patients who underwent TKA during 'catch up arthroplasty' weeks.
2. To compare these demographics and epidemiology with the demographics and epidemiology of national and international arthroplasty populations.
3. To determine if any of these demographic or epidemiological characteristics have any association with SSI and / or PJI.
4. To compare the SSI and PJI incidence rates after TKA during 'catch up arthroplasty' weeks with international populations.

2. Methodology

2.1 Research Questions

What are the overall post-operative SSI, and acute and delayed onset PJI rates in patients who underwent TKA in elective ‘catch up arthroplasty’ ‘move and walk’ weeks at HJH between 01 October 2015 and 31 August 2017? Do these rates differ from other international populations?

What are the demographics and what is the epidemiology of patients who underwent TKA in elective ‘catch up arthroplasty’ ‘move and walk’ weeks at HJH between 01 October 2015 and 31 August 2017? Do these demographics and does the epidemiology differ from the demographics and epidemiology of other national and international arthroplasty populations?

Do any of the demographic or epidemiological characteristics of patients who underwent TKA in elective ‘catch up arthroplasty’ ‘move and walk’ weeks at HJH between 01 October 2015 and 31 August 2017 have any association with SSI and / or PJI.

2.2 Research Design

This was a retrospective cohort study. Data were gathered from a retrospective review of patients’ inpatient and outpatient hospital files, as well as through a thorough, systematic review of relevant results recorded on the NHLS database.

2.3 Materials and Methods

Ethical clearance was granted by the Human Research Ethics Committee (Medical), University of the Witwatersrand (protocol number: M181101, see Appendix A). Furthermore, permission from the HJH Ethics and Research Committee, the HJH lab

and blood services coordinator and clinical manager, and the NHLS national data warehouse manager was granted (see Appendix B, C and D, respectively). All patients were assigned a study number to maintain anonymity, and patient identifiers (names, hospital number and identification number) were excluded from the data collection sheets to maintain confidentiality.

The secretary at the Department of Orthopaedics at HJH had a record of all elective arthroplasty cases done during these catch up weeks for the defined time period. These records included the patient's full name, hospital number, age at the time of the operation and the nature of the operative procedure performed. All of the patients' inpatient and outpatient files were then requested from the records department at HJH and scrutinised. The information that was gathered from each patient's file included: whether it was the first or second TKA recorded in the study, the patient's age, the patient's sex, the patient's race, the side of the TKR, the underlying diagnosis resulting in the TKR, the BMI classification, the smoking status, the presence of any comorbid risk factors for PJI, the use of any immune modifying drugs or steroids, the operative (skin to skin) time (OT), and the waiting period (time spent on the waiting list for TKA) (see Appendix E and Appendix F).

All the included patients also underwent a thorough individual search on the National Health Laboratory Service (NHLS) database. The primary investigator had access to the patients' results on the NHLS database which was accessed via the website https://trakcarelabwebview.nhls.ac.za. As the NHLS is a national service, all patients' results, regardless of the collection site, were displayed on the database. The name and surname, as well as the hospital / folder number of patients were inserted into the relevant fields on the NHLS website (as illustrated in Figure 2.1). All their logged biochemical, histological and microbiological results were sought for. All the evidence of PJI according to the MSIS criteria were captured on a Numbers spreadsheet (Apple Inc.) (see Appendix G). Only the results taken up to two years post-operatively were considered. In cases where there was doubt about the origin of a suspected infection, patient files were scrutinised for clarity.

The patients' results were analysed and positive results were classified into one of three outcome measures, namely: overall post-operative surgical site infection (OPS), prosthetic joint infection (PJI), and superficial surgical site infection (SSI).

OPS = PJI + SSI (see Appendix E). A positive PJI result was defined as an infection with clear evidence on the NHLS database, or in the patient's hospital file that fulfilled the revised 2018 MSIS criteria. A positive SSI was defined as a post-operative surgical site infection that did not fulfil the revised 2018 MSIS criteria for PJI. In all cases of confirmed PJI or SSI, patients' files were studied for the purpose of describing how these patients were diagnosed and managed, and to classify their infections.

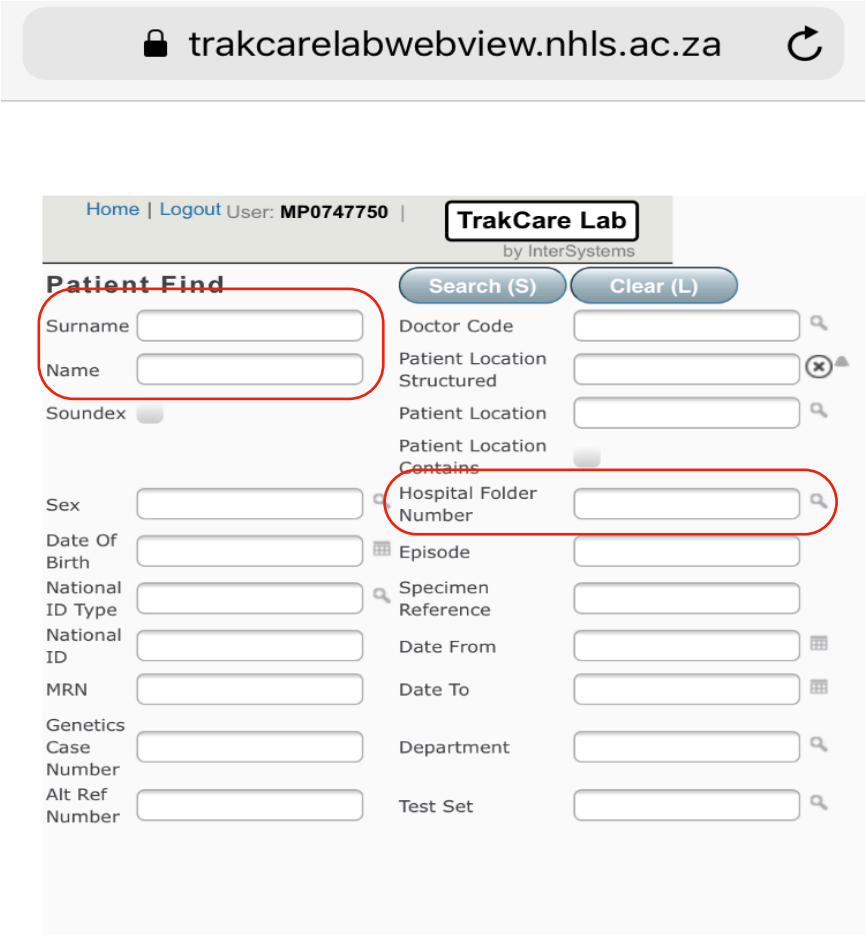

Figure 2.1: NHLS website database access page with highlighted fields that were searched.

2.4 Sample

All patients operated on during elective 'catch up arthroplasty' 'move and walk' weeks at HJH from its inception on 01 October 2015 until 31 August 2017 were considered for inclusion in this study. Patients included in the study were those who underwent a primary TKR during those weeks. Patients who underwent any operation other than a

primary TKR (hip arthroplasty cases, uni-compartmental knee replacements and revision TKR), and patients operated on outside ‘move and walk’ weeks were excluded from the study. No age restriction was applied.

2.5 Data Collection

The data were collected and tabulated on a data collection spreadsheet on Numbers (Apple Inc.).

2.6 Data Analysis

The results obtained from this study were tabulated in Numbers (Apple Inc.). A private statistician was hired to assist with the statistical analysis. Descriptive statistics were used to describe the characteristics of the population and these were displayed using graphs and charts. Categorical variables were analysed and represented as frequencies and percentages. The mean, standard deviation, median and interquartile ranges were reported for continuous data. Inferential statistics were performed on the data to seek any relationship between the variables and the three outcome measures, namely: OPS, SSI, and PJI. The Fisher Exact test was used when comparing percentages. The Student’s two sample t-test was used when comparing means for normally distributed data. The non-parametric Wilcoxon rank sum test was used when comparing medians for data that was not normally distributed.

The population’s overall early and delayed onset PJI, SSI and OPS rates were calculated and described as an incidence. All statistical tests were two sided and p-values less than or equal to 0.05 were considered statistically significant. All statistical procedures were done on SAS (SAS Institute Inc, NC, USA), (Release 9.4, running under Microsoft Windows). Graphs were created on Microsoft Excel and edited on Numbers (Apple Inc.).

3. Results

A total of 117 primary TKRs were included in the study. Of the initial proposed 120 patients, three were excluded. One patient was excluded as there was no record of the patient in the hospital records department and no record of the patient on the NHLS database. Two patients were excluded as their surgeries were not performed during the specified 'move and walk' weeks but rather on conventional elective arthroplasty lists due to acute medical conditions which arose during their admission. The 117 TKAs were performed on a total of 111 patients. Six patients had a TKR on both of their knees and all of these operations were performed on two separate occasions within the specified weeks and timeframe. A clinical trend was apparent in that 33.3% of the patients who had their second TKR performed in the audit developed a post-operative SSI, suggesting that there may be an association between a second TKR and infection, however this relationship was not statistically significant (p=0.098). Of the other procedures performed, 50.4% of the procedures were left TKRs and 49.6% were right TKRs (see Figure 3.1). There was no statistically significant association between the operated side and OPS, PJI or SSI. The operated side ratios of patients with and without OPS did not differ significantly (p=0.362).

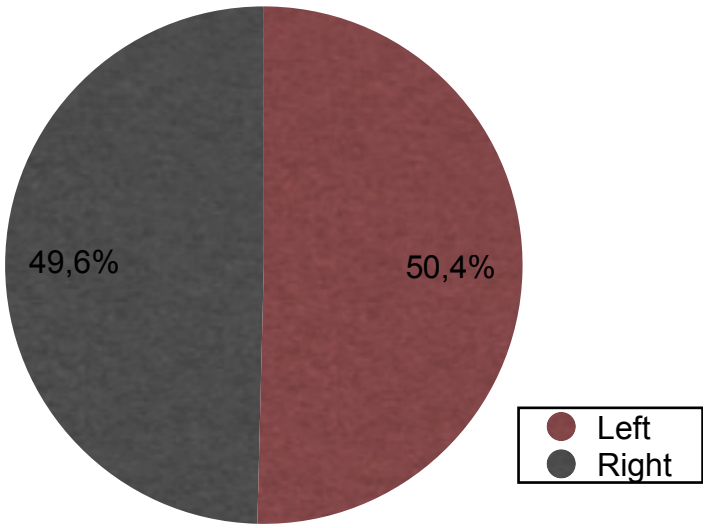

Figure 3.1: A pie chart showing the laterality distribution of TKAs performed in the study.

The mean waiting period (time from the patient being added to the waiting list to surgical completion of the operation) was 19.9 months (n=64, mean [SD] = 19.9 [+/- 8.0] months) and the median was 18.0 months (n=64, median [IQR] = 18.0 [16/21] months). The percentage of patients who waited between one and two years for their operation was 76.6%. The percentage of patients who waited in excess of 30 months for their procedure was 12.5% (see Figure 3.2). The shortest waiting period was five months and the longest was 48 months. There was a significant association between the waiting period and OPS. For the waiting period, when comparing the distributions with and without OPS, a statistically significant difference was displayed (p=0.046). The median waiting time in patients who developed OPS was 21 months compared to patients who did not develop OPS which was 18 months. This difference was statistically significant (p=0.022).

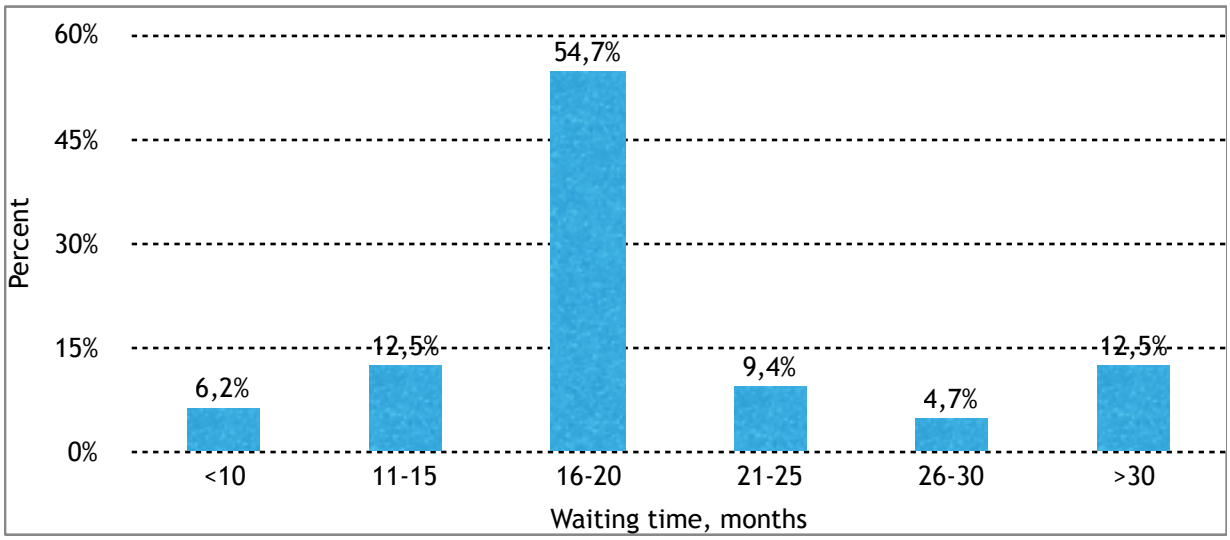

Figure 3.2: A bar graph showing the waiting period category distribution for TKA in the study.

The mean age of the population was 64.4 years old (n=117, mean [SD] = 64.4 [+/- 8,6] years) and the median age was 65 (n=117, median [IQR] = 65 [57/72] years). The youngest patient was 45 years old and the oldest patient was 84 years old. In total, 67.5% of the patients were between 50 and 69 years of age (see Figure 3.3). There was no significant association between age and OPS, PJI or SSI. The age distributions of patients with and without OPS did not differ significantly (p=0.351). Likewise, the mean ages of the patients with and without OPS also did not differ significantly (p=0.412).

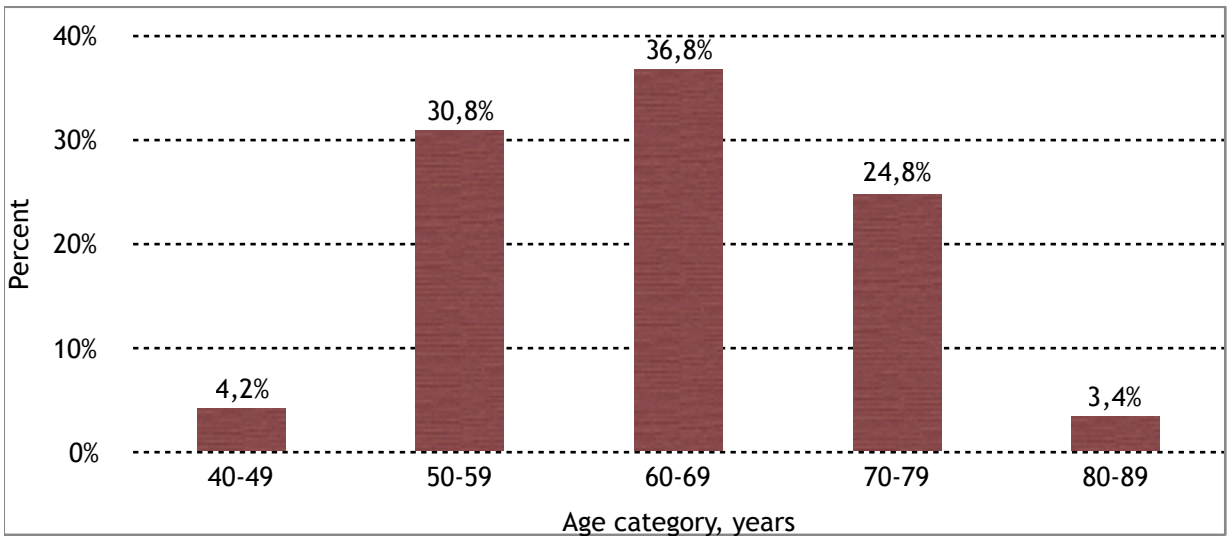

Figure 3.3: A bar graph showing the age category distribution for TKA performed in the study.

Of all the patients included in the study, 82.9% were female and 17.1% were male (see Figure 3.4). There was no association between gender and OPS, PJI or SSI. The gender ratios of patients with and without OPS did not differ significantly (p=0.688). The gender ratios of patients with and without post-operative PJI and SSI did not differ significantly (p=1.000 and p=0.687, respectively). With regard to race, 53.0% of the patients were Black African, 20.0% were Coloured, 19.0% were White and 8.0% were Indian (see Figure 3.5). Seventeen patients were an unknown race. There was a statistically significant overall association between race and OPS (p=0.025). The percentage of Coloured patients with OPS differed significantly from the percentage of patients without OPS (p=0.013). There was no significant overall association between PJI and race. The race distribution of patients with, and without PJI did not differ significantly (p=0.270).

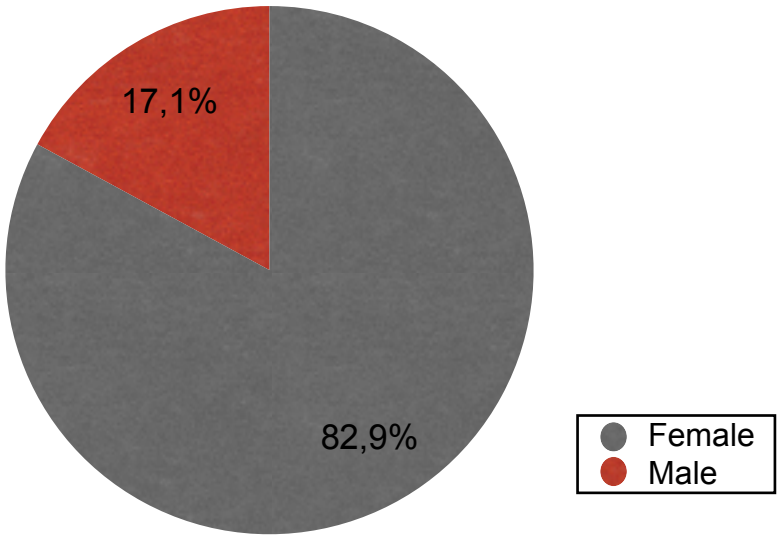

Figure 3.4: A pie chart showing the gender distribution of the patients included in the study.

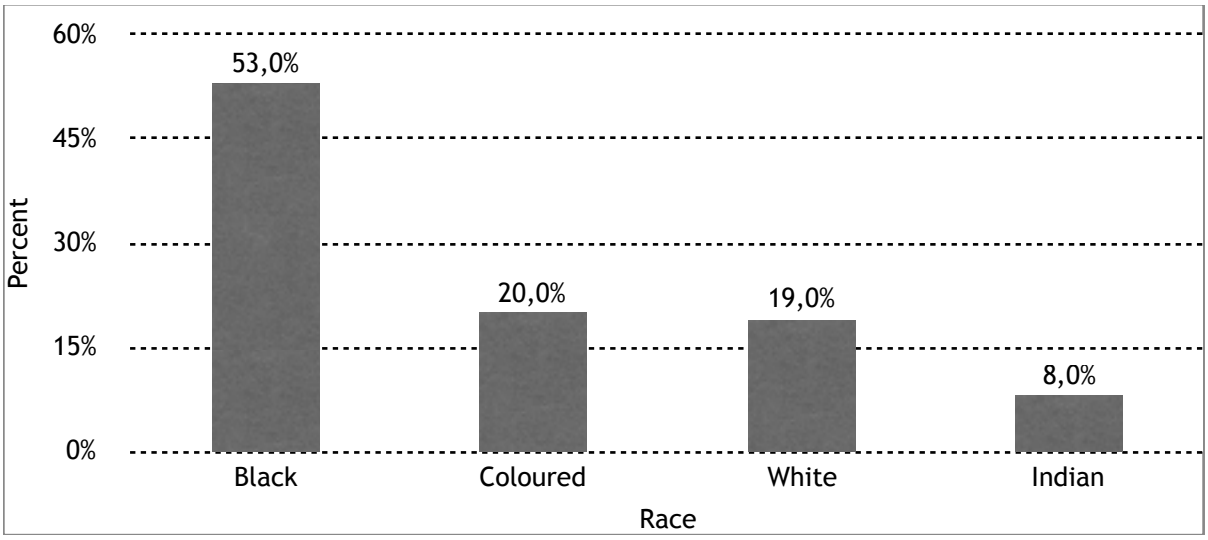

Figure 3.5: A bar graph showing the race category distribution of patients included in the study.

The underlying diagnosis of the pathology necessitating a TKR was recorded in 96 cases, 21 cases did not have a diagnosis recorded. Primary osteoarthritis (OA) was the underlying diagnosis in 58.3% of cases. Secondary OA was the underlying diagnosis in 10.5% of cases. In 28.1% of cases, OA was the underlying diagnosis,

however, differentiation was not made between primary or secondary subtypes (see Figure 3.6). Overall, OA was the underlying diagnosis in 96.9% of recorded cases. In the remaining 3.1% of the cases, the underlying diagnosis was an inflammatory arthritis. There was no statistically significant association between the underlying diagnosis and OPS. The underlying diagnosis distribution of patients with and without OPS did not differ significantly (p=1.000).

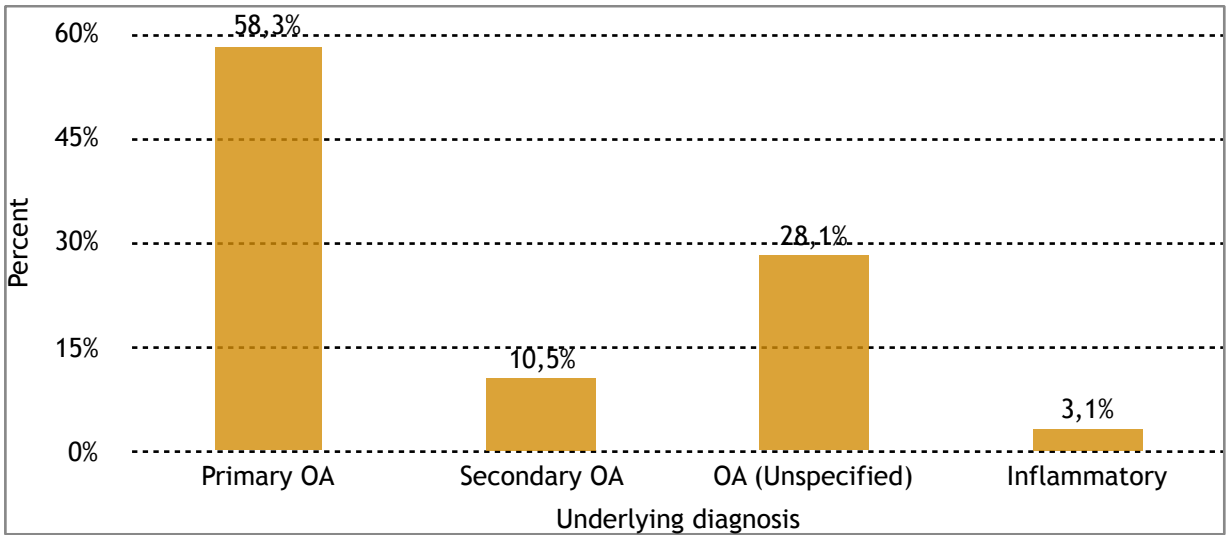

Figure 3.6: A bar graph showing the underlying diagnosis distribution of patients included in the study.

BMI was classified according the World Health Organisation's (WHO's) definition into six classes. No patients were underweight (BMI < 18.5), 20.0% of the patients were in the normal weight category (BMI 18.5 - 24.9), 22.4% of patients were in the pre-obesity category (BMI 25 - 29.9), 30.0% of patients were in the obesity class I category (BMI 30 - 34.5), 16.3% of patients were in the obesity class II category (BMI 35 - 39.9) and 11.3% of patients were in the obesity class III (BMI $\geq$ 40) (see Figure 3.7). Overall, 80.0% of patients were overweight and 57.6% of patients were classified as obese. There was no statistically significant association between any BMI class and OPS (p=0.844). There was a clinical trend apparent in that 75.0% of post-operative infections were diagnosed in a BMI overweight category, suggesting that there may be an association between being overweight and developing OPS, however this was not statistically significant (p=0.698). Likewise, there was no statistically significant relationship between all the BMI obese categories and OPS

(p=0.343). There was also no statistically significant association between any BMI category and post-operative PJI (p=0.0475), or post-operative SSI (p=0.867).

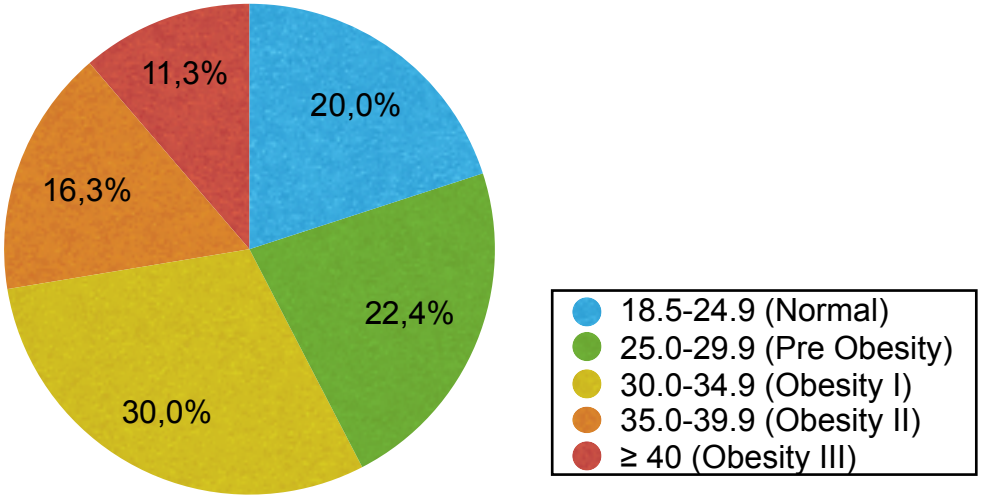

Figure 3.7: A pie chart showing the BMI category distribution of patients according to WHO's classification.

The mean OT was 106.4 minutes (n=63, mean [SD] = 106.4 [+/- 29.0] minutes) and the median OT was 105.0 minutes (n=63, median [IQR] = 105.0 [85.0-125.0] minutes). The shortest OT was 55.0 minutes and the longest OT was 175.0 minutes. Only 4.8% of the cases were completed within one hour. Overall, 65.1% of the cases took between one and two hours to complete. Furthermore, 7.9% of the cases took more than two hours and 30 minutes to complete (see Figure 3.8). There was a statistically significant association between OT and OPS. The OT category of patients with OPS differed significantly from those without OPS (p=0.040). Of the patients with recorded OTs, 80.0% of the infections occurred in operations with OTs between 120.0 and 150.0 minutes. When comparing OT taking more or less than two hours, there was a statistically significant difference between patients with and without OPS (p=0.026). However, the median OT of patients with and without OPS did not differ significantly (p=0.150). There was no statistically significant association between OT and PJI or SSI. The OT categories did not differ significantly in patients with and without PJI (p=0.349) or SSI (p=0.139). There was no statistically significant association with BMI overweight or BMI obese statuses and OT. OTs of more or less

than two hours did not differ significantly in patients with a normal BMI or overweight BMI statuses (p=0.740). Likewise, an OT of more or less than two hours did not differ significantly in patients with a non-obese BMI or an obese BMI status (p=0.763).

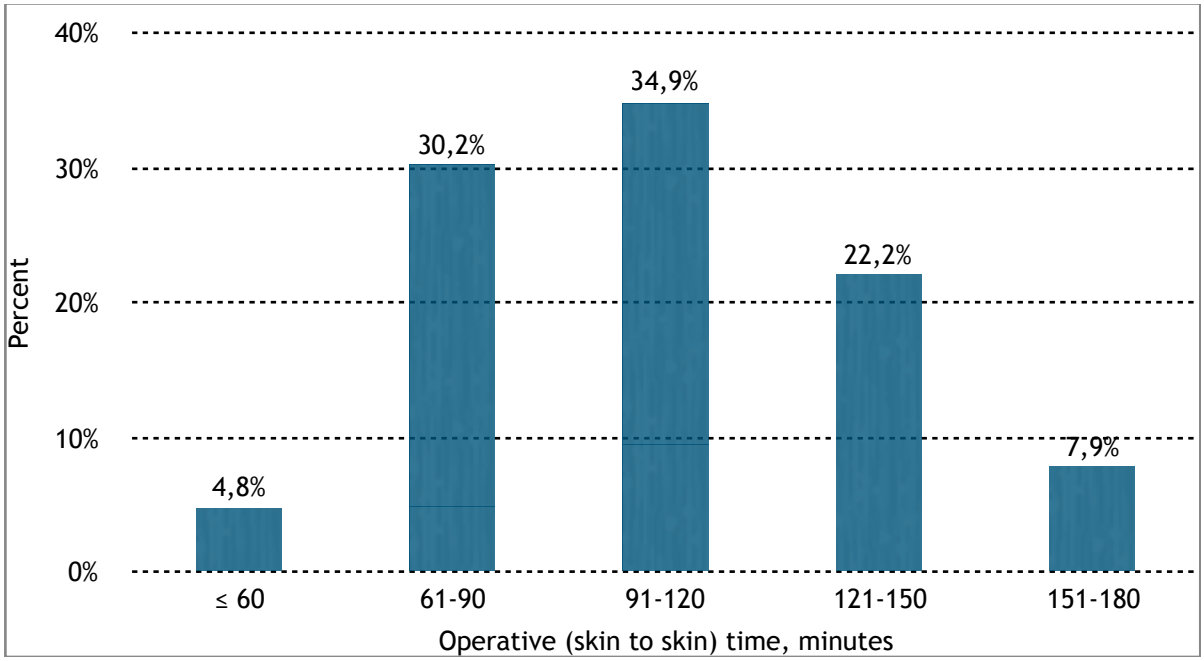

Figure 3.8: A bar graph showing the operating (skin to skin) time category frequency distribution of TKA performed in the study.

Sixty percent (60.0%) of the population had no identifiable comorbid diseases that were risk factors for PJI (see Figure 3.9). The most prevalent identifiable risk factor for PJI was diabetes mellitus which was present in 20.0% of the population. Of the 19 diabetic patients, 13 had pre-operative HbA1c levels recorded within two months of their operation. The mean HbA1c level was 7.6% (n=13, mean [SD] = 7.6 [+/- 2.2]%) and the median HbA1c level was 7.1% (n=13, median [IQR] = 7.1 [6.3-8.3]%). The lowest HbA1c level was 5.2% and the highest level was 12.8%. Seven of the 13 patients (53.8%) had a HbA1c level above 7.0%, and three of the 13 patients (15.4%) had a HbA1c level more than 9.0% (see Figure 3.10). The second most prevalent identifiable risk factor for PJI was venous insufficiency which was present in 5.3% of the population. The third most prevalent identifiable risk factors for PJI were shared by: an HIV positive status (3.2%), rheumatoid arthritis (3.2%) and a history of cancer (3.2%). Only one HIV positive patient had a recorded pre-operative CD4 count (489 cells/mm^3) and viral load (< 50 copies/ml). Two of the three patients (66.7%)

diagnosed with rheumatoid arthritis were on corticosteroids and / or DMARDs at the time of their surgery whilst the remaining patient was not on anti-rheumatic drugs. Less prevalent risk factors were peripheral vascular disease (2.1%), chronic kidney disease (1.1%), previous septic arthritis (1.1%) and multiple previous knee surgeries (1.1%). There was no statistically significant association between comorbid disease and OPS. The comorbid disease distributions of patients with and without OPS did not differ significantly (p=0.740). Likewise, there was no statistically significant association between DMARDs use and OPS. The DMARDs use ratios of patients with and without OPS did not differ significantly (p=1.000).

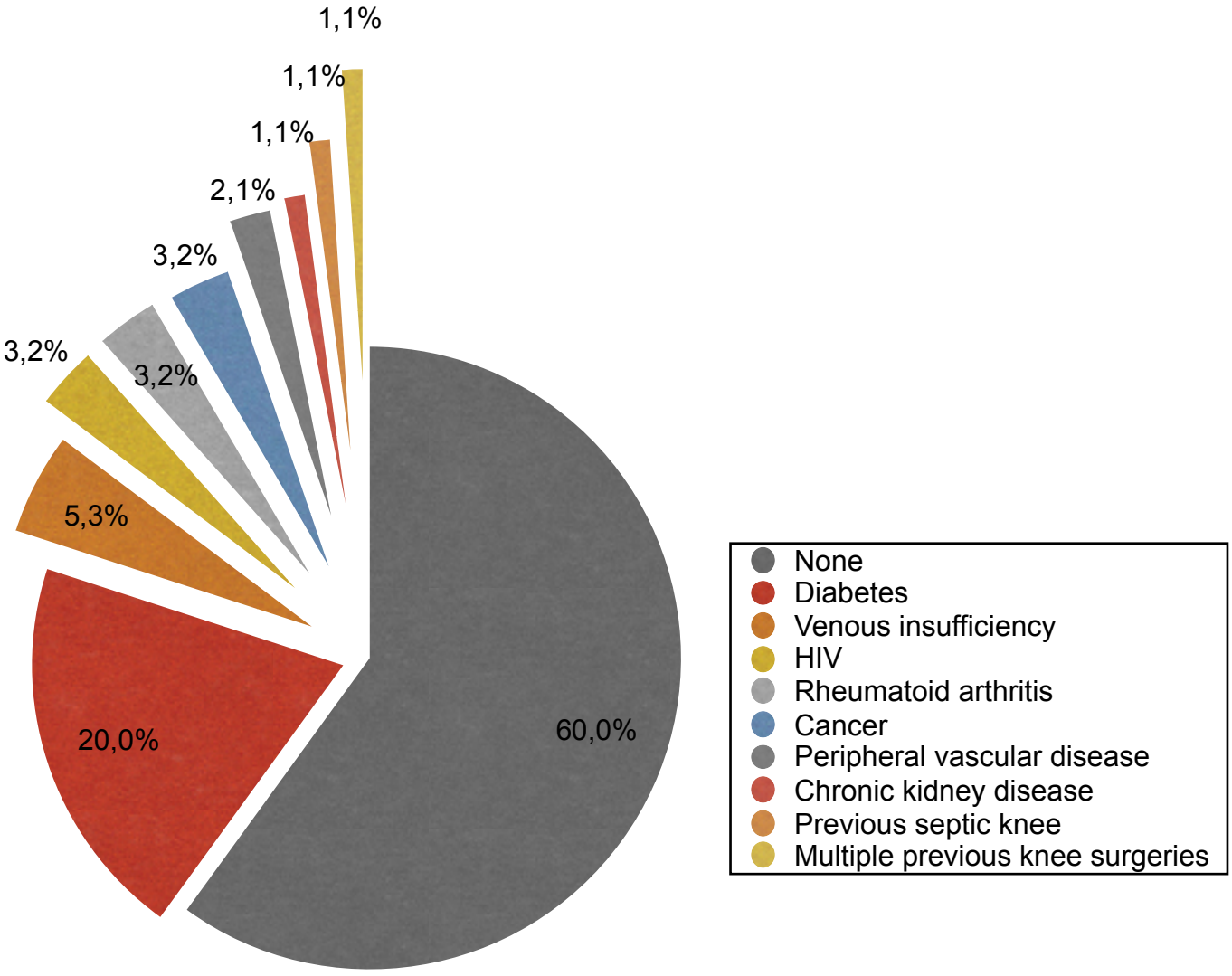

Figure 3. 9: A pie chart showing the comorbid risk factor distribution of patients who underwent TKR in the study.

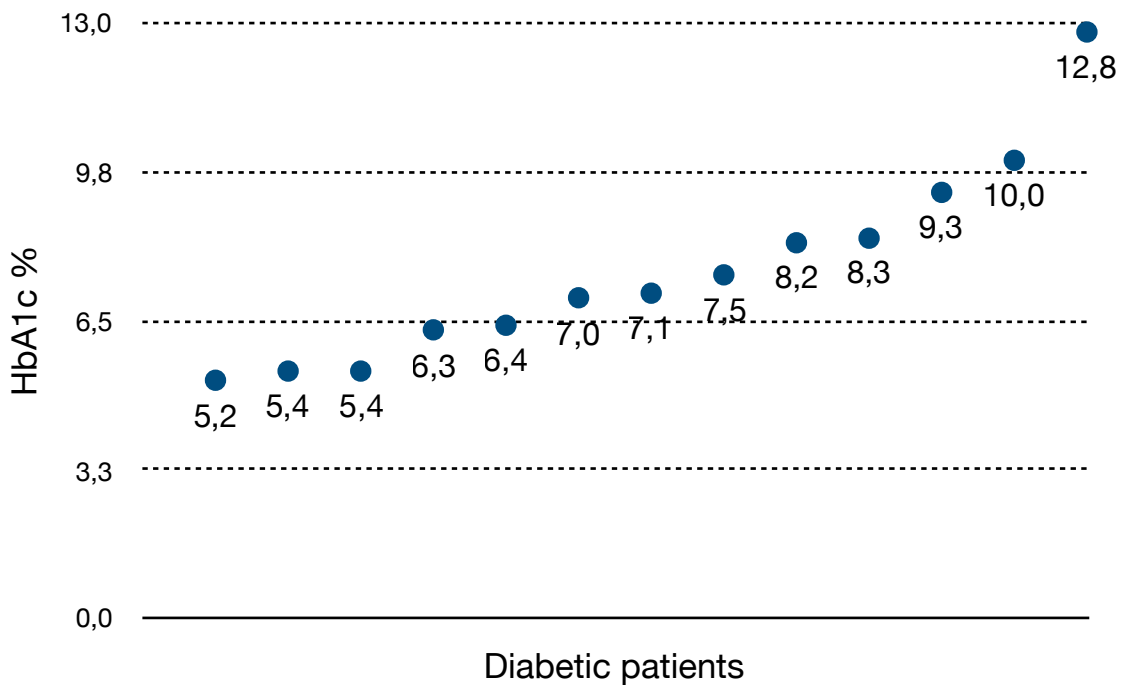

Figure 3.10: A scatter plot showing the HbA1c % distribution of diabetic patients who underwent TKR in the study.

Smoking status, either current or within the last one month pre-operatively, was known in 93 of the 117 patients (79.5%). Of these patients, 5.4% had a smoking positive status and 94.6% were non-smokers. There was no statistically significant association between smoking status and OPS. The smoking status ratios of patients with and without OPS did not differ significantly (p=1.000).

Of the 117 TKRs performed, a total of 12 patients complicated with OPS of musculoskeletal origin related to the procedure, within the defined timeframe for the study. The OPS incidence rate was 10.25%. Of the 12 septic cases, one fulfilled the criteria for the definition for a PJI. The PJI incidence rate was calculated to be 0.85%. The remaining 11 cases were classified as SSI. The post-operative SSI incidence rate was 9.40%.

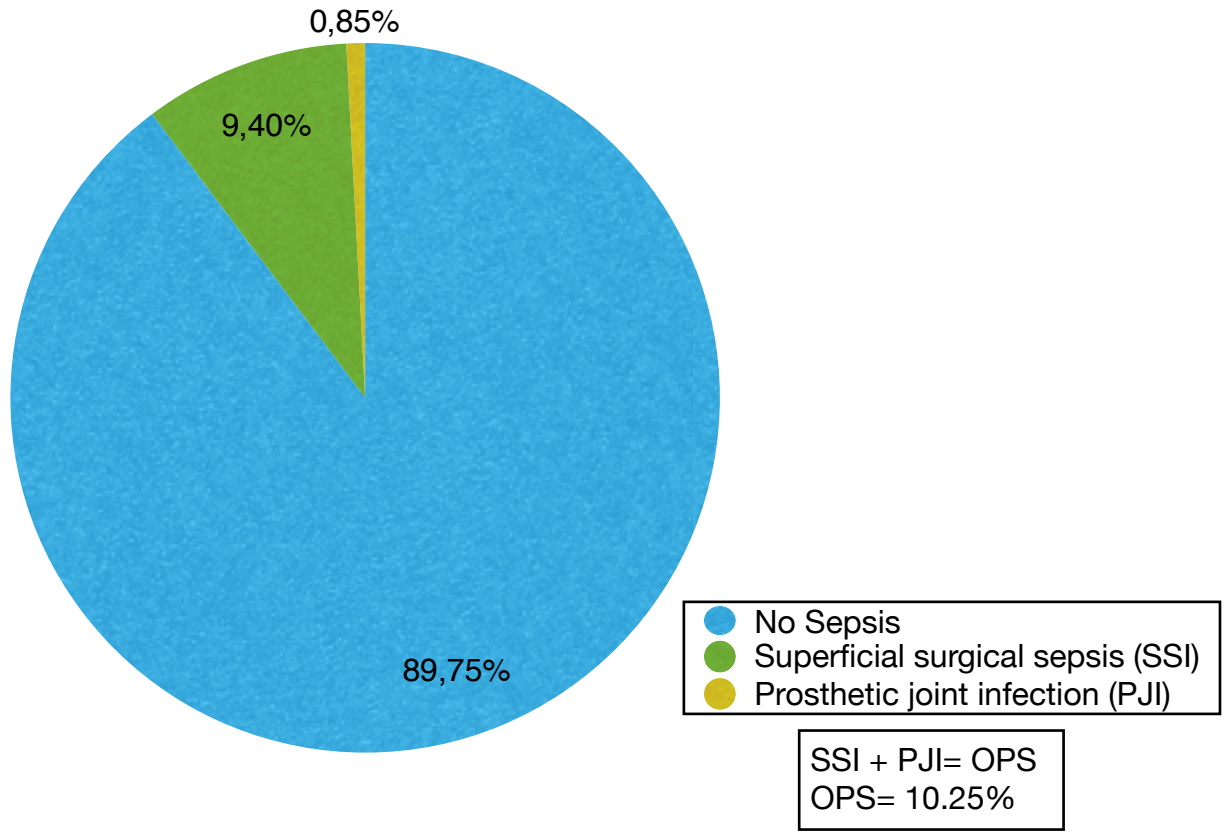

Figure 3.11: A pie chart summarising the post-operative septic outcome measures following TKR performed in the study.

Prosthetic joint infection cases:

Of the 117 TKAs performed, six patients were suspected of having a PJI. One of these patients developed this suspicion 33 months post-operatively, which fell outside the time frame defined for the study. Despite the time frame, the patient never met the definition for PJI, however the workup was still ongoing at the time of completion of data collection including a pending radionuclide scan. Of the remaining five patients, only one fulfilled the criteria for the definition of PJI, while the other three were classified as SSI.

The patient who fulfilled the criteria for the diagnosis of a PJI was a 76 year old Caucasian female. She had secondary (post-traumatic) OA of her left knee and was on the waiting list for TKA for 21 months. She had a history of previous breast cancer and was in remission and was not on any chemotherapy or radiation therapy at the time of her operation. She was a non-smoker and had a normal BMI according to the WHO classification. She had no other risk factors for PJI. She received a TKR in

August 2017 and the OT for her operation was 135 minutes. She presented five weeks post-operatively with a draining sinus communicating with her knee joint. Two initial pus specimens were sent off after her first debridement, and both cultured *Citerobacter braakii* and S*taphylococcus epidermidis,* both of which were sensitive to Cefepime. She met both major criteria according to the revised 2018 MSIS criteria and therefore fulfilled the definition of PJI. She was classified as an early onset PJI as her infection arose within three months post-operatively. According to the Tsukayama classification, she had a type IV (late chronic) infection as she presented more than one month post-operatively. She was planned for a two stage revision arthroplasty. She underwent her first stage prosthesis removal, debridement, and cement spacer, six weeks after her initial TKR, and was placed on a six week course of antibiotics. Subsequent to this, her wound broke down and she required a debridement one month after her first stage revision. At this stage her cultures from the wound grew a *Klebsiella pneumonia* sensitive to Ertapanem. Despite multiple re-debridements, replacement of the cement spacer and parenteral antibiotics, the infection never resolved and she eventually developed a carbapanem resistant *Klebsiella Pneumonia* infection. The second stage of the revision attempt was abandoned and she ultimately underwent a radical debridement, a knee fusion with an intra-medullary device, and also required soft tissue coverage with a gastrocnemius flap. These measures controlled her infection and resolved her PJI.

One other patient in the cohort developed a PJI that fulfilled the 2018 MSIS definition within the follow-up time frame, however the infection occurred in a knee that was not performed within the defined ‘move and walk’ weeks. The patient was a 65 year old Caucasian male. He had primary OA of both his left and right knee and was on the waiting list for 21 months for his left TKR and 12 months for his right TKR. His left TKR was performed in a ‘move and walk’ week in August 2017 which fell within the defined time frame for this study, while his right TKR was performed in a ‘move and walk’ week in August 2018 which fell outside the defined time period for the study. He had a history of previous prostate cancer and was in remission and was not on any chemotherapy or radiation therapy at the time of his operation. He was a non-smoker and had a BMI classified as type two obesity according to the WHO classification. He had no other risk factors for PJI. The OT for his left TKR was 105 minutes and 80 minutes for his right TKR. His left TKR healed well with no evidence of infection. Two weeks after his right TKR, he presented with a painful right knee, and raised septic

markers (white cell count [WCC] = 13.07, C-reactive protein [CRP] = 393 and erythrocyte sedimentation rate [ESR] = 119). He was taken to theatre where pus was found in the joint, a debridement was performed and the polyethylene liner was changed. The pus was sent for microbiological analysis and three separate specimens grew an *Escherichia coli* sensitive to ciproflaxacin. He met one major criteria according to the revised 2018 MSIS criteria and therefore fulfilled the definition of PJI. He was classified as an early onset PJI as his infection arose within three months post-operatively. According to the Tsukayama classification, he had a type IIB (deep early post-operative infection) infection as he presented less than one month post-operatively. He was treated on parenteral antibiotics, however two weeks later the infection remained and he developed a sinus tract communicating with the knee joint. Repeat pus cultures grew the same *Escherichia coli* organism. At this stage he had progressed to a Tsukayama type IV (late chronic) infection and underwent a two stage revision which resolved his PJI. This case was not counted towards the sepsis rates for this cohort as the infection occurred in a TKR that was performed outside the defined time period.

Superficial surgical site infection cases:

Eleven cases developed SSI. Five presented with pus oozing from the wound and six presented with an erythematous wound. Of the five patients who presented with pus draining, three had a record of pus being sent for microscopy, culture and sensitivity. Two specimens failed to grow an organism and one case grew a *Staphylococcus aureus* which was sensitive to penicillin (see Table 3.1 below**)**. Eight of the 11 cases with SSI resolved on a course of either oral or intravenous antibiotics. One of the 11 cases absconded and was lost to follow-up. One of the 11 cases required a superficial debridement and resolved subsequently with oral antibiotics.

Table 3.1: A summary of cases complicated by post-operative SSI.

Case no.	Age and sex	Clinical presentation	Lab work up	Specimen sent for MCS?	Microscopy/ Culture/ Sensitivity	Management	Outcome
1	**64 F**	Pus oozing from surgical wound spontaneously one month post op	WCC= 7.85 CRP= 62	Yes	*Staphylococcus aureus* sensitive to penicillin	Debridement and intravenous antibiotics	Infection resolved
9	**72 F**	Pus oozing from surgical wound spontaneously one month post op	None	No	N/A	Oral antibiotics	Infection resolved
10	**82 M**	Spontaneously sloughy wound no pus present one month post op	WCC= 10.29 CRP= 272	No	N/A	Intravenous antibiotics and local wound management	Infection resolved
57	**59 F**	Pus oozing from knee wound after a traumatic event six months post op	WCC= 9.51 CRP= 109	No	N/A	Intravenous antibiotics	Patient absconded before debridement. Lost to follow up
58	**62 F**	Erythematous wound two months post op	WCC= 10.9 CRP= 20	No	N/A	Oral antibiotics	Infection resolved
65	**54 F**	Pus oozing from surgical wound spontaneously three months post op	WCC= 7.97 CRP= 58 ESR= 67	Yes	Negative	Debridement and intravenous antibiotics	Failed debridement, two stage revision. Failed to meet MSIS definition for PJI
73	**67 F**	Erythematous wound two weeks post op	CRP= 47 ESR= 62	No	N/A	Oral antibiotics	Infection resolved
74	**67 F**	Erythematous wound two weeks post op	WCC= 9.83 CRP= 31 ESR= 18	No	N/A	Intravenous antibiotics	Infection resolved
81	**72 F**	Erythematous wound two weeks post op	WCC= 6.34 CRP= 35	No	N/A	Oral antibiotics	Infection resolved

Case no.	Age and sex	Clinical presentation	Lab work up	Specimen sent for MCS?	Microscopy/ Culture/ Sensitivity	Management	Outcome
83	**72 F**	Erythematous wound one week post op	WCC= 9.64 CRP= 319 ESR= 96	No	N/A	Intravenous antibiotics	Infection resolved
118	**49 F**	Pus oozing from surgical wound spontaneously one month post op	WCC= 6.52 CRP= 10 ESR= 6	Yes	Negative	Intravenous antibiotics	Infection resolved

Key: F: Female, M: Male, WCC = White cell count, CRP = C-reactive protein, ESR = Erythrocyte sedimentation rate

One of the 11 cases diagnosed as SSI was a case that was highly suspicious for PJI but never fulfilled the criteria for the diagnosis of PJI. This patient was a 65 year old Coloured female. She had primary OA of her right knee and was on the waiting list for a TKR for 17 months. She was a non-smoker and had a BMI classified as pre-obesity according to the WHO classification. She had no other risk factors for PJI. She received a TKR in November 2016, the OT for her operation was not recorded. She presented two months post-operatively with a painful knee, no draining sinus, and raised septic markers (WCC = 7.97, CRP = 58, ESR = 67). No synovial fluid analysis was performed pre-operatively. She underwent a debridement and polyethylene exchange. Tissue and synovial fluid from this debridement was sent for microbiological analysis and failed to grow any microorganisms, however numerous neutrophils were observed (reported as greater than 25 per low power field). According to the revised 2018 MSIS criteria, the patient had neither major criteria for PJI present. She had a score of three pre-operatively, which classified her as ‘possibly infected’. Her neutrophil count measured on microscopy was measured on a low power field whilst a positive measurement according to the revised 2018 MSIS criteria is measured on a high power field. Her intra-operative score was zero, which gave her a total final score of three, which was insufficient to make a diagnosis of PJI. Subsequent to this, she developed a SSI, but never developed a draining sinus. Multiple samples sent for microscopy and culture failed to grow any microorganisms. The pain in her knee persisted and her septic markers remained elevated, but at no time did she meet the MSIS criteria for the diagnosis of a PJI. She ultimately underwent a two stage revision which resolved her symptoms.

4. Discussion

Unlike many first world countries, very little data exists in the literature on local South African and SSA joint arthroplasty statistics. Sweden was the first country to establish a national orthopaedic joint registry, and since then many first world countries have also developed joint registries (30, 31). Malawi is the only country in SSA aside from South Africa to have an established, dedicated national joint registry (30). The present study represents a population from a single hospital in South Africa of 117 TKAs. In 2019, Davies et al. performed a systematic review of total joint replacement outcomes in SSA, which included seven studies which focused on TKA (30). Of these seven studies, only two had a population size in excess of 100 patients (one study from Botswana was conducted on 193 TKAs, and the other study was conducted in Malawi on 153 TKAs) (30, 32, 33).

The present study showed a mean waiting period for TKA just shy of 20 months. The shortest waiting period in the study was five months. Although difficult to accurately determine and compare, the median waiting periods displayed in many European countries, Canada and Australia vary between one and four months (34). These figures are significantly lower than the median waiting period in this cohort of 18 months. In 2016, Lizaur-Utrilla et al. displayed that waiting times in excess of six months for TKA negatively influenced pre-operative anxiety and post-operative satisfaction (35). Only 1.6% of patients within this cohort received their TKA within six months of being placed on the waiting list. Local data from a public hospital in Cape Town has shown waiting times for TKA similar to that displayed in this cohort (27). Patients waited on average 461 days (15.4 months) for TKA procedures at this Cape Town institution, but concern was raised as to how accurate this figure was (27). Likely explanations for the discrepancy in waiting times between these South African and international populations are: the large burden of trauma and infective cases that consume the majority of orthopaedic surgical time, and the resulting relative lack of elective theatre time in South African State hospitals (27). HJH instituted these ‘catch up arthroplasty’ ‘move and walk’ weeks in 2015 to help curb this demand. As a result, the waiting time in subsequent years is likely to decrease as the backlog is cleared. Statistical analysis revealed a significant association between waiting period and

OPS, and patients who developed OPS waited on average three months longer than patients who did not complicate with a septic outcome measure. The reason for this association may be related to the negative impact that waiting an excessive amount of time for elective TKA may have on one's psychology. Depression is a well known patient related risk factor for the development of post-operative SSI and PJI, and depression has a direct effect on the immune system which can predispose to infection (36, 37).

The present study showed a slight predominance of left TKAs performed (50.4% left TKA, 49.6% right TKA). This is in contrast to national figures which show a slight predominance for right TKAs (53.7% right TKA, 46.3% left TKA) and the global predominance of OA on the right knee compared to the left (38, 39). The slight left sided predominance in this study is likely a result of the relatively smaller population size, however it is evident that across the board the ratio of left to right TKA approximates 1:1.

The age distribution in the present study was normally distributed between the ages of 45 and 84 years and had a mean age of 64.4 years, and is comparable to local data from South Africa and SSA. Although no mean is reported, statistics from the South African National Joint Registry have shown that the majority of primary TKA cases are performed on patients in the 55-64 year old (30.0%) and the 65-74 year old (38.0%) age groups (38). The age distribution for primary TKA throughout SSA is similar with the mean population ages ranging from 62.6 to 67.3 years of age (30, 32, 33).

In a systematic review published in 2019, only one study out of seven looking at the demographics of TKA in SSA displayed a mean age outside this range at 59.3 years, however this study comprised a population of only eight TKAs performed on seven patients and was an outlier in terms of population size (30). The mean age of primary knee arthroplasty in populations throughout New Zealand, Europe and North America however are on average higher than those found in the present population and populations in SSA. The mean age in New Zealand is 68.0 years, in the United States of America it is 67.0 years, in Austria it is 69.5 years and in Sweden it is 68.9 years (31, 40-42). However, there is evidence that the mean age for TKA in many of

these regions is decreasing (43, 44). The reason for this discrepancy in SSA is not apparent.

In the present study, there was no significant association between age and OPS. International literature remains controversial with regard to the influence of age on PJI incidence rates after TKA. Some studies have demonstrated that older age is associated with post-operative SSI and PJI following TKA, and have attributed this to the fact that with advancing age there is a greater proportion of comorbidity burden, malnutrition and immune compromise (45). On the contrary, other studies have shown an association between younger age and post-operative SSI and PJI following TKA, and have attributed this to the higher proportion of patients in these younger age groups with inflammatory diseases and higher activity levels than older patients (46, 47).

In 2019, Inoue et al. performed a retrospective review from a single institution of 23 966 patients undergoing TKA and THA, and found that age alone was not an independent risk factor for the development of post-operative PJI (48). Patients in three different age groups were matched for confounding variables (sex, BMI, operation time, smoking, drug/alcohol abuse, AIDS etc.) and followed up for one year post-operatively (48). The results showed that there was a statistically significant difference in the incidence of major comorbidities / risk factors between the different age groups, but when adjusted for the variables, multivariate analysis showed no difference in the rates of PJI between the different age groups (48).

The gender distribution in the present study shows that more TKAs were performed on females, which is in keeping with national, and international populations, however the proportion to which females predominate is different. There is a well established body of knowledge in the literature which recognises that females are more affected with OA of the knee than males, particularly in the patellofemoral joint (49). This has been attributed to knee anatomic, kinematic and hormonal differences in males and females (49). The national South African primary TKA data show that 60.7% of the procedures were performed on females (males 39.3%), unlike the rate in this cohort which displayed that 82.9% of cases were performed on females (males 17.1%) (38). Lisenda et al. in 2016 displayed a female predominance for primary TKA of 62.0%

(males 38.0%) in a Botswana population which approximates South Africa's national figures (32). Likewise, the United States of America also shows a female predominance for primary TKA procedures in line with South African and Botswana figures of approximately 61.0% (40). Only Graham et al. in 2018 demonstrated a female predominance of 77.0% of primary TKA procedures (males 23.0%) in a ten year observational study in Malawi which approximated the very high female rate in the current study (33). In contrast to these figures, New Zealand performed almost as many male (48.5%) as female (51.5%) primary TKAs (41). In summary, the vast majority of populations display a male to female ratio of approximately 2:3, in New Zealand the ratio is approximately 1:1, and in the present population the ratio is 1:4. The reason for these international differences and the difference in the present population is not evident. Although female gender accounts for the majority of TKA procedures in the literature, there is a vast body of literature which demonstrates that male gender is an independent risk factor for developing both post-operative SSI as well as PJI (15, 47, 50-52). This was not the case in the present study as the gender ratios of patients with and without OPS, PJI and SSI did not differ significantly.

The present study showed a racial distribution that is similar to that of the national population in terms of overall racial category, however the overall percentages differed considerably (53). Nationally, the Black African population group is the most populous at 80.7%, followed by the Coloured population group at 8.8%, then the White population group at 7.9%, and the Indian/Asian population group is the least populous at 2.6% (53). The racial distribution in the present study showed that TKA was most frequently performed on Black patients (53.0%), followed by Coloured patients (20.0%), then White patients (19.0%), and lastly Indian patients (8.0%). Although Black patients were the most commonly operated race in the present study, the proportion in relation to other races was far less than what the national population represents. This may be attributed to the local community demographics of the areas that HJH serves, or cultural differences in disease pattern and health seeking behaviour. The South African National Joint Registry, like many other registries except the American Joint Replacement Registry, does not record racial demographics (31, 38, 40, 41). International literature has displayed that there are racial ethnic differences in OA severity (54). To the primary investigator's knowledge, there is no local data to support these differences apparent in the present study. The Coloured race in the present study had a significant association with OPS, although

this association should be interpreted with caution due to the low population size. The likelihood that race alone was independently associated with any septic outcome is low. A more likely scenario may be that the population group in the study had another underlying non-apparent variable which may predispose to infection. However, in 2013 Poultsides et el. in a cross sectional chart review of 784 335 files of an American healthcare database, demonstrated that race was an independent risk factor for post-operative SSI (47).

In the present study, OA was the underlying diagnosis in 96.9% of cases, and in the remaining 3.1% of cases, the underlying diagnosis was an inflammatory arthritis. This is representative of the spectrum of pathology that leads to TKA nationally and internationally (32, 33). Nationally, just like the present study, OA is the underlying diagnosis in the vast majority of TKA cases (95.4%) with inflammatory arthritis being the next most common diagnosis (3.4%) (38). Other underlying diagnoses of TKA cases performed nationally include fractures, avascular necrosis and tumor / sepsis which were not present in the present population, but all these diagnoses each comprised less than 1% of cases nationally (38). In 2009, an analysis of 43 148 primary and revision knee arthroplasties was performed from the Finnish Arthroplasty registry, and found that post-traumatic OA, unspecified OA and seropositive rheumatoid arthritis underlying diagnoses were associated with an increased risk of re-operations for the treatment of infection when compared to the underlying diagnosis of primary OA (50). There is a large body of literature which recognises the association between inflammatory arthritis (particularly poorly controlled and seropositive cases) and post-operative SSI and PJI (36, 37, 50, 55). The present study did not show an association between any underlying diagnosis and OPS, PJI or SSI.

The BMI distribution of TKA operated patients in the present study was similar to the BMI distribution nationally and internationally, however the proportion of patients in a normal weight BMI and obesity class III BMI categories was slightly higher in the present study. Many of the individually recorded BMIs in the present study were recorded in the clinical notes as a WHO BMI category which made the calculation of a mean impossible. Comparisons to international populations were difficult to make as not all the registries record population BMI statistics and those that did record

BMI, recorded it as an average (31, 40, 41). However, one study conducted in Glasgow Scotland in 2018 was conducted to seek a relationship between SSI and BMI, and described their population's BMI distribution as BMI categories (52). Twenty percent (20.0%) of TKAs performed in the present study were on patients with a normal BMI, compared to 11.0% nationally and 9.8% in the Glasgow study (38, 52). In the present study, 57.5% of TKAs performed were on patients with any obese BMI category, compared to 59.0% nationally and 58.3% in the Glasgow study (38, 52). The proportion of TKAs performed on BMI obese class III patients in the present study is higher than that nationally and in the Glascow study. In the present study, 11.3% of TKAs were performed on patients with a BMI obese class III category, compared to 8.7% in the Glascow study (52). Nationally, South Africa performed 8.0% of TKAs on patients with a BMI > 42 (38). This demonstrates that the population selected for these 'catch up arthroplasty' 'move and walk' weeks was not biased towards low risk BMI classes and is generally representative of national and international populations. BMI class III obesity has been shown in many studies to be a risk factor for SSI and PJI following TKA (15, 16, 52). One of the reasons for the increased incidence of post-operative sepsis in patients with a BMI in the class III obesity category is due to the relatively longer operating time taken for TKA in these very obese patients (8, 12). Unlike the Glascow study and other international papers, there was no association between any BMI category and post-operative SSI or PJI in the present study (15, 16, 52). Likewise, no association was demonstrated between higher BMI categories and OT in the present study. However, this association should be interpreted with caution due to the relatively low incidence of infections overall in the present study and because operations were performed by a number of different surgeons.

In the present study, the mean OT was 106.4 minutes (median = 105.0 minutes) and the majority of procedures took between 90.0 and 120.0 minutes. There was a statistically significant association between OTs that took in excess of 120.0 minutes and OPS, but not PJI or SSI. These results should be interpreted with caution due to the proportion of missing data and low sample size. OT is a statistic that is not routinely reported on in national joint registry data. The South African National Joint Registry does not record these OT statistics, and to the primary investigator's knowledge, no local statistics exist for comparison. The New Zealand Joint Registry in their 2018 annual report demonstrated a mean OT of 83.0 minutes for knee

arthroplasty procedures (41). This is significantly shorter than that reported in the present study, however the mean in New Zealand was not only calculated on conventional total knee arthroplasty cases alone, making the comparison difficult to interpret (41). In 2008, Ong et al. performed a retrospective chart review of two and half million medicare beneficiaries in the USA and demonstrated a median procedure time of 138.0 minutes for TKA procedures (56). Again, making a comparison was difficult with the present study as the procedure duration in the USA study included anaesthetic time and was not limited to cutting (skin to skin) time, however their findings revealed an association with longer procedure times and higher revision rates (56). In 2019, Anis et al. preformed an institutional review of 11 840 TKAs performed in Cleveland, USA and demonstrated a mean OT of 105.0 minutes (median=102) very similar to that found in the present study (57). Like in the present study, they also revealed that SSI rates were significantly higher in TKA with OTs in excess of 121.0 minutes (57). Additionally, PJI rates were also significantly higher in TKA with OTs in excess of 121.0 minutes, unlike the present study (57). In 2019, Ravi et al. performed a similar study in Ontario, Canada on 17 815 TKAs, and revealed that the median surgical duration was 106.0 minutes (58). In this study, surgical durations in excess of 100.0 minutes had a significantly higher rate of deep infection within one year following TKA, but did not look at SSI rates (58).

In the present study, there was no significant association between any comorbid diseases and OPS, PJI or SSI. Globally, the prevalence of many comorbid diseases varies between geographic regions so direct comparisons to different arthroplasty populations are difficult. There is a paucity of local data on the matter, and the South African National Joint Registry does not record data with regards to underlying diagnoses (38). The literature consistently supports the association between certain medical conditions namely: diabetes, rheumatologic disease and post-operative SSI and PJI (37, 45, 47, 50). Although no significant association has been demonstrated between a pre-operative HbA1c level and post-operative PJI, an HbA1c < 7.0% is considered well controlled and the recommendation for a safe pre-operative HbA1c is less than 8.0-9.0% prior to arthroplasty procedures (14). In the present study, more than half of the recorded HbA1c levels were above the 7.0% mark signifying well controlled disease, and 15.4% of diabetic patients had a HbA1c level above 9.0%. This suggests that the selected population is not biased in terms of diabetic control for patients at low risk of post-operative infection. Many other medical comorbidities

have been reported as risk factors for post-operative surgical site infections following TKA, with varying consistency in the literature but of relation to the present study are a HIV positive status, and a history of cancer. Although neither of these comorbidities had any significant association with post-operative SSI or PJI, both patients who met the revised 2018 MSIS criteria for PJI in the study had a history of prior malignancies. One of these was a male patient with previous prostate cancer who developed a PJI in a knee that was not operated on during the time defined for inclusion in the study. The other patient was a female with previous breast cancer and was the only case who met the inclusion criteria within the defined time period for the study. International literature has found an association between a history of cancer and the development of post-operative PJI and SSI following TKA (47). In the present study, only 3.2% of the population was HIV positive. No local data is available for comparison, however in 2018, Graham et al. performed a review of the short term outcomes of patients who underwent TKA on the Malawi National Joint Registry and found that 5.9% of patients were HIV positive (33). South Africa has a large burden of HIV positive patients with a current estimate of approximately 13.1% of the population living with the disease (53). The 3.2% prevalence of HIV positive patients in the present study is not representative of the national HIV burden, however little is still known about the demographics of OA in the local HIV population, and the effect that HIV and antiretroviral drugs have on OA of the knee (59).

In the present study, only 5.3% of patients had a current positive smoking status and there was no statistically significant association between smoking status and post-operative SSI or PJI. Currently in South Africa, approximately 17.6% of adults smoke tobacco, however four times more males than females smoke, more middle aged and young patients than older patients smoke, and the percentage of smokers in Gauteng province was the least of the provinces (60). Additionally, the Black African population group had the second lowest percentage of smokers (60). The majority of patients in the present study were of female gender, Black African population group, elderly and lived in Gauteng, so the 5.3% of smokers may be representative of the national demographic for these population characteristics. However, it cannot be excluded that there may have been a slight selection bias towards a smoking negative status in this population. International studies have demonstrated that there is a statistically significant association between a current smoking positive status and post-operative SSI and PJI (37, 51, 61). This was not the case in the present study, however, the

result should be interpreted with caution due to the relatively low incidence of post-operative infections and relatively low prevalence of smokers.

In the present study, the OPS incidence rate following TKR was 10.25%, with SSI making up the majority of cases (9.40%), and the early and delayed onset PJI rate was 0.85%. To the primary investigator's knowledge, no equivalent local data is published for direct comparison. In 2018, Campi et al. performed a study on 1 120 knee arthroplasties performed at a single institution in South Africa seeking their ten year survivorship rates (62). Only one patient in this study underwent a debridement for suspected infection one month post-operatively and they had no failures caused by infection, however all the procedures were uni-compartmental knee replacements (62). Uni-compartmental knee replacements was an exclusion criterion in the present study, and international literature has demonstrated lower overall complication rates (including post-operative SSI and PJI) in uni-compartmental knee replacements compared to TKA (63). In 2019, Davies et al. performed a systematic review on the outcomes of TKA performed in SSA and found a mean deep infection rate of 1.60% (range 1.70% - 2.60%) and SSI rates between 1.90% and 4.40% for TKA performed in Nigeria, Malawi, Botswana, Kenya, and Ghana (30). The limitation of the data from these studies is that their methodology and definition for the diagnosis of infection and follow-up periods were not defined and consistent therefore making it difficult to objectively compare to the present population (30, 32, 33, 64).

In 2017, Koh et al. performed a retrospective chart review of 11 134 TKAs performed in three tertiary hospitals in New Zealand, and found a risk for revision TKA due to PJI to be 2.00% (6). This study had many similarities to the present study and therefore was the most comparable study in terms of PJI incidence. Similar to the present study, they used the MSIS criteria as a definition for PJI cases, however they used the 2012 version (6). Like the present study, they excluded uni-compartmental knee replacements, however unlike the present study, they followed patients up for an average of five years (range one -16 years) (6). Their PJI rate was 2.00%, and in addition to early and delayed PJI cases, they also included late onset PJI cases. However, the authors did look at the PJI incidence per year and found that the greatest incidence, and the majority of cases, occurred within the first two years at a

rate of 1.00% which was comparable to the rate found in the present study (6). A SSI incidence was not described in their study.

In 2015, Crowe et al. performed a retrospective review of 3 836 TKAs performed at a single institution in New York, and found that 0.76% of primary TKAs were complicated by PJI (51). Unlike the present study, they used the Centres for Disease Control and Prevention's National Healthcare Safety Network criteria, and not the MSIS criteria as a definition for PJI cases (51). Unlike the present study, they followed patients up for one year (51). Therefore, their PJI incidence rate of 0.76% included only early and some delayed onset PJI cases. A SSI incidence rate was not described in their study.

Internationally, the vast majority of PJI incidence rates are derived from national joint registry data. There are many limitations on using national joint registry data for the determination of PJI incidence rates (6, 65). National joint registry data typically do not use defined criteria such as MSIS for PJI definition (6). These statistics, together with results from large retrospective multi-centre studies, often gather their data using operation codes (usually revision arthroplasty codes) from large databases (65). Many patients meeting defined MSIS criteria for PJI may be treated non-operatively (suppressive antibiotics) while others may be treated with debridement and retention of implants or arthrodesis. Such patients will be missed in studies of this nature and for these reasons, PJI rates may be underestimated, particularly in data derived from national joint registries (65). Despite these limitations, internationally the typical published PJI incidence rates following primary TKA vary between 0.32% and 1.93% (some of which are summarised in Table 4.1 below), similar to that displayed in the present study (65-68).

Table 4.1: A summary of some international publications describing PJI incidences, follow-up periods and relevant methodology (65-68).

Year (Author)	Country / Region	Study Population size	Follow up period	PJI incidence rate	Methodology
2009 (Jamsen et al.)	Finland	38 676	One year	0.52% at one year	Retrospective observational study from national joint registry data. Diagnosis of PJI based on ICD 10 coding and registry reported infections (no validated criteria)
2017 (Lenguerrand et al.)	England and Wales	679 010	One to ten years	0.32% at two years 0.75% at ten years	Retrospective observational study from national joint registry data. Diagnosis of PJI at the discretion of the treating surgeon (no validated criteria)
2018 (Wang et al.)	Taiwan	10 768	Two years	1.93% (2002-2006) 1.05% 2007-2010) and 0.76% (2011-2014)	Retrospective study from a single centre. PJI defined as an infection post TKR that required surgical intervention (arthrotomy and revision arthroplasty) (no validated criteria)
2018 (Kurtz et al.)	USA	2 528 579	One to five years	0.74% at one year 1.38% at five years	Retrospective review of Medicare database. PJI case defined as appropriate ICD 10 diagnostic code for PJI in the knee and accompanying revision TKA ICD 10 procedure code (no validated criteria)

The SSI incidence rate of 9.40% in the present study appears to be higher than that reported in the international literature (9, 47). In 2013, Poultsides et al. performed a retrospective review from a large in-patient database in the USA on 784 335 TKAs and found that only 0.31% of them developed pre-operative SSI (47). The only large limitation of this study was that the infections were identified using International Classification of Diseases (ICD) 9 diagnostic codes from inpatient data, which would have missed a large proportion of patients who were treated as out-patients (47). In the present study, 36.4% of patients who were diagnosed with a SSI were managed as an out-patient, and additionally not all SSIs were diagnosed in the immediate pre-operative period (27.3% of SSIs were diagnosed more than one month post-operatively). In 2018, Teo et al. prospectively followed up on 905 TKAs performed by a single surgeon from a single institution in Singapore and found an overall post-operative SSI incidence rate of only 1.10% (diagnosed within the first two weeks

post-operatively) (9). The population in this study however was significantly smaller and had a lower prevalence of many comorbidities compared to the present study (9). The above two studies display SSI rates after TKA that are very low, and in many instances lower than or equal to the incidence of PJI displayed in most of the articles reviewed in this research report.

The nature of the present study, being a retrospective cohort study, did present some limitations. Record keeping at government hospitals in South Africa is notoriously poor and in the present study resulted in missing data in some cases (69). However, the use of the electronic NHLS database did overlap in many instances of poor record keeping. Although one MSIS criterion for the diagnosis of PJI involves physical findings, all the patients with PJI being worked up for revision surgery require microbiological analysis of a specimen taken from their affected joint in order to correctly identify the offending pathogen. For this reason, it was felt that patients did not require an examination to determine whether there was any evidence of PJI. In cases where there was doubt about the origin of a suspected infection, patient files were scrutinised for clarity. Some of these limitations may have been circumvented if the study was designed as a prospective review where patients were physically examined on follow-up. However, a study of this nature would have been very demanding on time and resources which were outside the scope of this MMed research.

Possibly the greatest limitation with the present study was the overall population size and the limitation it had on seeking statistically significant relationships with the described variables. In comparison to much of the international data, this population is very small, but comparable to published populations from SSA (30). Unfortunately, the concept of the ‘move and walk’ week was only developed in 2015 at HJH and therefore a finite number of patients were available for analysis. As this was a new concept introduced at HJH, the follow-up time was limited to two years and as a consequence, only acute and delayed onset PJIs were sought for. Although the majority of PJIs generally occur within the first two years post-operatively, this may give a perception of a falsely low overall PJI rate of 0.85% in the present population, and comparisons could only relevantly be made to studies with a similar follow-up period.

There is risk for potential bias in the data with the selected population. The nature of these ‘catch up arthroplasty’ ‘move and walk’ weeks designed in South African State hospitals are to perform as many arthroplasties in one week as possible to decrease the long waiting times and lists. For this reason, a bias may be present that patients who are relatively “well”, and uncomplicated cases may have preferentially been selected for these weeks. However, through meticulous comparison of the patient demographics and variables in the present study and other national and international populations, it is clear that there are few differences, suggesting that a biased population was not selected. However, with this being said, the only way to know for certain if this was the case would have been to compare the population from these ‘move and walk’ weeks with a control group of patients performed on regular elective arthroplasty weeks at the same institution.

5. Conclusion

Waiting lists for elective total joint arthroplasties in South African State hospitals are some of the longest in the world, sometimes in excess of five years. As a result, HJH initiated elective lower limb ‘catch-up arthroplasty’ ‘move and walk’ weeks in an attempt to decrease these waiting times.

From this audit it was found that the average waiting time for total knee arthroplasty was 19.9 months. The average age of patients who underwent a TKA procedure was 64.4 years and the vast majority of these patients were female with a male to female ratio of 1:4. Age, gender, comorbid risk factors, underlying diagnosis and a positive smoking status were not associated with a post-operative surgical site infective outcome measure. The BMI distribution of patients who underwent TKA was similar to national and international populations however, unlike most international studies, the higher BMI categories were not associated with longer OTs or any post-operative surgical site infective outcome. The average OT was 106.4 minutes and was not associated with PJI, although an OT in excess of two hours was associated with OPS. Other variables in the present cohort which had a significant association with positive post-operative surgical site infective outcomes were the Coloured race and longer waiting times.

To the primary investigator's knowledge, this is the first study to objectively determine a PJI rate in SSA using validated (MSIS) criteria. Overall, the PJI incidence rate in this study was 0.85%, a rate which is lower than rates reported in SSA populations but is similar to international populations. The incidence of SSI was 9.40%, which unlike the PJI incidence, was higher than what has been reported in the international literature.

The paucity of data from South Africa and SSA on audits of this kind demonstrates that more studies of this nature are needed to understand the differences in demographics and epidemiology of total joint arthroplasty populations and how these differences translate into risks for post-operative surgical site infections in our region.

There is a need for more prospectively collected data, and data collected on larger populations to overcome some of the limitations present in this study.

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7. Appendices

Appendix A: Human Research Ethics Committee (Medical) clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Warren Meier

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M181101

NAME: (Principal Investigator)	Dr Warren Meier
DEPARTMENT:	Orthopaedics Helen Joseph Hospital
PROJECT TITLE:	Prosthetic Joint infection after Total Knee Arthroplasty - an audit from 'catch up arthroplasty' weeks at Helen Joseph Hospital
DATE CONSIDERED:	30/11/2018 (Conditional approval: 07/02/2019)
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof A. Aden and Dr L. Jacobs
APPROVED BY:	C B Penny Dr C B Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	01/04/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 19/02/2019.

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix B: Permission from HJH Ethics and Research Committee

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health
Helen Joseph Hospital
Enquiries: Dr. F.G Benson
Acting Chief Executive Officer
Tel :(011) 489-0306/1087
Fax :(011) 726-5425
E mail:Frew.Benson@gauteng.gov.za
Date: 14 March 2019

Dr. F.G. Benson
Acting Chief Executive Officer
Helen Joseph Hospital

Dear Dr. F. G. Benson

STUDY: Prosthetic joint infection after total knee Arthroplasty an audit form catch up arthroplasty week at Helen Joseph Hospital.

RESEARCHERS: Dr Warren Meier

Ethics: M181101

Above the study was discussed at the Research Committee meeting. We recommend that permission be granted for Helen Joseph Hospital to be used as a site for the above research, However , since this is individual /Patients.

Upon completion of the study, copy thereof should be submitted to Helen Joseph Hospital. It is duty of the researcher to collect the data to the relevant department after the Research Committee approved the study.

Thank you

Dr. Murimisi Mukansi
CHAIRPERSON
DATE:

Approved

Dr. F.G.Benson
Acting CHIEF EXECUTIVE OFFICER
DATE: 2019/3/25

Appendix C: Permission from HJH lab and blood services coordinator (page 1 of 2)

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

HELEN JOSEPH HOSPITAL

Enquiries:
Dr S Gaelejwue
Office of the clinical director
Email: gaelejwue@gauteng.gov.za

Dr Warren Meier
Unit 25, Terraces on 12th
No 122, 12th avenue
Rivonia
2191

29 October 2018

To the Helen Joseph Hospital Lab and blood services coordinator and clinical manager
HJH
1 Perth Road
Aukland Park
Johannesburg
Gauteng
2092

Re: Application to conduct research and access blood and microbiology results from NHLS

I am a registrar in the department of orthopaedics. I am requesting permission to conduct a retrospective review of all elective total knee arthroplaty patients performed at Helen Joseph Hospital during catch up 'move and walk' weeks between 01 October 2015 and 31 August 2017. I am looking for evidence on post operative prosthetic joint infection. I request permission from the NHLS to access biochemical, histological and microbiological results from patients operated on during these weeks. This research will form the basis for my MMed outlined below.

Introduction:

Total Knee Arthroplasty (TKA) is an effective means of eliminating pain and improving functional outcomes in patients requiring the procedure. The longevity and durability of these prostheses are ever improving, however the components do eventually fail. The two most common reasons for failure, and consequently revision TKA, are infection and aseptic loosening.

South African State hospitals have demonstrated very long waiting lists for Total Hip Arthroplasty (THA) and TKA, sometimes in excess of five years. In an effort to attempt to curb this demand, and decrease waiting times, a number of Johannesburg State hospitals including Helen Joseph Hospital (HJH), have initiated 'catch up arthroplasty' weeks.

Globally there has been an increasing trend to publish statistical data on lower limb arthroplasty cases in order to improve patient outcomes. For these reasons it is important to understand the South African population demographics of total joint arthroplasty patients managed at an institution and it is prudent to include prosthetic joint infection (PJI) rates when describing these audit statistics.

Aim:

To determine the rate of early and delayed onset prosthetic joint infection in patients undergoing total knee replacements during 'catch up arthroplasty' weeks at HJH between 01 October 2015 and 31 August 2017.

Appendix C: Permission from HJH lab and blood services coordinator (page 2 of 2)

Objectives:

1. To describe the characteristics of patients who underwent TKA during 'catch up arthroplasty' weeks at HJH.
2. To describe how prosthetic joint infections after TKA from 'catch up arthroplasty' weeks are diagnosed and managed at HJH.
3. To classify patients with prosthetic joint infection after TKA from 'catch up arthroplasty' weeks at HJH according to Tsukayama et al.
4. To compare the PJI rate after TKA during 'catch up arthroplasty' weeks at HJH with national and international populations.

Methodology:

This will be a retrospective cohort study of approximately 120 patients who were operated on during elective catch up arthroplasty "Move and Walk" weeks at HJH from 01 October 2015 to 31 August 2017. Biochemical, histological and microbiological results of patients will be retrieved via the NHLS database. All the evidence of PJI according to the Musculoskeletal Infection Society (MSIS) criteria (physical examination and biochemical, histological, and microbiological results) will be recorded. The data obtained from this study will be analysed using appropriate statistical tests together with the assistance of a biostatistician.

Ethical and financial considerations:

This study shall not cause harm to the research participants. Research numbers shall be assigned to each patient in order to maintain anonymity and all patient identifiers shall be excluded from the report to maintain confidentiality. The research will be entirely self funded and no additional cost shall be incurred by the Hospital/ NHLS.

I would greatly appreciate if permission would be granted for me to proceed with the study.

Sincerely

Dr Warren Meier

I hereby grant permission to Dr Meier to proceed with the above mentioned study.

(Yes) / No

(please circle relevant option)

Signed:



Name and rank/ position

HJH Laboratory & Blood Services Coordinator

Appendix D: Permission from NHLS national data warehouse manager

NATIONAL HEALTH LABORATORY SERVICE

Academic Affairs and Research
Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 386 6142
Fax: +27 (0)11 386 6296
Email: babatyi.kgokong@nhls.ac.za
Web: www.nhls.ac.za

22 March 2019

Applicant: Dr Warren Meier
Institution: University of the Witwatersrand
Department: Orthopaedics
Email: meier@vodamail.co.za
Cell: 072 279 4706

Re: Approval to access National Health Laboratory Service (NHLS) Data

Your application to undertake a research project "**Prosthetic joint infection after total knee arthroplasty-an audit from 'catch up arthroplasty' weeks at Helen Joseph Hospital**" using data from the NHLS database has been reviewed. This letter serves to advise that the application has been approved and the required data will be made available to you ***without patient names*** to conduct the proposed study as outlined in the submitted application.

Please note that final approval is granted on your compliance with the NHLS conditions of service and that the study can only be undertaken provided that the following conditions have been met.

- Processes are discussed with the relevant NHLS departments (i.e. Information Management Unit and Operations Office) and are agreed upon.
- Confidentiality is maintained at participant and institutional level and there is no disclosure of personal information or confidential information as described by the NHLS policy.
- A final report of the research study and any published paper resulting from this study are submitted and addressed to the NHLS Academic Affairs and Research office and the NHLS has been acknowledged appropriately.
- NHLS Data cannot be used to track patients as no pre-approval/consent is obtained from Patients.

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. Any data related queries may be directed to NHLS Corporate Data Warehouse, contact number: 011 386 6074 email: zarina.sabat@nhls.ac.za

PP: [signature]

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research

Appendix E: Data collection sheet 1- variables and outcomes

(page 1 of 5)

	Patient study number	First (1) or second (2) TKR in study	Age	Age category	Sex	Race category	TKA side	Underlying diagnosis category	BMI class	BMI overweight (Y/N)	BMI obese (Y/N)	Current Smoker (Y/N)	Comorbid risk factor category for PJI	DMARDS or Steroids (Y/N)	Cutting time (minutes)	Cutting time category	Cutting time more than 2 hours (Y=Yes, N=No)	Waiting period (months)	Waiting period category	Overall sepsis	Prosthetic joint infection	Superficial infection
Oct 15																						
* Suspected PJI: SSSI confirmed- doesn't meet PJI definition	1	1	64	3	F	3	Left	1	3	Y	Y	No	1	No						Y	N	Y
* Discarded file	2	1	42	1	M		Left													N	N	N
* File Missing	3	1	76	4	M		Left													N	N	N
*	4	1	67	3	F	3	Left	3	5	Y	Y	No	2	No						N	N	N
*	5	1	49	1	F	1	Left	1	5	Y	Y	No	2	No	130	4	Y			N	N	N
*	6	1	68	3	F	3	Right	3	2	Y	N	No	1	No						N	N	N
*	7	1	57	2	F	1	Right	1	5	Y	Y	No	2	No	110	3	N			N	N	N
*	8	1	56	2	F	1	Right	2				No	1	No	145	4	Y			N	N	N
* SSSI	9	1	72	4	F	1	Left	3	2	Y	N	No	1	No						Y	N	Y
* SSSI	10	1	82	5	M	3	Left	3	1	N	N	No	1	No						Y	N	Y
* Incomplete file	11	1	53	2	F	1	Left	1												N	N	N
*	12	1	56	2	F	1	Left	1				No	1	No						N	N	N
* Incomplete file	13	1	72	4	M	2	Left		1	N	N	No								N	N	N
*	14	1	71	4	F	2	Left	1	3	Y	Y	No	1	No	135	4	Y			N	N	N
*	15	1	62	3	F	4	Right	3	2	Y	N	No	1	No						N	N	N
15 patients																						
Apr 16																						
* Incomplete file	16	1	67	3	F	1	Left	1	3	Y	Y									N	N	N
*	19	1	52	2	F	3	Left	4	2	Y	N	No	4	Yes						N	N	N
*	20	1	62	3	F	1	Left	1				No	7	No	170	5	Y			N	N	N
*	21	1	68	3	F	1	Right	3				No	7	No						N	N	N
*	22	1	57	2	M	1	Left	2				No	1	No	110	3	N			N	N	N
*	23	1	72	4	F	1	Left	1	2	Y	N	No	1	No						N	N	N
* Incomplete file	24	1	59	2	F	1	Right													N	N	N
*	25	1	62	3	F	1	Left	1				No	1	No	160	5	Y			N	N	N
*	26	1	73	4	F	3	Right	3				No	1	No						N	N	N
* Incomplete file Patient Died	27	1	84	5	F	1	Left													N	N	N
*	28	1	71	4	F	3	Right	1	3	Y	Y	No	2	No	70	2	N			N	N	N
* File Missing	29	1	55	2	F		Left													N	N	N
*	30	1	68	3	F	1	Left	1	3	Y	Y	No	3	No						N	N	N
*	31	1	67	3	M	3	Right	3	3	Y	Y	No	2	No						N	N	N

Appendix E: Data collection sheet 1- variables and outcomes

(page 2 of 5)

	Patient study number	First (1) or second (2) TKR in study	Age	Age category	Sex	Race category	TKA side	Underlying diagnosis category	BMI class	BMI overweight (Y/N)	BMI obese (Y/N)	Current Smoker (Y/N)	Comorbid risk factor category for PJI	DMARDS or Steroids (Y/N)	Cutting time (minutes)	Cutting time category	Cutting time more than 2 hours (Y=Yes, N=No)	Waiting period (months)	Waiting period category	Overall sepsis	Prosthetic joint infection	Superficial infection
*	32	1	74	4	F	1	Right	3	2	Y	N	No	1	No						N	N	N
*	33	1	75	4	F	1	Left	1	1	N	N	No	1	No	90	2	N			N	N	N
16 patients																						
Aug 16																						
*	34	1	57	2	F	3	Left	1				No	3	No						N	N	N
*	35	1	55	2	F	4	Left	1	2	Y	N	No	2	No	105	3	N			N	N	N
*	36	1	68	3	F	1	Right	1	4	Y	Y	No	1	No	95	3	N			N	N	N
*	37	1	53	2	F	1	Right	1	3	Y	Y	No	1	No	140	4	Y			N	N	N
*	38	1	68	3	M	2	Left	2	1	N	N	No	1	No	70	2	N			N	N	N
*	39	1	54	2	M	2	Right	2	3	Y	Y	No	1	No	90	2	N			N	N	N
* Discarded file	40	1	49	1	F		Left													N	N	N
* Discarded file	41	1	59	2	F		Left													N	N	N
*	42	1	70	4	F	2	Left	4	1	N	N	No	4	Yes	60	1	N			N	N	N
*	43	1	52	2	F	3	Left	3	1	N	N	No	1	No	60	1	N			N	N	N
*	44	1	74	4	F	1	Left	1	3	Y	Y	No	1	No						N	N	N
* Incomplete file Suspected PJI Outside time for study	45	1	60	3	F	3	Right	1	5	Y	Y	No	2	No						N	N	N
*	46	1	55	2	F	1	Right	1	3	Y	Y	No	1	No						N	N	N
*	47	1	68	3	M	1	Right	1	3	Y	Y	No	1	No	115	3	N			N	N	N
*	48	1	62	3	M	1	Right	2	1	N	N	No	1	No	168	5	Y			N	N	N
*	49	1	53	2	M	1	Left	3	3	Y	Y	No	2	No	80	2	N			N	N	N
*	50	1	65	3	M	2	Left	3	2	Y	N	No	1	No	135	4	Y			N	N	N
*	51	1	58	2	F	1	Right	3	3	Y	Y	No	2	No	70	2	N			N	N	N
*	52	1	76	4	F	1	Left	1	2	Y	N	No	1	No	130	4	Y			N	N	N
*	53	1	73	4	F	1	Right	1				No	2	No						N	N	N
*	54	1	63	3	M	2	Right	2	3	Y	Y	No	2	No	105	3	N			N	N	N
*	55	1	73	4	F	1	Right	3	1	N	N	No	1	No	55	1	N			N	N	N
22 patients																						
Nov 16																						
*	56	1	54	2	F	4	Left	1				No	1	No				18	3	N	N	N
* Incomplete file Suspected PJI: SSSI confirmed- doesn't meet PJI definition	57	1	59	2	F	1	Right	3	1	N	N							17	3	Y	N	Y

Appendix E: Data collection sheet 1- variables and outcomes

(page 3 of 5)

	Patient study number	First (1) or second (2) TKR in study	Age	Age category	Sex	Race category	TKA side	Underlying diagnosis category	BMI class	BMI overweight (Y/N)	BMI obese (Y/N)	Current Smoker (Y/N)	Comorbid risk factor category for PJI	DMARDS or Steroids (Y/N)	Cutting time (minutes)	Cutting time category	Cutting time more than 2 hours (Y=Yes, N=No)	Waiting period (months)	Waiting period category	Overall sepsis	Prosthetic joint infection	Superficial infection
* Suspected PJI: SSSI confirmed- doesn't meet PJI definition	58	1	62	3	F	3	Left	1	5	Y	Y	No	3	No	80	2	N	18	3	Y	N	Y
*	59	2	73	4	F	1	Right	3	2	Y	N	No	1	No	85	2	N	16	3	N	N	N
*	60	1	56	2	F	1	Right	3				No	1	No				17	3	N	N	N
*	61	1	69	3	F	1	Right	1				No	1	No	68	2	N	17	3	N	N	N
*	62	1	81	5	M	1	Left	3	1	N	N	No	1	No	105	3	N	16	3	N	N	N
* File Missing	63	1	47	1	F		Left											40	6	N	N	N
*	64	1	67	3	F	1	Left	3	5	Y	Y	No	5	No	98	3	N	30	5	N	N	N
* Suspected PJI: SSSI confirmed- doesn't meet PJI definition	65	1	54	2	F	3	Right	1	2	Y	N	No	1	No				17	3	Y	N	Y
* File Missing	66	1	66	3	F		Left											16	3	N	N	N
* File Missing	67	1	69	3	M		Right											20	3	N	N	N
*	68	1	50	2	F	1	Right	1	4	Y	Y	Yes	1	No				14	2	N	N	N
* File Missing	69	1	75	4	F		Right											17	3	N	N	N
14 patients																						
Mar 17																						
*	70	1	60	3	F	2	Right											20	3	N	N	N
*	71	1	66	3	F	1	Right	1	3	Y	Y	No	1	No	105	3	N	20	3	N	N	N
*	72	1	69	3	F	4	Left	1	1	N	N	No	2	No	100	3	N	18	3	N	N	N
* SSSI	73	1	67	3	F	2	Left	1	4	Y	Y		1	No				23	4	Y	N	Y
* SSSI	74	1	67	3	F	3	Left	1	3	Y	Y	No	1	No	130	4	Y	28	5	Y	N	Y
*	75	2	74	4	F	1	Right	3	2	Y	N	No	1	No	95	3	N	34	6	N	N	N
*	76	1	60	3	F	4	Right	1	5	Y	Y	No	1	No	90	2	N	17	3	N	N	N
*	77	1	57	2	F	1	Right	3	1	N	N	No	1	No	70	2	N	17	3	N	N	N
*	78	1	78	4	F	1	Right	1	3	Y	Y	Yes	1	No	65	2	N	21	4	N	N	N
* File Missing	79	1	59	2	F		Left											18	3	N	N	N
*	80	1	59	2	F	1	Left	1	3	Y	Y	Yes	1	No	110	3	N	11	2	N	N	N
* SSSI	81	2	72	4	F	2	Right	1	2	Y	N	No	1	No				40	6	Y	N	Y
*	82	1	63	3	F	1	Right	1	2	Y	N	No	1	No				29	5	N	N	N
* SSSI	83	2	72	4	F	3	Left	1	2	Y	N	No	2	No	130	4	Y	34	6	Y	N	Y
* Incomplete file	84	2	60	3	F		Left											48	6	N	N	N
* Incomplete file	85	1	56	2	F	1	Right						2					17	3	N	N	N
*	86	1	57	2	F	1	Right	1	3	Y	Y	No	1	No	85	2	N	19	3	N	N	N
*	87	1	59	2	F	1	Left	1	4	Y	Y	No	1	No	110	3	N	34	6	N	N	N

Appendix E: Data collection sheet 1- variables and outcomes

(page 4 of 5)

	Patient study number	First (1) or second (2) TKR in study	Age	Age category	Sex	Race category	TKA side	Underlying diagnosis category	BMI class	BMI overweight (Y/N)	BMI obese (Y/N)	Current Smoker (Y/N)	Comorbid risk factor category for PJI	DMARDS or Steroids (Y/N)	Cutting time (minutes)	Cutting time category	Cutting time more than 2 hours (Y=Yes, N=No)	Waiting period (months)	Waiting period category	Overall sepsis	Prosthetic joint infection	Superficial infection
* File Missing	88	1	69	3	M		Left											8	1	N	N	N
19 patients																						
May 17																						
* Suspected infection, never confirmed doesn't meet PJI definition. No SSSI either	89	1	64	3	F	1	Right	1	5	Y	Y	No	1	No	120	3	N	35	6	N	N	N
*	90	1	65	3	F	2	Left	1	4	Y	Y	Yes	2	No	122	4	Y	32	6	N	N	N
*	91	1	65	3	F	1	Left						7	No				19	3	N	N	N
*	92	1	80	5	M	2	Right	1	2	Y	N	No	2	No	170	5	Y	11	2	N	N	N
*	93	1	61	3	F	1	Right	4	5	Y	Y	No	4	No	90	2	N	19	3	N	N	N
*	94	1	66	3	F	4	Left	1	1	N	N	No	2	No	100	3	N	19	3	N	N	N
* File Missing	95	1	59	2	F		Left											20	3	N	N	N
*	96	1	57	2	M	3	Right	2	4	Y	Y	No	10	No	110	3	N	20	3	N	N	N
* Second TKR in this study	98	2	75	4	F	1	Right	1	3	Y	Y	No	1	No	120	3	N	7	1	N	N	N
*	99	1	75	4	F	4	Right	3	2	Y	N	No	5	No	90	2	N	19	3	N	N	N
*	100	1	59	2	M	2	Right	2	3	Y	Y	Yes	9	No	115	3	N	18	3	N	N	N
* File Missing	101	1	76	4	F		Left											20	3	N	N	N
*	102	1	69	3	F	2	Right	1	4	Y	Y	No	1	No				16	3	N	N	N
13 patients																						
Aug 17																						
*	103	1	55	2	F	3	Right	1	4	Y	Y	No	1	No	130	4	Y	19	3	N	N	N
*	104	1	58	2	F	3	Right	1	1	N	N	No	1	No	110	3	N	21	4	N	N	N
*	105	1	63	3	F	1	Left	1	4	Y	Y	No	3	No	121	4	Y	5	1	N	N	N
*	106	1	76	4	F	3	Left	2	3	Y	Y	No	2	No	80	2	N	16	3	N	N	N
*	107	1	73	4	F	2	Left	1	2	Y	N	No	1	No	92	3	N	14	2	N	N	N
*	108	1	67	3	F	2	Left	1				No	1	No	88	2	N	15	2	N	N	N
*	109	1	75	4	F	4	Left	3	3	Y	Y	No	6	No	72	2	N	16	3	N	N	N
*	110	1	78	4	F	1	Right	1	4	Y	Y	No	1	No	70	2	N	16	3	N	N	N
*	111	1	59	2	F	1	Right	3				No	3	No				19	3	N	N	N
*	112	1	56	2	F	3	Right	1	4	Y	Y	No	1	No	125	4	Y	14	2	N	N	N
*	113	1	75	4	F	2	Right	1	1	N	N	No	8	No	175	5	Y	9	1	N	N	N

Appendix E: Data collection sheet 1- variables and outcomes

(page 5 of 5)

	Patient study number	First (1) or second (2) TKR in study	Age	Age category	Sex	Race category	TKA side	Underlying diagnosis category	BMI class	BMI overweight (Y/N)	BMI obese (Y/N)	Current Smoker (Y/N)	Comorbid risk factor category for PJI	DMARDS or Steroids (Y/N)	Cutting time (minutes)	Cutting time category	Cutting time more than 2 hours (Y=Yes, N=No)	Waiting period (months)	Waiting period category	Overall sepsis	Prosthetic joint infection	Supe infec
* Confirmed PJI but of knee done in M+W week after defined study period but within follow up	114	1	65	3	M	2	Left	1	4	Y	Y	No	8	No	105	3	N	21	4	N	N	N
*	115	1	69	3	F		Right	3				No	1	No				17	3	N	N	N
*	116	1	56	2	F	1	Right	3	4	Y	Y	No	2	No	115	3	N	16	3	N	N	N
* File Missing	117	1	68	3	F		Right											15	2	N	N	N
* SSSI	118	1	49	1	F	1	Right	1	3	Y	Y	No	1	No	122	4	Y	21	4	Y	N	Y
*	119	1	61	3	F		Right	3				No	1	No				15	2	N	N	N
* Confirmed PJI	120	1	76	4	F	2	Left	2	1	N	N	No	8	No	135	4	Y	21	4	Y	Y	N
18 patients																						
Grand total 117 knees																						

Key:									
BMI class:		**Race:**		**Risk factors:**		**Cutting time:**		**First or second TKR in study:**	
18.5-24.9 (Normal weight)	1	Black	1	None	1	≤ 60 mins	1	1	First
25-29.9 (Pre obesity)	2	White	2	Diabetes	2	61-90 mins	2	2	Second
30-34.9 (Obesity class 1)	3	Coloured	3	Venous insufficiency	3	91-120 mins	3		
35-39.9 (Obesity class 2)	4	Indian	4	Rheumatoid arthritis	4	121-150 mins	4	**Outcome**	
≥ 40 (Obesity class 3)	5			Peripheral vascular disease	5	151-180 mins	5	PJI	1
		Diagnosis:		Chronic kidney disease	6			Indeterminate	2
Age:		Primary OA	1	HIV	7	**Waiting period:**		Superficial infection	3
40-49	1	Secondary OA	2	Cancer	8	<10 months	1	Likely PJI but doesn't meet definition	4
50-59	2	OA (? primary/ secondary)	3	Prev septic knee	9	11-15 months	2		
60-69	3	Inflammatory	4	Mult prev knee surgeries	10	16-20 months	3	**Outcome columns:**	
70-79	4					21-25 months	4	Y	Yes
80-89	5					26-30 months	5	N	No
						> 30 months	6		

Appendix F: Diabetic patients HbA1c results

Patient study number	HbA1c
4	8.3%
28	7.5%
31	10.0%
35	6.3%
51	7.0%
53	12.8%
54	5.4%
72	8.2%
83	7.1%
85	9.3%
99	5.4%
106	6.4%
116	5.2%

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 1 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
Oct 15					
* Suspected PJI: SSSI confirmed- doesn't meet PJI definition	1	Pus swab, 2+ neutrophils, +ve S Aures sens Clox 05/12/2017 (ACUG85993NOF) Intracp specimens (ACXW4803NOF + ACXW4802NOF)- MCS- 1+ Neurrophils culture negative	WCC 7.85 CRP 62 Ward 4 05/12/2017 WCC 4.68 ESR 8 CRP 2 OOPD 09/02/2018	Not all MSIS criteria met (2011 or 2018= inconclusive)- insufficient investigations to make diagnosis of PJI	12/12/2017- Debridement of knee. No Poly exchange. No sepsis noted into knee joint. Subsequent follow up at OOPD 09/02/2018- no suspicion PJI
* Discarded file	2	Nil	ESR 20, CRP 3, WCC 10.7 (30/10/2015)- Ortho OPD		
* File Missing	3	Nil	WCC 5.93, CRP 2, ESR 2 (10/02/2017)- Ortho OPD WCC 5.48, CRP 3, ESR 2 (20/04/2017)- OPD WCC 5.43, CRP 4, ESR 4 OOPD (08/09/2017)- Ortho OPD		
*	4	Nil	Nil relevant		
*	5	Nil	Nil relevant		
*	6	Nil	Nil relevant		
*	7	Nil	Nil relevant		
*	8	Nil	Nil relevant		
* SSSI	9	Nil	Nil relevant		Post op- oozing wound (SSSI- cleared up on Oral Abx, no suspicion of PJI on follow up)
* SSSI	10	Negative Urine MCS/LP/BC (November 2015) Medical ward. No pus swab from knee wound	CRP 272, WCC 10.29 (November 2015 Medical ward). CRP 272, WCC 10.59 (December 2015 Medical ward) No ESR		Admitted 1 month post op to medical ward with sepsis of unknown origin. Had 2 open sloughy wounds on the knee without pus draining. Operated knee had a flexion contracture. Patient had a grade 2 bed sore. Orthos never consulted during admission. Patient DC on a wheelchair December 2015. No new follow up after December 2015 ? Demised
* Incomplete file	11	Nil	Nil relevant		
*	12	Nil	Nil relevant		Complicated post op By LRTI nosocomial- no evidence of PJI clinically
* Incomplete file	13	Nil	Nil relevant		
*	14	Nil	Nil relevant		
*	15	Nil	Nil relevant		
15 patients					

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 2 of 8)

	Patient study number	Microbiological Culture		Other relevant biochemical or histological result	Outcome of PJI	Other
Apr 16						
* Incomplete file	16	Nil		Nil relevant		
* Exclude from study!!!	17	?		?		No record of patient at records or NHLS
* Exclude from study!!!	18	Nil		Nil relevant		Surgery cancelled during move and walk week due to AKI, eventually done 12/05/2016. EXCLUDE FROM STUDY!!!
*	19	Nil		Nil relevant		
*	20	Nil		Nil relevant		
*	21	Nil		Nil relevant		
*	22	Nil		Nil relevant		
*	23	Nil		Nil relevant		
* Incomplete file	24	Nil		Nil relevant		
*	25	Nil		Nil relevant		
*	26	Nil		Nil relevant		
* Incomplete file Patient Died	27	Nil		Nil relevant		Patient died June 2017 Incomplete file
*	28	Pus swab +ve S Aureus sens clox (11/10/2016)- MRN64032992 (?? correct patient incorrect details ?? origin)		ESR 25, CRP 3 WCC 7 (16/02/2017) orth opd- nil clinical concern on follow up		
* File Missing	29	Blood culture (GNB- E.Coli sens amp) 27/05/2017 Urine MCS (GNB- E.Coli sens amp) 27/05/2017		WCC 8.39, CRP 2, ESR 5 (10/06/2016)- COPD WCC 17.6, CRP 233 (27/05/2017)- Medical admission		
*	30	Nil		Intra op Histological specimen taken to exclude gout. Biopsy shows features of a reactive synovium		
*	31	Nil		Nil relevant		Myocardial infarction post op ?? outcome
*	32	Nil		Nil relevant		
*	33	Nil		Nil relevant		
16 patients						

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 3 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
Aug 16					
*	34	Nil	ESR 17, WCC 6.93, CRP 2 (24/03/2017) Ortho OPD		Presented with Pain post TKR- PJI excluded ? PFJ overstuffing
*	35	Nil	Nil relevant		
*	36	Nil	Nil relevant		
*	37	Nil			
*	38	Nil	Nil relevant		
*	39	Nil	Nil relevant		
* Discarded file	40	Nil	Nil relevant		
* Discarded file	41	Nil	Nil relevant		
*	42	Nil	Nil relevant		
*	43	Nil	WCC 7.9 CRP 3 (12/09/2016) Ortho OPD		Patient presented with pain post TKR sepsis excluded
*	44	Nil	Nil relevant		
* Incomplete file Suspected PJI Outside time for study	45	Blood culture negative (07/09/2017) ICU Blood culture +ve 25/02/2019 ED: E.coli sens Amoxicillin	ESR 27, WCC 9.5, CRP 33 (07/10/2016) ortho OPD WCC 9.19 ESR 69 CRP 115 OOPD 24/05/2019 (OUTSIDE TIME FOR STUDY) WCC 9.06 ESR 96 CRP 105 OOPD 16/08/2019 (OUTSIDE TIME FOR STUDY)	Workup still pending ? Tsukayama type 3 or 4	?? Knee surgery 2018 ? reason- File missing! Suspected PJI (warm tender swollen knee, no draining sinus)- increased septic markers on 24/05/2019- OUTSIDE TIME FOR STUDY. Admission for CAP Feb 2019
*	46	Nil	Nil relevant		
*	47	Blood culture negative (05/10/2016)	WCC 44, CRP 270 (05/10/2016) Medicine		No evidence of PJI on follow up at OOPD
*	48	Nil	WCC 7.55 CRP 127 (14/03/2018) Emergency department- Septic hand- IDC on antibiotics		
*	49	Nil	Nil relevant		
*	50	Nil	Nil relevant		
*	51	Nil	Nil relevant		
*	52	Nil	WCC 3.92 CRP 4 ESR 22 OOPD 12/02/2017		Chronic knee pain post op- septic workup NAD
*	53	Nil	Nil relevant		
*	54	Nil	Nil relevant		
*	55	BC and urine MCS negative Ward 5 22/08/2019	WCC 11.55 CRP 280 ESR 87 22/08/2016		Post op nosocomial infection. No evidence PJI
22 patients					

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 4 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
Nov 16					
*	56				
* Incomplete file Suspected PJI: SSSI confirmed- doesn't meet PJI definition	57	2 negative blood cultures	13/05/2017 (ACDL5172NOF) CRP 109, WCC 9.51 ESR rejected with pus draining from surgical wound	Planned for debridement, failed to follow up	Incomplete file Patient fell in May 2017, presented with painful septic knee. Admitted on IV clox Discharged ? reason for the wknd to come back following week for debridement, failed to follow up
* Suspected PJI: SSSI confirmed- never doesn't meet PJI definition	58	K. Pneumonia UTI 19/06/2019 Uro OPD sens Nitrofurantoin.	CRP 20, WCC 10.9, ESR reject (27/01/2017) ortho OPD		Suspicion of PJI at OOPD 28/01/2017- never proven. OPD notes report chronically painfully knee but no Sinus. Oral abx
* Second TKR in this study	59	Nil	WCC 6.77 ESR 15 CRP 34 OOPD 20/04/2019		Second TKR in this study. Seen at OOPD 20/04/2018- ? OM ? BCC left leg. No suspicion PJI
*	60	Nil			
*	61	Nil	Nil relevant		
*	62	Nil	Nil relevant		
* File Missing	63	Nil	Nil relevant		
*	64				
* Suspected PJI: SSSI confirmed- doesn't meet PJI definition	65	Mult negative pus swabs and tissue MCS (05/09/2017, 10/03/2017, 28/02/2017, 27/02/2017, 01/02/2017) 1st stage revision (debridement and implant removal on 27/02/2019- MCS= Numerous neutrophils (3+), Culture negative (ABZD2169NOF/ AOZD2170NOF/ ABZD2171NOF) At revision TKR- Tissue MCS (ACPL7406NOF)- 3x negative samples Tissue MCS 05/09/2017- Negative ?? resason	WCC 7.97, ESR 67, CRP 58 (24/02/2017) ward 5 Removal of implants 27/02/2019- Histology: Evidence of recent surgical intervention with superimposed infection (ABZD2170NOF) OOPD 22/05/2018- WCC 7.71 ESR 16 CRP 9	?? How PJI diagnosed initially- No positive culture, no notes at OPD follow up on state of tissue. Feb 2017 after debridement and poly exchange- wound dehiscence: Dx as PJI (Failed attempt at debridement and polyethylene exchange) 2 stage revision TKR	1st operation 09/11/2016 Septic hardware 2/12 later Poly exchange and debridement 01/02/2017- Nil notes from records of in patient admission Implant removal 27/02/2017- complicated post op with wound dehiscence. Treated on a vac dressing and DC 20/3/2017 Revision TKR 2nd stage 05/09/2017- ? new admission September 2018- Multiple tissue MCS sent
* File Missing	66	Nil	Nil relevant		
* File Missing	67	Nil	Nil relevant		
*	68	Nil	Nil relevant		
* File Missing	69	Nil	Nil relevant		
14 patients					

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 5 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
Mar 17					
*	70	Knee fluid MCS- scanty 1+ lymph's, Negative culture 25/03/2018 Ward 4 (ACXW48702NDF)	CRP 12 ESR 33 WCC 7.4 02/03/2018 ward 4		
*	71	Joint aspiration 09/07/2019- negative MCS/ Fungal culture/ GXP	Pre op Septic markers 08/07/2019- Wcc 4.31, CRP <4 ESR 19 08/07/2015- RF 40 (raised N <20)	1 stage revision planned###	Aseptic loosening outside time of study
*	72	Urine MCS 16/03/2019- E. coli sens to Meropenem and Amikacin Blood culture 16/03/2019- Coagulase negative staph x 1 other blood culture negative	19/03/2019 (day 6 post op) CRP 114, WCC 8.95, ESR 17		Post op nosocomial sepsis- UTI treated with 1/52 IV antibiotics. No evidence of PJI
* SSSI	73		ESR 62, CRP 47 WCC reject (24/03/2017) Ortho OPD		Suspected superficial infxn- given 2/52 oral Abx, seen 1/52 later- no suspicion of PJI- DC
* SSSI	74		ESR 18, CRP 31 WCC 9.83 (24/03/2017) Ortho OPD		Suspected superficial infxn- admitted for IV antibiotics x 3/7 and Oral antibiotics for 1/52- Resolved. No draining sinus
* Second TKR in this study	75	Nil	WCC 6.85 CRP 2 ESR 5 OOPD (13/09/2017)		Second TKR in this study; Suspected PJI 13/09/2017, started on oral clox, septic markers negative- no evidence PJI on follow up
*	76	Nil	Nil relevant		
*	77				
*	78	Nil	Nil relevant		
* File Missing	79				
*	80	Nil	Nil relevant		
* SSSI Second TKR in this study	81	Nil	WCC 6.34 CRP 35 (24/03/2017) Ortho OPD	Resolved Superficial infection	Second TKR in this study; 2/52 post TKR wound erythematous (WCC 6 CRP 35)- given 2/52 oral antibiotics. Wound normal 2/52 later
*	82	Nil	Nil relevant		
* SSSI Second TKR in this study	83		ESR 98, CRP 319, WCC 9.64 (18/03/2017) ESR 88 (19/03/2017) Ward 4,	Resolved Superficial infxn	Second TKR in this study. Worry about early post op superficial sepsis- iv cox for 2/7 and topical antibiotics given. DVT negative. No clinical concern for infxn on F/U
* Incomplete file Second TKR in this study	84				Second TKR in this study; Incomplete file
* Incomplete file	85				Incomplete file
*	86	Nil	Nil relevant		
*	87	Nil	Nil relevant		
* File Missing	88	Nil	Nil relevant		
19 patients					

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 6 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
May 17					
* Suspected infection, never confirmed doesn't meet PJI definition. No SSSI either	89	Nil	WCC 6.33, CRP 12 OOPD 16/11/2018, ESR 15 OOPD 08/02/2019	Workup still pending	Consistently painful knee 1 year post TKR. Xray normal, being worked up for PJI: awaiting radionuclide scan, no aspirate
*	90	Nil	Nil relevant		
* Incomplete file	91	Nil	Nil relevant		
*	92	Nil	Nil relevant		
*	93	Nil	Nil relevant		
*	94	Nil	WCC 9.12 CRP 12 ESR 22 OOPD 14/09/2018		Superficial infxn of RIGHT TKR done 14/08/2018. No signs infxn Left TKR
* File Missing	95	Nil	Nil relevant		
*	96	Nil	Nil relevant		
* Exclude from study!!!	97				Cancelled during move and walk week- difficult case ?? time of definitive surgery
* Second TKR in this study	98	Nil			Second TKR in this study
*	99	Nil	WCC 7.11 CRP 10 ESR 8 UA 0.43 OOPD 17/11/2019. Knee pain, sepsis excluded		
*	100	Synovial biopsy at Poly exchange 12/12/2017: MCS- 1+ lymphocytes, No bacterial growth/ culture	WCC 6.38 ESR 11 OOPD 06/10/2017- Unstable knee - loose poly bloods excluded infective cause		Poly exchange 12/12/2017 due to instability, no sepsis
* File Missing	101				
*	102	Nil	Nil relevant		
13 patients					

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 7 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
Aug 17					
*	103				
*	104	Nil	Nil relevant		
*	105	Nil	Nil relevant		
*	106	Nil	Nil relevant		
*	107	Nil	Nil relevant		
*	108	Nil	WCC 6.61 CRP 2 ESR 7 OOPD 05/04/2019		Chronic painfull knee post op worked up for infen- excluded
*	109	Nil	Nil relevant		
*	110	2 x BC negative 20/08/2017	Wcc 12.33 CRP 189 20/08/2017 Ward 4 (Very soon post op)		Post op sepsis ? Nosocomial infxn, no evidence PJI
*	111				
*	112		WCC 6.05 CRP 11 ESR 5 OOPD 26/01/2019		No suspicion of PJI post op septic markers pulled for septic workup elsewhere (fost)
*	113	Fluid MCS (? Ascites) 02/11/2019- negative	WCC 9.19 CRP 226 HJH ED 12/10/2019		Presented 12/10/2017: 2/52 Post TKR with large sacral bedsore. Diagnosed as end stage Ovarian CA- TF to RMMAC 27/10/2019 ?? Follow up with records at RMMAC
* Confirmed PJI but of knee done in M+W week after defined study period but within follow up	114	Nil relevant for left knee Right knee: 05/08/2018 intra op debridement and poly exchange Pus MCS x 3 specimens = +ve E. Coli sens ciprofloxacin and Augmentin (ACYC6225NOF/ ACYC6223NOF/ ACYC6224NOF) 17/09/2019 Intra op Tissue MCS x 2 at first stage revision ACYC6230NOF= E.coli sens Ceftriaxone and augmentin 28/09/2019 joint aspirate in ward: ADLB03519NOF= E.coli sensitive only to Ciprobay and ceftriaxone 08/10/2018 intra op debridement and instalation of Lautenbach irrigation system (ACXH 4118NOF)- 3+ neutrophils. No culture	Nil relevant for left knee Right knee: Bloods on readmission 28/08/2018 WCC 13.07 CRP 393 ESR 119	Right knee: Debridement and poly exchange and IV Augmentin failed 2 stage revision and oral antibiotics (ciprobay ? duration) Tsukayama Type 2 ii (deep)	Right TKR done 17/08/2018 Readmitted 2/52 later with PJI. Arthrotomy and poly exchange done 5/9/2018- failed wound oozing pus 2weeks later 1st stage revision- debridement and cement spacer 17/09/2018 Debridement and instalation of lautenbach irrigation system and new cement spacer 09/10/2018 2nd stage revision TKR 04/03/2019. To date patient seems to have recovered. Now draining sinus 03/02/2020
*	115		Nil relevant		
*	116	Nil	WCC 6.41 CRP 12 ESR 10 18/06/2019 CHBAH OOPD WCC 7.56 CRP 61 ESR 27 02/07/2019 CHBAH MOPD		Need to scrutinise CHBAH records

Appendix G: Data collection sheet 2- NHLS results and outcome details (page 8 of 8)

	Patient study number	Microbiological Culture	Other relevant biochemical or histological result	Outcome of PJI	Other
* File Missing	117	Nil	Nil relevant		
* SSSI	118	BC negative, Sputum negative 19/09/2017 Medical ward, Knee aspirate (unsterile in ward) medical ward 18/09/2019 (ACPL6111NOF)= 0 leucs, 8840 polys, 0 Lymphs, Negative culture, GXP -ve	CRP 86 13/09/2017 Medical ward WCC 6.52 ESR 6 CRP 10 13/09/2019 OOPD		Admitted for Septic right knee 12/09/2017- diagnosed as superficial surgical site infxn. Treated on IV antibiotics. Seen at OOPD 13/09/2019- PJI excluded, ? Aseptic loosening
*	119	Nil	Nil relevant		
* Confirmed PJI	120	Pus swab positive (10/10/2017) 1st debridement after 1st stage revision: Citrobacter braakii x 2 specimens and Staphylococcus epidermidis sensitive to Cefepime Blood culture Enterococcus faecalis 23/11/2017 Wd 4 Blood culture Enterococcus faecalis 30/11/2019 Wd 4 Pus MCS 05/12/2018- Klebsiella pneumonia sens Ertapenem Tissue MCS 24/01/2018- at time of debridement and flap- +ve Klebs pneumonia (CRE) sens Amikacin only (ACXW5911NOF) Tissue MCS 30/01/2019- at time of flap debridement- +ve Klebs pneumonia (CRE) sens Amikacin and Colistin Tissue MCS 05/09/2018- At time of 2nd debridement and cement spacer- +ve Staph epidermis Sens Vanco and Rifampicin Tissue MCS 10/10/2018- Staphylococcus epidermis and Corynebacterium species, no sensitivity Tissue MCS 14/11/2018 at time of knee fusion (ADLF7779NOF) 2+ neutrophils no culture Tissue MCS 05/12/2018- Klebs pneumonia ESBL sens Ertapenem- Not treated with Erta	Numerous increased septic markers- not necessary to document- confirmed PJI with multiple positive Cultures of the same organism	Diagnosed PJI 5/52 post TKR- draining sinus 1. Debridement knee 10/10/2017 2. Debridement and 1st cement spacer 17/10/2017 3. Redebridement knee 14/11/2017 4.Redebridement knee 28/11/2017 5. Redebridement knee 13/12/2017 6. Redebridement knee 30/01/2018 7. Gastrocnemius flap for exposed hardware 20/12/2017 8. Debridement of knee and flap 26/01/2018 9. Redebridement 30/01/2018 10. Debridement and new cement spacer March 2018 11. Debridement and New cement spacer 05/09/2018 12. DRI, spacer removal and Knee fusion (IMN) and laulenbach irrigation 14/11/2018. 6/52 Iv Vanco then Linazolid 2/52 13. Debridement L knee 05/12/2018. Patient DC 12/12/2018. Seen 26/07/2019- wounds well healed PJI resolved	
18 patients					

Key:
Infection
Discarded/Missing file
Exclude from study
Incomplete file
Patient Died
Second TKR in study