Clinical and Confidence Outcomes Following Through-Knee versus Above-Knee Amputation: A Quantitative Study

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by

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ABSTRACT

Following surgery, patients with a major lower limb amputation face physical and mental health challenges. For clinicians and physiotherapists to reach a consensus and provide a suitable level of amputation for each patient, the understanding of post-operative outcomes based on varied levels of amputation must be established. The scientific literature has reported extensively on the clinical, biomechanical and rehabilitation outcomes of patients with an above-knee amputation (AKA). Many patients who receive an AKA may not have been considered for a through-knee amputation (TKA). Reported benefits of a TKA include an end weight-bearing residual limb, longer mechanical lever arm, which may be important for sitting balance and when mobilising with a prosthesis. However, patients are not considered for a TKA due to the historical association with poor wound healing. The aim of this thesis was to investigate and compare clinical and rehabilitation outcomes between patients with a TKA and patients with an AKA.

The first study was a systematic review and meta-analysis, thus aiming to compare the functional outcomes and balance confidence of patients with a TKA versus (vs.) AKA during activities of daily living. Existing literature suggested that patients with a TKA had a significantly increased walking distance during the six-minute walk test (6MWT).

The second overarching study aimed to perform a large-scale retrospective analysis of a case control series using data held within the NVR database, to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA. We found that TKA was more commonly performed in patients with diabetes, and is significantly associated with more elective admissions, fewer post-operative complications, and a lower mortality rate compared with AKA. Further, patients with a unilateral TKA had similar levels of successful wound healing as AKA patients, despite previous literature reporting of poor wound healing. Significantly more patients with a TKA were referred to amputation rehabilitation.

The aim of the final study was to compare the differences in ambulatory and non-ambulatory patients with a TKA and patients with an AKA, and to compare their balance confidence and falls history. Findings from this thesis indicated no differences between TKA and AKA when performing the six-minute walk test (6MWT), functional tests and self-reported balance confidence during daily tasks.

Keywords: Through-Knee Amputation, Above-Knee Amputation, Gait, Clinical.

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ABBREVIATIONS

Abbreviation	Term
ABC-UK	Activities-specific Balance Confidence UK
Amb	Ambulatory
AKA	Above-knee amputation
BACPAR	British Association of Chartered Physiotherapists in limb loss Absence Rehabilitation
BKA	Below-knee amputation
BMI	Body Mass Index
cm	centimetres
DARF	Data access request form
Diff	Difference
EQ-VAS	EuroQol Visual Analogue Scale
EQ-5D-5L	EuroQol 5-dimension 5-level
FIST	Function in Sitting Test
FRT	Functional reach test
g	grams
g/dL	Grams per decilitre
HRA	Health Research Authority
HQIP	Healthcare Quality Improvement Partnership
IQR	Interquartile
KD	Knee disarticulation
kg	kilograms
kg/m^2	kilograms per metre squared
LCI-5	Locomotor Capabilities Index-5

m	metres
mo	months
MAR	Missing at random
MCAR	Missing completely at random
MCS	Mental Component Score
MNAR	Missing not at random
MPK	Microprocessor knee
m/s	Metres per second
n	number of individuals in sample
NHS	National Health Service
Non-Amb	Non-Ambulatory
NMPK	Non-mechanical prosthetic knee
NVR	National Vascular Registry
P	P-value
PCS	Physical Component Score
QoL	Quality of life
RCT	Randomised controlled trial
RoBANS	Risk of bias in non-randomised studies
s	seconds
SD	Standard deviation (±)
SF-36	Short-Form Health Survey 36
SIGAM	Special Interest Group in Amputee Medicine
SMD	Standardised mean difference
TKA	Through-knee amputation
TUG	Timed-Up-and-Go

vs.	Versus
y	Years
2MWT	Two-minute walk test
6MWT	Six-minute walk test

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Publications

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Poster Presentation – Hull York Medical School Postgraduate Research Conference, July 2022.

DECLARATION

I confirm that this work is original and that if any passage(s) or diagram(s) have been copied from academic papers, books, the internet or any other sources these are clearly identified by the use of quotation marks and the reference(s) is fully cited. I certify that, other than where indicated, this is my own work and does not breach the regulations of HYMS, the University of Hull or the University of York regarding plagiarism or academic conduct in examinations. I have read the HYMS Code of Practice on Academic Misconduct, and state that this piece of work is my own and does not contain any unacknowledged work from any other sources. I confirm that any patient information obtained to produce this piece of work has been appropriately anonymised.

CHAPTER ONE: INTRODUCTION

1.1. Introduction

Most individuals can mobilise indoors and outdoors in a safe and efficient way. Performing daily motor tasks including walking, negotiating stairs, sitting in a chair or a motor vehicle, crossing obstacles and safely manoeuvring up and down a slope is important as they provide an individual with independence. However, there are a variety of circumstances that can influence the ability of an individual to perform motor tasks, therefore affecting their independence and confidence.

Lower limb amputation involves a surgical procedure to remove either all or part of an individual's limb, ranging from amputations at the level of the toe to the hip. Removal of a lower limb may have a devastating effect on a range of mechanical, physiological, and psychological factors for individuals. The type of amputation performed however, should consider providing individuals with the maximum level of motor functioning. The thesis will focus on adaptations to gait, balance, and balance confidence six months post-surgery between two levels of lower limb amputation.

There are four main levels of major lower limb amputation: below the knee, through the knee, above the knee and hip disarticulation. Despite lower limb amputations being performed most frequently at below-knee or above-knee levels, each level of amputation is a unique experience for every individual, with the problem of loss and replacement having different implications (Legro et al., 1999). Although through-knee amputation (TKA) represents less than 1% of all amputations within the UK (Moxey et al., 2010), this level of amputation is suggested to have many advantages. These advantages include less surgical blood loss, preservation of thigh muscles, a longer mechanical lever arm, and a weight-bearing residual limb (de Laat et al., 2014).

After a patient has had their lower limb amputation, they will undergo rehabilitation to learn how to mobilise with altered lower limb mechanics, and how to successfully complete functional motor tasks. However, the consequences that every patient is challenged with post-amputation are dependent on the person and their physical ability. The level of amputation may also have an impact on the ability to successfully perform activities of daily living. For most people with a lower limb amputation, the objective is to regain a level of mobility that will provide them with some independence. Not only will achieving mobility be of functional benefit, but it will influence their independence and quality of life (QoL), and costs encountered with everyday life.

One of the main challenges that patients with a TKA or above-knee amputation (AKA) encounter is replacing the functions of the knee joint, foot, and ankle, which help individuals adjust to uneven ground surfaces. The removal of anatomical segments correspondingly removes proprioceptive information surrounding the foot positioning in relation to the ground. Although this would contribute to the number of trips and falls experienced, there is also likely to be an impact on the level of confidence when performing activities of daily living. Assessing the risk of falling and how a patient with an amputation adapts to daily tasks is crucial to ensure that the correct support measures are in place. Clinical assessments can assist with rehabilitation and can be accomplished using questionnaires and gait analysis, with participants completing measures to investigate how gait patterns are altered and to determine the changes in mobility when completing certain activities (Davis et al., 1991; Wilken et al., 2012).

The lack of investigation into the gait and functional adaptations of TKA identifies a clear gap within the current literature. Few reports into TKA function, balance and balance confidence levels when performing activities of daily living have been made and there are currently no reports within the scientific literature on how the mobility and balance confidence differ between TKA and AKA (Murakami & Murray, 2016). The overarching aim of the thesis was to investigate clinical outcomes in patients with a TKA versus (vs.) patients with an AKA. Therefore, the objectives to achieve the overarching aim are:

- To investigate the surgical pre- and post-operative differences between TKA and AKA,
- To provide a comparison of functional outcomes between ambulatory patients with TKA and AKA when performing activities of daily living,
- To compare the functional outcomes between non-ambulatory patients with TKA and AKA when performing seated activities,
- To investigate self-reported balance confidence between ambulatory and non-ambulatory individuals with TKA and AKA when performing activities of daily living.

The information from the thesis will highlight areas of surgical, mobility, adaptations and differences that occur in both ambulatory and non-ambulatory functional status for patients with TKA and AKA. The investigations will benefit clinicians by providing objective information or justification of clinical decision making when determining which level of amputation to perform.

1.2. Impact of COVID-19

COVID-19 had a significant impact on my PhD. My planned research involving biomechanics was unable to continue due to the laboratory closure. Further, with the high level of vulnerability of the participant group in question, Health Research Authority (HRA) within the National Health Service (NHS) paused my study.

As the pandemic felt unlikely to allow completion of the thesis as originally planned, the supervisory team and I worked to change the main project to simplify the testing needed. A revised thesis project moved from gait biomechanics to using clinical data and tests to examine the differences between two levels of amputation. The change in methodology therefore resulted in a change of ethical approval, which was not approved until November 2020. Clinical data collection commenced, and despite having NHS and HRA approvals and University of Hull ethics, the lockdown and tier systems restricted the work I was able to complete on my research project. We managed to secure access to large databases broadly related to the project, however, given these are highly clinical datasets, I was required to undertake a significant amount of additional learning in both clinical surgical outcomes and in statistical methods required to analyse these data. Therefore, the project shifted the focus of the thesis to a retrospective clinical database analysis with the previously planned work as a smaller exploratory study.

1.3. Thesis Structure

The thesis begins with a literature review of lower limb amputation in Chapter Two. The review discusses the published literature relating to the biomechanics and functional outcomes of activities of daily living, balance, postural control, and post-surgical rehabilitation of lower limb amputations. The aim, objectives and hypotheses of the thesis are outlined at the end of the chapter.

Chapter Three is a systematic review and meta-analysis that compares the biomechanical, clinical tests, mobility and falls outcomes of TKA and AKA.

Chapter Four outlines the background and methodologies of three missing data handling techniques. The methodologies were utilised in Chapter Five, Six and Seven, respectively.

Chapter Five utilises the complete case analysis technique outlined in Chapter Four and provides a comparison of clinical and surgical pre- and post-operative data between TKA and AKA collected from the National Vascular Registry (NVR) database.

Chapter Six utilises the multiple imputation technique outlined in Chapter Four and provides a comparison of clinical and surgical pre- and post-operative data between TKA and AKA collected from the NVR database.

Chapter Seven utilises the propensity score matching technique outlined in Chapter Four and provides a comparison of clinical and surgical pre- and post-operative data between TKA and AKA collected from the NVR database.

Chapter Eight compares the results from the complete case analysis, multiple imputation and propensity score matching techniques presented in Chapter Five, Six and Seven, respectively. This chapter provides a comparison of clinical and surgical pre- and post-operative data between TKA and AKA collected from the NVR database.

Chapter Nine outlines the details of the ethical approval and eligibility criteria used for the clinical data collection. Further, Chapter Nine describes the experimental set up and procedures for data collection of the activities. A direct comparison of the clinical and functional outcomes between ambulatory and non-ambulatory TKA and AKA from the clinical data collection is presented within Chapter Nine.

Chapter Ten presents an overall summary of the thesis and its findings. The chapter will additionally interpret implications following surgical data and for each activity of daily living across the level of amputation that can be used in clinical practice. Limitations of the thesis and recommendations for future research will be address in Chapter Ten. Additionally, this chapter will outline the reflections of the COVID-19 pandemic.

Chapter Eleven provides a conclusion to the thesis.

CHAPTER TWO: LITERATURE REVIEW

2.1. Introduction

This literature review defines amputation and presents the national statistic values on lower limb amputation. The review uses key literature articles to describe the biomechanics of movement in able-bodied individuals before evaluating the literature investigating gait and balance of individuals with a lower limb amputation. The literature surrounding balance confidence and falls following lower limb amputation will be critically analysed. A summary of the literature is provided, followed by the specific objectives and hypotheses.

2.2. Causes of Lower Limb Amputation

The main reason for limb amputation is to mitigate the effects of damaged tissue, irretractable symptoms or if an individual's life may be at risk from processes within the affected limb (cancer or infection). In the UK and USA, 75% and 88% respectively of lower limb amputations are as result of peripheral vascular disease (van Schaik et al., 2019), 80% of which are associated with diabetes (Dillingham et al., 2002; Moxey et al., 2010). A diabetic lower limb amputation occurs every 30 seconds in the world (International Diabetes Federation, 2017). Diabetes is a lifelong condition that causes an individual's blood sugar levels to be high. For an individual with diabetes, their body either does not produce enough insulin, or cannot use its own insulin as efficiently as it should. Diabetes can lead to accelerated peripheral vascular disease, a blood circulation disorder that can cause the blood vessels outside of the heart and brain to narrow, block and spasm, causing pain and fatigue, particularly in the legs. As the blood vessels become narrowed, the level of blood flow reaching organs and limbs becomes limited. Chronically elevated blood glucose levels may also affect nerve function. Consequently, individuals may not be aware of a wound or ulcer that they have on their foot. Complications may include unhealed wounds resulting in tissue death, or further infection of tissue or bone, requiring limb amputation.

Although cancer amputations are rare, tumours proximal to the knee or hip joints may result in a lower limb amputation to save an individual's life by preventing the spread of cancerous or malignant cells to other body structures. Amputations due to trauma can be caused by landmines, road traffic accidents or work-related incidents (Clasper & Ramasamy, 2013).

2.3. Types of Lower Limb Amputation

The removal of a lower limb may have a significant impact on person's biomechanics, physiology, and psychology. There are several levels of amputation that can be performed when the limb is untreatable. Four main levels of leg amputation include below-knee amputation (BKA), TKA, AKA, and hip disarticulation. A BKA, known as a transtibial amputation, is performed across the shin and involves the surgical removal of the foot and ankle joint. A TKA or amputation about the knee is performed at or just above the knee level, whilst an AKA is performed at approximately the middle of the thigh. A through-hip amputation, known as hip disarticulation, is the surgical removal of the entire lower limb through the hip joint. Researchers have previously compared the gait biomechanics and mobility levels of BKA to AKA (Schmalz et al., 2007; Rougier & Bergeau, 2009; De Asha et al., 2014; Hendershot & Wolf, 2014). Much less is known about the clinical outcomes of AKA vs. TKA. These procedures and their relative merits and drawbacks are the focus of this thesis and are discussed in more detail below.

2.3.1. Above-Knee Amputation

An AKA, also known as a transfemoral amputation, is the surgical removal performed above the knee joint and along the femur. AKA may be performed across three areas of the femur, comprising of the bottom of the femur (distal femur), middle of the femur, and just below the groin (proximal femur). This level of amputation is commonly performed when there is presence of proximal disease, or wound healing failure and a BKA is not possible (Lim et al., 2018; Schmiegelow et al., 2018).

Some individuals undergoing an AKA may have the healing potential for a BKA, but may be non-ambulating, debilitated, or have a high risk of developing knee flexion contractures (Anderson, 2005). Previous literature stated that functional differences of a distal and proximal AKA are not as dramatic as the differences between a BKA and AKA (Anderson, 2005). If the residual limb is too short, there is an increased risk of contracture and muscle atrophy development. Contractures may contribute to muscle atrophy, repositioning of the adductor magnus and a wider gait, thus influencing energy expenditure (Jaegers et al., 1995a; Geertzen et al., 2019). The adductor magnus allows the femur to maintain a neutral position because of the lever arm length. The cross-sectional area and volume of the adductor magnus allows for the development of a greater adduction moment (Geertzen et al., 2019). As the adductor magnus attaches to the femur, the muscle would be more affected with a higher level of amputation. When amputations are performed at the distal level of the femur, there is a 70% reduction in the moment arm of the adductor magnus (Gottschalk, 2016; Geertzen et al., 2019). Following an AKA, the hip extensor and flexor muscles are atrophied. However, muscle atrophy is dependent on the level of amputation, with a higher level of atrophy occurring with a higher level of amputation (Geertzen et al., 2019). A reduction in muscle volume can alter the muscle forces, consequently reducing the control over the prosthetic limb (Smith et al., 2002; Geertzen et al., 2019).

The reported advantages of AKA include the avoidance of contracture complications and the surgical procedure is often more likely to heal quicker as it requires less intact vasculature to heal, when compared to BKA (Theriot et al., 2019). However, AKA can involve a significant amount of blood loss and requires transection of muscles from the patella and distal femur, thus reducing strength and control of the residual limb (Theriot et al., 2019). Patients with an AKA commonly encounter problems with socket fit for their subsequent prosthetic limb and have a higher level of energy expenditure when mobilising with a prosthesis, reducing the potential of achieving independent mobility (Aulivola et al., 2004; Göktepe et al., 2010). The level of energy expenditure to ambulate can increase by 65% in patients with an AKA compared to BKA (Theriot et al., 2019). Moreover, Bell et al. (2013) discovered that highly functional patients with an AKA and with a longer residual limb had a significantly faster self-selected walking speed of 1.37 metres per second (m/s) compared to 1.22m/s found amongst individuals with an AKA and a shorter residual limb. It therefore appears important to maintain the maximum amount of femoral length for better function, providing that the residual limb goes on to heal (Anderson, 2005).

2.3.2. Through-Knee Amputation

TKA, known as knee disarticulation (KD), is performed around the level of the knee joint and may also involve the removal of the femoral condyles, and patella (Baumgartner, 1979). All TKA procedures maintain the patella ligament and reinsert this to maintain the actions of the quadriceps muscle group. TKA is rarely performed and represents less than 1% of all amputations in the UK (Moxey et al., 2010), and 2% of lower limb amputations in the USA (Albino et al., 2014).

Many variations of this amputation exist and have been revised to assist with improving healing rates and prosthetic fit (Murakami & Murray, 2016). These variations include the KD, Mazet technique, Burgess or Youkey technique, and the Gritti-Stokes and Nellis/Van de Water technique. A KD TKA involves division of the limb through the knee joint with maintenance of all the femoral structures and re-attachment of the distal patella ligament to a posterior position (Figure 2.1). The Mazet technique (Figure 2.2) involves the excision of the patella and removal of the femoral condyles, allowing a less bulbous residual end, greater latitude in adjusting alignments and required stump adduction (Mazet & Hennessy, 1966). If there is a hip flexion contracture, the residual limb and socket may be set to flexion, which would be less noticeable with a small bulbous residual end (Mazet & Hennessy, 1966). The Burgess technique involves the removal of the patella and either all or part of the femoral condyles, similar to the Youkey technique (Burgess, 1977). This technique is suggested to have advantages including preservation of the end-bearing capacity at the TKA level, the transverse axis of the prosthetic knee will correspond to the sound limb whilst allowing knee mechanism control, increased prosthetic rotational control, and stability (Burgess, 1977). For Gritti-Stokes and Nellis/Van de Water amputations (Figure 2.3), the patella is attached to the distal end of the femur and is retained in position by wires or sutures or the tightness of attached tissues (Middleton & Webster, 1962). Muscle tendons serve the Gritti-Stokes amputation rather than muscle mass (Middleton & Webster, 1962). Gritti-Stokes amputations significantly decrease 30-day mortality compared to AKA (Theriot et al., 2019). Gritti-Stokes amputation has an increased limb length, improved assessment outcomes and improved rates of unassisted walking whilst wearing a prosthesis (Taylor et al., 2012).

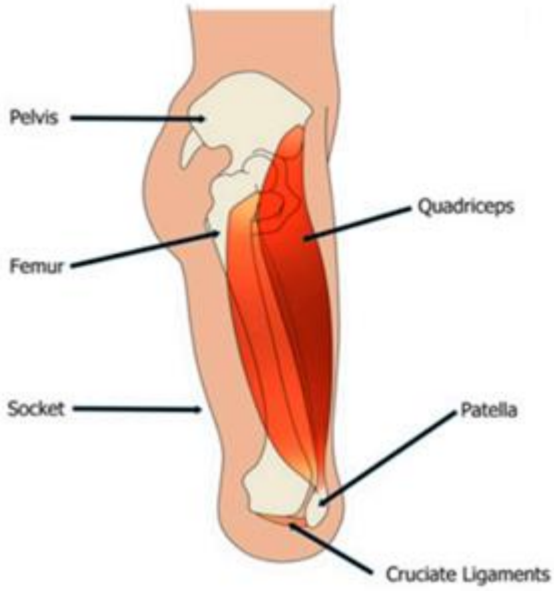

Figure 2.1. Knee disarticulation TKA technique as outlined by Panhelleux et al. (2021).

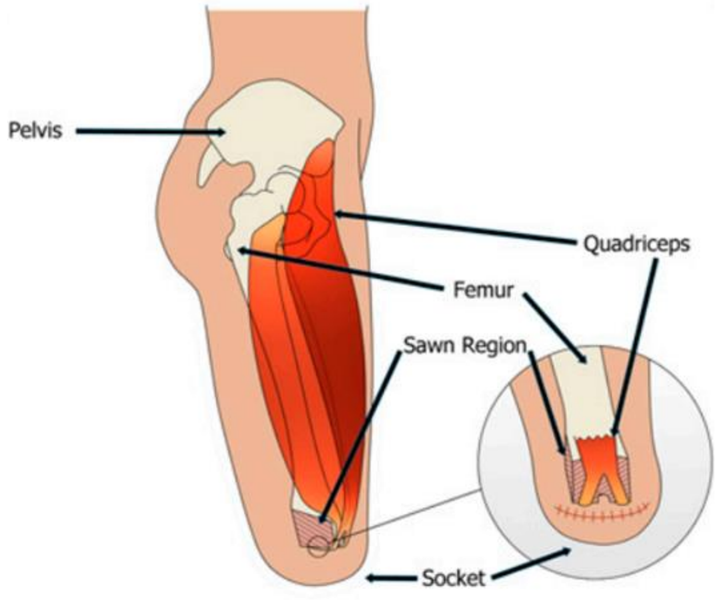

Figure 2.2. Mazet TKA technique as outlined by Panhelleux et al. (2021).

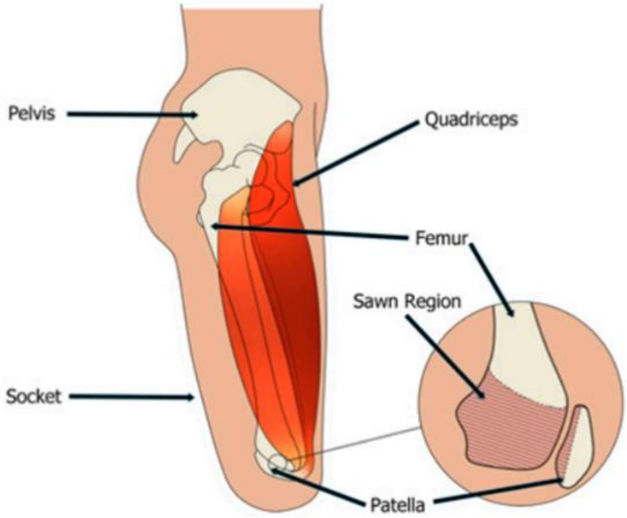

Figure 2.3. Nellis/Van de Water TKA technique as outlined by Panhelleux et al. (2021).

Despite few TKA procedures being performed, there are reportedly many advantages. These include less surgical blood loss, preservation of thigh muscles, a longer mechanical lever arm and a weight-bearing residual limb (Morse et al., 2008; de Laat et al., 2014). The TKA provides a stable and long-lasting residual limb allowing muscle control of the prosthetic limb (Mazet & Hennessy, 1966). Although individuals may experience prosthetic difficulties of a bulky prosthetic limb and an asymmetrical knee joint, TKA procedures are mainly performed on young, active males, with good lower limb strength (Burgess, 1977).

2.4. UK Lower Limb Amputation Statistics

According to the UK National Vascular Registry (NVR) Annual Report, there were 9,508 major lower limb amputations performed in the UK during the 2016-2018 period (Waton et al., 2019). The recorded amputations comprised of 4,983 BKA procedures, corresponding to 52.4% of the total number of amputations performed, and 4,525 AKA procedures, or 47.6% of all amputations performed. TKA procedures accounted for approximately 4% of all major lower limb amputations recorded in the NVR during 2016-2018 and were analysed with BKA data. Published data indicated a variation in the rates of lower limb amputations, ranging from 5.6-600 per 100,000 amongst diabetic individuals, and from 3.6-58.7 per 100,000 amongst the total population (Moxey et al., 2010; Davies et al., 2019). Diabetes causes more than 175 amputations in the UK every week (Diabetes UK, 2018). The risk of amputations because of diabetes compared to individuals without diabetes is reported to range between 7.4 and 41.3 times higher (Narres et al., 2017). However, the rate of major amputation in diabetic individuals has decreased by approximately 18% in the past 10 years (Davies et al., 2019), although it remains six times higher amongst diabetic individuals than non-diabetic individuals (Ahmad et al., 2016). Over 90% of annual major lower limb amputations can be attributed to arterial diseases (Ahmad et al., 2014). Amputations are costly to the NHS, with £1 in every £140 contributing towards foot care for patients with diabetes (Diabetes UK, 2018). Financial costings of major lower limb amputation on the NHS are estimated between £10,000 and £15,000 per procedure (Moxey et al., 2010).

2.5. Lower Limb Amputation Gait Performance

After a patient has had the surgical removal of their lower limb, the remaining muscles must compensate to facilitate walking with a prosthesis. The main concern for any patient following a lower limb amputation is whether they will be able to walk again. Patients who experience a lower limb amputation are faced with the task of adapting their established habits and movements to adjust to their new lower limb mechanics (Fiedler et al., 2014). Functional prosthetic limbs are prescribed to replace the missing anatomical structures and can increase a patient's QoL and function by allowing them to ambulate independently (Pell et al., 1993; Brown et al., 2012; Uchytil et al., 2014; Lim et al., 2018). Other factors that influence a patient's ability to ambulate include their age, level of amputation, comorbidities and time since amputation (Keagy et al., 1986; Leung et al., 1996; Davies & Datta, 2003; Hamamura et al., 2009; Frengopoulos, 2017; Frengopoulos et al., 2018). Social status, rehabilitation care, prosthetic fit and function are additional factors that can influence the functional outcome of patients with an amputation (Czerniecki & Gitter, 1996). There are observed compensatory mechanisms in the profiles of patients with a lower limb amputation in comparison to able-bodied individuals. However, there are some circumstances when individuals are not provided with a prosthesis and alternatively mobilise using a wheelchair (Fiedler et al., 2014). This may be because of the severity of the limb loss, and or the reduced capabilities of the individual (Fiedler et al., 2014). In some cases, however, prosthetics and wheeled mobility aids complement each other during different activities of daily living or situations (Fiedler et al., 2014). It is suggested that mobility assessment of patients with lower limb amputations may contribute to individual case management, influence the comfort of the residual limb, and impact the efficiency of gait ambulation (Beyaert et al., 2008; Kark et al., 2012; Esquenazi, 2014).

2.5.1. Lower Limb Prosthetic Components

Following a lower limb amputation, one of the main rehabilitation goals is to restore a patient's independence to increase their mobility and their ability to undertake a variety of activities of daily living (Schaffalitzky et al., 2012; Arifin et al., 2017). To achieve this rehabilitation goal, a patient with a lower limb amputation will be prescribed with a prosthesis. A prosthesis is an externally applied device that consists of a single component, or an assembly of components, that are used to replace an absent or deficient lower limb segment (Arifin et al., 2017). Defining a rehabilitation goal and selecting appropriate interventions require consideration of the capabilities, functional demands, and the goals of the individual (Fiedler et al., 2014). Further, van der Linde et al. (2004) mentioned that prosthetic prescription is based on adjusting the mechanical characteristics of a prosthesis to meet the functional requirements of the prosthesis user. Prosthetic limbs are necessary if a patient's rehabilitation goal is to restore their locomotor abilities (Fiedler et al., 2014). The prescribed prosthesis may even help to restore function that exceeds the immediate pre-operative level of function (Fiedler et al., 2014).

Common prosthetic components can include a socket, interface systems, joints, terminal devices, and a foot. Patients with a lower limb amputation must have the correct prosthetic components prescribed according to their amputation level, amputation aetiologies, and their activity level (Arifin et al., 2017; Wanamaker et al., 2017). Prosthesis use for patients with different levels of lower limb amputation requires complex adaptation strategies, within the affected and intact limbs during everyday gait and locomotor tasks (Vrieling et al., 2008; Varrecchia et al., 2019). The two main factors that influence the gait amongst patients with a lower limb amputation are the level of amputation and the type of prosthesis (Varrecchia et al., 2019). Users of lower limb prosthetic devices experience an increased risk of tripping and falling, and this is associated with amputation level, age, and comorbidities (Fiedler et al., 2014). According to Schaffalitzky et al. (2012), prosthesis users should be matched with the most suitable technology to meet their physical needs, fully restore functionality, and to ensure that patients are psychologically and socially satisfied. Further, patients with a lower limb amputation must learn about the behaviour of their prosthetic limb as it will differ to their original limb (Fiedler et al., 2014). Therefore, high-quality prosthetic services are crucial to provide individuals with independence and allow social integration.

2.5.1.1. Prosthetic Knee Components

Prosthetic knee components are designed for patients who have amputations at or above the knee, lack the biological knee joint, and tibia and fibula bones. Patients with a higher level of amputation require a socket, a bucket-shell that supports the affected limb and attaches the prosthetic knee joint. A pylon and a prosthetic foot are also required. Prosthetic knee components support a range of functional abilities, and they differ between models (Hafner et al., 2007; Fiedler et al., 2014).

There are two main types of prosthetic knees: the mechanical knee (NMPK) and the microprocessor knee (MPK). Mechanical knees use a mechanical hinge to replace the knee joint and are the most popular knees used within prosthetic limb services. In addition, individuals who have a lower mobility level, and who tend to be older with comorbidities, are most often fitted with basic mechanical prosthetic knees (Lansade et al., 2018). The hinge is often controlled by either friction, a hydraulic system, or a locking mechanism (Kaufman et al., 2012). Alternatively, an MPK uses a sensor, a microprocessor, software, resistance, and a battery. The microprocessor, which is the knee’s internal computer, controls an internal fluid. The computer monitors each phase of the gait cycle using sensors. The monitoring and control of the internal fluid allows the microprocessor knee to adjust to a variety of external environments. An MPK provides a greater degree of control of the prosthetic knee, and they are designed to help patients walk with a more stable and efficient gait pattern. Furthermore, they allow a more precise adjustment of knee resistance and allow patients with an AKA or TKA to walk more safely in demanding situations including step-over-step stair ascent and descent, and walking on slopes (Kaufman et al., 2012).

Previous literature has investigated the differences in NMPK and MPK joints in TKA and AKA (Theeven et al., 2011; Theeven et al., 2012; Prinsen et al., 2017a; Lansade et al., 2018). Theeven et al. (2011) discovered that two higher functional groups performed the Assessment of Daily Activity Performance in Transfemoral amputees (ADAPT) significantly faster using the MPK in comparison to the NMPK. Theeven et al. (2012) discovered that participants’ perception regarding ambulation, residual limb health, satisfaction and utility during walking were significantly greater with the MPK compared to the NMPK. Prinsen et al. (2017a) reported no significant differences in walking speed and peak prosthetic knee flexion during the swing phase, but vaulting was significantly reduced when walking with the MPK compared to the NMPK. Lansade et al. (2018) found that the Timed-Up-and-Go (TUG) test time was shorter, and the Locomotor Capabilities Index-5 (LCI-5) score was improved with

MPK than the NMPK. Furthermore, prosthesis satisfaction and QoL were significantly improved with the MPK in their study (Lansade et al., 2018). Despite the slight variation in randomised controlled trial (RCT) design, the authors failed to make a comparison of TKA and AKA, as the results were combined for amputation level.

2.5.1.2. Prosthetic Ankle Components

It is difficult to reproduce the complex anatomy and function of the human foot and ankle. The prosthetic foot, however, is an integral prosthesis component following major lower limb amputation (Stevens et al., 2018). Prosthetic feet, determined as the distal interface between the environment and the individual, are important for the transmission of forces and motion (Fogelberg et al., 2016). Prosthetic feet are designed and prescribed to provide stability to patients with a lower limb amputation by reducing the amount of body sway controlled by the stiff ankle joint (Arifin et al., 2015). The ankle joint is important in maintaining balance in activities that involve body movements (Buckley et al., 2002; Ku et al., 2014). There are many mechanical variations of prosthetic feet, with design features attempting to replicate the shock absorption in loading response, the leverage required during terminal stance, and the propulsion required from terminal stance to pre-swing (Stevens et al., 2018). Functions of the prosthetic foot are determined using a range of mechanisms, these including the mechanical joint axes, compressive foams, and bumpers. In addition, prosthetic feet have elastic materials that are designed to deform during loading, and then return to their original shape, releasing the energy stored to provide power during the gait cycle (Stevens et al., 2018).

Prosthetic feet are classified into key categories that reflect on differences in technologies and functional performance. The solid-ankle-cushion-heel foot consists of a solid ankle block with a rigid forefoot and has a compressive material within the heel. The single-axis foot comprises of a single mechanical hinge to replicate the function of the ankle. Furthermore, the multiple-axis foot includes flexible elements that allow dampening movements across all three planes of motion, and the flexible-keel foot includes flexible elements of the forefoot to provide progression of the centre of pressure in the stance phase (Stevens et al., 2018). The energy-storage-and-return foot is built of elastic materials that deform during loading and store potential energy that is used during the gait cycle. Whilst walking is the primary focus of rehabilitation and research, the success or failure of regaining foot functioning from a prosthesis can impact an individual's identity and comfort level during social interactions (Fogelberg et al., 2016).

2.5.2. Lower Limb Amputation Gait

Following lower limb amputation, patients will first learn how to ambulate over level ground. However, navigating daily environments requires level walking, and negotiating steps, stairs, and obstacles, for example. Previous literature has investigated movement patterns of patients with an AKA when performing these tasks. But it is also important to understand other tasks, including sit-to-stand, and reaching for items when sitting.

Functional levels following amputation is often assessed using K-levels or Special Interest Group of Amputee Medicine (SIGAM) mobility grades. K-levels are important as they determine the functional mobility of patients following amputation and assist prosthetists when prescribing an appropriate level of prosthesis componentry. There are five K-levels, ranging from levels 0 to 4 (Physiopedia, 2022a), and are outlined in Table 2.1.

Table 2.1. K-levels of mobility described by Physiopedia (2022a).

K-level	Description
K0	The patient does not have the ability or potential to ambulate or transfer safely with or without assistance, and a prosthesis does not enhance QoL or mobility.
K1	Patient has the ability or potential to use a prosthesis for transfers or ambulation in level surfaces at a fixed cadence. Defined as household ambulators.
K2	Defined as community ambulators, patients have the ability or potential for ambulation with the ability to transverse low-level environmental barriers such as curbs, stairs, or uneven surfaces.
K3	Patients have the ability or potential for ambulation with variable cadence. Defined as community ambulators who could transverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic use beyond simple locomotion.
K4	Patients have the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels. Describes the prosthetic demands of the child, active adult, or athlete.

As mentioned, the SIGAM mobility grades are a single-item scale, consisting of six categories that describes clinically useful levels of mobility in patients with lower limb amputations (Ryall et al., 2003). SIGAM mobility grades range from A to F are outlined in Table 2.2.

Limited indoor walking ability, defined as K-level 1 users or SIGAM mobility grades B to Cc, means that patients can complete transfers from a wheelchair to a bed or toilet facilities, ensuring independence and self-esteem (Rommers et al., 2001). Limited outdoor walking ability, defined as K-level 2 users or SIGAM mobility grades up to Dc allows patients to take part in social activities within their local community (Rommers et al., 2001). It is important to understand the functional levels amongst patients with TKA vs. patients with AKA.

Table 2.2. SIGAM grade classifications.

Grade classification	Description
A	Not using a limb/use for cosmesis only
B	Transfers/short distances
Ca	Walk indoors with a frame
Cb	Walk indoors with 2 sticks/crutches
Cc	Walk indoors with one stick/crutch
Db	Walk outdoors with 2 sticks or crutches
Dc	Walk outdoors with one stick or crutch
E	Occasional walking aid use
F	Walk anywhere in any weather without a walking aid

2.5.2.1. Temporal-Spatial Parameters

A variety of compensatory mechanisms may be observed within the gait patterns of AKA and TKA. The compensatory mechanisms include altered temporal-spatial characteristics during gait. Previous literature has investigated the gait pattern of AKA compared to able-bodied individuals (Bae et al., 2007; Wentink et al., 2013; Sturk et al., 2018), and previous research has compared level walking temporal-spatial parameters between patients with a TKA and AKA (Schuett et al., 2018; Sturk et al., 2018).

Joint forces, temporal-spatial variables and stance time is detrimental to patients with amputations when walking (Carpes et al., 2010; Highsmith et al., 2010; Ramakrishnan et al., 2018). Walking speed calculated from walking tests is an indicator of walking ability (van Velzen et al., 2006), and is a predictor of community mobility in populations, including for patients with a lower limb amputation (van Velzen et al., 2006; Batten et al., 2019). Further, walking speed can be influenced by age, gender, amputation level, and comorbidities (Batten et al., 2019).

Previous studies have reported slower walking speeds in patients with a lower limb amputation compared to able-bodied individuals (Boonstra et al., 1993; Pinzur, 1993; Hoffman et al., 1997; Bae et al., 2007; Goujon-Pillet et al., 2008; Hendershot & Wolf, 2014; Esposito et al., 2015; Guirao et al., 2017; Hendershot et al., 2018; Sturk et al., 2018). Sturk et al. (2018) reported average walking speeds during level walking for able-bodied individuals (1.4m/s ± 0.13), K4 users (1.16m/s ± 0.29) and K3 users (0.89m/s ± 0.13), thus a slower walking speed may relate to allowing extra time to plan movements or having a lower gait confidence. Furthermore, previous lower limb amputation gait studies have reported lower step lengths (Farahmand et al., 2006; Uchytil et al., 2014; Jarvis et al., 2017; Brandt & Huang, 2019), and an increased stance time (Farahmand et al., 2006; Vallery et al., 2011; Esquenazi, 2014; Jarvis et al., 2017; Kobayashi et al., 2020) in patients with amputations compared to able-bodied individuals. Although, Schuett et al. (2018) found no difference in walking speed, step width, cadence and step length between TKA and AKA, whereas Pinzur (1993) reported a faster walking speed in patients with TKA, resulting in a lower energy cost during ambulation compared to AKA. Schuett et al. (2018) recruited four males with TKA and contralateral BKA of trauma aetiology, aged between 23 and 41 years. They also recruited four males with AKA and contralateral BKA of trauma aetiology, aged between 22 to 27 years. Although the type was not specified, patients within their study were encouraged to wear their own custom prosthesis. Their power analysis determined a total of 56 patients with TKA and a matched same-sized cohort were required to identify minimum clinically important change in ambulation, thus concluding that a larger study with more participants would be required to make any definitive conclusions of gait temporal-spatial parameters in TKA and AKA. Lower limb symmetry in collected temporal-spatial parameters could influence the gait pattern interpretation.

Gait asymmetries can contribute to gait pathology (Moreno Hernandez, 2007; Kaufman et al., 2012; Uchytil et al., 2014). Patients with a lower limb amputation often present with gait asymmetries to protect their residual limb from increased loading by relying on their intact limb where possible (Nolan et al., 2003; Farahmand et al., 2006). However, asymmetry in temporal-spatial parameters between the intact and prosthesis reduces because of increased walking speed (Andriacchi et al., 1977; Murray et al., 1980; Jaegers et al., 1995b; Isakov et al., 1996; Nolan et al., 2003), reportedly up to 0.34% by Nolan et al. (2003). A possible explanation for asymmetries in temporal-spatial parameters during level walking may be due to a lack of confidence or discomfort when weight bearing through their prosthetic limb (Nolan et al., 2003; Highsmith et al., 2010; Sawers & Hafner, 2013; Brandt et al., 2017; Riveras et al., 2020). It is expected that patients with a higher K-level would walk faster and have independent mobility to complete functional tasks, while patients with a lower K-level have a slower walking speed (Batten et al., 2019). Batten et al. (2019) recruited two patients with KD, 30 patients with AKA and 78 patients with BKA. They discovered a greater median walking speed amongst patients recruited collectively with higher K-levels than those of a lower K-level (K4 1.06m/s and K1 0.17m/s, respectively). Despite Batten et al. (2019) recruiting patients with KD, they were unable to include separate median scores for gait speed due to the small sample size.

However, temporal-spatial gait parameters such as reduced velocity, swing time, stride length and increased stride time are potential markers for gait deficits and determine the risk of falling amongst individuals with reduced mobility and numerous diseases and conditions (Schülein et al., 2017). There are many pathological conditions that affect movement, but lower limb amputation has a detrimental impact on the functional mobility of a patient as their locomotor system is altered (van Velzen et al., 2006). Batten et al. (2019) discovered a greater median walking speed in individuals with non-vascular amputations compared to dysvascular amputations (0.63m/s and 0.5m/s, respectively). It is important to understand functional outcomes following lower limb amputation, so patients are provided with effective rehabilitation resources (Davies & Datta, 2003).

2.5.2.2. Walking

Following amputation patients are often prescribed with a prosthesis and undertake rehabilitation. The main rehabilitation goal after amputation is to enable patients to walk again and regain a level of functional ability that they had prior to their amputation (Brooks et al., 2001; Salih et al., 2016; Davie-Smith et al., 2017a). Walk tests can be completed as part of rehabilitation and to monitor treatment effectiveness across patients with lower limb amputations (Brooks et al., 2001). Several walk tests can be conducted based on the patients' needs and are used frequently in clinical settings to assess the functional walking of patients with a lower limb amputation (Batten et al., 2019), including time-based sub-maximal tests such as the two-minute walk test (2MWT), the six-minute walk test (6MWT), or fixed distance tests including the 10-metre walk test (Brooks et al., 2001). Additionally, patients with a lower limb amputation may complete the Timed-Up-and-Go (TUG) test and the L-test during their rehabilitation stages. The TUG test is a performance-based measure of functional mobility that was developed to identify mobility and balance impairments in adults (Wellmon, 2007, cited in Cameron and Monroe, 2007). The test requires sit-to-stand, walking, turning, and stand-to-sit. The L-test is a modification of the TUG test (Deathe & Miller, 2005), including the same testing procedures but with the walking path representing an "L" shape.

The 2MWT and 6MWT are measures of self-paced walking and functional capacity and can be used across a variety of health conditions, including lower limb amputation (Brooks et al., 2001). Both tests measure the distance a patient can walk in two-minutes or six-minutes. The 2MWT has good construct validity with similar walking measures (Brooks et al., 2001; Deathe et al., 2009), and has been used extensively throughout lower limb amputation research (Brooks et al., 2001; Andrysek et al., 2011; Reid et al., 2015; Karatzios et al., 2019). Further, the 2MWT is often used when ambulatory patients cannot walk for six-minutes (Brooks et al., 2001). Karatzios et al. (2019) recruited 12 patients with Gritti-Stokes amputations due to trauma, tumour and ischaemic causes, and 12 patients with an AKA due to trauma, tumour and ischaemic causes. Their results from the 2MWT indicated that overall, patients with a Gritti-Stokes amputation walked 122.75 metres (m), compared to 149.42m for AKA. These results contrasted with Reid et al. (2015), with 6 patients with a KD walking an average distance of 153.77m, and 28 patients with an AKA walking an average distance of 136.72m. Although amputation aetiologies were reported and include trauma, vascular, cancer, congenital and infection, it is unclear the specific aetiologies for KD and AKA (Reid et al., 2015). A Cochrane review by Barr and Howe (2018) aimed to identify and summarise the evidence evaluating prosthetic rehabilitation interventions following unilateral AKA or TKA in older dysvascular patients. They identified one study that met their inclusion criteria, therefore preventing drawing a conclusion.

On the other hand, the 6MWT was developed by the American Thoracic Society (2002) and is a sub-maximal exercise test that is used to assess aerobic capacity and endurance over six minutes. Clinicians including physiotherapists may use the 6MWT with patients with a lower limb amputation and assess longer walking distance abilities, as walking six-minutes reportedly allow patients to achieve distances exceeding 300m (Gailey et al., 2002; Resnik et al., 2011). The 6MWT has been validated for use with lower limb amputations (Reid et al., 2015; Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021). Walking distances have varied between TKA and AKA, with 17 patients with a TKA walking between 338.5m and 493m within six minutes, and 90 patients with an AKA walking between 302.3m and 450.2m (Reid et al., 2015; Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021).

The TUG test is a performance measure that incorporates walking, turning whilst walking, balance and transfers (Resnik et al., 2011). This measure determines the fall risk and measures the progress of balance, sit-to-standing, and walking in patients. Previous literature suggests that the TUG test is appropriate for older patients who are frailer or who use walking aids (Lafont et al., 1998; Lin et al., 2014). The TUG test can be used at any time during prosthetic rehabilitation, or to monitor changes in mobility after intervention or after discharge. The TUG test has good inter-rater and inter-rater reliability and is valid in lower limb amputations (Schoppen et al., 1999; Resnik et al., 2011). Further, this performance measure has been validated for use with lower limb amputations (Schoppen et al., 1999; Pernot et al., 2000; Reid et al., 2015; Hafner et al., 2017; Karatzios et al., 2019). In two of the studies, 19 patients with TKA of trauma, tumour and vascular aetiologies completed the TUG test in 16.2 seconds (s) compared to 14.9s in 48 patients with an AKA of trauma, tumour and vascular aetiologies (Hafner et al., 2017; Karatzios et al., 2019). The TUG test is an indicator of fall risk in those with a lower limb amputation, with a cut-off score greater than 19s indicating a greater risk of falling (Physiopedia, 2022b).

The L-Test of functional mobility (L-Test) is a performance measure that is used to assess physical function and dynamic balance ability. It is a modification of the TUG test and is designed to overcome the ceiling effect of the TUG found in higher-functioning patients (Kim et al., 2015). The L-Test provides an assessment of walking over a greater distance and involves turning in two directions. Further, it can be used to assess physical function in individuals with lower limb amputations and who are using a prosthesis (Deathe & Miller, 2005). The L-Test has been validated for use with lower limb amputations (Deathe & Miller, 2005; Rushton et al., 2015; Frengopoulos, 2017). Frengopoulos (2017) compared the L-test time taken across patients with BKA of vascular aetiology, patients with BKA of non-vascular aetiology, and patients with AKA or patients with bilateral amputations of any aetiology. Their results indicated that patients with an AKA or patients with bilateral amputations initially completed the L-Test in an average time of 36.10s, compared to 31.31s for patients with BKA of vascular aetiology, and 23.49s for patients with BKA of non-vascular aetiology.

2.5.2.3. Limitations to Amputation Clinical Outcomes Literature

The literature reviewed provides a detailed descriptive analysis of walking ability in patients with an AKA and have indicated a variety of compensatory mechanisms that are apparent in the gait of AKA. However, there are aspects within the literature that prevent the application of their findings to alternative levels of amputation.

Previous studies have compared the temporal-spatial parameters in individuals with a TKA and AKA (Pinzur, 1993; Kobayashi et al., 2013; Schuett et al., 2018). The age ranges of individuals with a TKA and AKA in the study by Schuett et al. (2018) ranged from 22 years to 41 years, thus having an average age of 24 years in individuals with an AKA and 32 years in individuals with a TKA. Causes of amputation have varied within the literature, with Pinzur (1993) focusing on vascular amputations and Schuett et al. (2018) focusing on traumatic amputations. Pinzur (1993) did not mention the age range of participants in their study, although the cause was related to peripheral vascular disease. Kobayashi et al. (2013) recruited one patient with a TKA aged 12 years who had their limb removed due to congenital fibular hemimelia and one patient with an AKA aged 42 years who had their limb removed due to trauma. Five patients with a TKA due to peripheral vascular disease reportedly walked at a preferred walking speed of approximately 0.32m/s in comparison to five patients with an AKA due to peripheral vascular disease who reportedly walk at a preferred speed of 0.23m/s (Pinzur, 1993), although it is unclear from this study the ages of the participants. However, patients with a TKA due to trauma reportedly walk at a preferred speed of 1.18m/s in comparison to patients with an AKA who walk at a preferred speed of 1.20m/s. The step cadence reported in literature of patients with a TKA appears different, with a cadence of 104 steps per minute (steps/min; Schuett et al., 2018) to 111 steps/min (Kobayashi et al., 2013). The cadence reported in patients with an AKA is comparable in both studies and was 106 steps/min (Kobayashi et al., 2013; Schuett et al., 2018). The difference in values in patients with a TKA could be as a result to the ages of patients with lower limb amputations used within the studies, as Kobayashi et al. (2013) recruited a 12-year-old individual with an amputation whilst Schuett et al. (2018) recruited patients with amputations aged between 23 to 41 years. However, there are so few studies reporting temporal-spatial parameters, in which some are double case-studies thus the data cannot be generalised.

Several studies investigated TKA and AKA; however, the literature has failed to compare the kinematic gait and temporal-spatial outcomes of patients with an AKA to individuals with a TKA (Vrieling et al., 2009; Highsmith, 2012; Fey et al., 2014; Prinsen et al., 2017a; Prinsen et al., 2017b; Crozara et al., 2019; Kobayashi et al., 2020). Alternatively, authors have combined the results of the patients with TKA and AKA. There are a variety of inconsistencies in participant characteristics amongst studies, therefore their findings from the literature may not apply to the younger and elderly populations. In previous studies, the participant age range was 18 to 85 years (Vrieling et al., 2009; Highsmith, 2012; Fey et al., 2014; Prinsen et al., 2017a; Prinsen et al., 2017b; Crozara et al., 2019; Kobayashi et al., 2020). One of these studies investigated participants between the age of 18 to 30 years (Vrieling et al., 2009) and an additional study restricted the age of participants between 18 and 85 years (Highsmith, 2012), whereas alternative studies did not restrict the age ranges (Fey et al., 2014; Prinsen et al., 2017a; Prinsen et al., 2017b; Crozara et al., 2019; Kobayashi et al., 2020). Additionally, patients with a lower limb amputation that participated in the studies had different causes of amputations. Highsmith (2012) did not mention the causes of amputation within the literature. The majority of patients with amputations had an amputation as a result of trauma, vascular and infections (Vrieling et al., 2009; Fey et al., 2014; Prinsen et al., 2017a; Prinsen et al., 2017b; Crozara et al., 2019; Kobayashi et al., 2020), and some amputations were as a result of tumours and cancer (Vrieling et al., 2009; Kobayashi et al., 2020), and osteosarcoma (Fey et al., 2014; Prinsen et al., 2017a; Prinsen et al., 2017b). It is likely that due to TKA being a rare procedure, recruiting from this population may contribute to the wide-ranging patient characteristics. Issues with possible recruiting bias and a small sample size can cause an influence on the comparison made between studies and therefore it is important to consider these factors when interpreting results from similar literature.

The literature previously listed also uses a range of methodological approaches to collect temporal-spatial parameters, kinetics, and kinematic data. In most studies mentioned above, all patients with a lower limb amputation were asked to walk at their preferred walking speed (Vrieling et al., 2009; Fey et al., 2014; Prinsen et al., 2017a; Crozara et al., 2019; Kobayashi et al., 2020). However, Prinsen et al. (2017a) manipulated walking speed on a treadmill: preferred, 70% preferred walking speed and 115% preferred walking speed. Patients with a lower limb amputation tend to walk at their preferred walking speed. Secondly, patients with traumatic amputations reportedly walk at a quicker preferred walking speed (Fey et al., 2014; Schuett et al., 2018) compared patients with a vascular amputation (Pinzur, 1993; Crozara et al., 2019). Patients with amputations due to peripheral vascular disease rarely achieve walking and prosthetic ability of those with amputations due to trauma or cancer, as they do not possess the energy expenditure to overcome the metabolic demands of walking with a prosthesis (Pinzur, 1993; Ettema et al., 2021). Therefore, comparing results between patients with a lower limb amputation with different causes of amputation may be problematic. A clear comparison of gait between patients with a TKA and patients with an AKA has evidently been challenging, thus requiring further exploration as to whether amputation aetiology impacts gait parameters between these two cohorts.

2.5.3. Balance and Postural Control

2.5.3.1. Seated Balance and Postural Control

Individuals spend most of their time sitting, with the exact amount of time determined by aspects of their life including profession, lifestyle and health (Hägg & Nielsen, 2016). Seated balance involves the ability to maintain the body's posture without falling over and to balance the body mass over the base of support (Dean et al., 1999a; Pedersen et al., 2016), returning to equilibrium position following perturbations (Andersson & Winters, 1990; Vette et al., 2010). The ability to balance whilst sitting and reaching for a range of objects within and beyond the arm's length is critical to an individual's independent living (Alexander, 1994; Dean & Shepherd, 1997; Dean et al., 1999a; Messier et al., 2005) and QoL (Dean et al., 1999a; Messier et al., 2005). Secondly, the ability to maintain equilibrium during perturbations when sitting down is critical for many activities including wheeled mobility (Ousley, 2015). Performance during seated reaching tasks requires coordination of the trunk and upper limbs motion (Son et al., 1988; Dean & Shepherd, 1997). Postural stability can be maintained through a combination of body segments, including bones, ligaments, tendons, and muscles (Riedel et al., 1992). The responsibility of lower limbs during seated activities are not only to provide a larger base of support, but the lower limbs reportedly play a vital, active role in balance (Dean & Shepherd, 1997; Dean et al., 1999b). There are a variety of factors that can influence the role of the lower limbs whilst maintaining balance during seated activities, including the distance and direction of the reach, seat height, and the extent of thigh support on the seat (Arborelius et al., 1992; Dean & Shepherd, 1997). During a reach, it has been suggested that the lower limbs and the trunk act in unison to stabilize the body to minimize the centre of mass displacement (Kaminski, 2007).

Measurements of sitting postural control should take into consideration the multidirectional functions and foot support as they have an impact on sitting balance (Chari & Kirby, 1986; Kerr & Eng, 2002). The lower limbs contribute widely to the performance of reaching whilst in a seated position, calculating to approximately 30 centimetres (cm) difference between having both feet positioned on the ground with thigh support, compared to having both feet positioned off the ground with ischial support (Chari & Kirby, 1986). The Function in Sitting Test (FIST) was developed to provide sitting balance measures (Gorman et al., 2014a). It consists of 14 functional sitting tasks that quantify performance whilst assessing postural control and function and demonstrates excellent intra-rater and inter-rater reliability (Gorman et al., 2014a). The FIST may fill a gap in sitting balance abilities, which could provide clinicians with a measure of balance recovery until standing balance tests are appropriate (Gorman et al., 2014a). The FIST has not been used in lower limb amputation research but has been used in patients with neurological conditions (Gorman et al., 2014b) and sitting balance dysfunction (Gorman et al., 2014a).

2.5.3.1.1. Lower Limb Amputation Seated Balance and Postural Control

Many patients with amputations lead a sedentary life, with those patients who cannot tolerate a prosthesis having a wheelchair for transportation. In addition to walking performance, the postural changes and the increasing load of the amputated limb may increase additional blood flow discrepancies in patients with a vascular amputation (Gauthier-Gagnon et al., 1986; Duclos et al., 2009), and pain within the back and leg

(Hagberg & Brånemark, 2001). The asymmetrical weight-bearing can further cause postural asymmetries amongst patients with a lower limb amputation that is difficult to correct using training (Gauthier-Gagnon et al., 1986; Duclos et al., 2009). The literature has reported comparison of patients with an AKA performance of seated balance against patients with a BKA and able-bodied individuals (Hendershot & Nussbaum, 2013). Two studies combined the results of patients with an AKA, BKA and able-bodied individuals and presented a variety of distance and velocity parameters together (Overgaard et al., 2018; Butowicz et al., 2019). One study investigated patients with an AKA only (Hägg & Nielsen, 2016).

In the study by Hendershot and Nussbaum (2013), prosthesis users with trauma, congenital deformity and cancer amputation aetiologies performed seated maximum voluntary contractions for trunk flexion and extension for left and right lateral bending, collecting center of pressure data and electromyographic data of bilateral lumbar (L3) erector spinae, rectus abdominis, and external oblique muscles. Four patients with an AKA aged 39.0 years ± 12.0 years experienced a larger anterior-posterior and medio-lateral root mean square distance compared to four patients with a BKA aged 43.0 years ± 26.1 years and eight able-bodied individuals. Participants were instructed to sit on an unstable chair that was rigidly attached above a force platform. Center of pressure velocity in antero-posterior and medio-lateral directions were slower in patients with a lower limb amputation than able-bodied. The increase of center of pressure sway measures in patients with a lower limb amputation suggests these individuals may have weaker core muscles in both directions (Hendershot & Nussbaum, 2013). Patients who are not predicted to walk or stand following their amputation may be prescribed a cosmetic prosthesis as it may improve sitting forward reaching abilities (Chari & Kirby, 1986). In a study by Overgaard et al. (2018), three patients with an AKA and two patients with a BKA were instructed to sit quietly on a chair with a pressure mat and with their feet off the ground and facing forwards. Amputation aetiologies including atherosclerosis gangrene and diabetes mellitus, gender and ages were reported; however it was unclear for which amputation level these related to. Recordings were completed under conditions including with and without the prosthetic limb. A 4-week rehabilitation and prosthesis fitting programme was provided for new patients with amputations who were eligible for a prosthesis. The first stage of the programme was an inpatient intensive training programme, consisting of functional training (gait training, weight-bearing, balance training, transfers) twice a day, lasting one week for patients with BKA and two weeks for patients with AKA (Overgaard et al., 2018). The remaining of the 4-week rehabilitation and prosthesis fitting programme was outpatient-based with strength- and gait-training occurring weekly. Postural control and QoL were assessed at baseline and after the 4-week rehabilitation and prosthesis fitting programme. Despite the standing force plate measures, TUG test and Berg Balance Scale results improving after completing the rehabilitation programme, the results illustrated that there was a trend of a worsened seated postural control in patients with and without a prosthesis after the rehabilitation programme (Overgaard et al., 2018), showing an increase in total center of pressure excursion total length and velocity, further implying that seated postural control was dependent on both legs acting as lever arms. However, the authors outlined that the three patients with AKA had somewhat better seated postural control compared to the two patients with BKA both with and without a prosthesis (Overgaard et al., 2018). Upon critically interpreting these findings, you would expect patients with an AKA to have worsening seated postural control due to the discrepancy contribution of a shortened mechanical lever arm and an increase in additional blood flow discrepancies compared to BKA. The authors used a stable sitting platform, which may not have fully explored seated postural control.

2.5.3.2. Standing Balance and Postural Control

The ability to stand upright on two feet is crucial for independence and as a precursor to completing activities of daily living (Winter et al., 1998; Buckley et al., 2002; Moe-Nilssen & Helbostad, 2002; Vrieling et al., 2008; Kozáková et al., 2009; Ku et al., 2014; Charkhkar et al., 2020). Standing postural control is essential to maintain an individual's balance (Koceja et al., 1999).

Standing balance is maintained by keeping the body's centre of pressure within the support base (Horak et al., 1989; Blackburn et al., 2000; Buckley et al., 2002; Gillette et al., 2003; Vanicek et al., 2009). Postural control relies on an individual's ability to predict, detect, and encode passive and dynamic disturbance to posture characteristics (Horak et al., 1989). Standing balance can be achieved by a combination of coordinated joint rotations that involve the centre of pressure movement between the two feet (Gillette et al., 2003). Proactive or reactive adjustments amongst able-bodied individuals are characterised by motor patterns that occur and are required to adjust the positioning of the body's centre of mass (Winter, 1995). The ankle joint and lower limb musculature contribute extensively to maintaining balance by shifting the centre of pressure towards a less efficient hip strategy (Horak & Nashner, 1986; Vrieling et al., 2008; Damayanti Sethy et al., 2009; Geurts & Mulder, 2009). Adjusting the foot placement during standing balance can change the constraints of the lower limbs and may alter postural responses (Gillette et al., 2003). Maintaining balance and postural control can be achieved using somatosensory (proprioception, joint and cutaneous), visual, and vestibular sensory sources of feedback (Winter, 1995; Blackburn et al., 2000; Kozáková et al., 2009; Arifin et al., 2015). Sensory information allows changes to be detected regarding the body's position of the centre of gravity, and correcting them where necessary (Horak et al., 1989).

2.5.3.2.1. Lower Limb Amputation Standing Balance

Patients with a lower limb amputation experience impairment in postural control (Buckley et al., 2002; Geurts & Mulder, 2009; Kozáková et al., 2009; Rougier et al., 2009; Hlavackova et al., 2011; Kristensen et al., 2014; Wong et al., 2014). Specific anatomical structures, responsible for XYZ are missing and compensatory adjustments are needed to maintain postural control when compared to able-bodied individuals (Vrieling et al., 2008). Patients with a lower limb amputation tend to have a reduced postural control ability due to the loss of the somatosensory and neuromuscular feedback from their lower limb but also the lack of the foot and ankle to allow smaller compensatory movements of shift in weight to maintain balance. Previous literature has investigated balance and postural control when standing in patients with an AKA (Hlavackova et al., 2011; Highsmith et al., 2014) compared to able-bodied individuals (Fernie & Holliday, 1978; Vrieling et al., 2008) and BKA (Fernie & Holliday, 1978; Buckley et al., 2002; Vrieling et al., 2008; Damayanti Sethy et al., 2009; Rougier et al., 2009; Nederhand et al., 2012; Kristensen et al., 2014). Hlavackova et al. (2011) recruited eight patients with trauma AKA and were instructed to stand still on a plantar pressure data acquisition system with their eyes closed. Results found a larger body weight distribution was applied to the intact limb and more regular centre of foot pressure was applied to the intact limb compared to the affected limb, thus highlighting the non-equally contribution of control. Two studies included patients with a TKA, AKA and BKA to make direct comparisons to able-bodied individuals (Geurts et al., 1991; Geurts et al., 1992). Geurts et al. (1991) recruited two patients with a TKA due to vascular and infection aetiologies, and two patients with an AKA due to trauma and infection aetiologies. They found that the balance behaviour of the amputation cohort was less efficient during the dual-task condition compared to single-task condition of the Stroop test, thus indicating that lower limb amputations affect postural control in the sagittal plane and frontal plane. Summers et al. (1988) included patients with a TKA, AKA, BKA, and a through-hip amputation.

There are several tests that can be used to measure dynamic balance, including the functional reach test (FRT). The FRT measures the difference between the arm's length and a maximal forward reach when using a stable support base (Leifsdóttir & Tómasdóttir, 2021). Leifsdóttir and Tómasdóttir (2021) recruited one patient with a lower limb amputation and performed the FRT. The authors reported that the lowest distance reached was from the participant with an amputation, and the second lowest score was from the oldest participant. They concluded that age and lower limb loss may influence balance. However, the participant's level of amputation was unclear, and they only recruited one participant with an amputation, thus warranting further exploration. Further, Hill et al. (2020) investigated the lateral reach test rather than a forward reach. They recruited nine patients with an AKA, with the distance reached greater on the side of their intact limb was compared to their affected side. Damayanti Sethy et al. (2009) investigated the effect of balance training on balance control of patients with a unilateral lower limb amputation. They recruited 30 patients with an AKA and BKA, and split patients into an experimental group who received Phyaction balance exercise with conventional training (entailing of a platform board that swayed over a diameter of 40cm in medio-lateral and antero-posterior positions), and control group who received conventional training only. The results indicated that patients with lower limb amputations in the experimental group were able to reach further after completing training compared to the control group. However, there was no discussion of which level of amputation reached further. When comparing scores between patients with a lower limb amputation (Hill et al., 2020) to community-dwelling adults with disability when performing activities of daily living (Lin et al., 2004), community-dwelling adults aged between 65 and 74 years were able to reach an average of 15.8cm (Lin et al., 2004), compared to 10.9cm reached in patients with a lower limb amputation (Hill et al., 2020). However, there has been suggestions that FRT does not measure dynamic balance, but it could indicate other valuable information about balance (Wernick-Robinson et al., 1999; Leifsdóttir & Tómasdóttir, 2021), such as trunk and lower extremity range of motion and strength, willingness to risk loss of balance, or fear of falling (Wernick-Robinson et al., 1999).

Patients with a lower limb amputation are reported to show asymmetry during weight-bearing, including larger center of pressure displacements under the prosthesis foot (Summers et al., 1988; Geurts et al., 1991; Rougier et al., 2009; Hlavackova et al., 2011). Additionally, they use their intact limb as their primary control during static and dynamic activities (Geurts et al., 1991; Kozáková et al., 2009; Kristensen et al., 2014; Arifin et al., 2015), and rely on visual feedback to maintain balance and posture due to the loss of somatosensory information in the prosthesis (Vrieling et al., 2008; Arifin et al., 2015; Sadeghisani et al., 2016; Charkhkar et al., 2020). Further, balance problems in patients with vascular amputations may be because of diabetic neuropathy in the remaining limb and retinopathy impairing vision (Burger & Marinček, 2001).

2.5.3.3. Limitations to Lower Limb Amputation Literature

Previous literature has investigated the performance of activities of daily living in patients with an AKA and determined the kinematic joint profiles, although they may appear different compared to able-bodied individuals. There have been no studies reporting a direct comparison of the kinematic joint profiles for individuals with TKA and AKA when performing activities of daily living. The lack of literature investigating activities of daily living in patients with an AKA indicates that further investigation into these tasks would be beneficial and a direct comparison to patients with a TKA may assist amputation physiotherapists and clinicians when determining on the level of amputation to perform.

Previous studies that have investigated balance and postural control have provided a clear description to how patients with a lower limb amputation perform specific tasks. Although the literature has determined how patients with a BKA and AKA adapt their postural control, the literature fails to incorporate patients with a TKA to determine how their postural control are affected during quiet standing. It is important to determine the differences in quiet standing across a range of amputation levels to ensure the differentiate postural characteristics accordingly. If lower limb amputation results are combined within a research study, it is likely to mask the differences in balance and postural control associated with different causes and levels of amputation. Postural control differs between AKA and BKA, due to the role of the prosthesis componentries. For patients with a BKA, the patella is preserved as the procedure is performed through the tibia and fibula, thus providing stability when compensating through a prosthetic ankle. However, for patients with an AKA, the procedure is performed through the femur thus losing the patella and lower limb skeletal and musculature. For mobilising, this cohort of patients require a prosthetic ankle and knee, significantly affecting their gait. Changes in gait for a patient with an AKA include pelvic tilt, pelvic obliquity, and hip abduction (Kowal et al., 2021), which contribute to center of pressure displacement and consequently reducing postural control. Although the literature has identified balance and postural control differences between able-bodied individuals and patients with a lower limb amputation, it is difficult to make a comparison within studies as a range of methodologies are used.

Authors of studies have assessed lower limb amputation standing balance using clinical measures, including the one leg balance test (Burger & Marinček, 2001; Eijk et al., 2012) and the Berg Balance Scale (Major et al., 2013; Wong et al., 2015a). The Berg Balance Scale has been validated for use with lower limb amputations, is reported to have good validity and reliability, and is designed to assess the balance of an individual using a 14-tasked scale (Major et al., 2013). Although Burger and Marinček (2001) recruited patients with a BKA and AKA to compare with healthy able-bodied male individuals, the single leg balance test results showed no difference in standing time in lower limb amputations. However, they discovered that patients with amputations due to trauma were able to perform the one leg balance test for longer in comparison to patients with a lower limb amputation due to peripheral vascular disease (Burger & Marinček, 2001). They suggested that patients with an amputation due to peripheral vascular disease may have more problems with balance because of diabetic neuropathy and retinopathy due to the disease (Burger & Marinček, 2001). The results from the Berg Balance Scale by Major et al. (2013) determined that a combined average score from 30 patients with a unilateral and bilateral BKA and AKA of 51 were lower than the reported score of 54 by Yazicioglu et al. (2007). Participants within the study by Yazicioglu et al. (2007) performed the Berg Balance Scale, Houghton Scale of prosthetic use, and Locomotor capabilities index. However, the 24 participants recruited for this study had BKA or chopart's amputations. Despite research being completed using lower limb amputations to assess standing balance, there is no comparison of TKA and AKA.

2.5.4. Flexibility

Physical capacity can be assessed using flexibility (van Velzen et al., 2006). Flexibility is the ability of a joint to move through a maximum unrestricted range of motion (Mayorga-Vega et al., 2014). There are several variables that affect the loss of joint flexibility, these being injury, lack of stretching, or inactivity. Range of motion is influenced by the mobility of soft tissues that surround the joint, including muscles, ligaments, tendons and skin. Sitting balance, bed mobility and transfers are enabled by strong, flexible back and abdominal rotators, extensors and flexors, and hip extensors (Esquenazi & DiGiacomo, 2001). Maintaining a high level of flexibility is an important factor of health-related fitness, and can prevent risk of falling, postural deviations or gait limitations (Cuberek et al., 2013). Flexibility can be measured using the sit-and-reach test. Sit-and-reach tests are widely used measures of flexibility in hamstrings and the lower back (Holt et al., 1999; Castro-Piñero et al., 2010; Mayorga-Vega et al., 2014; Cuberek et al., 2013).

2.5.4.1. Lower Limb Amputation Flexibility

Sufficient lower limb flexibility following amputation is crucial to preparation of the residual limb for a prosthesis to avoid contractures (Esquenazi & DiGiacomo, 2001). Further, adequate range of motion at the ankle, knee and hip of the intact limb is required to assist with prosthesis use and transfer abilities (Esquenazi & DiGiacomo, 2001). Losing the dorsiflexion ability in the intact limb may be more problematic for patients with vascular disease as increased stress is placed on the plantar structures, leading to foot deformities and breakdown of the foot (Esquenazi & DiGiacomo, 2001). Further problems may arise from weak muscles, deceased muscular endurance and poor balance (Burger & Marinček, 2001).

Lower limb flexibility was assessed in patients with a lower limb amputation using the sit-and-reach test (Burger & Marinček, 2001), as part of the Fullerton Functional Fitness Test (Miotto et al., 1999; Rikli & Jones, 1999). They recruited healthy sedentary men, 17 patients with a BKA and 11 patients with an AKA. The results indicated that patients with a BKA could reach 41.5cm, compared to patients with an AKA who could reach 39.5cm. Patients with amputations due to peripheral vascular disease could reach 43.4cm, compared to 37.2cm in trauma amputations, identifying no significant differences between the cohorts (Burger & Marinček, 2001). The difference in distance reached in patients with a BKA and AKA may be influenced by the level of amputation; patients with an AKA lose two main joints and many muscles are cut (Jaegers, 1993), suggesting that strength and flexibility from a longer lever may influence the sit-and-reach test. However, patients with a TKA were not included in their study.

2.5.5. Falls

2.5.5.1. Falls Background

A fall is described as an event that results in an individual coming to rest unintentionally on the ground (Dionyssiotis, 2012). Falls often occur when postural control is obstructed by an external perturbation (Miller & Deathe, 2004; Vrieling et al., 2008; Damayanti Sethy et al., 2009). The number of falls represent a significant public health risk, approximating to 12 million able-bodied individuals falling each year (Stevens et al., 2006; Wong et al., 2015a). Falls can be categorised into three different types according to the factor of the incident (Mata et al., 2017). An accidental fall occurs when an individual stumbles or slips and may be influenced by environmental factors (Mata et al., 2017). An anticipated physiological fall occurs when individuals show symptoms that can indicate the probability to fall and are often assessed using clinical measures (Mata et al., 2017). An unanticipated physiological fall is unpredictable and can be associated with fainting (Mata et al., 2017).

Falls have many different causes, with the elderly having several predisposing risk factors (El Miedany et al., 2011). Falls can be markers of poor health, declining function, and significant morbidity (Miller et al., 2001a; Ülger et al., 2010; Rice et al., 2015). Issues in proprioception and coordination, changes in body weight, muscular strength and endurance reductions, sight and hearing problems, loss of sensation and existence of cognitive function disorders can increase the risk of falling (Ülger et al., 2010). A fall can lead to a range of injuries, from a scrape or bruising to significant impairments including concussions, fractures, or death (Miller et al., 2001b; Rice et al., 2015; Mata et al., 2017). Furthermore, researchers suggest that faller and non-faller older individuals experience psychological difficulties relating to falls (Tinetti et al., 1990; Jørstad et al., 2005; Major et al., 2013). These psychological consequences are categorised as fear, self-efficacy, activity avoidance, and loss of confidence (Tinetti et al., 1990; Jørstad et al., 2005). Fear of falling, described as the avoidance of activities that an individual can perform (Hunter et al., 2018), is a common fear amongst community-dwelling older individuals (Howland et al., 1993; Jørstad et al., 2005).

2.5.5.2. Falls in Lower Limb Amputations

Lower limb amputations cause alterations in ambulatory skills amongst patients (Pauley et al., 2006; Ülger et al., 2010). Key factors that hinder the ability for patients with a lower limb amputation to achieve maximum functional capacities are falls and the fear of falling (Kaufman et al., 2014). Falls are mainly associated with a functional disability, and can indicate a reduction in independence, mobility, and an individual’s self-imposed restriction towards activities of daily living (Tinetti et al., 1994; Miller & Deathe, 2004). Patients with a lower limb amputation experience a higher number of falls compared to able-bodied individuals (Arifin et al., 2015; Wong et al., 2015a; Wong et al., 2016a; Mundell et al., 2017), due to the deficits when controlling movements in the anterior-posterior and medial-lateral positions (Arifin et al., 2015). Approximately 50% of individuals with a lower limb amputation sustain a falls-related injury, with 60% of fallers reporting that falls negatively affect their activities of daily living (Kulkarni et al., 1996; Shirota et al., 2015). Falls occur more commonly when patients with lower limb amputations are wearing their prosthesis and are performing activities of daily living, including walking (Kulkarni et al., 1996; Hunter et al., 2018). There are two aspects of balance and mobility that are identified as being high-risk factors for falls and their injuries: the inability to step quickly in different directions and the inability to safely turn around whilst walking (Dite et al., 2007). Patients with a lower limb amputation face challenges regarding these two risk factors when completing activities of daily living (Dite et al., 2007). Alternative identified risk factors of falling reported by Pauley et al. (2006) and Ülger et al. (2010) are lower limb weakness (Edelberg, 2001), cognitive impairment (Tinetti et al., 1988), postural hypotension (Bumin et al., 2002), abnormal proprioception (Woolley et al., 1997), polypharmacy (Edelberg, 2001), foot problems (Edelberg, 2001), and peripheral artery disease (Gardner & Montgomery, 2001). The consequences of falling amongst patients with a lower limb amputation involve sustaining injuries that require ongoing medical treatment or experiencing psychological issues that may impact future prosthesis functioning (Kulkarni et al., 1996; Gooday & Hunter, 2004; Pauley et al., 2006; Yu et al., 2010; Felcher et al., 2015; Hunter et al., 2017; Hunter et al., 2018). Fear of falling is present amongst 49.2% of patients with a lower limb amputation when using a prosthesis (Miller et al., 2001a; Hunter et al., 2018).

According to the literature, patients with an AKA fall at a similar rate to balance-impaired individuals (Miller et al., 2001a; Shirota et al., 2015), including the elderly (Miller et al., 2001b; Chang et al., 2004; Pauley et al., 2006; Mundell et al., 2017). Patients with an AKA have a yearly fall incidence of between 64% and 66% (Kulkarni et al., 1996; Miller et al., 2001a; Crenshaw et al., 2013). The fall-related costs for patients with an AKA are similar to older adults (Mundell et al., 2017). Falls are associated with a fear of falling and a lower level of confidence (Miller et al., 2001a; Chihuri & Wong, 2018). As falling is common amongst patients with a lower limb amputation, nearly half report a fear of falling (Miller et al., 2001b; Major et al., 2013; Wong et al., 2015a). Miller et al. (2001a) discovered that 52.4% of patients with an AKA or BKA who wore their prosthesis daily experienced a fall within the prior 12 months. Amongst the fallers, 75% of patients with a lower limb amputation fell more than once, and 40.4% of patients with amputations suffered an injury (Miller et al., 2001a). Major et al. (2013) reported that 12 months prior to examination, 66.7% of patients with a lower limb amputation were wearing their prosthesis at the time of their fall. Of the reported fallers, 43.3% of patients with a lower limb amputation fell more than once, with 57% of those patients with a lower limb amputation sustaining an injury (Kulkarni et al., 1996). Hunter et al. (2018) reported that 7.4% of patients with a lower limb amputation fell during their rehabilitation and were wearing their prosthesis at the time of falling. Secondly, 25.9% of patients with a BKA and AKA reported that the fear of falling affected their activities of daily living at follow-up. Patients with a lower limb amputation within the study by Hunter et al. (2018) considered falls to be preventable and thus ranked falls and prevention as an important health concern. Chihuri and Wong (2018) reported that amongst their 114 patients with a BKA and 125 patients with an AKA, 65.8% of patients that had more than two falls did not sustain an injury, although there was no significant difference in Berg Balance Scale score in patients with a lower limb amputation who sustained an injury vs. no injury. However, Chuhuri and Wong (2018) reported the Berg Balance Scale scores as an average of items 6, 10 and 11, thus not representative against the three thresholds outlines from the score (0-20 high falls risk, 21-40 medium falls risk, 41-56 low falls risk). Miller et al. (2002) reported that 47.6% of patients with an AKA and BKA had fallen in the 12 months prior to participation, with 19.8% sustaining an injury. Miller et al. (2001b) reported that 52.4% of patients with an AKA and BKA had fallen in the 12 months prior to participating in the research. Yu et al. (2010) recruited 370 patients with a BKA, AKA and TKA, and reported the incidence of falling was 16.5%, with 44.3% of falls occurring during the daytime between 07.00 and 15.00 hours, and 36.1% occurring from 15.00 to 23.00 hours. Further, 62.3% of falls occurred within the bedroom, and 18% of falls occurred within the bathroom (Yu et al., 2010). Injuries were sustained in 60.7% of patients with a lower limb amputation, with most injuries sustained on the residual limb (Yu et al., 2010). Further, Yu et al. (2010) reported patients with an AKA to have less of a fall risk in comparison to BKA, contradicting previous research (Miller et al., 2001a). Despite Yu et al. (2010) recruiting patients with a TKA in their study, they did not individually identify the falls and injuries sustained with TKA as an individual level of amputation. This may explain the contrast in results, however further research is warranted to investigate falls in patients with TKA.

An alternative method that can assess falls is using the Tinetti assessment. This measure investigates the perception of balance and stability during activities of daily living and their fear of falling. This assessment has not been performed in patients with a TKA in the wider literature.

2.5.6. Quality of Life and Self-Reported Measures in Lower Limb Amputations

Confidence is a predictor of engagement in activity rather than the skill or ability of an individual (Bandura, 1982; Miller & Deathe, 2004). An individual's balance confidence or perception of their ability to maintain balance differs from their objectively measured balance ability (Wong et al., 2015a). Patients with a lower limb amputation and a better level of functional balance ability may feel more confident within their community and would engage in activities that have the potential to expose them to falls, for example stepping up a raised curb (Wong et al., 2016a). However, having psychoemotional feelings including a fear of falling or a decreased level of confidence may hinder their physical function, mobility, ability of perform activities of daily living, and integration within the community in addition to having a physical impairment (Miller et al., 2002; Wong et al., 2015b). A reduction in balance confidence amongst patients with a lower limb amputation may be likely given the altered gait pattern associated with prostheses, the loss of proprioception and the altered postural sway (Miller & Deathe, 2004). Balance confidence and QoL can be measured using self-report measures including questionnaires (Hart et al., 2015; Wong et al., 2015a). Individuals who experience lower limb amputation often experience complex and variable emotions, including depression, anxiety and other psychological responses (Sarroca et al., 2021; Rahim et al., 2022). It is reported that post-operative outcomes such as pain increases rates of depression and anxiety (Rahim et al., 2022), affecting the QoL of patients with amputations (Sarroca et al., 2021).

There are numerous outcome measures that can be used throughout lower limb amputation research. The rational for selecting these outcomes of interest are that many, if not all, are recommended in the British Association of Chartered Physiotherapists in limb loss Absence Rehabilitation (BACPAR) toolbox. BACPAR is a Professional Network of the Chartered Society of Physiotherapy, and it provides a nationwide network for physiotherapists involved in limb absence and prosthetic rehabilitation. Further, BACPAR supports the promotion of evidence-based practice and research and is committed to education.

2.5.6.1. Quality of Life

2.5.6.1.1. EQ-5D-5L

The EQ-5D-5L is a preference-based tool for describing and evaluating an individual's health-related QoL (Conner-Spady et al., 2015). It has been used to estimate utilities of patients with type 2 diabetes in large questionnaires in a range of countries (Mata et al., 2016). The EQ-5D-5L is based on a descriptive system that is comprised of five health dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Conner-Spady et al., 2015; Wang et al., 2016). The dimension of the self-reported measure has five response categories of no problems, some problems, and extreme problems (Conner-Spady et al., 2015; Wang et al., 2016).

Davie-Smith (2017) indicated that patients with lower limb amputations because of diabetes reported to have a higher QoL 6 months and 12 months post-amputation, compared to patients with non-diabetic amputations. Patients with an AKA had a lower QoL 6 months and 12 months post-amputation compared to BKA. Patients with a TKA were included in their study, but the results were combined with AKA as there was only three individuals with TKA.

2.5.6.1.2. Short-Form Health Survey 36

The Short-Form Health Survey 36 (SF-36) is the most used health-related QoL measure across physical activities and research (Findler et al., 2001; Barnett et al., 2013; Hart et al., 2015). The SF-36 measures health-related QoL in adults and is an easy self-administering tool (Hart et al., 2015). It is a multi-dimensional scale comprising of 36 items, 8 health-related categories and 2 other categories. The dimensions within the SF-36 are vitality, physical functioning, bodily pain, general health, physical role functioning and mental health (Hagberg et al., 2004; Gunawardena et al., 2006; Barnett et al., 2013).

Previous research in Sweden (Hammarlund et al., 2011) and Turkey (Burçak et al., 2021) investigated QoL, functional status, and pain in individuals with a lower limb amputation, including TKA. Hammarlund et al. (2011) discovered that patients with TKA had significantly lower physical functioning and significantly higher emotional role compared to the normative Swedish data they used. However, there was no significant differences between the levels of amputation (Hammarlund et al., 2011). Although Burçak et al. (2021) examined TKA, the results were combined with AKA for the mechanical prosthesis component and microprocessor prosthesis component groups. The reasoning for the authors combining TKA and AKA results were due to the small number of patients with TKA recruited (n=4).

2.5.6.2. Locomotor Capabilities Index-5

The Locomotor Capabilities Index (LCI-5) is a 14-item questionnaire that is designed to measure the walking ability of patients with lower limb amputations (Larsson et al., 2009). The LCI-5 is validated for use in patients with lower limb amputations. It has good test-retest reliability, contrast validity and internal consistency. The LCI-5 is easy to administer and has been proposed to evaluate ambulatory skills using a prosthesis (Franchignoni et al., 2004). The questionnaire computes the global, basic, and advanced locomotor skills (Gauthier-Gagnon & Grisé, 2006). The LCI-5 is composed of 14 questions on different locomotor activities and is based on basic and advanced activities. Results taken from the LCI-5 are interpreted using a 5-level, ranging from 0 not being able to and 4 able to accomplish the activity.

Further, 144 patients with a lower limb amputation were recruited for their study, however all results were combined and presented as one score. The mean basic LCI-5 score was 17.1 ± 5.5 and the advanced LCI-5 score was 11.3 ± 7.8, thus higher scores reflecting greater locomotor capabilities with a prosthesis and less dependence on assistance from individuals or aids. Although the authors presented mean and median scores for each level of the questionnaire, there were no separate scores for the different levels of amputation. Glemne et al. (2012) investigated the perioperative characteristic and functional outcomes in patients with lower limb amputations. Three patients with a TKA were recruited as part of their study. Despite combining the results of all levels of amputation (unilateral BKA, AKA and TKA, and amputations with existing contralateral amputations), the LCI-5 score 6 months post amputation was significantly lower than the score recorded before amputation (LCI-5 post amputation 21 vs. before amputation 24, p=0.039).

2.5.6.3. Houghton Scale of Prosthetic Use

The Houghton Scale of prosthetic use has been applied for classifying individuals after prosthetic rehabilitation according to walking ability categories (Wong et al., 2016b). It is a self-administered tool with and is scored out of 12, the first 3 items attempt to capture prosthesis wearing habits, and the fourth question has dichotomous items that investigate comfort levels when negotiating outdoors (Devlin et al., 2004). The results of the scale are reported as a higher score indicating greater function and were determined by three categories of ambulation: i) community (having a score more than or equal to 9), ii) limited community and household (score of between 6-8) and iii) limited household (having a score less than or equal to 5).

Previous literature has investigated the Houghton Scale of prosthetic use (Hagberg et al., 1992; Miller et al., 2001b; Devlin et al., 2004; Wong et al., 2016b; Repo et al., 2018). Hagberg et al. (1992) recruited 59 patients with BKA, TKA, and AKA. The results of their study indicate that 41% of patients with TKA wore their prosthesis for 9 or more hours per day, in comparison to 22% of patients with AKA. No patients with a TKA reported wearing their prosthesis less than 25% of waking hours, compared to 28% of individuals with AKA who stated that they never wore their prosthesis. Wong et al. (2016b) recruited 145 patients with unilateral lower limb amputations, 23 patients with bilateral lower limb amputations and 12 patients who did not list their level of amputation. Despite recruiting 2 TKA and 63 AKA, the authors combined the results of all participants to gain an average Houghton Scale score of 7.6. They discussed that vascular and non-vascular amputation aetiologies were represented throughout the Houghton Scale of prosthetic use category, however people with vascular amputations were significantly more likely to be in the limited household category than the community category (Wong et al., 2016b). Repo et al. (2018) recruited 124 patients with lower limb amputations as part of adapting the Houghton Scale into Finnish and assessing the psychometric properties. Although they recruited three patients with a TKA, results of the study were combined into one score. There was no statistics presented for any other level of amputation except for BKA.

2.5.6.4. Activities-specific Balance Confidence Scale-UK

The Activities-specific Balance Confidence Scale (ABC-UK) is a self-administered questionnaire that assesses balance confidence when performing daily tasks (Powell & Myers, 1995; Cleary & Skornyakov, 2014). The ABC-UK has 16 items and individuals are asked to rate their level of confidence on a scale between 0 to 100% when performing activities including climbing stairs, reaching above the head, and walking across different surfaces (Miller & Deathe, 2004; Cleary & Skornyakov, 2014). Previous research illustrates that the ABC-UK distinguishes fallers from non-fallers (Lajoie & Gallagher, 2004; Moore et al., 2011).

Further, previous literature has investigated using the ABC-UK amongst individuals with lower limb amputations (Miller et al., 2001b; Miller et al., 2002; Miller & Deathe, 2004; Sakakibara et al., 2011). Miller et al. (2002) recruited 435 patients with lower limb amputations, including TKA. The mean ABC scores were presented as a mean for AKA and BKA only, as the 5 TKA were combined with the AKA group due to recruitment numbers. Despite this, the ABC score was lower in AKA compared to BKA. Miller and Deathe (2004) recruited 11 patients with TKA, however, they also combined this level of amputation with AKA. In addition, when presenting the descriptive statistics for the literature, the authors combined all levels of amputation and presented scores as baseline ABC and follow up ABC, thus preventing any further discussion of the differences between levels of amputation.

2.5.6.5. Limitations to Amputation Falls, Confidence and Quality of Life

Previous literature has investigated the falls, fear of falling and confidence levels amongst individuals with lower limb amputations. Although the literature has incorporated TKA, most studies have not reported a direct comparison of falls and confidence amongst individuals with TKA and AKA. The lack of literature investigating those two levels of amputation combined within studies makes it clear that there is insufficient evidence of the differences between the fall risk, QoL and confidence surrounding TKA, and especially in comparison to AKA. This could be because of TKA being rarely performed, but nevertheless, TKA should ideally be investigated separately to determine the QoL, falls and confidence levels experienced when performing activities of daily living. The results reported for QoL and confidence could correlate to the surgical procedure itself and thus, be a greater influence on the level of amputation performed.

2.6. Summary and Rationale

The literature has investigated a variety of activities including individuals with varied levels of lower limb amputations. Although their reported findings have helped to understand some level of activity for individuals with lower limb amputations, it has not fully investigated the clinical and functional differences between patients with TKA and AKA. It is understandable why previous authors have combined TKA results with either BKA or AKA, because of TKA representing 1% of amputations within the UK. Nevertheless, it is important to understand whether there is any clinical and functional difference between these TKA and AKA, and if there is, to highlight what these differences are. The information would provide various healthcare service providers, including surgeons, prosthetists, and physiotherapists, with the significant information regarding TKA function and outcomes.

2.6.1. Aims, Questions and Hypotheses

The aim of the PhD thesis is to compare the clinical and functional outcomes between individuals with TKA and AKA.

The research questions and the hypotheses are as follows:

1. Are there differences in post-operative complications between TKA and AKA?

    Hypothesis: Patients with TKA will have better post-operative outcomes compared to AKA.

2. Are there differences in functional outcomes between TKA and AKA?

Hypothesis: Patients with TKA will have improved functional outcomes compared to AKA patients.

3. Do TKA and AKA walk the same distance during the 2MWT and 6MWT?

Hypothesis: Patients with TKA will walk further than AKA during the 2MWT and 6MWT due to their longer residual limb and more intact thigh musculature.

4. Does the time taken to complete tasks vary amongst patients with TKA vs. AKA?

Hypothesis: Patients with TKA will complete tasks more quickly than AKA.

5. Are patients with a TKA at a reduced risk of falling compared to AKA on the Berg Balance Scale?

Hypothesis: Patients with TKA are at a reduced risk of falling in comparison to AKA.

6. Do balance confidence scores differ between patients with TKA and AKA?

Hypothesis: Patients with TKA will trip and fall less compared to patients with AKA, although balance confidence levels will be similar between the two levels of amputation.

CHAPTER THREE: SYSTEMATIC REVIEW AND META-ANALYSIS OF FUNCTIONAL OUTCOMES AND BALANCE CONFIDENCE

3.1. Introduction

Global vascular guidelines for chronic limb-threatening ischaemia management have prioritised future research to examine whether the data for post-operative mobility using a prosthesis can justify performing a TKA rather than an AKA (Conte, 2019). The reported advantages of a TKA include reduced surgical blood loss, preservation of thigh muscles, a longer mechanical lever arm, and a weight-bearing residual limb, thus providing greater ambulatory stability (Pinzur, 2004; Smith, 2004; Robinson et al., 2010; de Laat et al., 2014). The reported disadvantages of TKA include a poor cosmetic result with asymmetrical knee levels and poor primary healing (Jensen, 1996; Smith, 2004).

A direct comparison of the biomechanical and rehabilitation outcomes of patients with a TKA vs. AKA is lacking (Murakami & Murray, 2016). It is unknown how the biomechanical gait and functional outcomes compare between patients with a TKA vs. AKA. Poor rehabilitation outcomes are most common amongst individuals with an AKA, as less than 30% of patients with these amputations achieve community prosthetic ambulation (Davies & Datta, 2003). However, prosthetic ambulation rates for patients with a TKA range between 13% to 75% (Murakami & Murray, 2016). There are theoretical biomechanical advantages for improved gait for patients with a TKA (Schuett et al., 2018), although they may be hindered due to lack of prosthetist experience, and the shorter space for both ankle and knee components in the lower leg segment (Smith, 2004). Previous researchers have advised that future studies should provide an insight into patients with a TKA vs. AKA performing activities of daily living (Theeven et al., 2012; Theeven et al., 2013; Stevens & Wurdeman, 2019).

It is important to determine which level of amputation provides better mobility and functional outcomes. The aim of this systematic review and meta-analysis was to compare the functional outcomes and balance confidence of patients with a TKA vs. AKA during activities of daily living.

In parallel to this thesis, a Cochrane review was conducted to assess the effects of TKA vs. AKA on clinical and rehabilitation outcomes and complication rates for all patients undergoing vascular and non-vascular major lower limb amputation. The author of this thesis made substantial contributions, including protocol drafting, acquisition of trial reports, trial selection, data extraction, data analysis, data interpretation, review drafting and future review updates, guarantor of the review. The reference of this article can be found in the Dissemination section of the thesis.

3.2. Methods

A protocol was developed and registered on PROSPERO database (identifier CRD42020177221). A patient, intervention, comparison and outcome (PICO) framework was developed to meet the aims and objectives to determine the quantitative differences between patients with a TKA and patients with an AKA (Table 3.1).

Table 3.1. PICO Framework Formula.

Acronym	Definition	Keywords
P	Population	Individuals with lower limb amputation
I	Intervention	TKA
C	Comparison	AKA
O	Outcomes	Biomechanical outcomes, functional outcomes and balance confidence

3.2.1. Searches

Databases including CINAHL, EMBASE Medline, PubMed, Cochrane and ClinicalTrials.gov were searched for terms relating to published, unpublished, in press or in progress studies (including RCTs) comparing patients with a TKA vs. AKA. Patients with amputations, including those from vascular and diabetic causes, comprising of infection, tissue loss, pain, and ischaemia; as well as non-vascular causes including trauma, malignancy, and congenital malformation were included. Bilateral amputations were also included, however, as due to the expected difference in functional outcomes following multiple amputations compared to a unilateral amputation, sensitivity analysis was completed to determine their effect on the outcomes. Studies including patients with an AKA were included only if TKA outcomes were reported separately. Studies were excluded if there was no separation of AKA with TKA data, if they were qualitative, if they included children or animals, or if they were literature reviews or editorials. Studies were excluded if the full text was not available in English.

3.2.1.1. Search Strategy

A search strategy was devised, and search terms were created to assist with finding relevant trials. The search strategy was based on terms related to TKA and AKA, including ((“through-knee” AND “amput*”) OR (“gritti-stokes” or “knee disarticulation” OR “youkey” or “mazet” OR “burgess”)) AND ((“above-knee” AND “amput*”) OR (“transfemoral”)). In addition, activities of daily living were searched with the above search terms and (“gait” OR “function*” OR “perform*” OR “activit*” OR “mobili*” OR “ambulat*” OR “biomechanic*” OR “movement*”).

3.2.1.2. Outcome Measures

The primary outcome was walking speed. Walking speed was measured as the distance walked divided by the time taken to walk that distance. This was converted and standardised across all papers to be reported as m/s. The secondary outcomes that were compared amongst the completed activities of daily living between the two levels of amputation include temporal-spatial parameters, kinematic parameters, kinetic parameters, time taken, distance walked, balance confidence and falls efficacy, and level of prosthetic ambulation.

3.2.2. Data Collection and Analysis

3.2.2.1. Selection of Studies

The lead reviewer merged the search results and discarded any duplicated results. The lead and a second reviewer then independently reviewed the titles and abstracts to determine which studies were potentially eligible. Conflicts were discussed to reach consensus when necessary. This process was then repeated with full texts of the studies that were appropriate for inclusion. The study selection process is shown in a PRISMA diagram in Figure 3.1 (Liberati et al., 2009).

3.2.2.2. Data Extraction

The data were independently extracted, and relevant data were collected from the included studies. Authors were contacted for their raw data when TKA outcomes were not reported separately but were included within the study population.

3.2.2.3. Quality Assessment

The lead and second reviewer assessed the included studies for risk of bias using the risk of bias in non-randomised studies (RoBANS) tool (Park et al., 2011). The risk was rated as either low, high, or unclear. Disagreements were discussed between the review authors, and a third reviewer to reach consensus when necessary. The risk of bias was rated by selection of participants, confounding variables, intervention (exposure) measurement, blinding of outcome assessment, incomplete outcome data and selective outcome reporting. The RoBANS tool is illustrated in Appendix A, and the risk of bias report for each study is illustrated in Figure 3.2. A checklist by Downs and Black (1998) was used to assess studies by their methodological quality. This comprised 27 questions based on reporting, external validity, internal validity, and power. The possible score ranges from 0-28 and can be viewed in Appendix B.

3.2.2.4. Data Analysis

All available data were extracted, and authors were contacted to request missing or additional data. Intention-to-treat analysis was completed where necessary, with incidents of loss to follow-up reported. The extracted data were synthesised using Microsoft Excel and statically analysed using RevMan. A meta-analysis was performed when there were sufficient data for reported outcome measures. A fixed-effect model meta-analysis was used when there was no or minimal heterogeneity. A random-effects model was used if there was a high level of heterogeneity. The mean difference between treatment groups and a 95% confidence interval were used for continuous outcome measures (walking speed, temporal-spatial parameters including step and stride length, kinematic parameters, kinetic parameters, time taken, distance walked, balance confidence and falls, and level of prosthetic ambulation). The standardised mean difference (SMD) was used if different scales were used to measure the same perception. A narrative approach was used to synthesise the data when there were insufficient data for a meta-analysis. A sub-group analysis was conducted when there were sufficient data for the levels of amputation and the different types of prosthetic componentry.

3.2.2.5. Assessment of Heterogeneity and Reporting Bias

The heterogeneity of the included studies was considered methodologically and statistically. Heterogeneity was assessed using Chi^2 and I^2 with interpretation guidelines being followed (Higgins et al., 2011). Further, funnel plots and tables were used to report bias, and statistical advice was obtained for interpretations for outcomes with more than 10 studies (Higgins et al., 2011).

3.3. Results

3.3.1. Searches

A total of 395 studies were identified within the extensive database searches (Figure 3.1). Two studies were excluded from the review as they were not quantitative. Secondly, 56 studies were excluded as they did not include patients with a TKA and AKA. Thirdly, 62 studies were excluded as the data were combined for patients with a TKA and AKA. The remaining exclusion reasons are listed in Figure 3.1. Following these, a total of 28 studies met the inclusion criteria and were included within the review. These 28 studies, listed in Table 3.2, represent a total of 641 patients with a unilateral TKA, 10 patients with a bilateral TKA, 1,880 patients with a unilateral AKA, and 20 patients with a bilateral AKA. The study designs were cross-sectional, case studies, prospective, retrospective, and cross-over (Table 3.2).

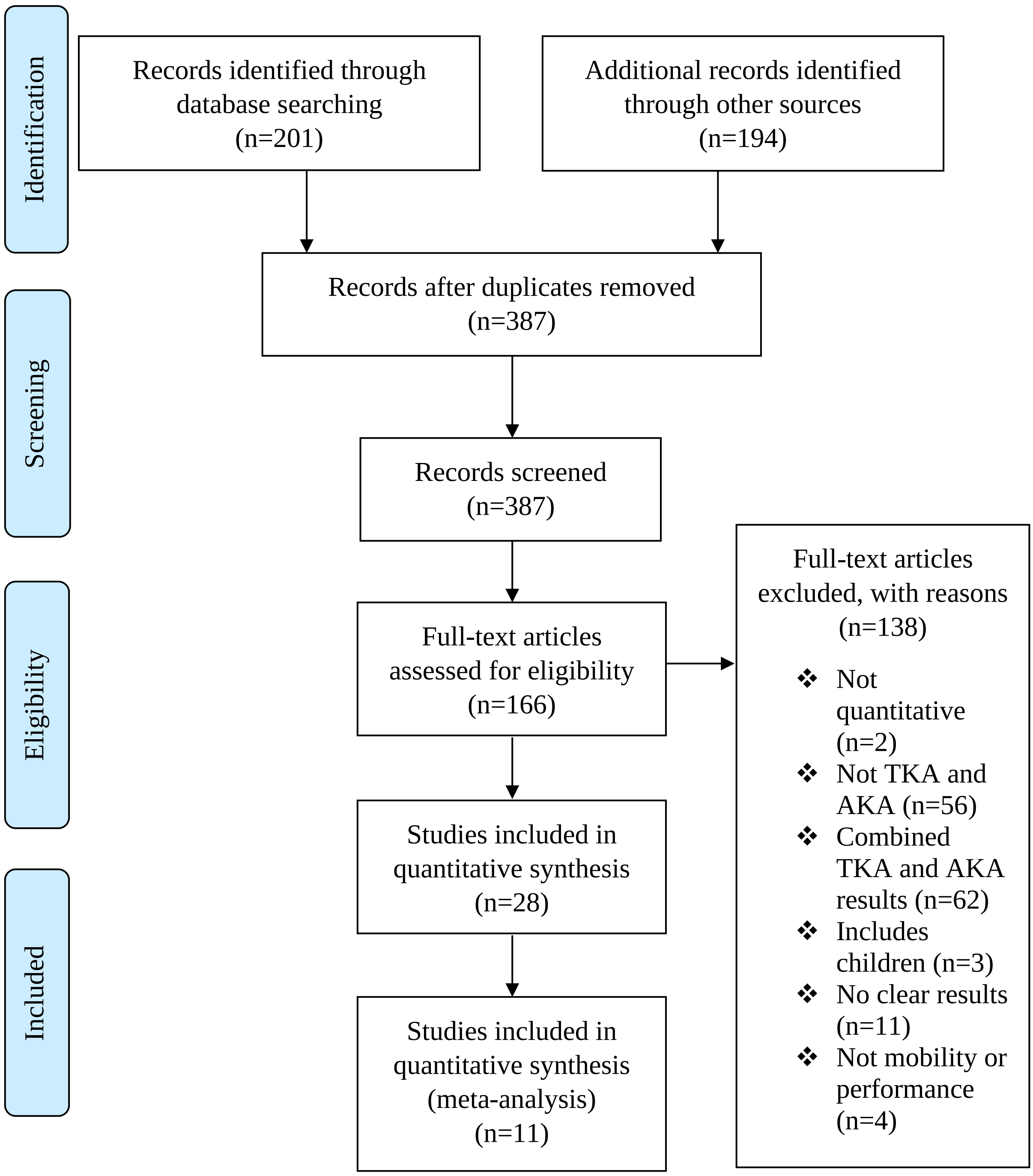

Figure 3.1. PRISMA flow diagram.

Table 3.2. Study Characteristics of included studies.

Study Authors	Participants	Study Design	Tests Used	Outcome Measures
Alsancak & Guner (2018)	1 AKA, 1 TKA and 8 able-bodied	Cross-sectional	Three-dimensional gait analysis	Temporo-spatial parameters, kinematics, and kinetics
Andrysek et al. (2011)	1 TKA and 11 AKA	Cross-over	2MWT and 20 metre walk-test	2MWT distance, 2MWT walking speed and time taken
Bailey & MacWhanell (1997)	2 TKA, 1 AKA and 7 BKA	Cross-sectional	Walking between parallel bars	Distance walked
Boonstra et al. (1993)	8 TKA and 16 AKA	Test-retest	Three-dimensional gait analysis on a 10-metre walkway	Walking speed
Burçak et al. (2021)	4 TKA and 29 AKA	Single subject	6MWT and SF-36	6MWT distance, 6MWT walking speed, and SF-36 scores
Esfandiari et al. (2018)	94 TKA, 458 AKA and 29 hip disarticulation	Cross-sectional	Amputee Mobility Predictor with a prosthesis	Amputee Mobility Predictor with a prosthesis score
Furtado et al. (2015)	1 TKA and 35 AKA	Cross-sectional	Toronto Extremity Salvage Score, Quality of Life – Cancer Survivors scale and Brief Pain Inventory	Toronto Extremity Salvage Score, Quality of Life – Cancer Survivors scale and Brief Pain Inventory scores
Gailey et al. (2010)	9 TKA and 109 AKA	Cross-sectional	Questionnaires on prosthetic devices, functional capability, health status, comorbidities, and combat-associated injuries	Number of prosthetic devices used, functional capability, health status, comorbidities, and combat-associated injuries scores

Gökşenoğlu & Yildirim (2019)	6 TKA and 20 AKA	Case studies	Questionnaires including LCI-5, Amputee Body Image Scale and Beck Depression Inventory	LCI-5, Amputee Body Image Scale and Beck Depression Inventory scores
Hafner et al. (2017)	7 TKA and 36 AKA	Cross-sectional	Prosthetic Limb Users Survey of Mobility and measures of physical function, mobility, Amputee Mobility Predictor with a prosthesis, TUG, Patient Reported Outcomes Measurement Information System-Physical Function, Prosthesis Evaluation Questionnaire-Mobility Subscale, and ABC	Measures of physical function, mobility, Amputee Mobility Predictor with a prosthesis, TUG time, Patient Reported Outcomes Measurement Information System-Physical Function, Prosthesis Evaluation Questionnaire-Mobility Subscale, and ABC scores
Hagberg et al. (1992)	17 TKA, 18 AKA and 24 BKA	Case studies	Questionnaire on prosthetic rehabilitation, and assessment of prosthetic replacement	Prosthetic use and grade of rehabilitation among prosthesis users
Houghton et al. (1989)	27 Gritti-Stokes, 54 TKA and 91 AKA	Case studies	Rehabilitation questionnaire	Prosthetic rehabilitation score
Houghton et al. (1992)	15 Gritti-Stokes, 15 TKA and 193 AKA	Case studies	Rehabilitation questionnaire	Prosthetic rehabilitation score
Karatzios et al. (2019)	12 TKA and 12 AKA	Prospective	Prosthetic Limb Users Survey of Mobility Short Form-12, 2MWT, TUG, Prosthetic Profile of the Amputee	2MWT distance, 2MWT walking speed, TUG time, Prosthetic Limb Users Survey of Mobility Short Form-12, Prosthetic Profile of the Amputee

			Locomotor Capabilities Index and ABC	Locomotor Capabilities Index and ABC scores
MacKenzie et al. (2004)	18 TKA and 34 AKA	Prospective	Sickness Impact Profile, degree of independence in transfers, walking, and climbing stairs, and 100-ft. timed walking test	SIP score, percentage of independent activity completion, percentage of a greater self-selected walking speed, percentage of inability to perform activities without help
Met et al. (2008)	39 TKA and 34 AKA	Retrospective	Special Interest Group in Amputee Medicine Mobility (SIGAM)	SIGAM score
Möller et al. (2018)	10 TKA and 32 AKA	Cross-sectional	Questionnaires including General Self-Efficacy Score, prosthetic use, mobility, and health	Questionnaires including General Self-Efficacy Score, prosthetic use, mobility score, global health score and problem score
Möller et al. (2019)	6 TKA, 23 AKA and 16 able-bodied	Cross-sectional	10-metre walk, 6MWT, ABC	Time taken, step count, prosthetic use, ABC score, 6MWT distance, and 6MWT walking speed
Möller et al. (2020)	6 TKA and 23 AKA	Cross-sectional	6MWT distance, prosthetic use, and ABC questionnaire	6MWT distance, 6MWT walking speed, prosthetic use, and ABC score
Onat et al. (2017)	54 TKA and 268 AKA	Retrospective	Nottingham Extended Activities of daily living activities Daily Living Scale	Nottingham Extended Activities of daily living activities Daily Living Scale score
Pernot et al. (2000)	43 TKA and 52 AKA	Prospective cohort	Barthel index, self-reported walking distance, duration of daily use of the prosthesis, the	Functional levels, walking distance, prosthetic use, use of walking aids,

			use of walking aids, TUG, and the Sickness Impact Profile	TUG time and Sickness Impact Profile score
Pinzur et al. (1992)	5 TKA, 5 AKA 5 Symes, 5 BKA, 5 Midfoot and 5 able-bodied	Cross-sectional	Self-selected walking on a treadmill	Walking speed
Polfer et al. (2019)	10 TKA and 18 AKA	Retrospective	Lower Limb Outcome Questionnaire, Tegner Activity Scale, SF-36, and Prosthetic Evaluation Questionnaires	Lower Limb Outcome Questionnaire, activity scale, SF-36 and Prosthetic Evaluation Questionnaires scores
Reid et al. (2015)	6 TKA and 28 AKA	Case series	2MWT, 6MWT, TUG, LCI-5, Houghton, and ABC	2MWT distance, 2MWT walking speed, 6MWT distance, 6MWT walking speed, TUG time, LCI-5, Houghton, and ABC scores
Schuett et al. (2018)	4 TKA with contralateral BKA and 4 AKA with contralateral BKA	Retrospective case series	Three-dimensional gait analysis	Walking speed, cadence, step width, step length, stride width, single-limb support, total stance time on each side, vertical ground reaction forces at early stance and late stance
Sherman et al. (2019)	2 TKA with contralateral AKA and 2 AKA with contralateral AKA	Case series	activPAL monitor following 2 weeks in-patient rehabilitation and consecutive 2 weeks away from rehabilitation	Daily step count
Taylor et al. (2005)	27 TKA and 216 AKA, 14 bilateral BKA/AKA and 4 bilateral BKA/TKA	Retrospective review	Review of clinical records in the vascular outpatient office	Prosthetic wear rates, ambulation status post-operatively and after 1 year

			and prosthetic rehabilitation clinics	
Yusuf et al. (1997)	144 TKA and 117 AKA	Retrospective review	Questions on mobility and prosthetic limb use	Stanmore mobility grade after rehabilitation

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Able-bodied controls (CON); Below-knee amputation (BKA).

3.3.2. Data Quality

The risk of bias using the RoBANS tool was low overall (Figure 3.2). Further, the scores of the methodological quality scores based on the Downs and Black checklist are illustrated in Table 3.3. The mean methodological scores across all studies were mean 13.9 ± 3.5, and median of 14, with a range of 5 to 20.

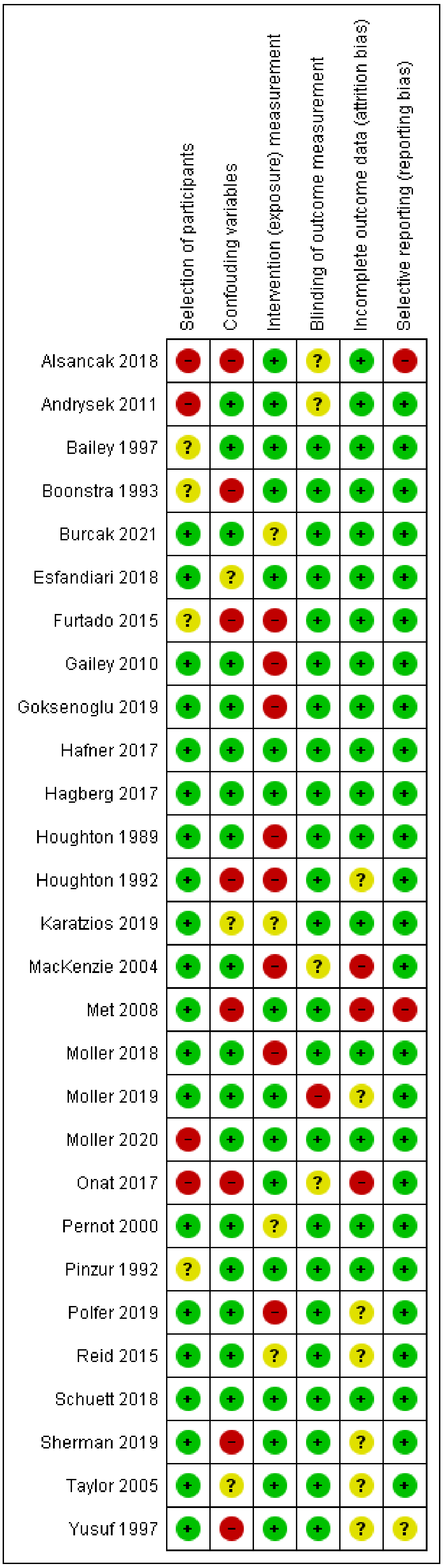

Figure 3.2. Risk of Bias summary.

Table 3.3. Methodological quality assessment using the Downs and Black Checklist.

	Reporting										External validity			Internal validity - bias							Internal validity - confounding						Power	
Study	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**Sum**
Alsancak (2018)	1	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	5
Andrysek 2011)	1	1	1	1	2	1	1	1	0	1	0	0	0	0	0	0	0	0	1	1	0	1	0	0	1	0	0	15
Bailey (1997)	1	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	8
Boonstra (1993)	1	1	0	1	0	1	1	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	8
Burçak (2021)	1	1	1	0	2	1	1	0	0	1	0	0	1	0	0	0	1	1	0	1	1	1	0	0	0	0	0	14
Esfandiari (2018)	1	1	1	0	0	1	1	0	0	1	1	1	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	13
Furtado (2015)	1	1	1	0	2	1	1	0	0	1	0	0	1	0	0	0	0	1	0	1	1	1	0	0	0	0	0	13
Gailey (2010)	1	1	1	1	2	1	1	0	0	1	1	1	1	0	0	0	1	1	1	0	1	1	0	0	1	0	1	19
Gökşenoğlu (2019)	1	1	1	0	2	1	1	0	0	1	0	0	1	0	0	0	0	1	0	1	1	0	0	0	0	0	0	12
Hafner (2017)	1	1	1	1	2	1	1	0	0	1	0	0	1	0	0	0	1	1	1	1	1	1	0	0	1	0	1	18
Hagberg (1992)	1	1	1	1	2	1	0	0	1	0	1	1	1	0	0	0	0	1	0	0	1	1	0	0	0	0	0	14
Houghton (1989)	1	1	0	1	0	1	1	0	0	1	1	0	1	0	0	0	1	1	0	0	1	1	0	0	1	0	0	13
Houghton (1992)	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	1	0	0	1	1	0	0	0	1	0	11
Karatzios (2019)	1	1	1	1	2	1	1	0	1	1	0	0	1	0	0	0	0	1	1	1	1	1	0	0	0	1	1	18
MacKenzie (2004)	1	1	1	1	2	1	1	0	1	1	1	1	1	0	0	0	1	1	0	0	1	1	0	0	1	1	0	19
Met (2008)	1	0	1	1	2	1	1	0	0	0	1	1	1	0	0	0	0	1	1	1	1	1	0	0	0	0	0	15
Möller (2018)	1	1	1	1	2	1	1	0	0	1	0	0	1	0	0	0	1	1	1	1	1	0	0	0	1	0	0	16
Möller (2019)	1	1	1	1	2	1	1	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0	1	0	0	13

Möller (2020)	1	1	1	1	0	1	1	1	0	1	0	0	1	0	0	0	1	1	1	1	0	1	0	0	0	0	0	14
Onat (2017)	1	1	1	1	0	1	1	0	0	0	0	0	1	0	0	0	1	1	1	1	1	0	0	0	0	0	0	12
Pernot (2000)	1	1	1	1	2	1	1	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0	0	0	1	0	20
Pinzur (1992)	1	1	1	1	2	1	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	10
Polfer (2019)	1	1	1	1	2	1	1	0	0	1	0	0	1	0	0	0	1	1	1	1	1	1	0	0	1	0	0	17
Reid (2015)	1	1	1	0	0	1	1	0	0	1	1	1	0	0	0	0	0	1	0	1	1	1	0	0	1	0	0	13
Schuett (2018)	1	1	1	1	2	1	1	0	1	1	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0	1	0	17
Sherman (2019)	1	1	1	0	2	1	1	0	0	0	0	0	1	0	0	0	1	1	0	1	1	1	0	0	1	0	0	14
Taylor (2005)	1	1	1	1	2	1	1	0	0	1	1	1	0	0	0	0	1	1	0	0	1	1	0	0	0	0	0	15
Yusuf (1997)	0	0	1	1	0	1	1	0	1	0	1	1	0	0	0	0	0	1	1	1	1	1	0	0	0	1	0	13

Key: 1 = Yes addressed; 0 = Not addressed or unable to determine.

Question 5, 2 = Yes addressed; 1 = Partially addressed; 0 = Not addressed.

3.3.3. Meta-Analysis

A meta-analysis on walking speed (Pinzur et al., 1992; Boonstra et al, 1993; Andrysek et al., 2011; Reid et al., 2015; Alsancak and Guner, 2018; Schuett et al, 2018; Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021), 2MWT distance (Andrysek et al., 2011; Reid et al., 2015; Karatzios et al., 2019), 2MWT walking speed (Andrysek et al., 2011; Reid et al., 2015; Karatzios et al., 2019), 6MWT distance (Reid et al., 2015; Möller et al., 2019; Burçak et al., 2021), 6MWT walking speed (Reid et al., 2015; Möller et al., 2019; Burçak et al., 2021), TUG test (Hafner et al., 2017; Karatzios et al., 2019), ABC-UK (Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020), and LCI-5 (Gökşenoğlu and Yildirim, 2019; Karatzios et al., 2019) were completed using the available data from the searches. Patient characteristics from the meta-analysis are shown in Table 3.4. It is important to note, that the characteristics were combined with other levels of amputation for many studies and were unavailable. Although, cause of amputation and prosthesis components were similar between the two levels of amputation (Table 3.4). Table 3.5 indicates the results from the meta-analysis, reported as mean and standard deviation, difference and test for overall effect.

Walking speed was reported across nine studies; however, the meta-analysis did not find a significant effect despite the small increase in patients with a TKA (Table 3.5). Additionally, there was no overall effect on 2MWT distance and 2MWT walking speed between patients with a TKA and patients with an AKA (Table 3.5). However, 6MWT distance was significantly greater in patients with a TKA (p=0.04). The meta-analysis results are outlined in Chapter Three, Sections 3.3.4, 3.3.5 and 3.3.6.

Table 3.4. Patient characteristics included within the meta-analysis.

Patient Characteristics	TKA (n = 65)	AKA (n = 207)
Age (years)	55.8 years	44.3 years
Gender	Male (n=31) Female (n=11)	Male (n=111) Female (n=27)
Cause of Amputation	Trauma (n=18), Vascular (n=9), Ischaemic (n=5), Tumour (n=5)	Trauma (n=65), Vascular (n=13) Infection (n=2), Ischaemic (n=3), Tumour (n=20)
Time since Amputation (range)	1 year to 28 years	1 year to 52 years
Prosthetic Components	Mechanical (n=20) Microprocessor (n=18)	Mechanical (n=74) Microprocessor (n=63)
Study Design	Cross Sectional (n=5), Cross-over (n=1), Test-retest (n=1), Pragmatic (n=1), Case Studies (n=2), Prospective (n=1)	

Table 3.5. Meta-analysis outcome results.

Outcome	TKA (n = 65)	AKA (n = 207)	Difference	P	Effect Size (Cohen's d)	
Walking Speed (m/s)	1.12 ± 0.26	1.13 ± 0.25	0.05 [-0.37, 0.46]	p=0.83	0.1	Small
2MWT Distance (m)	145.0 ± 19.4	144.6 ± 6.9	7.46 [-4.12, 19.03]	p=0.21	0	Negligible
2MWT Walking Speed (m/s)	1.21 ± 0.16	1.21 ± 0.06	0.06 [-0.03, 0.16]	p=0.19	0	Negligible
6MWT Distance (m)	412.3 ± 49.1*	369.0 ± 47.6*	40.24 [0.93, 79.55]	p=0.04*	0.5	Medium
6MWT Walking Speed (m/s)	1.05 ± 0.13	1.01 ± 0.11	0.08 [-0.08, 0.25]	p=0.33	0.4	Medium
TUG Test	16.2 ± 4.9	15.0 ± 3.7	0.59 [-4.62, 5.81]	p=0.82	0.3	Medium
ABC-UK	81.0 ± 2.8	77.0 ± 5.3	4.48 [-2.96, 11.92]	p=0.24	0.8	Large
LCI-5	36.9 ± 4.1	46.1 ± 9.1	0.20 [-3.60, 4.00]	p=0.92	1.1	Large

Key: Metres per second (m/s); Two-minute walk test (2MWT); metres (m); Six-minute walk test (6WMT); Timed-Up-and-Go (TUG); Activities-specific Balance Confidence-UK (ABC-UK); Locomotor Capabilities Index-5 (LCI-5).

TKA and AKA scores reported as mean (± standard deviation); Difference scores reported as inverse variation for fixed-effect methods with 95% CI; * Indicates an overall effect p<0.05.

3.3.4. Biomechanical Outcomes

3.3.4.1. Temporal-Spatial Parameters

Walking speed was calculated for 42 patients with a TKA and 106 patients with an AKA across nine studies. Despite the variance in walking speed across studies (Table 3.6), walking speed was similar between the two groups overall. A total of 42 patients with a TKA had an average walking speed of 1.12m/s, and 106 patients with an AKA had an average walking speed of 1.10m/s, and a meta-analysis did not reach significance (p=0.83). Taking into consideration that some of the patients had bilateral amputations, a separate sensitivity analysis was completed on the unilateral amputations only. Walking speed was similar in patients with a unilateral TKA and patients with a unilateral AKA (1.11m/s and 1.09m/s, respectively; p=0.82).

Cadence, measured as the number of steps per minute, was reported across 5 patients with a TKA and 5 patients with an AKA in two studies (Table 3.7). This was similarly reported between patients with a TKA and patients with an AKA (109 steps/min and 110 steps/min, respectively), and was not statistically significant in the meta-analysis (p=0.56).

Step count was measured in two studies using different methodologies (Table 3.8). In one study (Möller et al., 2019), step count was calculated during 14metre walking trials at self-selected walking speed, with patients achieving a similar step count (Table 3.8). In the second study (Sherman et al., 2019), step count was calculated using the activPAL activity monitor during in-patient rehabilitation for two weeks and the following two weeks at home. The activPAL was fitted to a prosthesis of each participant. The start time and date, stop time and date, elapsed time in days, and daily number of unilateral monitor-side steps per day recorded. The average step count varied between TKA and AKA, and during in-patient rehabilitation and recordings at home (Table 3.8).

Stride length of the intact and prosthetic limb was reported by Alsancak and Guner (2018) for one patient with a TKA and one patient with an AKA. Secondly, step length, measured as the distance between the point of initial contact of one foot to the point of initial contact of the opposing foot, was reported by Schuett et al. (2018) for four bilateral patients with a TKA and four bilateral patients with an AKA. Further, step width, measured as the lateral distance between the heels when both feet touch the ground (Osoba et al., 2019), was reported by Schuett et al. (2018) for four bilateral patients with a TKA and four bilateral patients with an AKA. Values for stride length, step length and step width were similar between patients with a TKA and patients with an AKA.

Table 3.6. Walking speed meta-analysis.

Study	Sample Size	TKA (m/s)	AKA (m/s)	Diff
Alsancak & Guner (2018)	1 TKA, 1 AKA	1.49 ± 0	1.51 ± 0	0.02
Andrysek et al. (2011)	2 TKA, 22 AKA	1.32 ± 0.01	1.23 ± 0.25	0.09
Boonstra et al. (1993)	8 TKA, 16 AKA	1.19 ± 0.25	1.04 ± 0.21	0.15
Karatzios et al. (2019)	12 TKA, 12 AKA	1.02 ± 0.41	1.25 ± 0.36	0.23
Möller et al. (2019)	5 TKA, 23 AKA	1.02 ± 0.56	1.09 ± 0.51	0.07
Möller et al. (2020)	2 TKA, 12 AKA	1.02 ± 0.56	1.04 ± 0.54	0.02
Pinzur et al. (1992)	5 TKA, 5 AKA	0.58 ± 0	0.41 ± 0	0.17
Reid et al. (2015)	3 TKA, 11 AKA	1.28 ± 0.35	1.14 ± 0.25	0.14
Schuett et al. (2018)	4 TKA, 4 AKA	1.22 ± 0.17	1.22 ± 0.1	0
Total	42 TKA, 106 AKA	1.12 ± 0.26	1.10 ± 0.25	p=0.83

Key: metres per second (m/s); Through-knee amputation (TKA); Above-knee amputation (AKA); Difference (Diff); Standard deviation (± SD); P-value (P). Scores reported as mean ± SD.

Table 3.7. Cadence meta-analysis.

Study	Sample Size	TKA (steps/min)	AKA (steps/min)	Diff
Alsancak & Guner (2018)	1 TKA, 1 AKA	114 ± 0	116 ± 0	2
Schuett et al. (2018)	4 TKA, 4 AKA	103 ± 5	106 ± 6	3
Total	5 TKA, 5 AKA	109 ± 2.7	110 ± 3	p=0.56

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); steps per minute (steps/min); Difference (Diff); Standard deviation (± SD); P-value (P). Scores reported as mean ± SD.

Table 3.8. Step count in included studies.

Study	Sample Size	TKA	AKA	Diff
Möller et al. (2019)	6 TKA, 23 AKA	15.4 ± 2.0	14.9 ± 2.2	0.5
Sherman et al. (2019)	2 TKA/AKA, 2 AKA/AKA (in-patient)	2224.5 ± 753.5	1751 ± 1120	473.5
Sherman et al. (2019)	2 TKA/AKA, 2 AKA/AKA (home)	998.5 ± 640.5	1730.5 ± 1524	732
Total	8 TKA, 27 AKA	1079.5 ± 465.3	1165.5 ± 882.1	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Difference (Diff); Standard deviation (± SD). Scores reported as mean ± SD.

3.3.4.2. Kinematic Parameters

The peak kinematic parameters were reported for both intact and prosthetic limbs for one patient with a TKA and one patient with an AKA by Alsancak and Guner (2018). Their results are not comparable as it is a non-statistical reporting article on a case study.

3.3.4.3. Kinetic Parameters

Maximum hip external flexion and extension moments were reported for the intact and prosthetic limb by Alsancak and Guner (2018). A peak hip external flexion moment was identified in the prosthetic limb of one patient with a TKA and one patient with an AKA (0.81Nmm/kg and 0.55Nmm/kg, respectively). Additionally, peak hip external extension moment was reported in the intact limb of one patient with a TKA and one patient with an AKA (-2.16Nmm/kg and -5.2Nmm/kg, respectively). The results from this study cannot be compared due to the nature of the study design.

3.3.5. Functional Outcomes

3.3.5.1. Distance Completed

The 2MWT was measured and reported in three studies (Andrysek et al., 2011; Reid et al., 2015; Karatzios et al., 2019). The average distance walked during each study following TKA and AKA are reported in Table 3.9. The studies are contrasting in results, and a meta-analysis was conducted to determine any significance (Figure 3.3). Figure 3.3 illustrates a forest plot of the distance walked during the 2MWT in three studies, with 17 patients with a TKA and 45 patients with an AKA. An average of the distance walked indicated minimal difference between patients with a TKA and patients with an AKA (145m ± 19.4m and 146.6m ± 6.9m, respectively). A meta-analysis of the results from these three studies did not reach significant difference in 2MWT distance ($p=0.21$).

6MWT distance was reported in three studies (Reid et al., 2015; Möller et al., 2019; Burçak et al., 2021). The average distance walked during six-minutes was 412.3m ± 49.1m following a TKA, and 369m ± 47.6m following an AKA (Table 3.10). Figure 3.4 indicates a forest plot of these results. A meta-analysis concluded that patients with a TKA overall had a significantly greater walking distance compared to patients with an AKA (p=0.04).

Table 3.9. 2MWT distance walked within the included studies.

Study	Sample Size	TKA (metres)	AKA (metres)	Diff
Andrysek et al. (2011)	2 TKA, 22 AKA	158.4 ± 1.7	174.7 ± 29.4	16.3
Karatzios et al. (2019)	12 TKA, 12 AKA	122.8 ± 49.4	149.4 ± 43.6	26.6
Reid et al. (2015)	3 TKA, 11 AKA	153.8 ± 41.8	136.7 ± 38.6	17.1
Total	17 TKA, 45 AKA	145 ± 19.4	144.6 ± 6.9	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Difference (Diff); Standard deviation (± SD). Values reported as mean ± SD.

Study or Subgroup	Through-Knee Amputation Mean	SD	Total	Above-Knee Amputation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Andrysek 2011	158.4	1.7	2	147.65	29.43	22	85.5%	10.75 [-1.77, 23.27]
Karatzios 2019	122.8	49.4	12	149.4	43.6	12	9.6%	-26.60 [-63.88, 10.68]
Reid 2015	153.8	41.8	3	136.7	38.6	11	4.9%	17.10 [-35.41, 69.61]
Total (95% CI)			**17**			**45**	**100.0%**	**7.46 [-4.12, 19.03]**

Heterogeneity: Chi² = 3.60, df = 2 (P = 0.17); I² = 44%
Test for overall effect: Z = 1.26 (P = 0.21)

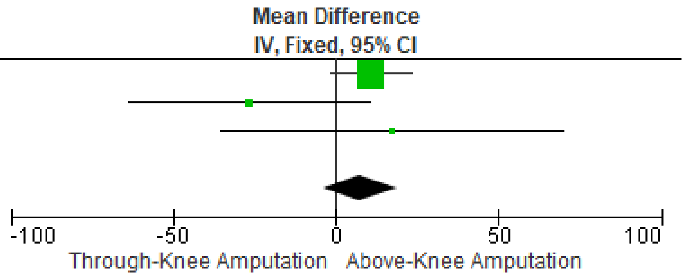

Figure 3.3. Forest plot of 2MWT distance within the included studies.

Table 3.10. 6MWT distance within the included studies.

Study	Sample Size	TKA (metres)	AKA (metres)	Diff
Burçak et al. (2021)	8 TKA, 58 AKA	355.6 ± 59.9	316.7 ± 64.7	38.9
Möller et al. (2019)	5 TKA, 21 AKA	440.4 ± 101.7	409.6 ± 165.6	30.8
Reid et al. (2015)	4 TKA, 11 AKA	441 ± 98.3	380.8 ± 119.7	60.2
Total	17 TKA, 90 AKA	412.3 ± 49.1	369 ± 47.6	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Difference (Diff); Standard deviation (± SD). Values reported as mean ± SD.

	Through-Knee Amputation			Above-Knee Amputation				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Burcak 2021	355.6	59.9	8	316.7	64.7	58	77.3%	38.90 [-5.82, 83.62]
Moller 2019	440.4	101.7	5	409.6	165.6	21	11.9%	30.80 [-83.05, 144.65]
Reid 2015	441	98.3	4	380.8	119.7	11	10.8%	60.20 [-59.31, 179.71]
Total (95% CI)			**17**			**90**	**100.0%**	**40.24 [0.93, 79.55]**

Heterogeneity: Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 2.01 (P = 0.04)

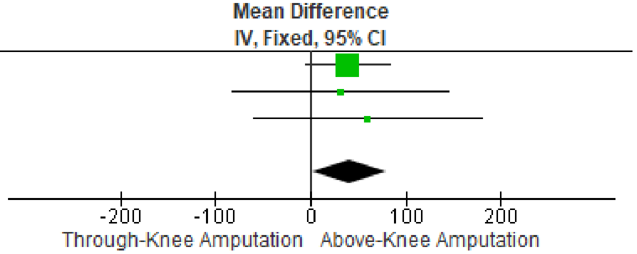

Figure 3.4. Forest plot of 6MWT distance within included studies.

3.3.5.2. Timed Tasks

The TUG test was reported in four studies (Pernot et al., 2000; Reid et al., 2015; Hafner et al., 2017; Karatzios et al., 2019), however, data were only available for two studies (Table 3.11). The TUG times differed in these two studies (Table 3.11), but an average showed that patients with an AKA performed the TUG at a similar speed to those with a TKA (15.0s ± 8.3s and 16.2s ± 12.5s, respectively). It would be expected that both levels of amputation would have a higher risk of falls as their score was greater than 14 seconds. A meta-analysis was completed using these results and can be viewed in Figure 3.5. There was no difference in TUG scores (Table 3.11), and meta-analysis did not reach significance (p=0.82).

The time taken to walk 10 metres was reported by Möller et al. (2019). Patients with a TKA walked 10m in an average time of 8.9s ± 2.2s, and patients with an AKA walked 10 metres in 9.1s ± 2.1s. The walking speed for patients with a TKA and patients with an AKA during the 10-metre walk test was similar (TKA 1.17m/s ± 0.26m/s and AKA 1.16m/s ± 0.30m/s, respectively).

Table 3.11. Timed-Up-and-Go test results within the included studies.

Study	Sample Size	TKA (s)	AKA (s)	Diff
Hafner et al. (2017)	7 TKA, 36 AKA	19.7 ± 17.1	17.6 ± 10.4	2.1
Karatzios et al. (2019)	12 TKA, 12 AKA	12.7 ± 7.9	12.4 ± 6.2	0.3
Total	19 TKA, 48 AKA	16.2 ± 12.5	15.0 ± 8.3	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Seconds (s); Difference (Diff); Standard deviation (± SD). Values reported as mean ± SD.

Study or Subgroup	Through-Knee Amputation Mean	SD	Total	Above-Knee Amputation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Hafner 2017	19.67	17.12	7	17.57	10.43	36	15.8%	2.10 [-11.03, 15.23]
Karatzios 2019	12.71	7.92	12	12.4	6.17	12	84.2%	0.31 [-5.37, 5.99]
Total (95% CI)			**19**			**48**	**100.0%**	**0.59 [-4.62, 5.81]**

Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.22 (P = 0.82)

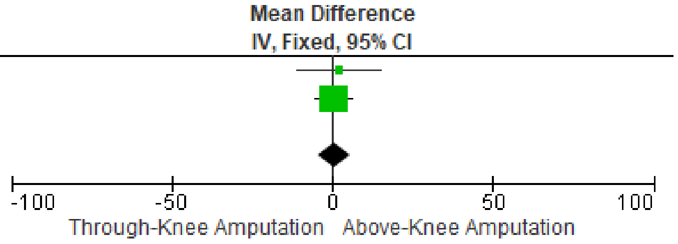

Figure 3.5. Forest plot for the Timed-Up-and-Go test within the included studies.

3.3.5.3. Mobility and Level of Prosthetic Ambulation

The percentage of patients with a TKA and patients with an AKA who received a prosthesis following the loss of their lower limb was identical at 38% in one study (Met et al., 2008). Functional outcomes were determined by the SIGAM mobility grades in a study by Met et al. (2008). K-levels and SIGAM mobility grades are outlined in Chapter Two (Table 2.1 and Table 2.2). Met et al. (2008) reported that 67% of patients with an AKA had a SIGAM grade A vs. 65% of patients with a TKA, indicating that they had abandoned wearing their limb or they had use of a cosmetic limb only. Secondly, 15% of patients with a TKA had SIGAM grade D vs. 13% of patients with an AKA. Four percent of patients with a TKA had SIGAM grade F vs. no patients with an AKA (SIGAM grade F represents normal or near normal gait). Similarly, Hagberg et al. (1992) investigated function after lower limb amputation and used an ordinal scale to grade the rehabilitation amongst prosthesis users. A greater portion of patients with a TKA were able to walk outdoors, walk up and down stairs, travel in a car, and perform household chores compared to patients with an AKA, but the exact number was unclear. Met et al. (2008) found no significance for prosthesis supply or for SIGAM.

Hagberg et al. (1992) found that 28% of AKA did not use their prescribed prosthesis, vs. 0% in TKA. Almost double the TKA reportedly wore their prosthetic limb between 6-9 hours/day compared to AKA (11% and 6%, respectively). Findings were similar when wearing their prosthetic limb greater than 9 hours, with a greater percentage of patients with a TKA wearing their prosthetic limb for longer compared to patients with an AKA (41% and 22%,92uestiotively). These findings were corroborated by Taylor et al. (2005), with reports of prosthesis wear rates of 61.6% in patients with a TKA compared to 44.5% in patients with an AKA. Further, findings from both studies contrasted to those reported by Houghton et al. (1992), with the percentage of limb wearers being higher in patients with an AKA compared to patients with a TKA and patients with a Gritti-Stokes (30%, 1% and 3%, respectively). Yusuf et al. (1997) utilised the Stanmore mobility grades to determine the rehabilitation of lower limb amputations. A greater percentage of individuals with a Gritti-Stokes in a study by Yusuf et al. (1997) used a cosmetic limb compared to patients with an AKA (8.1% and 0%, respectively). Additionally, their study had a greater percentage of individuals with a Gritti-Stokes who were indoor walkers only compared to patients with an AKA (37.8% and 16.7%, respectively). Thirdly, a greater percentage of patients with a Gritti-Stokes amputation had independent mobility compared to patients with an AKA (13.5% and 8.3%, respectively). Contradictory to the above studies, Furtado et al. (2015) reported that the patient with a TKA in their study were wheelchair users and did not use a prosthesis or walking aids, whereas 62.9% of patients with an AKA in their study used a prosthesis and 89.3% patients with an AKA in their study used walking aids. Overall prosthesis use was recorded using the Questionnaire for Persons with a Transfemoral Amputation in three studies (Möller et al., 2018; Möller et al., 2019; Möller et al., 2020).

Walking distances were recorded for patients with a TKA and patients with an AKA by Pernot et al. (2000). In their study, more TKA were non-ambulatory vs. AKA (4 patients vs. 2 patients, respectively). However, more patients with an AKA were able to walk between 0-50m compared to patients with a TKA (44.4% and 33.3%, respectively), and more patients with an AKA were able to walk between 50-500 metres compared to patients with a TKA (33.3% and 25%, respectively). Despite patients with an AKA walking further distances, only one patient with a TKA reportedly walked further than 50m. All patients with a TKA in a study by Gailey et al. (2010) were able to walk following the loss of their limb, compared to 6.4% of patients with an AKA who were unable to walk. A higher percentage of patients with a TKA were able to walk with varying speeds over uneven obstacles compared to patients with an AKA (44.4% and 22.9%, respectively). Further, a greater percentage of patients with an AKA were able to complete a variety of low-impact and high-impact activities vs. patients with a TKA (29.3% and 22.2%, respectively). Houghton et al. (1989) investigated the rehabilitation outcomes following lower limb amputation and reported that 68% of patients with a TKA were satisfactory rehabilitated compared to 54% of patients with an AKA and 52% of patients with a Gritti-Stokes amputation. Satisfactory rehabilitated was defined as a score of nine or greater. Further, their study reported that 88% of patients with a TKA never used a wheelchair, compared to 86% of patients with an AKA and 86% of patients with a Gritti-Stokes amputation. Of those who were wheelchair users, fewer TKA patients used a wheelchair outside compared to patients with a Gritti-Stokes amputation and AKA patients (5.6%, 25.9% and 12.1%, respectively). Although these values are relatively small, the authors reported following statistical analysis, patients with a TKA significantly rehabilitated better than the AKA cohort ($p<0.02$).

Onat et al. (2017) evaluated the differences in activities of daily living when transitioning from their prescribed prosthesis to a microprocessor knee. There was a significant increase reported between pre- and post-activity scores when using the Nottingham Extended Activities of Daily Living Activities Scale, with patients with an AKA having a higher score vs. patients with a TKA (60.5 and 57.2, respectively; $p=0.001$). The Amputee Mobility Predictor and Amputee Mobility Predictor with Prosthetic use was utilised in two studies (Hafner et al., 2017; Esfandiari et al., 2018).

3.3.6. Self-Reported Measures

3.3.6.1. Self-Reported Measures

The ABC-UK data were collected in five studies (Reid et al., 2015; Hafner et al., 2017; Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020). Two of the studies (Reid et al., 2015; Hafner et al., 2017) did not report their findings and did not state their reasoning. In three studies (Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020), balance confidence scores were similar in patients with an AKA vs. patients with a TKA (Table 3.12). A meta-analysis was conducted on the ABC-UK scores reported across three studies (Figure 3.6). However, the meta-analysis found no significant difference between AKA and TKA scores (p=0.24).

The LCI-5 was completed by Gökşenoğlu and Yildirim (2019). Following a TKA their confidence score was 34, and 52.5 following an AKA. Karatzios et al. (2019) utilised the Prosthetic Profile of the Amputee Locomotor Capabilities Index, with capabilities to perform tasks being similar between patients with a TKA and patients with a TKA (39.8 and 39.6, respectively). There was no significant difference associated from the meta-analysis of these results (p=0.92).

Prosthetic Limb Users Survey of Mobility was utilised in two studies (Hafner et al., 2017; Karatzios et al., 2019), and assessed a patient's perceived capacity to perform different activities that vary in difficulty when using their prosthesis. The average scores reported by Hafner et al. (2017) following TKA were 52.1 ± 6.9, and AKA 49.9 ± 7.7. Similarly, the average scores reported by Karatzios et al. (2019) following TKA were 50.4 ± 5.7, and AKA 48.9 ± 9.5.

The Prosthesis Evaluation Questionnaire was utilised in two studies (Hafner et al., 2017; Polfer et al., 2019), thus measuring prosthesis-related QoL and prosthesis-related function in individuals with amputations. The ambulation Prosthesis Evaluation Questionnaire score recorded by Polfer et al. (2019) following an AKA was 66.3, and the score for patients with a TKA was 62. Hafner et al. (2017) reported the Prosthesis Evaluation Questionnaire Mobility Subscale as the combination of ambulation and transfer subscales from the Prosthesis Evaluation Questionnaire. Scores for TKA on average was 2.1, and 2.5 for an AKA.

Table 3.12. ABC-UK scores within the included studies.

Study	Sample Size	TKA	AKA	Diff
Karatzios et al. (2019)	12 TKA, 12 AKA	80.1 ± 16.8	82.4 ± 18.2	2.3
Möller et al. (2019)	6 TKA, 23 AKA	78.8 ± 8.5	71.8 ± 24.7	7.0
Möller et al. (2020)	6 TKA, 23 AKA	84.2 ± 8.9	76.9 ± 26.2	7.3
Total	24 TKA, 58 AKA	81.0 ± 11.4	77.0 ± 23.0	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Difference (Diff); Standard deviation (± SD). Values reported as mean ± SD.

Study or Subgroup	Through-Knee Amputation Mean	SD	Total	Above-Knee Amputation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Karatzios 2019	80.1	16.8	12	82.4	18.2	12	28.5%	-2.30 [-16.31, 11.71]
Moller 2019	78.8	8.5	6	71.8	24.7	23	37.7%	7.00 [-5.17, 19.17]
Moller 2020	84.2	8.9	6	76.9	26.2	23	33.8%	7.30 [-5.56, 20.16]
Total (95% CI)			**24**			**58**	**100.0%**	**4.45 [-3.02, 11.93]**

Heterogeneity: $Chi^2 = 1.25$, df = 2 (P = 0.54); $I^2 = 0\%$
Test for overall effect: Z = 1.17 (P = 0.24)

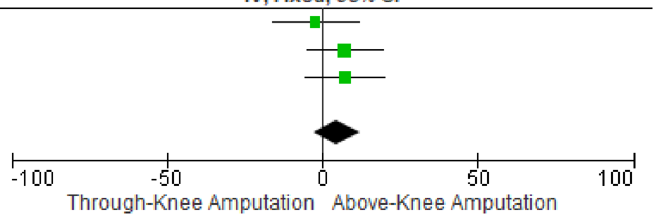

Figure 3.6. Forest plot of ABC-UK scores within the included studies.

3.3.6.2. Quality of Life

SF-36 was included in two studies (Polfer et al., 2019; Burçak et al., 2021). Burçak et al. (2021) determined the physical function attribute of the SF-36 for TKA was 46.1 ± 10.5, and 43.2 ± 11.2 for AKA. Further, Polfer et al. (2019) reported the physical function attribute of the SF-36 for TKA was 59, and 57.5 for AKA.

The Patient Reported Outcome Measure Information System Physical Function was reported by Hafner et al. (2017). Patients with a TKA and patients with an AKA had a similar score (39.9 and 39.8, respectively), indicating that both levels of amputation had good physical function in this study.

The Toronto Extremity Salvage Score evaluates physical disability after treatment for limb sarcoma and was reported by Furtado et al. (2015). Patients with an AKA had a score of 53.5, and patients with a TKA had a score of 17.3. A higher score indicates the ability to complete more activities. Although, the one patient with a TKA in their study did not receive a prosthesis and had no use of walking aids, indicating that they were non-ambulatory and therefore limited in activities.

3.3.7. Sub-group Analysis

There were several studies that compared functional outcomes when using a NMPK and an MPK (Andrysek et al., 2011; Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021). Andrysek et al. (2011) compared the differences between a simplified automatic stance phase lock (SASPL) prosthesis and an MPK when completing the 2MWT. Patients with a TKA walked on average 159.6m with the MPK compared to 157.2m with the SASPL. Although these distances were approximately 12m further than patients with an AKA, distances walked with both prostheses for patients with an AKA were identical (MPK 147.5m and SASPL prosthesis 147.8m, respectively).

The 6MWT distance and walking speed when using a MPK and NMPK was compared in three studies (Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021), and these results can be viewed in Table 3.13. In two of these studies, led by the same author, (Möller et al., 2019; Möller et al., 2020), patients with a TKA walked with a NMPK an average of 361.5m ± 139.3m (Table 3.14) compared to an average of 493m ± 24.9m with an MPK. Secondly, in the same studies with the same author (Möller et al., 2019; Möller et al., 2020), patients with an AKA walked an average of 375.8m ± 192.9m with a NMPK, compared to 450.2m ± 123.2m with an MPK. These findings were similar to Burçak et al. (2021). A meta-analysis conducted and illustrated in Table 3.13 outlined no significances between 6MWT distance and level of amputation with the NMPK (p=0.46). However, the meta-analysis found a significant effect between 6MWT distance and level of amputation with the MPK (Figure 3.7; p=0.03).

Table 3.14 indicates the results when comparing sub-groups of prosthesis components to level of amputation. Möller et al. (2019) used the timed 10-metre walk test to compare the differences between walking with MPK and NMPK. Two studies (Möller et al., 2019; Möller et al., 2020) compared the ABC confidence scores between MPK and NMPK. Burçak et al. (2021) compared the physical functioning QoL between the MPK and NMPK.

Andrysek et al. (2011) used the timed 20-metre walk test to compare the differences between walking at a self-selected walking speed and a fast-walking speed with SASPL and MPK. One patient with a TKA walked 159.6m with the MPK, compared to 11 patients with an AKA who walked an average of 147.5m. Secondly, one patient with a TKA walked 157.2m metres with the SASPL prosthesis, compared to 11 patients with an AKA who walked an average of 147.8m.

Table 3.13. 6MWT distance prosthesis componentry sub-group results.

	TKA (metres)		AKA (metres)	
Study	**NMPK**	**MPK**	**NMPK**	**MPK**
Burçak et al. (2021)	338.5 ± 74.9	372.8 ± 44.4	302.3 ± 65.9	331.0 ± 61.1
Möller et al. (2019)	361.5 ± 139.3	493.0 ± 24.9	375.8 ± 192.9	450.2 ± 123.2
Möller et al. (2020)	361.5 ± 139.3	493.0 ± 24.9	375.8 ± 192.9	450.2 ± 123.2

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Mechanical knee (NMPK); Microprocessor knee (MPK); Standard deviation (± SD). Scores are reported as mean ± SD.

Study or Subgroup	Through-Knee Amputation Mean	SD	Total	Above-Knee Amputation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Burcak 2021	372.8	44.4	4	331	66.1	29	57.3%	41.80 [-7.92, 91.52]
Moller 2019	493	24.9	3	450.2	123.2	10	21.4%	42.80 [-38.59, 124.19]
Moller 2020	493	24.9	3	450.2	123.2	10	21.4%	42.80 [-38.59, 124.19]
Total (95% CI)			**10**			**49**	**100.0%**	**42.23 [4.60, 79.85]**

Heterogeneity: Chi² = 0.00, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 2.20 (P = 0.03)

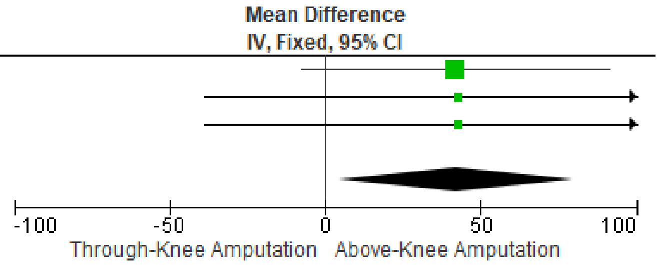

Figure 3.7. Forest plot for 6MWT distance prosthesis componentry sub-group analysis.

Table 3.14. Sub-group comparisons for prosthesis componentry and level of amputation.

		TKA		AKA	
Study	**Activity**	**NMPK**	**MPK**	**NMPK**	**MPK**
Möller et al. (2019)	10 metre timed walk (s)	n=2 10 ± 3.7	n=4 8.4 ± 1.6	n=12 10.1 ± 2.2	n=11 8.1 ± 1.6
Möller et al. (2019)	ABC-UK	n=2 72.2 ± 0.4	n =4 82.1 ± 8.8	n=12 60.4 ± 28.1	n=11 84.3 ± 12.2
Möller et al. (2020)	ABC-UK	n=2 76.9 ± 0.9	n=4 87.9 ± 8.9	n=12 64.9 ± 29.9	n=11 90.0 ± 12.8
Burçak et al. (2021)	SF-36	n=4 39.4 ± 11.0	n=4 52.9 ± 3.4	n=29 37.1 ± 10.6	n=29 49.3 ± 8.2

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Mechanical knee (NMPK); Microprocessor knee (MPK); Seconds (s); Activities-specific balance confidence UK (ABC-UK); Short Form 36 (SF-36). Standard deviation (± SD). Scores are reported as mean ± SD.

3.4. Discussion

This systematic review aimed to compare the biomechanical gait and functional outcomes of patients with a TKA and patients with an AKA when performing activities of daily living, and to examine the balance confidence and QoL between the two levels of amputation. It is evident that patients with a TKA have not been excluded from research, however their results have not been explored thoroughly across all aspects. The studies included in the review used a variety of methods to assess numerous aspects of function and varied in quality.

The main findings of the systematic review and meta-analysis were that following a meta-analysis, 6MWT distance was significantly greater following TKA than AKA. Additionally, the sub-group meta-analysis of the 6MWT identified that completing the test whilst wearing a MPK, patients with a TKA walked significantly further than those with an AKA. There were no other significant findings identified from the meta-analysis.

3.4.1. Studies

There was a total of 611 patients with a unilateral TKA and 1,880 patients with a unilateral AKA included within this systematic review. Additionally, there were 10 bilateral patients with a TKA and 20 bilateral patients with an AKA. It is unclear whether the patients with a TKA or AKA included within the study were predominantly males or females, or the causes of amputations across each case, therefore these factors could not be investigated in depth. From the available meta-analysis patient characteristics, the included patients had a variety of amputation indications (trauma, vascular disease, and cancer), The variety of study designs used (cross-sectional, case studies, observational, prospective, retrospective, and cross-over) demonstrates that it is possible to capture TKA quantitative data in numerous ways. Although, there were 138 studies excluded as they did not meet the inclusion criteria. Identified studies are limited by a small number of patients with a TKA and varied methods, therefore preventing a meta-analysis of most of the available data. Initially upon screening, numerous studies utilised a mixed methodology approach, which although employing mixed methods can gain a better understanding of connections and contraindications between qualitative and quantitative (Shorten & Smith, 2017), the purpose of the systematic review and meta-analysis was to quantitatively scope the literature and review data to determine quantitative differences between TKA and AKA.

Quality of the included studies were calculated using the RoBANS tool and the Downs and Black checklist. The risk of bias was low across all 28 studies, with the lowest results stemming from blinding of outcome assessments and selective outcome reporting. However, some studies had a high selection bias caused by the inadequate selection of participants (Andrysek et al., 2011; Onat et al., 2017; Alsancak & Guner, 2018; Möller et al., 2020). Inadequate consideration of confounding variables caused eight studies to be at high-risk bias (Houghton et al., 1992; Yusuf et al., 1997; Met et al., 2008; Furtado et al., 2015; Onat et al., 2017; Alsancak & Guner, 2018; Sherman et al., 2019). Confounding factors can mask an association, or falsely demonstrate an association between cohorts and the outcome (Skelly et al., 2012). Thus, ensuring that bias is avoided from adjusting for variables that are not confounders are as important as identifying and minimising confounding (Howards, 2018). Intent of performing TKA rather than AKA must be considered a possible confounder in these studies. Anecdotal reports suggest that TKA in the UK are often performed when patients are young and expected to heal well and mobilise with a prosthesis or when patients are expected to be bed bound and benefit from enhanced stump length in optimising sitting balance. The varied indication for amputations suggests a very mixed patient population within the studies and the TKA patients included may either be a distinct group who were expected to perform particularly well or particularly badly in terms of functional tests.

The methodological quality using the Downs and Black checklist varied, with a minimum quality value of 5 and a maximum quality value of 20 across studies. Most studies clearly described reporting category well, including the hypothesis, aims or objectives (Table 3.3, item 1), and outlined the main outcomes to be measured within their introduction or methods (Table 3.3, item 2). Inclusion and exclusion criteria were described (Table 3.3, item 3), along with the main findings and estimates of random variability in the data (Table 3.3, item 7). Following internal validity bias, statistical tests were used in most studies, therefore the answers were predominantly yes (Table 3.3, item 18). Questions that had a poor methodological value included blinding study subjects (Table 3.3, item 14-15), and data dredging (Table 3.3, item 16). Methodological quality could have been higher across all studies and the checklist should be used in future studies to ensure methodological quality is maintained and bias risk is reduced.

3.4.2. Biomechanical Outcomes

Biomechanical gait outcomes were investigated in numerous studies, with a variety of aspects taken into consideration. Walking speed as an indicator of walking capacity was calculated across nine studies (Pinzur et al., 1992; Boonstra et al., 1993; Andrysek et al., 2011; Reid et al., 2015; Alsancak and Guner, 2018; Schuett et al., 2018; Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020), and appeared similar across all studies. Although this parameter has been calculated from activities including 2MWT, 6MWT, 10-metre walk test and other tests, a meta-analysis of studies did not identify a significant difference between TKA and AKA. The identified studies did not individually report significant differences in their results as they initially combined levels of amputation, or their sample size was insufficient to calculate a difference statistically. Although there was insufficient information regarding characteristics, walking speed is known to vary between amputation aetiology, with traumatic amputations having a walking speed up to 1.3m/s, compared to 0.75m/s in dysvascular amputations (Roffman et al., 2016). Previous research has suggested that patients with a traumatic amputation may walk faster on a prosthesis than patients with a dysvascular amputation due to the difference in their overall health, as patients with vascular disease will often be older and may feel fatigued as well as having other issues limiting mobility such as diseased blood vessels in their legs (Waters et al., 1976). Cadence, measured as the number of steps per minute, was also not significant following a meta-analysis. Measuring cadence and walking speed can describe the quality of steps during daily life (Kim et al., 2020). Step count was measured in two studies, however the results from Sherman et al. (2019) appeared somewhat different between in-patient rehabilitation and at-home mobilising. Initially reviewing the results, patients with a TKA took an average of 473 steps more than AKA during in-patient rehabilitation, whereas patients with an AKA took an average of 732 steps more than TKA when at-home mobilising. Although it is unclear if these findings are significant, it could be argued as to whether patients with a TKA abandoned their prosthetic limb and utilised a non-ambulatory approach to mobilising when at home. The TKA has a total end weight-bearing residual limb, thus providing greater comfort, proprioception, and stability (Hagberg et al., 1992; Pinzur, 1993;

Nehler et al., 2003). TKA patients may rest a stump on furniture to stand or may simply have had a longer stride than AKA patients and taken less steps to accomplish similar mobility in this sample.

Parameters including stride length, step length and step width were less frequently included, and results were available from two studies (Alsancak & Guner, 2018; Schuett et al., 2018). These parameters were similarly reported between TKA and AKA, although these were reported across one patient with a unilateral TKA, one patient with a unilateral AKA, four bilateral patients with a TKA, and four bilateral patients with an AKA. These parameters should be examined in depth in future as they may assist to understand and compare the gait pattern following TKA vs. AKA.

Kinematic parameters were measured by Alsancak and Guner (2018). However, there was no statistical comparison between the two levels of amputation as they recruited one patient with a TKA and one patient with an AKA. Although asymmetries are clear from their results, it is unclear from the study how their data were collected and computed, therefore no conclusions can be drawn. Alsancak and Guner (2018) reported the use of three-dimensional gait analysis but did not specify activity selection. Further, they did not specify how data was recorded, nor specify how they analysed their results; thus the study robustness is 108uestionable. They did not justify the use of measurements (reported as Nmm/kg). Similarly, kinetic parameters were reported by Alsancak and Guner (2018), with one patient with a unilateral TKA and one patient with a unilateral AKA. It is difficult to draw conclusions on the biomechanical differences between these two levels of amputation as they did not recruit more than one of each participant in the study.

3.4.3. Functional Outcomes

A meta-analysis identified no significant differences between TKA and AKA when completing the 2MWT (p=0.21). However, 6MWT distance reported across three studies (Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021) identified that patients with a TKA walked significantly further than those with an AKA, on average 43m further. All three studies reported an increased walking distance between 30.8m and 60.2m in the TKA cohort compared to the AKA cohort. Maintaining a longer residual limb allows the rectus femoris, vastus lateralis, vastus medialis and vastus intermedius muscles to stay intact and reduce muscular imbalance compared to the intact limb (Baumgartner, 1979), thus generating more power to drive the limb forwards during walking or when completing household activities. The TKA provides a better suspension, thus allowing better control over the prosthesis (O'Keeffe & Rout, 2019). All four muscles allow extension of the knee joint and stabilises the patella, which are beneficial when getting up and down from a chair, walking, or climbing stairs. Anatomical contributions may allow patients with a TKA to tolerate end weight-bearing thus walk further, compared to the anatomical contributions of AKA, who do not have an end weight-bearing residual limb and have muscular imbalance due to muscles being divided in the thigh. Individuals with a TKA or AKA require a higher energy expenditure when walking with a prosthesis compared to patients with a BKA due to the greater prosthesis componentry required. However, they may be unable to expend as much energy as their blood flow is reduced, therefore reducing in their exercise ability and possibly walking distance.

The TUG test was reported and measured in a meta-analysis for two studies (Hafner et al., 2017; Karatzios et al., 2019). Although the biomechanical advantages of the TKA longer lever and end-weight bearing residual limb would have assisted with stability and walking during this task, the total scores were similar between patients with a TKA and AKA, and the meta-analysis found no significant difference. Karatzios et al. (2019) reported the average time to complete the TUG test was 12.7s ± 7.9s for TKA, and 12.4s ± 6.2s for AKA. These average scores indicate that both levels of amputation were at risk of falling, as a cut-off score of 19 seconds indicated that patients with lower limb amputations were at greater risk of falling (Physiopedia, 2022b). Compared to TUG scores of the TKA cohort 19.7s ± 17.1s and AKA cohort 17.6s ± 10.4s reported by Hafner et al. (2017), the recorded times by Karatzios et al. (2019) are somewhat lower (TKA 12.7s ± 7.9s vs AKA 12.4s ± 6.2s). Half of the patients with a TKA in the study by Karatzios et al. (2019) were due to trauma, and may have a faster walking speed compared to amputations of other aetiologies. Although, these results cannot be confirmed between the two studies as it is unclear as to the specific aetiologies of amputations included in the study by Hafner et al. (2017).

3.4.4. Mobility and Prosthetic Ambulation

Several studies documented and compared mobility and prosthetic ambulation differences between TKA and AKA (Houghton et al., 1989; Hagberg et al., 1992; Houghton et al., 1992; Yusuf et al., 1997; Pernot et al., 2000; Taylor et al., 2005; Met et al., 2008; Gailey et al., 2010; Furtado et al., 2015; Hafner et al., 2017; Esfandiari et al., 2018; Onat et al., 2017). Results were conflicting between studies, for example, Met et al. (2008) reported that 67% of patients with a TKA and 65% of patients with an AKA had a SIGAM score A, thus indicating abandonment of their prosthesis, whereas Hagberg et al. (1992) reported that no patients with a TKA and 28% of patients with an AKA had abandoned use of their prescribed prosthesis. Additionally, Taylor et al. (2005) reported that 61.6% of TKA wore prostheses compared to 44.5%

AKA, whereas Houghton et al. (1992) reported that 30% of the patients with a TKA in their study were limb wearers compared to 3% AKA. These studies presented contrasting results; therefore it is difficult to determine the consensus as to which level of amputation may provide better mobility and prosthetic ambulation. A TKA could be beneficial to ambulatory patients due to the longer mechanical lever from the thigh and the end weight-bearing residual limb, thus generating more power to drive the limb forwards during walking with a prosthetic limb. The daily use of prostheses in patients with a TKA compared with patients with an AKA may be indicative of an increased ease of use, better functional ability, and greater acceptability (Hagberg et al., 1992; Lineham et al., 2017). However, a TKA may also be beneficial to those patients who are non-ambulatory, as the longer the residual limb, the greater the stability and balance when seated (Siev-Ner et al., 2000). Additionally, as the data collection techniques were sporadic amongst the literature, a meta-analysis could not be conducted to determine any significant differences.

3.4.5. Self-Reported Measures

Balance confidence and QoL were measured using the ABC-UK (Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020), LCI-5 (Gökşenoğlu & Yildirim, 2019; Karatzios et al., 2019), Prosthetic Limb Users Survey of Mobility (Hafner et al., 2017; Karatzios et al., 2019), Prosthesis Evaluation Questionnaire (Hafner et al., 2017; Polfer et al., 2019), SF-36 (Polfer et al., 2019; Burçak et al., 2021), the Patient Reported Outcomes Measurement Information System-Physical Function (Hafner et al., 2017), and Toronto Extremity Salvage Score (Furtado et al., 2015). Although these measures are widely used in lower limb amputation research, no differences were found. A meta-analysis on the ABC-UK and LCI-5 determined no significant differences between TKA and AKA. It is interesting to note that there was no difference in balance confidence, defined as the belief that the individual has the capability to perform an activity or action without losing their balance (Miller & Deathe, 2011). The TKA residual limb provides stability and proprioceptive responses that are essential for balance in ambulatory and non-ambulatory individuals (Pinzur, 1992; Siev-Ner et al., 2000), thus may assist with transfers and performing everyday activities. Balance confidence may vary depending on the time from amputation, which could have been explored more in-depth in studies looking at balance confidence. Further, there was no difference in SF-36 physical function between TKA and AKA. The ability to mobilise with a prosthesis has a direct impact on a person's QoL (Agrawal et al., 2017; Davie-Smith et al., 2017b).

3.4.6. Sub-group Analysis

A meta-analysis found a significant difference between TKA and AKA when completing the 6MWT with an MPK. Microprocessors provide a greater method of control with a prosthetic knee, by continuously controlling flexion and extension of the knee joint with a microcomputer system during the stance and swing phase (Şen et al., 2020). Further, they allow the prosthetic knee to respond to the immediate needs of a user's cadence or walking speed whilst adjusting to extrinsic conditions (Şen et al., 2020). Combining the features of an MPK and the biomechanical advantages of a TKA may have influenced the increased distance in patients with a TKA. The longer lever of a TKA stump may simply be more effective at triggering sensors in the MPK to respond, thus benefiting the TKA group in terms of walking function.

3.5. Limitations

Despite the findings of the systematic review and meta-analysis, limitations were apparent. Firstly, the systematic review was searching for published, unpublished, in press or in progress journal articles for inclusion. Some of these unpublished journal articles may or may not have been peer-reviewed, in which journal articles should have been through a rigorous process prior to publication to increase publication quality. However, this is not achievable for every publication (Larson & Chung, 2012). Secondly, identified studies within this review were limited by a small number of participants and varied methods. These therefore have prevented high quality meta-analysis of much of the available data.

3.6. Conclusion

This systematic review assessed and meta-analysed the results of biomechanical, functional outcomes, and balance confidence and QoL following TKA vs. AKA. It highlights the importance of examining TKA vs. AKA, as the evidence cannot provide sufficient conclusions. Furthermore, results show that despite a variety of methods and small number of participants being included across 28 studies, patients with a TKA walked significantly further during the 6MWT than patients with an AKA. Findings suggest that TKA may provide further functional benefits over AKA during activities of daily living. We recommend that where appropriate, studies separate TKA from other levels of amputation to build on the foundation of research surrounding TKA. This systematic review also identified several areas in which the quality of reporting must be improved (for example, including more participant characteristic information, sample size justification, and follow-up of patients). These factors combined could enable more robust research, thus examining these two levels of amputation in more detail.

CHAPTER FOUR: ESTABLISHING STATISTICAL DATA ANALYSIS AND HANDLING MISSING DATA

Chapters Four to Eight are a separate part of the thesis and centres on data collated from the NVR database. Chapter Four will outline missing data techniques, with Chapters Five, Six and Seven applying each of the missing data techniques to the NVR datasets for analysis. Chapter Eight will compare the results collectively for the missing data techniques.

4.1. Introduction

Missing data, or missing values, is specified as the data that are not stored for a particular variable of interest (Kang, 2013). Examples of missing data include incomplete sequencing, missing files, or missing data entries. Missing data are an ongoing problem that is faced during research and clinical aspects (Kang, 2013; Madley-Dowd et al., 2019), as statistical methods presume there is complete information for all variables (Soley-Bori, 2013). However, the amount of missing data can have a significant impact on conclusions that could be drawn from the data (Kang, 2013). Additionally, it can present various problems for investigators, including reducing the statistical power, causing bias, reducing the representativeness of samples, and complicated analysis leading to validity issues and wrong conclusions (Kang, 2013; Madley-Dowd et al., 2019).

4.1.1. Types of Missing Data

According to the literature (Manly & Wells, 2015; Jakobsen et al., 2017; Hughes et al., 2019), there are three types of missing data, including missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR).

MCAR causes large standard errors due to the reduction in sample size (Sterne et al., 2009; Jakobsen et al., 2017), but indicates that there is no relationship between missingness and observed or unobserved covariates being studied. Additionally, incomplete datasets are representative for the entire dataset (Jakobsen et al., 2017). Data are categorised as MCAR when the data are missing by design, if the data are lost, or if the data are not recorded due to equipment failure. Examples of MCAR include a lost questionnaire in the post, a damaged blood sample, or electrical equipment that ran out of batteries. With data that are MCAR, the main statistical advantage is that the analysis remains unbiased. MAR allows a prediction of missing values based on participants with complete data (Sterne et al., 2009; Jakobsen et al., 2017), but indicates that the missingness is still random due to observed values within the model and not due to the missing values. An example of data that are MAR is if an individual misses an examination due to Illness, it may be predictable from previous data about their health, but it would not be related to the examination itself. MAR does not mean missing data can be overlooked; it should be accounted for when feasible. MNAR indicates that the missingness is dependent on the values of the missing data (Sterne et al., 2009; Jakobsen et al., 2017). An example of when data are MNAR is if a set of weighing scale mechanisms wear out over time, causing more missing data, which is not noticed as time progresses.

4.1.2. Missing Data Techniques

There are three techniques that are often used to handle missing data when it is either MAR, MCAR, or MNAR. These techniques include complete case analysis, multiple imputation, and propensity score matching, and will be subsequently described in Chapter Four, Sections 4.2, 4.3, and 4.4, drawing on their background, methodological approach, advantages and disadvantages.

4.2. Handling Missing Data Technique 1: Complete Case Analysis

4.2.1. Background

The most frequent approach to omit missing data is to use complete case analysis for the remaining data. Complete case analysis is a missing data handling technique which involves patient records being analysed if they have complete data fields and have no missing data. Complete case analysis, also known as listwise deletion, has become the default option for analysis in majority of statistical software packages (Kang, 2013). If there is a large enough sample size and data are assumed to not be MCAR, complete case analysis may be a useful strategy. The advantage to this analysis is that it only identifies the individuals that have complete variables (Hughes et al., 2019). However, the disadvantages of using complete case analysis are that not many variables are often completed in large datasets, which can result in a smaller number of patient records being analysed (Soley-Bori, 2013).

4.2.2. Methods

For the complete case analysis purposes, patient case records were selected in IBM SPSS if there was a valid response for age, gender, and whether overall the patient had comorbidities (Figure 4.1). Age, gender, and overall comorbidities were considered the most important identifiers. Additionally, patient records who had either a unilateral TKA or unilateral AKA were selected at this process. Chi-square analysis was completed when examining all categorical variables against level of amputation. Non-parametric independent tests were performed for continuous variables, with Mann-Whitney tests performed for body mass index (BMI) and overall hospital length of stay, and the Kruskal-Wallis test performed for ordinal variables including patient frailty level.

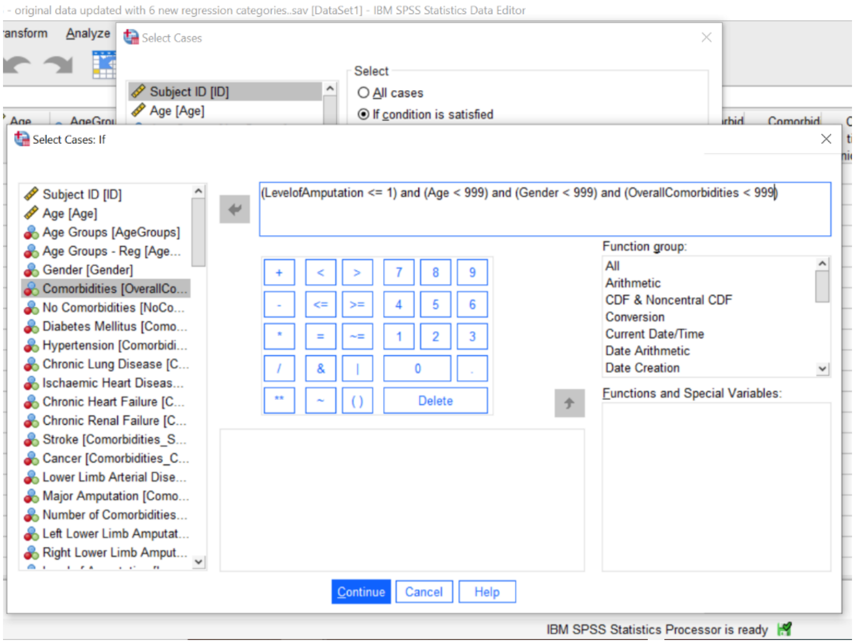

Figure 4.1. Screenshot of selecting complete case analysis.

4.3. Handling Missing Data Technique 2: Multiple Imputation

4.3.1. Background

Multiple imputation is an attractive method for handling missing data (Kang, 2013) and was first proposed by Rubin (1976). Multiple imputation allows the analysis of incomplete data with regular data analysis tools. This technique narrows uncertainty about missing data by calculating several different options, and subsequently several different datasets are created. Instead of substituting a single value for each missing value, the missing data are replaced with numerous credible values which contain variability yet uncertainty of the correct value (Kang, 2013). In the previous years, multiple imputation was rarely used (Eekhout et. Al., 2012; Rombach et. Al., 2018) or never used (Van Ginkel et. Al., 2010), and instead listwise deletion was used.

Multiple datasets are created using multiple imputation and analysed individually before obtaining a combined pooled value (Figure 4.2). Advantages of multiple imputation include the reduction of bias and errors, improve validity and accuracy, increasing the precision, and results in robust statistics (Statistics How To, 2017a). On the contrary, the disadvantages of multiple imputation include it is not good for unbiased estimates of relationships, there are some errors within the estimates, and it assumes that the data are MAR (Lodder, 2013; Bursa, 2017). Another disadvantage to multiple imputation, is that researchers may have to think about the imputation model in addition to the analysis model, as imputation models should contain all variables in the analysis model (Bursa, 2017; Hughes et al., 2019).

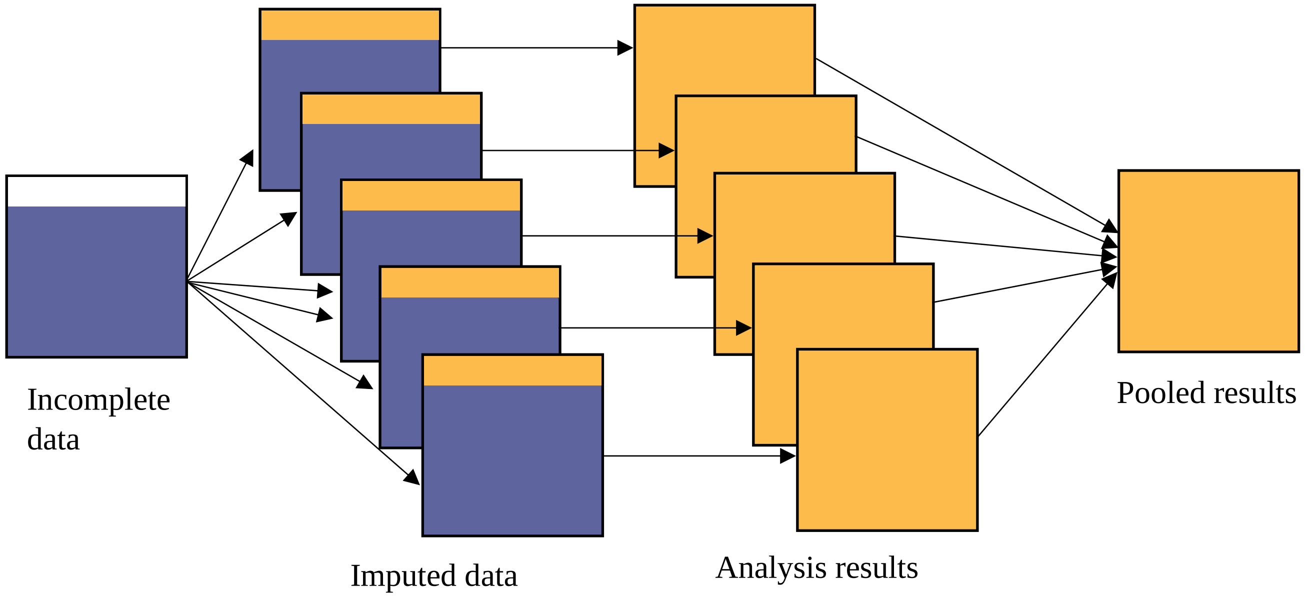

Figure 4.2. Multiple imputation process.

4.3.2. Methods

For the analysis purposes, multiple imputation was performed in IBM SPSS. This imputation method is accounted for by adding error variance to the predicted values and the uncertainty in estimating the regression coefficients found in the imputation model. Predictors used are listed in Table 4.1. All predictors and outcomes that had missing data and were recorded as code 999 were variables that required imputing. Variables with missing data and percentages can be found in Table 4.1. A total of 5 imputations were selected at default by IBM SPSS, and a new dataset was created, thus allowing the multiple imputation data to be opened in a new dataset rather than running into the original document.

The imputation method used was a custom method named "fully conditional specification". This fully conditional specification method, known as the Markov Chain Monte Carlo method, is suitable for data that has an arbitrary pattern of missing values. The maximum number of iterations was changed from the default number of 10 to 50, as it was recommended that there were 10 iterations per imputation (Raghunathan et al., 2002; Heymans & Eekhout, 2019). Maximum iterations specify the number of iterations or steps taken by the Markov Chain Monte Carlo used by the fully conditional specification method. For each outcome in the variable list, and for each iteration specified, the fully conditional specification method applies a univariate model using all available variables in the model as predictors. It then imputes the missing values for the variable being applied. The method continues until the maximum number of iterations are reached, and the imputed values at the maximum iteration are saved to the new imputed dataset. The model type for continuous variables was chosen as "predictive mean matching". Predictive mean matching is a modification of linear regression, which matches the computed imputed values from the regression model to the closest observed value. The minimum and maximum imputed values were defined for continuous variables when the linear regression model is selected in the method tab. The current range of variable values from the database were obtained and were adjusted accordingly. Descriptive statistics of imputed variables were exctracted and the iteration history dataset was requested, which contains the means and standard deviations of the imputed continuous variables for each iteration.

Upon completion of multiple imputation analysis, a new SPSS dataset was formed with imputed values stacked below each other, and the imputed values marked in yellow. It is important for imputed values to remain marked in yellow to allow further statistical analysis to be successful. Descriptive statistics and independent t-tests were then completed for continuous variables to determine the pooled mean, standard deviation, and median. Chi-square analysis was completed when examining all categorical variables for each level of amputation. This analysis gave a pooled count and percentage of all categorical variables for each level of amputation. In addition, logistic regression was performed to determine the relationship between the level of amputation and outcome of interest.

Table 4.1. Missing data factor list for multiple imputation model.

Predictor or Outcome Name	Percentage of missing data (%)
Age	0.1
Body Mass Index (BMI)	40.4
Haemoglobin	15.7
Smoking Status	23
Amputation Indication	1.4
Procedure Time	0.1
Return to Theatre	1.3
Further Surgery	7.1
Post-Operative Complications	0.1
Overall Hospital Length of Stay	0.3
Discharge Status	0
Discharge Destination	63.1
Amputation Rehabilitation Referral	0.1
30-days Re-admission	13.6
30-days Vascular Re-admission	95.5
30-days Mortality	36.2
30-days Wound Healing	43.9
Patient Frailty	77.9

4.4. Handling Missing Data Technique 3: Propensity Score Matching

4.4.1. Background

Matching has become a prevalent approach to estimate treatment effects (Caliendo & Kopeinig, 2008). Propensity score was introduced by Rosenbaum and Rubin (1983) to adjust a treatment effect for confounders in non-randomised studies and is the probability that a unit with certain characteristics will be assigned to the experimental group (Thoemmes, 2012). The propensity score is the conditional probability of being in the experimental condition, given the set of observed characteristics that were taken prior to their amputation. The scores can be used to eliminate selection bias in observational studies by balancing the characteristics of participants between the control and experimental groups (Statistics How To, 2017b). When these characteristics are balanced, it is easier to match participants with multiple characteristics. The closer the score is to 0, the stronger the prediction that the patient would be in the experimental group (unilateral TKA); and the closer the score is to 1, the stronger the prediction that the participant would be in the control group (unilateral AKA). Propensity score matching creates a set of patients in the control and experimental groups with similar propensity scores. A matched set consists of at least one patient in the control group and one patient in the experimental group, with similar propensity scores. The propensity score is defined as the probability of receiving treatment based on a measured covariate:

$$e(x) = P(Z=1 \mid X)$$

where e(x) is an abbreviation for the propensity score, P is the probability, Z=1 is a treatment indicator with 0 accounting for the control and 1 accounting for the treatment, the "|" symbol indicates conditional on, and X is the set of observed covariates (Thoemmes, 2012). One-to-one matching without a replacement allows the matching of an experimental participant to a control participant who has a similar propensity score (Shadish & Steiner, 2010). Those two matched participants are removed from the pool, and then the next experimental participant is matched to the next similar control group participant (Staffa & Zurakowski, 2018). This process continues until all experimental group participants have a match, or until no further matches are possible. Upon completion of propensity score matching, they can be used in different analyses to compare the two groups. When propensity score matching is accounted for, selection bias is eliminated (Streiner & Norman, 2012). If crucial variables have been overlooked, groups may remain unbalanced, and the results of the study can cause bias (Streiner & Norman, 2012). One issue with propensity score matching, is that a considerable large amount of data could be lost and jeopardise the study results when individual records are excluded. Further, this may reduce power and limit the generalisation (Shadish & Steiner, 2010).

4.4.2. Methods

For the study, propensity score matching was completed with the levels of amputation as the group indicator (patients with a unilateral TKA and patients with a unilateral AKA), and gender, age as a categorical measure, and overall comorbidities all as predictors, thus allowing a pairing of the two levels of amputation within IBM SPSS (Figure 5.3). The case ID was selected as the patient's personal subject ID, and a match tolerance of 0 was selected as the matches were to be as close as possible. The match ID variable was the value of which codes were matched.

Sampling without replacement was used to allow all experimental participants to be paired, and if not paired, they were removed from the analysis. Maximum execution performance was used within the propensity score matching as it maximised the performance in selecting matches by using the maximum speed and minimum memory usage, which was recommended when using large datasets (Rubin, 1988). A random number seed of 1 was utilised to repeat the analysis and find the closest match. Upon each subject ID receiving a propensity score match ID, those who were matched received a value greater than 1, and those who were not matched received a blank value. Blank cases were excluded from further analysis. The most successful matches were determined by computing a variable that satisfied the condition (level of amputation), with those successful matches paired to the alternate level of amputation. Upon pairing, cases were sorted ascending by their matched amputation level.

Analysis of the baseline characteristics of age, gender and overall comorbidities were performed to determine the balance between the two levels of amputation. Successful matching was determined by both groups being balanced for the baseline characteristics. Further analysis of each factor and outcome were carried out using Chi-square and non-parametric tests for categorical and continuous variables, respectively. As the p-values comparing the baseline characteristics between the treatment and control group were driven by sample size (Austin, 2008; Austin, 2009; Staffa & Zurakowski, 2018), the baseline characteristics matched upon, and the matched baseline characteristics were compared to assess the matching quality.

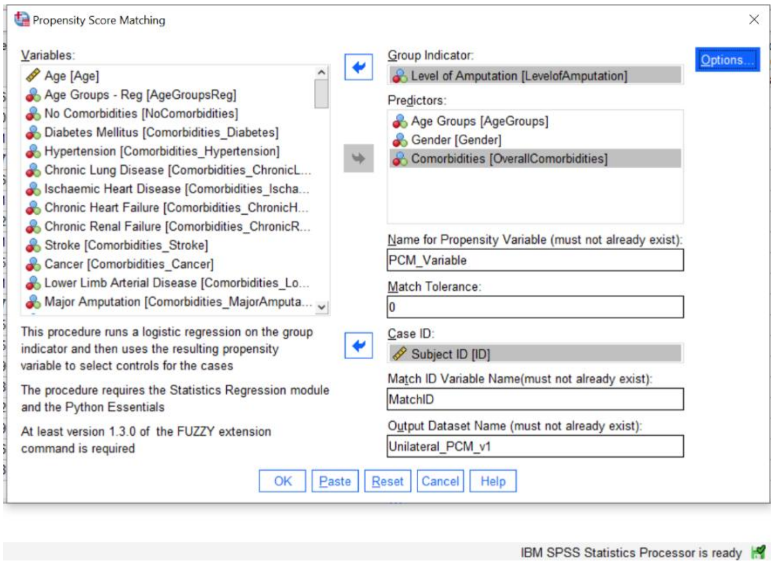

Figure 4.3. Propensity score matching set-up in IBM SPSS.

4.5. Discussion

The aim of this chapter was to outline the background of the three missing data types, and to discuss the background and methodological approach of the three different handling missing data techniques.

When completing statistical data analysis, it is crucial to have all data available, as missing data reduces the power of any given trial. However, this may not always be the case and some data are expected to be missing, although a target sample size may be increased to allow for missing data. Having complete data allows analysis to be as accurate as possible, and that differences are not because of chance. If there are large numbers of missing data, there is the potential of not detecting important differences between treatments or clinical practice. Having missing data is not an impediment, but it is important to perform the correct analysis based on the missingness. More consideration should be in place when designing a study or completing clinical databases to allow complete and accurate analysis.

Each of the handling missing data techniques have their advantages and disadvantages should this analysis be needed. Complete case analysis may not be viable for all data, but it can be useful when identifying the number of individuals with complete information for each variable and can still provide an estimate for those with complete data. However, complete case analysis can give unbiased estimates when data are MNAR. When the data are MCAR, complete case analysis is inefficient but may lead to unbiased associations (van der Heijden et al., 2006). Although, if the data were MCAR, complete case analysis can cause potential issues (Pigott, 2001). Nevertheless, when the data missing are not MCAR, it can also be inefficient and lead to biased results (Rubin, 1976; Greenland & Finkle, 1995; Vach, 1997; Schafer & Graham, 2002; van der Heijden et al., 2006). With multiple imputation, the goal is to obtain estimates of missing values rather than the expected values of sufficient statistics (Pigott, 2001), and numerous values for each missing data observation are generated. Standard methods of analysis can be used once imputations are performed, and standard errors of estimates can be obtained. Each iteration of data generates one completed data set; therefore, thousands of iterations may be obtained to complete up to five datasets for further analysis. Additionally, an issue with multiple imputation is the number of completed data sets required for multiple imputation (Pigott, 2001). Schafer (1997) suggested that having five completed datasets may result in unbiased results, although it may suffice for analysis and provide inferences that are efficient and practically valid. Propensity score matching, on the other hand, allows the mimicking of some characteristics of an RCT (Austin, 2011). Although propensity score matching does not produce gold standard levelled evidence like an RCT, it is a highly effective method to balance groups and may lead to instinctive analysis (Staffa & Zurakowski, 2018). As confounding influences of covariates can cause bias with effect estimates, propensity score matching allows an approach to omit confounding bias. By using matching, balance of the covariates is created, and the confounding effect has the potential to be minimised or entirely removed (Thoemmes, 2012). On this basis, propensity score matching has become increasingly popular in the wider research context (Khan et al., 2013; Hsu et al., 2017; Lim et al., 2018; Staffa & Zurakowski, 2018; Kim et al., 2020; Traven et al., 2019; Qi et al., 2020; Haug et al., 2021), with Lim et al. (2018) using this technique to evaluate surgical outcomes of TKA and AKA. According to Staffa and Zurakowski (2018), propensity score matching is an important methodological technique to obtain a balance of observed relevant covariates and allows a more objective group comparison.

4.6. Conclusion

In summary, if a dataset or trial has missing data, it is important to determine whether that missing data are at random, completely at random, or not at random. Each of the handling missing data techniques outlined have their advantages and disadvantages, and equally can be as vital to make inferences on the data at hand.

CHAPTER FIVE: NATIONAL VASCULAR REGISTRY – COMPLETE CASE ANALYSIS

5.1. Introduction

The NVR measures the quality and the care outcomes for patients who undergo a major vascular surgery in NHS hospitals, in which vascular departments within the UK can improve the quality of care received by those patients. To date, all analysis of amputation data within the NVR has compared AKA and BKA outcomes. It is accepted that a BKA allows enhanced recovery over amputations at a higher level (Waton et al., 2016). Patients with a TKA have always been grouped with patients with an AKA for clinical and functional outcomes literature (Kristensen et al., 2015; Liu et al., 2015; Reid et al., 2015; Prinsen et al., 2017a; Prinsen et al., 2017b; Möller et al., 2018; Mundell et al., 2018; Karatzios et al., 2019; Möller et al., 2019; Welke et al., 2019; Möller et al., 2020; Burçak et al., 2021) however, TKA was categorised with BKA within recent NVR annual reports (Waton et al., 2019; Waton et al., 2020) and the literature (Jensen et al., 2017).

The numerous variations of TKA procedures, along with a lack of surgical experience and consensus around the patient criteria who could potentially benefit from a TKA, may be causing surgeons to favour an AKA over a TKA. This study aimed to perform a large-scale retrospective analysis of a case control series using data held within the NVR database, and to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA. Examples of post-operative outcomes include post-operative complications, discharge status and destination, 30-day mortality, 30-day wound healing, and prosthetic rehabilitation referral.

5.2. Methods

5.2.1. Data Request Application Form

A 20-section data access request form (DARF) was completed as part of the application process and included sections based on project details, data summary, data type, and data fields. The form was submitted to Healthcare Quality Improvement Partnership (HQIP) and the HQIP application was approved (application number HQIP356). Upon approval, depersonalised data were exported into Microsoft Excel by the NVR manager and was electronically transferred via a File Transfer Protocol Secure using a file sharing system at the Royal College of Surgeons. The data file was encrypted by the NVR manager before uploading it to the file transfer system.

5.2.2. Data Analysis

The de-personalised patient level data were sorted and cleaned in Microsoft Excel. Upon cleaning, missing data were recorded as code 999. The cleaned data were processed into IBM Statistical Package for the Social Sciences (IBM SPSS, version 27) software for analysis. Complete case analysis were determined by complete information of the patient's age, gender, and overall comorbidities, and were analysed using methods outlined in Chapter Four, Section 4.2.2. Non-parametric independent tests and chi-square were used within the IBM SPSS software to determine any significant differences in clinical outcomes between patients with a unilateral TKA and patients with a unilateral AKA. Non-parametric independent t-tests were used for continuous variables including age, body mass index (BMI), haemoglobin, overall hospital length of stay and critical care length of stay, when data were non-normally distributed. Chi-square were used for categorical variables including gender, comorbidities, rehabilitation referral, 30-day mortality, and wound healing.

5.3. Results

During the years of 2016 and 2019, there were a total of 497 unilateral TKA procedures and 6,757 unilateral AKA procedures within England and Wales with complete case records for age, gender, and overall comorbidities. Patient characteristics are described in Chapter Five, Section 5.3.1, and remaining outcomes are outlined subsequently.

5.3.1. Patient Characteristics

Patient characteristics are described in Table 5.1, Table 5.2, Table 5.3 and Table 5.4.

Patients within the study were of a similar age (Table 5.1), and there was no significant difference in age between the two levels of amputation (p=0.075). There was a significantly higher percentage of patients with a TKA who were under 60 years old at the time of their amputation compared to patients with an AKA (24.3% and 19%, respectively), $\chi^2(1) = 8.362$, p=0.004. Although amputations were more frequent amongst males (Table 5.1), there was no association between gender and level of amputation, $\chi^2(1) = 0.754$, p=0.385.

Patients within the study had a similar BMI (Table 5.2), thus there was no significant effect between BMI and level of amputation (p=0.076). The BMI groups (underweight, healthy, overweight and obese) were determined by their overall BMI (NHS, 2019a). There was no significant association found between BMI group and level of amputation (Table 5.2).

Haemoglobin levels were similar between patients with a TKA and patients with an AKA (Table 5.2), thus there was no significant association found (p=0.370). Anaemia was refined as patients who were male and had a haemoglobin level equal to or lower than 13.5 grams per decilitre (g/dL), and patients who were female and had a haemoglobin level equal to or lower than 12g/dL. There was no significant association found between haemoglobin level and level of amputation, $\chi^2(1) = 0.524$, $p=0.469$.

Pre-operative comorbidities reported in the NVR included diabetes mellitus, hypertension, ischaemic heart disease, and major amputation (Table 5.3). There were 449 (90.3%) patients with a TKA and 6,027 (89.2%) patients with an AKA who had pre-operative comorbidities. Patients with a TKA had a significantly higher presence of diabetes mellitus compared to patients with an AKA, $\chi^2(1) = 10.259$, $p=0.001$. Patients with a TKA had a significantly lower presence of chronic lung disease compared to AKA, $\chi^2(1) = 4.518$, $p=0.034$. There were no significant differences between the levels of amputation and alternative comorbidities (Table 5.3). Further, there were no significant differences in smoking history between the two levels of amputation (Table 5.3; $p>0.05$).

Incidence of patient frailty was determined as the number of patients that were frail at the time of their amputation. Patient frailty was categorised as not frail, mild frailty, moderate frailty, and severe frailty, as recorded in the Patient Frailty Score Guidance (Vascular Services Quality Improvement Programme, 2019). Not frail was determined as the patient was well or managing well and were routinely walking. Mild frailty was determined as evident slowly such as difficulty when walking outside. Moderate frailty was defined as if the patient needed help with some personal care or housekeeping, and severe frailty was defined by the patient being completely dependent for personal care. The incidence of patient frailty was determined between the two levels of amputation. Significantly more patients with a TKA were frail compared to patients with an AKA (Table 5.4), $\chi^2(1) = 4.240$, $p=0.039$. There was no significant association between the two levels of amputation and mild, moderate, and severe frailty, independently ($p>0.05$).

Table 5.1. Patient characteristics following complete case analysis.

Characteristic	TKA	AKA	P
Age (years)	**N=497**	**N=6757**	0.075
- Mean (± SD)	69.1 ± 13.3	70.4 ± 12.5	
- Median (IQR)	71.3 (60.6-78.9)	71.7 (62.7-79.4)	
Age Group, n (%)	**N=497**	**N=6757**	
- Under 60 years	121 (24.3)	1,286 (19)	0.004*
- 60-70 years	109 (21.9)	1,720 (25.5)	0.081
- 70-80 years	153 (30.8)	2,176 (32.2)	0.513
- 80+ years	114 (22.9)	1,575 (23.3)	0.850
Gender, n (%)	**N=497**	**N=6757**	0.385
- Male	326 (65.6)	4,560 (67.5)	
- Female	171 (34.4)	2,197 (32.5)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage) unless stated; * signifies a significant difference of $p<0.005$.

Table 5.2. Patient BMI and haemoglobin characteristics following complete case analysis.

Characteristic	TKA	AKA	P
BMI (kg/m^2)	**N=326**	**N=4314**	0.076
- Mean (± SD)	27.2 ± 8.4	26.1 ± 6.7	
- Median (IQR)	25.7 (22-30.9)	25.2 (21.6-29.4)	
BMI Group, n (%)	**N=326**	**N=4314**	
- Underweight (<18.5 kg/m^2)	34 (10.4)	388 (9)	0.385
- Healthy (18.5-24.9 kg/m^2)	116 (35.6)	1,713 (39.7)	0.142
- Overweight (25-29.9 kg/m^2)	88 (27)	1,227 (28.4)	0.576
- Obese (>30 kg/m^2)	88 (27)	986 (22.9)	0.088
Haemoglobin (g/dL)	**N=427**	**N=5810**	0.370
- Mean (± SD)	10.9 ± 2.2	10.8 ± 2.2	
- Median (IQR)	10.6 (9.3-12.1)	10.5 (9.2-12)	
Haemoglobin Level, n (%)	**N=427**	**N=5810**	0.469
- Anaemic	369 (86.4)	4,946 (85.1)	
- Not Anaemic	58 (13.6)	864 (14.9)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Body mass index (BMI); Standard deviation (SD); Interquartile range (IQR); kilograms per metres squared (kg/m^2); grams per decilitre (g/dL); Values reported as count (percentage) unless stated.

Table 5.3. Patient comorbidities and smoking status following complete case analysis.

Characteristic	TKA, n (%)	AKA, n (%)	P
Comorbidities	**N=497**	**N=6757**	
- No Comorbidities	48 (9.7)	730 (10.8)	0.426
- Diabetes Mellitus	249 (50.1)	2,887 (42.7)	0.001*
- Hypertension	311 (62.6)	4,225 (62.5)	0.983
- Chronic Lung Disease	113 (22.7)	1,832 (27.1)	0.034*
- Ischaemic Heart Disease	210 (42.3)	2,778 (41.1)	0.618
- Chronic Heart Failure	71 (14.3)	878 (13)	0.410
- Stroke	58 (11.7)	874 (12.9)	0.416
- Chronic Renal Failure	100 (20.1)	1,351 (20)	0.946
- Cancer	16 (3.2)	168 (2.5)	0.316
- Lower Limb Arterial Disease	0 (0)	4 (0.1)	0.587
- Major Amputation	24 (4.8)	392 (5.8)	0.368
Smoking Status	**N=495**	**N=6736**	
- Never	95 (19.2)	1,123 (16.7)	0.148
- Ex-smoker	243 (49.1)	3,275 (48.6)	0.839
- Current or stopped within 2 months	157 (31.7)	2,338 (34.7)	0.177

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

Table 5.4. Patient frailty following complete case analysis.

Factor	TKA, n (%)	AKA, n (%)	P
Frail	**N=120**	**N=2049**	0.039*
- Yes	87 (72.5)	1,295 (63.2)	
- No	33 (27.5)	754 (36.8)	
Frailty Level	**N=120**	**N=2049**	
- Not Frail	33 (27.5)	754 (36.8)	0.039*
- Mild Frailty	27 (22.5)	367 (17.9)	0.205
- Moderate Frailty	37 (30.8)	601 (29.3)	0.726
- Severe Frailty	23 (19.2)	327 (16)	0.353

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

5.3.2. Pre-Operative Factors

5.3.2.1. Admission Type

The total elective and non-elective admissions were compared between the two levels of amputation (497 TKA and 6757 AKA). There was a significantly higher number of patients with a TKA (131, 26.4%) who had an elective admission compared with patients with an AKA (1,180, 17.5%), $\chi^2(1) = 24.737$, $p<0.001$ (Figure 5.1).

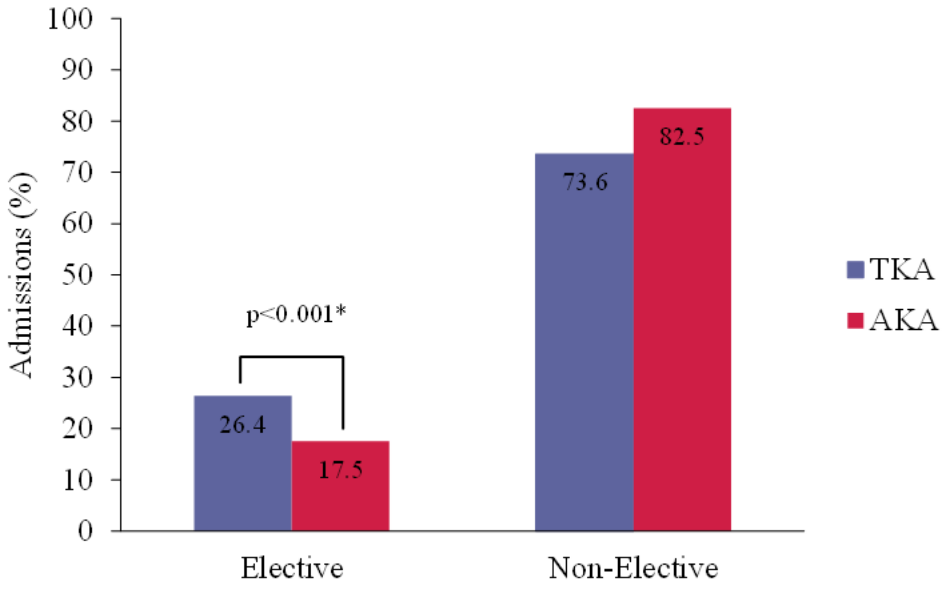

Figure 5.1. Admission type following complete case analysis.

5.3.2.2. Amputation Indication

There were seven amputation indications reported in the NVR database. These indications included acute limb ischaemia, chronic limb ischaemia, tissue loss, and trauma (Table 5.5). There was a significantly higher number of patients with an AKA because of acute limb ischaemia compared to patients with a TKA, $\chi^2(1) = 21.446$, $p<0.001$. Secondly, there was a significantly higher number of patients with an AKA because of chronic limb ischaemia compared to TKA, $\chi^2(1) = 4.237$, $p=0.040$. However, there was a significantly higher number of patients with a TKA due to tissue loss compared to patients with an AKA, $\chi^2(1) = 16.568$, $p<0.001$.

Table 5.5. Amputation indication following complete case analysis.

Factor	TKA, n (%)	AKA, n (%)	P
Amputation Indication	**N=496**	**N=6669**	
- Acute Limb Ischaemia	63 (12.7)	1,431 (21.5)	<0.001*
- Chronic Limb Ischaemia	90 (18.1)	1,474 (22.1)	0.040*
- Neuropathy	8 (1.6)	78 (1.2)	0.382
- Tissue Loss	224 (45.2)	2,403 (36)	<0.001*
- Uncontrolled Infection	95 (19.2)	1,116 (16.7)	0.165
- Trauma	11 (2.2)	85 (1.3)	0.078
- Aneurysm	5 (1)	82 (1.2)	0.664

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

5.3.2.3. Time of Procedure

The time of procedure was determined as the time the procedure began when there was knife-to-skin contact. Table 5.6 indicates the number of patients, total percentage, and p-value for the time of procedure for patients with a TKA and patients with an AKA. Significantly more patients with a TKA had their procedure performed during core daytime hours of 07:00 to 19:00, $\chi^2(1) = 5.987$, $p=0.014$.

Table 5.6. Time of procedure following complete case analysis.

Factor	TKA, n (%)	AKA, n (%)	P
Time of Procedure	**N=497**	**N=6751**	0.014*
- 07:00 – 19:00 hours	476 (95.8)	6,271 (92.9)	
- 19:00 – 07:00 hours	21 (4.2)	480 (7.1)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

5.3.3 Post-Operative Factors

5.3.3.1. Critical Care Admission from Theatre

The incidence of critical care admission from theatre was determined as the number of patients that were admitted to critical care within hospital following the surgical procedure of a major lower limb amputation. The length of critical care stay was determined as the number of days, if any, following a patient's lower limb amputation, where they were admitted to critical care within hospital. Table 5.7 highlights the critical care admission rates and critical care length of stay following their initial amputation. There were significantly fewer patients with a TKA who were admitted to critical care compared to patients with an AKA, $\chi^2(1) = 9.289$, $p=0.002$. However, there was no significant difference in critical care length of stay between the two levels of amputation ($p=0.072$).

Table 5.7. Critical care admission and critical length of stay following complete case analysis.

Critical Care	TKA	AKA	P
Admission, n (%)	**N=497**	**N=6757**	0.002*
- Yes	54 (10.9)	1,082 (16)	
- No	443 (89.1)	5,675 (84)	
Length of Stay (days)	**N=54**	**N=1082**	0.072
- Mean (± SD)	4.4 ± 6.3	5 ± 6.9	
- Median (IQR)	2 (1-4)	3 (2-5)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of $p<0.005$.

5.3.3.2. Incidence of Return to Theatre

The incidence of return to theatre was determined as the number of patients that returned to theatre following their major lower limb amputation. Return to theatre within the NVR was removed from the amputation dataset in January 2019 and replaced with further surgery. The type of further surgery was compared between patients with a TKA and patients with an AKA.

There was no significant association found between the two levels of amputation and return to theatre, $\chi^2(1) = 3.209$, $p=0.073$ (Table 5.8). For those who had further surgery, a similar percentage of patients with a TKA and patients with an AKA had received angioplasty with a stent (0.2% and 0.1%, respectively), a major lower limb amputation (1.1% and 1.2%, respectively), and other forms of surgery (1.6% and 1.7%, respectively). There were no significant differences in further procedures between groups ($p>0.05$).

Table 5.8. Return to theatre rates and types of further surgery following complete case analysis.

Post-Operative Factor	**TKA, n (%)**	**AKA, n (%)**	**P**
Return to Theatre	**N=481**	**N=6694**	0.073
- Yes	49 (10.2)	528 (7.9)	
- No	432 (89.8)	6,166 (92.1)	
Further Surgery Type	**N=445**	**N=6361**	
- None	432 (89.8)	6,166 (91.8)	0.129
- Angioplasty with Stent	1 (0.2)	5 (0.1)	0.315
- Major Lower Limb Amputation	5 (1.1)	74 (1.2)	0.940
- Other	7 (1.6)	106 (1.7)	0.882

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

5.3.3.2.1. Incidence of Revision of Amputation

The incidence of revision of amputation was determined as the number of patients who were revised to a higher level of amputation following their original major lower limb amputation. Incidence of revision of amputation was determined between the two levels of amputation. Further surgery with a multi-code response was added to the NVR dataset in January 2019, which resulted in incomplete responses previously.

Table 5.8 indicates there was a similar percentage of patients with a TKA and an AKA who had a major lower limb amputation following their initial amputation (1.1% and 1.2%, respectively). No significant difference between the two levels of amputation was determined, $\chi^2(1) = 0.006$, $p=0.940$. It should be noted that there were no minor lower limb amputations reported in the NVR database.

5.3.3.3. Incidence of Post-Operative Complications

The incidence of complications was determined as the number of patients who experienced complications following their major lower limb amputation. The number of post-operative complications were determined by the total number of post-operative complications that each patient experienced. Table 5.9 indicates the post-operative complications experienced by patients with a TKA and AKA following their initial surgery. Patients with a TKA experienced significantly fewer cardiac complications post-operatively compared to patients with an AKA, $\chi^2(1) = 5.414$, $p=0.020$. Further, patients with a TKA experienced significantly fewer respiratory complications post-operatively compared to patients with an AKA, $\chi^2(1) = 6.624$, $p=0.010$. There were no significant differences between the two levels of amputation and independently cerebral, renal failure, limb ischaemia and paraplegia ($p>0.05$).

The number of post-operative complications patients had varied between the two levels of amputation (Table 5.9). Patients with a TKA had no more than five post-operative complications, however, patients with an AKA had up to 10 post-operative complications. There was no significant difference between level of amputation and number of post-operative complications, $\chi2(10) = 7.504$, $p=0.677$. When investigating those patients who had post-operative complications, only one patient with a TKA had five or more post-operative complications (Table 5.9), therefore those with complications following a TKA had fewer overall number of complications compared to patients with an AKA. These findings were not significant between the two levels of amputation, $\chi2(1) = 2.133$, $p=0.144$.

Table 5.9. Post-operative complications following complete case analysis.

Post-Operative Complications	TKA, n (%)	AKA, n (%)	P
Complication Type	**N=496**	**N=6753**	
- None	396 (79.8)	5,133 (76)	0.053
- Cardiac	26 (5.2)	552 (8.2)	0.020*
- Respiratory	34 (6.9)	708 (10.5)	0.010*
- Cerebral	3 (0.6)	106 (1.6)	0.088
- Renal Failure	20 (0.4)	280 (4.1)	0.902
- Haemorrhage	6 (1.2)	100 (1.5)	0.627
- Limb Ischaemia	17 (3.4)	240 (3.6)	0.883
- Paraplegia	2 (0.4)	72 (1.1)	0.156
- Post-Operative Confusion	4 (0.8)	88 (1.3)	0.340
- Major GI Complication	1 (0.2)	19 (0.3)	0.744
- Surgical Site Infection	8 (1.6)	118 (1.7)	0.825
- Other	12 (2.4)	251 (3.7)	0.136
Number of Complications	**N=496**	**N=6753**	
- 0	396 (79.8)	5,133 (76)	0.053
- 1	81 (16.3)	1,179 (17.4)	0.522
- 2	10 (2)	207 (3.1)	0.186
- 3	5 (1)	96 (1.4)	0.448
- 4	3 (0.6)	76 (1.1)	0.281
- 5	1 (0.2)	40 (0.6)	0.263
- 6	0	12 (0.2)	0.347
- 7	0	5 (0.1)	0.544
- 8	0	3 (0.0)	0.639
- 9	0	1 (0.0)	0.786
- 10	0	1 (0.0)	0.786
Complications	**N=100**	**N=1220**	0.144
- 1 to 4	99 (99)	1,558 (96.2)	
- 5+	1 (1)	62 (3.8)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

5.3.3.3.1. Incidence of Surgical Site Infection

The incidence of surgical site infection was determined as the number of patients who experienced a surgical site infection following their major lower limb amputation. Surgical site infection was similar in patients with an AKA and patients with a TKA (Table 5.9). Further, there was no significant difference between level of amputation and surgical site infection, $\chi^2(1) = 0.049$, p=0.825.

5.3.3.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were calculated as the number of patients that died prior to discharge and the number of patients that died within 30 days of receiving a major lower limb amputation, respectively. In-hospital and 30-day mortality were determined between the two levels of amputation. Table 5.10 displays the in-hospital and 30-day mortality rates in complete case records recorded in the NVR for patients with a TKA and patients with an AKA. In-hospital mortality was significantly higher in patients with an AKA compared to patients with a TKA (10.8% and 6.2%, respectively; $\chi^2(1) = 10.170$, p=0.001). Further, 30-day mortality was significantly higher in patients with an AKA compared to patients with a TKA (11.9% and 6.6%, respectively; $\chi^2(1) = 8.221$, p=0.004).

Table 5.10. In-hospital and 30-day mortality rates following complete case analysis.

Outcome	TKA, n (%)	AKA, n (%)	P
Mortality Rates	**N=497**	**N=6757**	0.001*
- In-Hospital mortality	31 (6.2)	728 (10.8)	
- Survived	466 (93.8)	6029 (89.2)	
Upon Discharge	**N=331**	**N=4547**	0.004*
- 30-day mortality	22 (6.6)	539 (11.9)	
- Survived	309 (93.4)	4008 (88.1)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

5.3.4. Discharge Outcomes

5.3.4.1. Overall Hospital Length of Stay

Overall length of stay (LOS) was calculated as the number of days that each patient stayed in hospital following their major lower limb amputation and was determined between the two levels of amputation. Table 5.11 illustrates the mean, median and interquartile ranges for both levels of amputation. Overall hospital LOS was similar between patients with a TKA and patients with an AKA (p=0.408).

Table 5.11. Overall hospital length of stay (days) following complete case analysis.

Outcome	TKA	AKA	P
Overall Hospital LOS	**N=496**	**N=6742**	0.408
- Mean (± SD)	30.9 ± 23	31.6 ± 30.8	
- Median (IQR)	22 (12.3-38)	23 (13-40)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Standard deviation (SD); Interquartile range (IQR).

5.3.4.2. Discharge Destination

Discharge destination was determined as the number of patients that were discharged to their own residence, to rehabilitation, to a different hospital, or to intermediate care following their major lower limb amputation. Discharge destination was determined between the two levels of amputation.

Table 5.12 displays the discharge destinations for complete case records recorded in the NVR for patients with a TKA and patients with an AKA. Significantly more patients with a TKA were discharged to their own residence compared to patients with an AKA (51.4% and 43.9%, respectively; $\chi^2(1) = 3.878$, $p=0.049$).

Table 5.12. Discharge destination following complete case analysis.

Outcome	TKA, n (%)	AKA, n (%)	P
Discharge Destination	**N=183**	**N=2949**	
- Deceased	31 (16.9)	728 (24.7)	-
- Own Residence	94 (51.4)	1,294 (43.9)	0.049*
- Rehabilitation	24 (13.1)	355 (12)	0.654
- Other Hospital	22 (12)	407 (13.8)	0.497
- Intermediate Care	12 (6.6)	165 (5.6)	0.584

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Values reported as count (percentage) unless stated.

5.3.4.3. Wound Healing Rates

Wound healing rates were determined as the number of patients who had successful wound healing 30 days after a major lower limb amputation and were determined between the two levels of amputation. Wound healing was successful in over 75% of patients within the study (Table 5.13). However, the rates were similar between both levels of amputation and there was no significant association, $\chi^2(1) = 1.395$, $p=0.238$.

Table 5.13. Wound healing rates following complete case analysis.

Outcome	TKA, n (%)	AKA, n (%)	P
Wound Healing Rates	**N=292**	**N=4089**	0.238
- Yes	232 (79.5)	3,125 (76.4)	
- No	60 (20.5)	964 (23.6)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

5.3.4.4. Incidence of Re-admission within 30 days

Incidence of re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital. The incidence of vascular re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital for vascular reasons. The incidence of re-admission within 30 days and incidence of vascular re-admission within 30 days was determined between the two levels of amputation.

Table 5.14 indicates the 30-day hospital re-admission rates in patients with a TKA and AKA. There was no significant difference between the two levels of amputation (p=0.547).

Of these re-admissions, 4 (7.5%) of patients with a TKA and 77 (8%) of patients with an AKA were re-admitted for vascular reasons. There was no significant association between the two levels of amputation (p=0.903).

Table 5.14. 30-day hospital re-admission rates following complete case analysis.

Outcome	TKA, n (%)	AKA, n (%)	P
Re-admission 30 days	**N=424**	**N=5946**	0.547
- Yes	39 (9.2)	497 (8.4)	
- No	385 (90.8)	5,449 (91.6)	
Vascular Re-admission 30 days	**N=53**	**N=961**	0.903
- Yes	4 (7.5)	77 (8)	
- No	49 (92.5)	884 (92)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

5.3.4.5. Incidence of Referral to Rehabilitation

Incidence of referral to rehabilitation was determined as the number of patients that were referred to rehabilitation and/or limb fitting on the condition of being alive at discharge from hospital. The incidence of referral to rehabilitation was determined between the two levels of amputation.

Data were available for 497 TKA and 6757 AKA. A total of 352 (70.8%) patients with a TKA and 4,134 (61.2%) patients with an AKA were referred to amputation rehabilitation (Figure 5.2). Overall, significantly fewer patients with an AKA were referred to amputation rehabilitation compared to patients with a TKA, $\chi^2(1) = 18.246$, $p<0.001$.

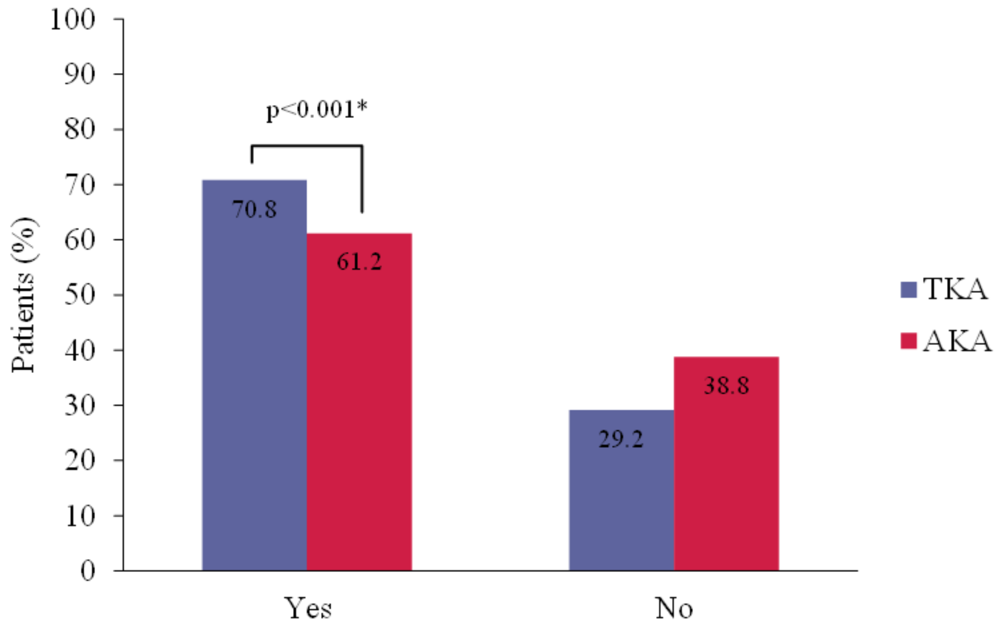

Figure 5.2. Amputation rehabilitation referrals following complete case analysis.

5.4. Discussion

The aim of this study was to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA. To our knowledge, this is the first study that compared the clinical outcomes of patients with a TKA and AKA within the NVR database.

A higher percentage of patients with a TKA had diabetes mellitus compared to patients with a unilateral AKA. Secondly, more patients with a TKA had an elective admission prior to their amputation, and more of the TKA were performed during core daytime hours. Fewer patients with a TKA experienced cardiac and respiratory post-operative complications. In-hospital and 30-day mortality were significantly lower in patients with a TKA, and more patients with a TKA were discharged to their own residence. A greater number of patients with a TKA were referred to amputation rehabilitation in comparison to patients with an AKA, and more patients with a TKA had successful wound healing even though no difference in surgical site infection post amputation was determined. Despite this, there were a higher percentage of patients with a unilateral TKA that were frail compared to patients with an AKA.

5.4.1. Patient Characteristics

More patients with a TKA were under the age of 60 years, which is significantly greater than those reported in patients with an AKA. This is the only study who has investigated the differences between age and age groups on level of amputation. Panhelleux et al. (2021) suggested that patients with a TKA are younger than those with an AKA, with mean ages of 64 years and 70 years, respectively. Lim et al. (2018), who used retrospective data to determine post-operative mortality risks, showed a similar difference in age between patients with a TKA and patients with an AKA (64.7 years and 70.7 years, respectively) to those reported by Panhelleux et al. (2021). It might be that a TKA is suitable for patients who are younger as they have the potential to mobilise better and have an increased QoL. However, as more patients with a TKA in this study were frail and trauma amputations were low, it does not explain this finding.

Patients who have a major lower limb amputation often have multiple comorbidities (Fang et al., 2017), including coronary heart disease, hypertension, cerebrovascular disease, diabetes mellitus, chronic kidney disease, and smoking-related diseases (Melsom & Danjoux, 2011). Over 50% of patients with a TKA in the study had diabetes mellitus, compared to 42.7% of patients with an AKA. A greater percentage of patients with a TKA in a study by Lim et al. (2018) had diabetes mellitus compared to patients with an AKA. Diabetes mellitus can lead to peripheral vascular disease, which can cause blood vessels to narrow, thus reducing blood flow to the legs and feet. Peripheral neuropathy can prevent pain and wounds, or ulcers can become infected, and those with diabetes mellitus can have poorer wound healing than those without diabetes. Patients with type 2 diabetes mellitus have an increased prevalence of lipid abnormalities, which could contribute to an increased risk of cardiovascular events (García-Esquinas et al., 2015). Additionally, it is known that poor glycaemic control can increase the risk of long-term complications in patients with diabetes mellitus (García-Esquinas et al., 2015). Patients with a TKA in this study predominantly had their amputations because of Infection or tissue loss, Ih could be related to diabetes mellitus complications. However, Albino et al. (2014) stated that a TKA procedure is commonly performed following trauma. Although there were more patients in this study who had a TKA due to trauma reasons compared to patients with an AKA, this percentage was extremely low and was not the main amputation indication in patients who had a TKA.

A higher percentage of patients with a TKA were frail compared to patients with an AKA. These findings are supported by Schmiegelow et al. (2018), who stated that patients with a TKA or higher are frail. Patients requiring a major lower limb amputation for peripheral arterial disease tend to be elderly, frail, and presenting multiple comorbidities (Monaro et al., 2017). Frailty places patients at a greater risk of adverse outcomes, including hospital admission, a worsening disability, and death (Partridge et al., 2012; Monaro et al., 2017). Surgeons may have been selecting patients who were frail, those who were experiencing difficulties with walking and independent living, or those they felt were more likely to be bedbound following a TKA procedure. Numerous factors are known to be associated with frailty, including diabetes mellitus (Assar et al., 2019; Kong et al., 2021), loss of skeletal muscle strength (García-Esquinas et al., 2015), malnutrition (Kong et al., 2021), sociodemographic factors such as age and education level (García-Esquinas et al., 2015; Thein et al., 2018), physical factors such as blood pressure and body weight (García-Esquinas et al., 2015; Thein et al., 2018), and biological factors such as haemoglobin, albumin and high-density lipoprotein cholesterol (García-Esquinas et al., 2015; Thein et al., 2018). Additionally, outcomes including mortality, increased hospital re-admissions, and post-operative complications have been correlated with an increase in frailty amongst the literature (Dasgupta et al., 2009; Fang et al., 2017). Diabetes mellitus impairs skeletal muscle function, vascular function, and hormonal milieu (García-Esquinas et al., 2015; Chhetri et al., 2017; Kong et al., 2021), and diabetes mellitus contributions from a poor glycaemic and lipid control may increase the risk of frailty amongst those patients who have diabetes mellitus within this study. Moreover, it was stated by van Aalst et al. (2019) that although disabling symptoms because of limb ischaemia can be an indication for surgery, patients who are frail may have a decreased ability to recover from procedures. With the above associated factors in mind (age, diabetes mellitus, BMI, haemoglobin), most patients in this study with a TKA were aged between 70-80 years (30.8%), had diabetes mellitus (50.1%), had a median BMI of 25.2 kg/m^2 although 35.6% of patients were classified as having a healthy BMI, and a median haemoglobin of 10.6 g/dL with 86.4% of patients being anaemic. Although there were missing data for frailty, these factors may be associated with an increased risk of frailty amongst patients with a TKA. Moreover, patients with a TKA in this study had a higher presence of diabetes mellitus and higher prevalence of frailty, yet discharge outcomes appeared greater. For instance, frailty can be associated with loss of skeletal muscle strength, and diabetes mellitus is known to impair skeletal muscle function, yet more patients with a TKA were referred to rehabilitation, and more patients were discharged to their own residence. It is surprising that post-operative outcomes were better for those patients who have received a TKA because of their frailty status and that they were seen to be bedbound post discharge. Frailty within the NVR was categorised into four groups, with not frail indicating the patient was well or managing well and routinely walking, mild frailty indicating the patient was evidently slowing including having difficulty walking outside, moderate frailty indicating the patient needed help with some personal care or keeping house, and severe frailty indicating the patient was completely dependent for personal care. Although frailty may have been measured across each centre using different tools such as the Edmonton Frail Scale or the Electronic Frailty Index, patient frailty was significantly greater in TKA in this study. However, there were small numbers with reported frailty scores and it is unclear as to which validated tool was used to confirm each frailty status. It is important that the same validated tool is used by vascular surgeons to ensure that the data is representative for each cohort. As missing data appeared greater amongst this factor, this warrants further investigation.

5.4.2. Hospital Admissions

Patients with a TKA were more often elective admissions compared to patients with an AKA. Elective admissions are planned, thus suggesting that surgeons may be unfamiliar with the TKA surgical procedure and have a lack of experience when performing this level of amputation. Secondly, these results could suggest that trainees, who may be more likely to be performing the out of hours amputations, may be less confident to leave a longer residual limb, or that they may be unfamiliar with the procedure due to the lower number of TKA. Further, 95.8% of TKA procedures were performed during core daytime hours of 07:00 to 19:00, compared with 92.9% of AKA procedures. Major lower limb amputations should be undertaken on a planned operating list during normal working hours (Waton et al., 2019).

The current study highlights that most major lower limb amputations were performed within their recommendations and during normal core working hours. Those amputations that were performed out of hours could not wait until the following day. Patients with a TKA had greater indications of tissue loss and controlled infection, with 4.8% of patients having overnight amputations due to trauma. In comparison, those patients with an AKA had overnight amputations due to acute limb ischaemia, followed by tissue loss and uncontrolled infection, with trauma accounting for 1.7% of all overnight AKA procedures. Although the indications overall were different between TKA and AKA procedures for acute limb ischaemia, chronic limb ischaemia and tissue loss, amputation indications are not associated with the procedure time.

5.4.3. Risk of Post-Operative Complications

A variety of factors influence the risk of complications following a major lower limb amputation, including age, level of amputation, and general health (NHS, 2019b). Patients with a TKA experienced fewer cardiac and respiratory post-operative complications compared to patients with an AKA. It is thought that a proximal leg amputation is associated with a greater risk of developing cardiovascular diseases than distal amputations (Naschitz & Lenger, 2008; Mundell et al., 2018), and patients with a dysvascular AKA were more likely at risk of a cardiac event (Mundell et al., 2018). Ambler et al. (2020) investigated hospital mortality rates amongst patients with a BKA, TKA and AKA. They reported that 6.6% of patients in their study had cardiac post-operative complications, and 9.7% had respiratory post-operative complications. Further, Aulivola et al. (2004) reported that 10.2% of patients with a BKA and patients with an AKA had cardiac complications. However, both studies included TKA procedures, but they did not separate their findings to compare levels of amputation independently. It is reported that the risk of serious complications is lower in elective amputations than in emergency amputations (NHS, 2019b). Whilst patients with a TKA in this study had a higher presence of diabetes mellitus and frailty, they would be expected to suffer more post-operatively. As discussed in Chapter Five, Section 5.4.1, patients with diabetes mellitus are more likely to be frail than those without diabetes mellitus (Umegaki, 2016; Sinclair et al., 2017; Assar et al., 2019; Kong et al., 2021). Patients who are frail have a reduced ability to recover from procedures or a stressful event (Khan et al., 2019; Pandit et al., 2021), thus frailty is a predictor of mortality (Hajek et al., 2016; van Aalst et al., 2019). Conversely, cardiac and respiratory post-operative complications, in-hospital mortality and 30-day mortality in this study were significantly lower following a TKA.

Although surgery is frequently performed out of hours and on emergency admissions, this can create challenges for perioperative planning, thus reducing the time available for medical optimisation pre-operatively (Melsom & Danjoux, 2011). Despite AKA being performed more out of hours, the post-operative complications may be expected to increase. However, these procedures are more urgent and are therefore performed out of hours. It could be suggested that surgeons have more time to perform their amputations and are more cautious with complications that could be prompted.

5.4.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were significantly lower in patients with a TKA than patients with an AKA. The findings from this study contrasted with Lim et al. (2018), who reported similar rates of mortality amongst both levels of amputation (Molina & Faulk, 2021). Mortality at 90 days, reported by Jensen (1983), were higher in patients with an AKA than TKA (40% and 21%, respectively). Additionally, mortality rates at 90 days reported by Schmiegelow et al. (2018) were lower in patients with a TKA than patients with an AKA (38% and 44%, respectively). Further, Jensen (1983) reported that mortality was higher in patients with an AKA than TKA at 1 year (54% and 39%, respectively), 3 years (70% and 58%, respectively), and 5 years (77% and 67%, respectively). On the contrary, 30-day mortality reported by Kristensen et al. (2012) was greater in patients with a TKA than patients with an AKA (50% and 31%, respectively). According to Fortington et al. (2013), older age, proximal amputation levels and multi-morbidity are associated with mortality following an amputation. Additionally, the type of rehabilitation setting, and physical independence grade may contribute to mortality rates post amputation (Kristensen et al., 2012).

5.4.5. Hospital Discharge

A higher percentage of patients with a TKA than patients with an AKA were discharged to their own residence following their amputation. The overall findings were consistent with Kayssi et al. (2017), with 48% of patients following unilateral and bilateral amputations in their study were discharged to their own residence with services. Dillingham et al. (2003) examined the post-acute rehabilitation services following a lower limb amputation. They included patients with a TKA and AKA, although both amputations were included as part of the AKA group. However, most patients within the AKA level in their study (52%) were discharged to skilled nursing facilities, and 30.4% discharged to their own residence, which although is a large number of patients, is not the highest discharge destination. Fortington et al. (2013) investigated the short-term and long-term outcomes following a major lower limb amputation and included patients with a TKA. However, their findings were combined for all levels of amputation, and their findings indicated that 53% of patients were discharged to care following their amputation. Further, Nijmeijer et al. (2017) stated that 60% of patients with a TKA in their study were discharged to a nursing facility, whereas only 4.4% of patients were discharged home following their amputation. Parameters including physical condition, social factors, age, and comorbidities are influencing factors in determining the discharge destination (Rommers et al., 1997). More patients with a TKA may have been discharged home following their amputation due to the advantages offered by the TKA procedure. The TKA procedure provides stability and proprioceptive responses that are essential for balance in ambulatory and non-ambulatory individuals (Pinzur, 1992; Siev-Ner et al., 2000), thus assisting with transfers and performing everyday activities. Secondly, patients with a TKA who were discharged to their own residence were more likely to be frail, however, the increased number of elective admissions for this procedure may have assisted with prior living alterations, thus facilitating discharge to their own residence. Additionally, as there were fewer non-elective (emergency) admissions, patients with a TKA may have been less unwell during their stay. This could be evident from the significantly fewer cardiac and respiratory post-operative complications experienced, and significantly fewer patients with a TKA were admitted to critical care following their amputation. Furthermore, there were significantly more amputation indications of tissue loss amongst those patients with a TKA, however, it is unclear whether those patients experiencing tissue loss were because of a traumatic injury or because of tissue damage from sepsis or gangrene. Despite this, more patients with a TKA may have been less unwell and as a result, were discharged to their own residence. Surgical site infection was miniscule amongst the recorded data, which raises the question of if these data were not recorded, not inputted into the dataset, or there were fewer cases of surgical site infection following amputations. Sands et al. (1996) stated that decreasing hospital lengths of stay and increasing use of ambulatory surgery may comprise the accuracy of surveillance data, with previous studies reporting that surgical site infections occur after hospital discharge (Sands et al., 1996; Woelber et al., 2016).

5.4.6. Referral to Rehabilitation

A greater number of patients with a TKA were referred to rehabilitation than patients with an AKA. The TKA provides a longer lever arm and a weight-bearing end residual limb (Mensch, 1983; Siev-Ner et al., 2000; Anderson, 2005; Morse et al., 2008; Jackson et al., 2012; Lim et al., 2018). These results were surprising, as more patients with a TKA were frail with a potential loss of skeletal muscle strength, and thus not expected to mobilise. Additionally, as there was a greater prevalence of diabetes mellitus in patients with a TKA, it is important to mention that diabetes mellitus impairs skeletal muscle function and vascular function (Kong et al., 2021). However, given that there were 26.4% elective admissions, this may account and allow for better planning and pre-operative preparation, or counselling where necessary. Despite more patients with a TKA being referred to rehabilitation, it is unclear whether they were referred to prosthetic rehabilitation and cast for a prosthesis. The outcomes of their referral were unclear, such as whether they had a cosmetic limb for appearance only whilst using a wheelchair, or they may have received a prosthesis but abandoned its use. Physiotherapists have occasionally referred patients to a prosthesis rehabilitation consultant to emphasise to patients that they are not suitable for a prosthetic limb and will be unable to walk, and so, their referrals may be preferably to access allied health professional services.

However, for those that may have received a prosthesis, prosthetic gait is facilitated by this long and strong lever arm for the thigh muscles and preservation of the hip function, thus providing greater ambulatory stability (Jensen et al., 1982; Pinzur, 2004; Smith, 2004; Robinson et al., 2010; de Laat et al., 2014). Further, Aulivola et al. (2004) stated that less than one third of patients with an AKA are likely to rehabilitate with a prosthesis. This is due to the increased energy expenditure required as the amputation is performed proximally (Waters & Mulroy, 1999; Crowe et al., 2019). Met et al. (2008) reported an identical percentage of patients with a TKA and AKA who were fitted with a prosthesis. Previous studies who have investigated ambulation and prosthesis use between patients with a TKA and patients with an AKA are comparable. A greater percentage of patients with a TKA could walk more than 50 metres outdoors on level ground and in good weather less than or equal to 50 metres with or without the use of walking aids compared to patients with an AKA, and 4% of patients with a

TKA had normal or near normal gait (Met et al., 2008). Similarly, a greater percentage of patients with a TKA were able to walk outdoors, walk up and down stairs, travel in a car, and perform household chores compared to patients with an AKA (Hagberg et al., 1992). However, in some cases, not all individuals who received a lower limb amputation were suitable for a prosthesis. Numerous studies have revealed that approximately one quarter of patients with an AKA receive a prosthesis (Nehler et al., 2003; Fletcher et al., 2002; Webster et al., 2012; Mundell et al., 2016; Mundell et al., 2018). Patients who are not suitable for a prosthesis may mobilise using a wheelchair and use their remaining stump to weight bear or as a functional lever to transfer from a chair to a bed (Siev-Ner et al., 2000). Although, it is reported that patients who mobilise with a prosthesis have approximately a 60% reduction in the risk of mortality (Mundell et al., 2018). Whilst Mundell et al. (2018) concluded that patients mobilising with a prosthesis have a decreased risk of mortality from non-cardiac events and was due to survival following an amputation, it is important to note that regular physical activity including walking may decrease the risk of mortality, and has several benefits on overall health, including increased blood flow. It is unclear whether the reduction in mortality reported is because of patients being less unwell and generally fitter, or whether patients who mobilise with a prosthesis maintain a greater QoL and fitness, resulting in a longer lifespan.

5.4.7. Wound Healing

Surgical wounds are expected to heal successfully without complications (Harker, 2006). However, poor wound healing has been previously associated with TKA in some of the literature (Jensen et al., 1982; Cull et al., 2001; Morse et al., 2008; Albino et al., 2014; Murakami & Murray, 2016; Lim et al., 2018; Bergman & Metcalfe, 2020). However, the findings of this study contrast with previous statements, indicating that patients with a TKA have similar wound healing success compared to patients with an AKA. Importantly, the findings from this study were supported by literature who reported successful wound healing rates of between 70% and 100% in patients with a TKA (Newcombe & Marcuson, 1972; Jensen et al., 1982; Moran et al., 1990; Bowker et al., 2000; Nellis & Van de Water, 2002; Morse et al., 2008; Jackson et al., 2012). According to the literature (Eneroth and Persson, 1993; Harker, 2006), important factors for wound healing following an amputation include the patient's age, nutritional status, smoking status, and the presence of comorbidities including diabetes mellitus, renal failure, and anaemia. Additionally, site selection is crucial as healing depends on the adequacy of perfusion (Harker, 2006), and healing depends on the technical precision of the surgeon (Dean, 1995; Harker, 2006). Although there were a greater percentage of patients in this study with a TKA who had diabetes mellitus, were anaemic, were ex-smokers, and fewer patients with a TKA had chronic renal failure, over 79% of patients with a TKA in this study had successful wound healing after 30 days. These findings support the literature since the healing rates of patients with a TKA are similar, or greater in this study, to patients with an AKA (Murakami & Murray, 2016). Of the remaining 21% of wounds that did not heal following a TKA, 2% of these were because of surgical site infection, with the remaining 19% being unclear of the cause. Potential wound healing complications associated with lower limb amputations include slow healing, dehiscence, splitting open of a closed wound, skin blistering, bone erosion, haematoma, and stump oedema (Harker, 2006). Additionally, the 19% could not have been recorded, or may have never healed. However, it is important to acknowledge that these are non-randomised data in a retrospective registry dataset, there could be publication bias within the literature which may have been produced by individuals who were keen to promote TKA and may likely be in higher volume centres with a greater experience of TKA who subsequently may see better results than those centres that perform fewer TKA.

A greater percentage of patients with a TKA had a revised amputation. Although wound healing success rates were surprisingly high in patients with a TKA, it is unclear what the cause for revision was, and the level of revision they had. There were no more uncontrolled infections on admission, and no more surgical site infections recorded following a TKA. For conclusions to be drawn regarding wound healing, a detailed, coded response should be added to the registry dataset.

5.5. Conclusion

Findings suggest that TKA may provide better outcomes in certain aspects of post amputation care over AKA, with patients experiencing fewer cardiac and respiratory complications, more patients were discharged to their own residence, 30-day mortality was lower, and more patients were referred to amputation rehabilitation. Despite previous reports of poor wound healing with a TKA, this study suggests wound healing is potentially more successful, and warrants further investigation to compare this closely. As there is a large amount of missing data, it is important to determine the true differences between patients with a TKA and patients with an AKA by utilising statistical techniques to handle missing data. These techniques are outlined in Chapter Four, with subsequent chapters reporting the application of thse techniques on the data. Limitations are outlined collectively in Chapter Eight, Section 8.5.

CHAPTER SIX: NATIONAL VASCULAR REGISTRY – MULTIPLE IMPUTATION ANALYSIS

6.1. Introduction

The NVR measures the quality and the care outcomes for patients who undergo a major vascular surgery in NHS hospitals, in which vascular departments within the UK can improve the quality of care received by those patients. To date, all analysis of amputation data within the NVR has compared AKA and BKA outcomes. It is accepted that a BKA allows enhanced recovery over amputations at a higher level (Waton et al., 2016). Patients with a TKA have always been grouped with patients with an AKA for clinical and functional outcomes literature (Kristensen et al., 2015; Liu et al., 2015; Reid et al., 2015; Prinsen et al., 2017a; Möller et al., 2018; Mundell et al., 2018; Karatzios et al., 2019; Möller et al., 2019; Welke et al., 2019; Möller et al., 2020; Burçak et al., 2021) however, TKA was categorised with BKA within recent NVR annual reports (Waton et al., 2019; Waton et al., 2020) and the literature (Jensen et al., 2017).

The numerous variations of TKA procedures, along with a lack of surgical experience and consensus around the patient criteria who could potentially benefit from a TKA, may be causing surgeons to favour an AKA over a TKA. This study aimed to perform a large-scale retrospective analysis of a case control series using data held within the NVR database, and to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA.

6.2. Methods

6.2.1. Data Request Application Form

A 20-section DARF was completed as part of the application process. The process is outlined in Chapter Five, Section 5.2.1.

6.2.2. Data Analysis

The de-personalised patient level data were sorted and cleaned in Microsoft Excel. Upon cleaning, missing data were recorded as code 999. The cleaned data were processed into IBM Statistical Package for the Social Sciences (IBM SPSS, version 27) software for analysis. Multiple imputation technique as outlined in Chapter Four, Section 4.3.2 was utilised for this analysis.

6.3. Results

During the years of 2016 and 2019, there was a total of 497 unilateral TKA procedures and 6,764 unilateral AKA procedures within England and Wales. Patient characteristics are described in Chapter Six, Section 6.3.1, and remaining outcomes are outlined subsequently.

6.3.1. Patient Characteristics

Patient characteristics are described in Table 6.1, Table 6.2, Table 6.3 and Table 6.4.

Table 6.1 indicates patient characteristics following TKA and AKA. Patients with a TKA were significantly younger than patients with an AKA (p=0.025). There was no significant association between age group and level of amputation (Table 6.1). Although amputations were more frequent amongst males (Table 6.1), there was no association between gender and level of amputation (p=0.381).

BMI was somewhat significantly higher in patients with a TKA (Table 6.2; p=0.019). The BMI groups (underweight, healthy, overweight and obese) were determined by their overall BMI (NHS, 2019a). There was no significant association between BMI groups and level of amputation (Table 6.2).

Haemoglobin was similar between patients with a TKA and patients with an AKA (Table 6.2), thus there was no significant association (p=0.429). Anaemia was refined as patients who were male and had a haemoglobin level equal to or lower than 13.5g/dL, and patients who were female and had a haemoglobin level equal to or lower than 12g/dL. There was no significant association between haemoglobin level and level of amputation (p=0.793).

Pre-operative comorbidities reported in the NVR included diabetes mellitus, hypertension, ischaemic heart disease, and major amputation (Table 6.3). Patients with a TKA had a significantly higher presence of diabetes mellitus compared to patients with an AKA (p=0.001). Patients with a TKA had a significantly lower presence of chronic lung disease compared to AKA (p=0.033). There were no significant differences between the levels of amputation and alternative comorbidities (Table 6.3). There were no significant differences in smoking history between the two levels of amputation (Table 6.3).

Incidence of patient frailty was determined as the number of patients that were frail at the time of their amputation. Patient frailty was categorised as not frail, mild frailty, moderate frailty, and severe frailty, as recorded in the Patient Frailty Score Guidance (Vascular Services Quality Improvement Programme, 2019). The incidence of patient frailty was determined between the two levels of amputation and results are presented in Table 6.4. There was no significant association between the two levels of amputation and patient frailty (Table 6.4).

Table 6.1. Patient characteristics following multiple imputation.

Characteristic	TKA	AKA	P
Age (years)	**N=497**	**N=6764**	0.029*
- Mean (± SD)	69.1 ± 13.3	70.4 ± 12.6	
- Median (IQR)	-	-	
Age Group, n (%)	**N=497**	**N=6764**	
- Under 60 years	121 (24.3)	1,288 (19)	0.004*
- 60-70 years	109 (21.9)	1,722 (25.5)	0.081
- 70-80 years	153 (30.8)	2,178 (32.2)	0.513
- 80+ years	114 (22.9)	1,576 (23.3)	0.853
Gender, n (%)	**N=497**	**N=6764**	0.381
- Male	326 (65.6)	4,566 (67.5)	
- Female	171 (34.4)	2,198 (32.5)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of $p<0.005$.

Table 6.2. Patient BMI and haemoglobin characteristics following multiple imputation.

Characteristic	TKA	AKA	P
BMI (kg/m^2)	**N=497**	**N=6764**	0.019*
- Mean (± SD)	26.8 ± 7.9	26.1 ± 6.7	
- Median (IQR)	-	-	
BMI Group, n (%)	**N=497**	**N=6764**	
- Underweight (<18.5 kg/m^2)	50 (10.1)	601 (8.9)	0.493
- Healthy (18.5-24.9 kg/m^2)	180 (36.2)	2,686 (39.7)	0.166
- Overweight (25-29.9 kg/m^2)	139 (28)	1,937 (28.6)	0.739
- Obese (>30 kg/m^2)	128 (25.7)	1,540 (22.8)	0.149
Haemoglobin (g/dL)	**N=497**	**N=6764**	0.429
- Mean (± SD)	10.6 ± 2.2	10.5 ± 2.2	
- Median (IQR)	-	-	
Haemoglobin Level, n (%)	**N=497**	**N=6764**	0.793
- Anaemic	435 (87.5)	5,887 (87)	
- Not Anaemic	62 (12.5)	877 (13)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Body mass index (BMI); Standard deviation (SD); Interquartile range (IQR); Kilograms per metre squared (kg/m^2); Grams per decilitre (g/Dl); Values reported as count (percentage) unless stated.

Table 6.3. Patient comorbidities and smoking status following multiple imputation.

Characteristic	TKA, n (%)	AKA, n (%)	P
Comorbidities	**N=497**	**N=6764**	
- No Comorbidities	48 (9.7)	730 (10.8)	0.430
- Diabetes Mellitus	249 (50.1)	2,891 (42.7)	0.001*
- Hypertension	311 (62.6)	4,231 (62.6)	0.992
- Chronic Lung Disease	113 (22.7)	1,834 (27.1)	0.033*
- Ischaemic Heart Disease	210 (42.3)	2,784 (41.2)	0.632
- Chronic Heart Failure	71 (14.3)	879 (13)	0.410
- Stroke	58 (11.7)	874 (12.9)	0.421
- Chronic Renal Failure	100 (20.1)	1,352 (20)	0.943
- Cancer	16 (3.2)	168 (2.5)	0.314
- Lower Limb Arterial Disease	0 (0)	4 (0.1)	0.588
- Major Amputation	24 (4.8)	393 (5.8)	0.364
Smoking Status	**N=497**	**N=6764**	
- Never	95 (19.1)	1,128 (16.7)	0.155
- Ex-smoker	244 (49.1)	3,292 (48.7)	0.868
- Current or stopped within 2 months	158 (31.8)	2,344 (34.7)	0.194

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

Table 6.4. Patient frailty following multiple imputation.

Outcome	TKA, n (%)	AKA, n (%)	P
Frail	**N=497**	**N=6764**	0.398
- Yes	403 (81.1)	5,301 (78.4)	
- No	94 (18.9)	1,460 (21.6)	
Frailty Level	**N=497**	**N=6764**	
- Not Frail	94 (18.9)	1,460 (21.6)	0.398
- Mild Frailty	124 (24.9)	1,555 (23)	0.496
- Moderate Frailty	187 (37.6)	2,156 (37.2)	0.858
- Severe Frailty	92 (18.5)	1,233 (18.2)	0.903

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

6.3.2. Pre-Operative Factors

6.3.2.1. Admission Type

Elective and non-elective admissions were compared between the two levels of amputation (497 TKA and 6764 AKA). There was a significantly higher percentage of patients with a TKA who had an elective admission compared to patients with an AKA (Figure 6.1; $p<0.001$).

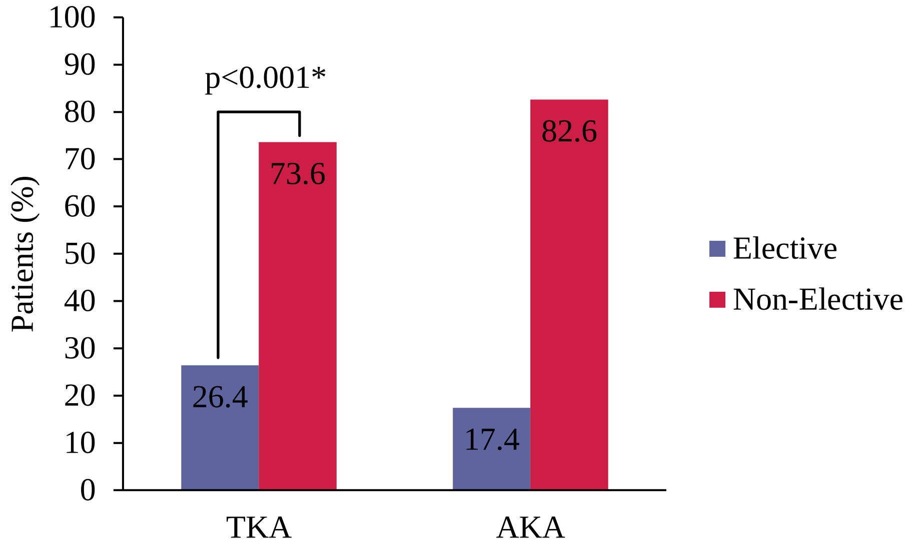

Figure 6.1. Admission type following multiple imputation.

6.3.2.2. Amputation Indication

There were seven amputation indications reported in the NVR database. These indications included acute limb ischaemia, chronic limb ischaemia, tissue loss, and trauma (Table 6.5). There was a significantly higher number of patients who had an AKA because of acute limb ischaemia compared to patients with a TKA ($p<0.001$). Secondly, there was a significantly higher number of patients who had an AKA because of chronic limb ischaemia compared to TKA ($p=0.042$). However, there was a significantly higher number of individuals who had a TKA due to tissue loss compared to patients with an AKA ($p<0.001$).

Table 6.5. Amputation indication following multiple imputation.

Factor	TKA, n (%)	AKA, n (%)	P
Amputation Indication	**N=497**	**N=6764**	
- Acute Limb Ischaemia	63 (12.7)	1,450 (21.4)	<0.001*
- Chronic Limb Ischaemia	90 (18.2)	1,4795 (22.1)	0.042*
- Neuropathy	8 (1.6)	79 (1.2)	0.386
- Tissue Loss	225 (45.3)	2,437 (36)	<0.001*
- Uncontrolled Infection	95 (19.1)	1,133 (16.8)	0.168
- Trauma	11 (2.2)	87 (1.3)	0.087
- Aneurysm	5 (1)	83 (1.2)	0.672

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

6.3.2.3. Time of Procedure

The time of procedure was determined as the time the procedure began when there was knife-to-skin contact. Table 6.6 indicates the number of patients, total percentage, and p-value for the time of procedure for patients with a TKA and patients receiving an AKA. Significantly more patients with a TKA had their procedure performed during core daytime hours of 07:00 to 19:00 (p=0.014).

Table 6.6. Time of procedure following multiple imputation.

Factor	TKA, n (%)	AKA, n (%)	P
Time of Procedure	**N=497**	**N=6764**	0.014*
- 07:00 – 19:00 hours	476 (95.8)	6,282 (92.9)	
- 19:00 – 07:00 hours	21 (4.2)	482 (7.1)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

6.3.3 Post-Operative Factors

6.3.3.1. Critical Care Admission from Theatre

The incidence of critical care admission from theatre was determined as the number of patients that were admitted to critical care within hospital following the surgical procedure of a major lower limb amputation. The length of critical care stay was determined as the number of days, if any, following a patient's lower limb amputation, where they were admitted to critical care within hospital.

Table 6.7 highlights the critical care admission rates and critical care length of stay following their initial amputation. There were significantly fewer patients with a TKA who were admitted to critical care compared to patients with an AKA ($p<0.001$). However, there was no significant difference in critical care length of stay between the two levels of amputation ($p=0.513$).

Table 6.7. Critical care admission and critical care length of stay following multiple imputation.

Critical Care	TKA	AKA	P
Admission, n (%)	**N=497**	**N=6764**	<0.001*
- Yes	54 (10.9)	1,084 (16)	
- No	443 (89.1)	5,680 (84)	
Length of Stay (days)	**N=497**	**N=6764**	0.513
- Mean (± SD)	4.4 ± 6.3	5 ± 6.9	
- Median (IQR)	-	-	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of p<0.005.

6.3.3.2. Incidence of Return to Theatre

The incidence of return to theatre was determined as the number of patients that returned to theatre following their major lower limb amputation. Return to theatre within the NVR was removed from the amputation dataset in January 2019 and replaced with further surgery. The type of further surgery was compared between patients with a TKA and patients with an AKA.

There was no significant association found between the two levels of amputation and return to theatre (Table 6.8). For those who had further surgery, a similar percentage of patients with a TKA and patients with an AKA had received angioplasty with a stent (0.2% and 0.1%, respectively), a major lower limb amputation (1.1% and 1.2%, respectively), and other forms of surgery (1.6% and 1.7%, respectively). There were no significant differences in further procedures between groups ($p>0.05$).

Table 6.8. Return to theatre rates and types of further surgery following multiple imputation.

Post-Operative Factor	**TKA, n (%)**	**AKA, n (%)**	**P**
Return to Theatre	**N=497**	**N=6764**	0.077
- Yes	50 (10.1)	530 (7.8)	
- No	447 (89.9)	6,234 (92.2)	
Further Surgery Type	**N=497**	**N=6764**	
- None	477 (89.9)	6,234 (92.2)	0.077
- Angioplasty with Stent	1 (0.2)	5 (0.1)	0.714
- Major Lower Limb Amputation	5 (1.1)	74 (1.2)	0.961
- Other	7 (1.6)	106 (1.7)	0.810

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

6.3.3.2.1. Incidence of Revision of Amputation

The incidence of revision of amputation was determined as the number of patients who were revised to a higher level of amputation following their original major lower limb amputation. Incidence of revision of amputation was determined between the two levels of amputation. Further surgery with a multi-code response was added to the NVR dataset in January 2019, which resulted in incomplete responses previously.

There was a similar percentage of patients with a TKA and AKA who had received a major lower limb amputation following their initial amputation (1.1% and 1.2%, respectively). No significant difference between the two levels of amputation was determined (p=0.961). There were no minor lower limb amputations reported in the NVR database.

6.3.3.3. Incidence of Post-Operative Complications

The incidence of complications was determined as the number of patients who experienced complications following their major lower limb amputation. The number of post-operative complications were determined by the total number of post-operative complications that each patient experienced.

Table 6.9 indicates the post-operative complications experienced by patients with a TKA and AKA following their initial surgery. Post-operative complications were apparent in patients with a TKA and patients with an AKA following their initial lower limb amputation. Patients with a TKA experienced significantly fewer cardiac complications post-operatively compared to patients with an AKA (p=0.019). Further, patients with a TKA experienced significantly fewer respiratory complications post-operatively compared to patients with an AKA (p=0.009). There were no significant differences found between the two levels of amputation and independently cerebral, renal failure, limb ischaemia and paraplegia ($p>0.05$).

The number of post-operative complications patients had varied between the two levels of amputation (Table 6.9). Significant fewer patients with a TKA had no post-operative complications ($p=0.008$). Patients with a TKA had no more than five post-operative complications, however, patients with an AKA had up to 10 post-operative complications. When investigating those patients who had post-operative complications, only one patient with a TKA had five or more post-operative complications (Table 6.9). There was no significant difference between the two levels of amputation ($p=0.173$).

Table 6.9. Post-operative complications following multiple imputation.

Post-Operative Complications	TKA, n (%)	AKA, n (%)	P
Complication Type	**N=497**	**N=6764**	
- None	397 (79.9)	5,141 (76)	0.052
- Cardiac	26 (5.2)	554 (8.2)	0.019*
- Respiratory	34 (6.8)	710 (10.5)	0.009*
- Cerebral	3 (0.6)	107 (1.6)	0.101
- Renal Failure	20 (0.4)	282 (4.2)	0.913
- Haemorrhage	6 (1.2)	100 (1.5)	0.623
- Limb Ischaemia	17 (3.4)	241 (3.6)	0.866
- Paraplegia	2 (0.4)	72 (1.1)	0.156
- Post-Operative Confusion	4 (0.8)	88 (1.3)	0.335
- Major GI Complication	1 (0.2)	20 (0.3)	0.835
- Surgical Site Infection	8 (1.6)	119 (1.8)	0.862
- Other	12 (2.4)	252 (3.7)	0.133
Number of Complications	**N=497**	**N=6764**	
- 0	397 (79.9)	5,141 (76)	0.053
- 1	81 (16.3)	1,179 (17.4)	0.520
- 2	10 (2)	207 (3.1)	0.188
- 3	5 (1)	98 (1.5)	0.423
- 4	3 (0.6)	76 (1.1)	0.331
- 5	1 (0.2)	40 (0.6)	0.281
- 6	0	12 (0.2)	0.993
- 7	0	5 (0.1)	0.994
- 8	0	3 (0.4)	0.994
- 9	0	1 (0.0)	0.995
- 10	0	1 (0.0)	0.995
Complications	**N=100**	**N=1624**	0.173
- 1 to 4	99 (99)	1,561 (96.1)	
- 5+	1 (1)	63 (3.9)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

6.3.3.3.1. Incidence of Surgical Site Infection

The incidence of surgical site infection was determined as the number of patients who experienced a surgical site infection following their major lower limb amputation. The incidence of surgical site infection was determined between the two levels of amputation. Surgical site infection was similar in patients with an AKA and patients with a TKA (Table 6.9). Further, there was no significant difference between level of amputation and surgical site infection (p=0.862).

6.3.3.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were calculated as the number of patients that died prior to discharge and the number of patients that died within 30 days of receiving a major lower limb amputation, respectively. In-hospital and 30-day mortality were determined between the two levels of amputation. Table 6.10 displays the in-hospital and 30-day mortality rates for patients with a TKA and patients with an AKA following multiple imputation. In-hospital mortality was significantly higher in patients with an AKA compared to patients with a TKA (10.8% and 6.2%, respectively; p=0.001). Further, 30-day mortality following their amputations were significantly higher in patients with an AKA compared to patients with a TKA (8.8% and 5.4%, respectively; p=0.030).

Table 6.10. In-hospital and 30-day mortality rates following multiple imputation.

Outcome	TKA, n (%)	AKA, n (%)	P
Mortality Rates	**N=497**	**N=6764**	0.001*
- In-Hospital mortality	31 (6.2)	731 (10.8)	
- Survived	466 (93.8)	6033 (89.2)	
Upon Discharge	**N=497**	**N=6764**	0.030*
- 30-day mortality	27 (5.4)	597 (8.8)	
- Survived	460 (94.6)	6167 (91.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

6.3.4. Discharge Outcomes

6.3.4.1. Overall Hospital Length of Stay

Overall length of stay was calculated as the number of days that each patient stayed in hospital following their major lower limb amputation. Overall length of stay was determined between the two levels of amputation. Table 6.11 illustrates the mean, median and interquartile ranges for both levels of amputation. Overall hospital LOS was similar between patients with a TKA and patients with an AKA, and there was no significant difference between these two levels of amputation (p=0.580).

Table 6.11. Overall hospital length of stay (days) following multiple imputation.

Outcome	TKA	AKA	P
Overall Hospital LOS	**N=497**	**N=6764**	0.580
- Mean (± SD)	30.8 ± 27.8	31.6 ± 30.8	
- Median (IQ)	-	-	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of p<0.005.

6.3.4.2. Discharge Destination

Discharge destination was determined as the number of patients that were discharged to their own residence, to rehabilitation, to a different hospital, or to intermediate care following their major lower limb amputation. Discharge destination was determined between the two levels of amputation. Table 6.12 displays the discharge destinations for patients with a TKA and patients with an AKA. There was no significant association between discharge destination and level of amputation ($p>0.05$).

Table 6.12. Discharge destination following multiple imputation.

Outcome	TKA, n (%)	AKA, n (%)	P
Discharge Destination	**N=497**	**N=6764**	
- Deceased	31 (6.2)	731 (24.8)	-
- Own Residence	279 (56.1)	3,559 (56.2)	0.252
- Rehabilitation	80 (16.1)	963 (14.2)	0.538
- Other Hospital	74 (14.9)	1,075 (15.9)	0.632
- Intermediate Care	33 (6.6)	436 (6.5)	0.947

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Values reported as count (percentage) unless stated.

6.3.4.3. Wound Healing Rates

Wound healing rates were determined as the number of patients who had successful wound healing 30 days after a major lower limb amputation and were determined between the two levels of amputation. Wound healing was successful in over 78% of patients within the study (Table 6.13). However, the rates were similar between both levels of amputation and there was no significant association (p=0.359).

Table 6.13. Wound healing rates following multiple imputation.

Outcome	TKA, n (%)	AKA, n (%)	P
Wound Healing Rates	**N=497**	**N=6764**	0.359
- Yes	403 (81.1)	5,301 (78.4)	
- No	94 (20.5)	1,460 (21.6)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

6.3.4.4. Incidence of Re-admission within 30 days

Incidence of re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital. The incidence of vascular re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital for vascular reasons. The incidence of re-admission within 30 days and incidence of vascular re-admission within 30 days was determined between the two levels of amputation.

Table 6.14 indicates the 30-day hospital re-admission rates in patients with a TKA and AKA. There was no significant difference between the two levels of amputation (p=0.517).

Of these re-admissions, there were similar percentages of patients with a TKA and AKA who were re-admitted for vascular reasons (Table 6.14). There was no significant association between the two levels of amputation (p=0.447).

Table 6.14. 30-day hospital re-admission rates following multiple imputation.

Outcome	TKA, n (%)	AKA, n (%)	P
Re-admission 30-days	**N=497**	**N=6764**	0.517
- Yes	47 (9.5)	577 (8.5)	
- No	450 (90.5)	6,187 (91.5)	
Vascular Re-admission 30-days	**N=497**	**N=6764**	0.447
- Yes	266 (53.5)	3,511 (51.9)	
- No	231 (46.5)	3,253 (48.1)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

6.3.4.5. Incidence of Referral to Rehabilitation

Incidence of referral to rehabilitation was determined as the number of patients that were referred to rehabilitation and/or limb fitting on the condition of being alive at discharge from hospital. The incidence of referral to rehabilitation was determined between the two levels of amputation (497 TKA and 6764 AKA).

A total of 352 (70.8%) patients with a TKA and 4,136 (61.1%) patients with an AKA were referred to amputation rehabilitation (Figure 6.2). Overall, significantly more patients with a TKA were referred to amputation rehabilitation compared to patients with an AKA ($p<0.001$).

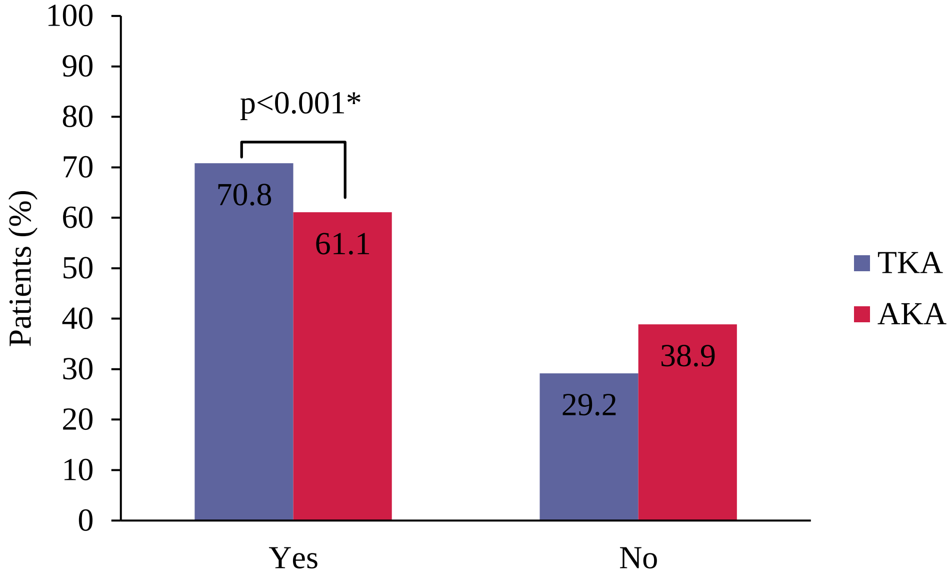

Figure 6.2. Amputation rehabilitation referrals following multiple imputation.

6.4. Discussion

The aim of this study was to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA when undertaking multiple imputation.

The main findings from this analysis indicate that patients with a TKA were significantly younger and have a significantly higher BMI. Secondly, a higher percentage of patients with a TKA had diabetes mellitus and chronic lung disease compared to patients with an AKA. Thirdly, more patients with a TKA had an elective admission prior to their amputation, and significantly more TKA were performed during core daytime hours. There were significantly fewer TKA who had amputations due to acute limb ischaemia and chronic limb ischaemia, although there was significantly more TKA who had amputations due to tissue loss. There were significantly fewer patients with a TKA who were admitted to critical care, and significantly fewer patients with a TKA had post-operative complications. For those who had post-operative complications, significantly fewer patients with a TKA experienced cardiac and respiratory post-operative complications. In-hospital and 30-day mortality were significantly lower in patients with a TKA. A significantly greater number of patients with a TKA were referred to amputation rehabilitation in comparison to patients with an AKA. There was successful wound healing following TKA and AKA, although there was no significant difference determined.

6.4.1. Patient Characteristics

More patients with a TKA were under the age of 60 years, which is significantly older than those reported in patients with an AKA. This is the only study that has investigated the differences between age on level of amputation. A review by Panhelleux et al. (2021) suggested that patients with a TKA are younger than those with an AKA, with mean ages of 64 years and 70 years, respectively. Lim et al. (2018) used retrospective data to determine post-operative mortality risks and showed a similar difference in age between patients with a TKA and patients with an AKA (64.7 years and 70.7 years, respectively) to those reported by Panhelleux et al. (2021). It might be that a TKA is suitable for patients who are younger as they have the potential to mobilise better and have an increased QoL.

Patients with a TKA had a significantly greater BMI than those with an AKA. Although the different is not large, the mean BMI recorded for TKA was 26.8 kg/m^2 compared to AKA 26.1 kg/m^2, illustrating that both cohort means are in the overweight classification. These findings suggest that most individuals undergoing an amputation are overweight or obese. Obesity, however, is a risk factor for amputation (Rosenberg et al., 2013), and amputation may contribute to further weight gain, thus further influencing a decline in patient health (Rosenberg et al., 2013). Following, obesity has been associated with the development and progression of cardiovascular disease and hypertension (Rosenberg et al., 2013), elevated cholesterol (Rosenberg et al., 2013), elevated blood glucose levels (National Institutes of Health National Heart, Lung and Blood Institute, 1998; Flegal et al., 2007; Rosenberg et al., 2013), increased mortality (Flegal et al., 2005; Rosenberg et al., 2013) and an increased risk of disability (Vincent et al., 2010; Rosenberg et al., 2013). Studies including TKA and AKA (Fortington et al., 2013; Lim et al., 2018; Ambler et al., 2020) did not report BMI, therefore no comparison can be made.

Patients with a lower limb amputation frequently have numerous comorbidities (Fang et al., 2017). Over 50% of patients with a TKA and 42.7% of patients with an AKA had diabetes mellitus. A greater percentage of patients with a TKA in a study by Lim et al. (2018) had diabetes mellitus compared to patients with an AKA. Additionally, significantly more patients with a TKA had a higher presence of chronic lung disease. Chronic lung disease may be caused by smoking tobacco, or inhaling chemical fumes, dust or air pollution (National Cancer Institute, 2022). Approximately 80% of patients with a TKA in this study were ex-smokers or current smokers, however there was no significant association determined between smoking status and level of amputation. There could be a causal affect and therefore requires further investigation.

Patients with a TKA had amputations because of infection or tissue loss, which could be related to diabetes mellitus complications. Patients with a TKA had significantly fewer amputations due to acute limb ischaemia and chronic limb ischaemia. Acute limb ischaemia is defined as a sudden decrease in limb perfusion that threatens viability of the limb (Norgren et al., 2007; Creager et al., 2012). Chronic limb ischaemia on the other hand, is caused by collateral blood vessels which may circumvent an occluded artery (Creager et al., 2012). Reported causes of ischaemia include hypertension, cigarette smoking, and diabetes mellitus (Brown & Juergens, 1972; Gordon & Kannel, 1972; Santilli & Santilli, 1999). Van Aalst et al. (2019) stated that disabling symptoms because of limb ischaemia can be an indication for surgery. Although 62.6% of patients with a TKA had hypertension, and 80.9% had a history of smoking, these were not significant following a TKA and therefore these cannot explain this finding. However, patients with a TKA had a significantly higher presence of diabetes mellitus. Although patients with diabetes mellitus are at an increased risk of developing chronic limb ischaemia due to peripheral arterial disease (Santilli & Santilli, 1999; Ying et al., 2022), this does not explain the finding as significantly fewer patients with a TKA had amputations due to acute limb ischaemia and chronic limb ischaemia. Ischaemia results in tissue damage, thus could have been recorded as tissue loss rather than ischaemia.

6.4.2. Hospital Admissions

Elective admissions were primarily used for patients with a TKA, thus suggesting that surgeons may be unfamiliar with the TKA surgical procedure and may have a lack of experience when performing this level of amputation. Secondly, these results could suggest that trainees, who may be more likely to be performing the out of hours amputations, may be less confident to leave a longer residual limb, or that they may be unfamiliar with the procedure due to the lower number of TKA. Approximately 96% of TKA procedures were performed during core daytime hours of 07:00 to 19:00, compared with approximately 93% of AKA procedures. According to Waton et al. (2019), lower limb amputations should be undertaken on a planned operating list during normal working hours. Amputations that were performed out of hours in the current study could not wait until the following day. Although the indications overall were significantly different between TKA and AKA procedures for acute limb ischaemia, chronic limb ischaemia and tissue loss, amputation indications are not associated with the procedure time.

6.4.3. Risk of Post-Operative Complications

Significantly fewer patients with a TKA were admitted to critical care following their amputation. Critical care is required when a patient is seriously ill and requires intensive treatment or close monitoring. Additionally, critical care is appropriate for patients requiring advanced respiratory support, or patients requiring support of two or more organs (Smith & Nielsen, 1999). This supports other findings of this study, as a variety of factors influence the risk of complications following a major lower limb amputation, including age, level of amputation, and general health (NHS, 2019b). Moreover, patients with a TKA experienced fewer cardiac and respiratory post-operative complications compared to patients with an AKA. It is thought that a proximal leg amputation is associated with a greater risk to developing cardiovascular diseases than distal amputations (Naschitz & Lenger, 2008; Mundell et al., 2018), and patients with a dysvascular AKA were more likely at risk of a cardiac event (Mundell et al., 2018). Further, cardiac and respiratory post-operative complications, in-hospital mortality and 30-day mortality in this study were significantly lower following a TKA, thus explaining why significantly fewer patients with a TKA were admitted to critical care following their initial surgery.

6.4.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were significantly lower in patients with a TKA than patients with an AKA. Although different statistical values, this is consistent with findings for this outcome in Chapter Five and is discussed in Section 5.4.4.

6.4.5. Referral to Rehabilitation

A larger number of patients with a TKA were referred to rehabilitation than patients with an AKA. These findings are consistent to the findings for this outcome in Chapter Five and is discussed in Section 5.4.6.

6.4.6. Wound Healing

The findings of this study indicated that patients with a TKA have greater wound healing success than failed wound healing. Poor wound healing has been previously associated with TKA (Jensen et al., 1982; Cull et al., 2001; Morse et al., 2008; Albino et al., 2014; Murakami & Murray, 2016; Lim et al., 2018; Bergman & Metcalfe, 2020). Importantly, the findings from this study were supported by literature who reported successful wound healing rates of between 70% and 100% in patients with a TKA (Newcombe & Marcuson, 1972; Jensen et al., 1982; Moran et al., 1990; Bowker et al., 2000; Nellis & Van de Water, 2002; Morse et al., 2008; Jackson et al., 2012). These findings are consistent with those identified in Chapter Five and is discussed in Section 5.4.7.

6.5. Conclusion

Findings suggest that TKA may provide better outcomes in certain aspects of post amputation care over AKA, with patients experiencing fewer cardiac and respiratory complications, 30-day mortality was lower, and more patients were referred to amputation rehabilitation. Despite previous reports of poor wound healing with a TKA, this study suggests wound healing is potentially more successful, and warrants further investigation to compare this closely. Limitations are outlined collectively in Chapter Eight, Section 8.5.

CHAPTER SEVEN: NATIONAL VASCULAR REGISTRY – PROPENSITY SCORE MATCHING

7.1. Introduction

The NVR measures the quality and the care outcomes for patients who undergo a major vascular surgery in NHS hospitals, in which vascular departments within the UK can improve the quality of care received by those patients.

This study aimed to perform a large-scale retrospective analysis of a case control series using data held within the NVR database, and to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA.

7.2. Methods

7.2.1. Data Request Application Form

A 20-section DARF was completed as part of the application process. The process is outlined in Chapter Five, Section 5.2.1.

7.2.2. Data Analysis

The de-personalised patient level data were sorted and cleaned in Microsoft Excel. Upon cleaning, missing data were recorded as code 999. The cleaned data were processed into IBM Statistical Package for the Social Sciences (IBM SPSS, version 27) software for analysis. Propensity score matching as outlined in Chapter Four, Section 4.4.2 was utilised for this analysis.

7.3. Results

During the years of 2016 and 2019, there were a total of 497 unilateral TKA procedures matched on age, gender, and overall comorbidities to 497 unilateral AKA procedures within England and Wales. Patient characteristics are described in Chapter Seven, Section 7.3.1, and remaining outcomes are outlined subsequently.

7.3.1. Patient Characteristics

Patient characteristics are described in Table 7.1, Table 7.2, Table 7.3 and Table 7.4.

Patients within the study were of a similar age (Table 7.1), and there was no significant difference in age between the two levels of amputation (p=0.607). Patients were matched upon age groups and gender, therefore there was no significant difference between levels of amputation (Table 7.1). Although, amputations were more frequent amongst males (Table 7.1).

Patients with a TKA had a significantly greater BMI compared to patients with an AKA (Table 7.2; p=0.005). Further, significantly more patients with a TKA were obese compared to AKA, $\chi^2(1) = 7.579$, p=0.006.

Haemoglobin levels were similar between patients with a TKA and patients with an AKA (Table 7.2), thus there was no significant association (p=0.924). There was no significant association between haemoglobin level and level of amputation, $\chi^2(1) = 1.778$, p=0.182.

Pre-operative comorbidities reported in the NVR are outlined in Table 7.3. Patients with a TKA had a significantly higher presence of diabetes mellitus compared to patients with a AKA, $\chi^2(1) = 6.809$, p=0.009. Patients with a TKA had a significantly lower presence of chronic lung disease compared to AKA, $\chi^2(1) = 4.436$, p=0.035. Further, patients with a TKA had a significantly lower presence of cancer compared to AKA $\chi^2(1) = 8.789$, p=0.003. There were no significant differences between the levels of amputation and alternative comorbidities (Table 7.3). Additionally, there were significant fewer patients with a TKA who were current or had stopped smoking within 2 months of their amputation compared to AKA, $\chi^2(1) = 4.652$, p=0.031 (Table 7.3).

Incidence of patient frailty was determined as the number of patients that were frail at the time of their amputation. Patient frailty was categorised as not frail, mild frailty, moderate frailty, and severe frailty, as recorded in the Patient Frailty Score Guidance (Vascular Services Quality Improvement Programme, 2019). Significantly fewer patients with a TKA were frail compared to patients with an AKA, $\chi^2(1) = 8.476$, p=0.004 (Table 7.4). Further, of those patients who were frail, there were significantly fewer patients with a TKA who were moderately frail compared to AKA, $\chi^2(1) = 4.146$, p=0.042 (30.8% and 41.6%, respectively).

Table 7.1. Patient characteristics following propensity score matching.

Characteristic	TKA	AKA	P
Age (years)	**N=497**	**N=497**	0.607
- Mean (± SD)	69.1 ± 13.3	69.9 ± 12.5	
- Median (IQR)	71.3 (60.7-78.9)	71.3 (62.7-79.4)	
Age Group, n (%)	**N=497**	**N=497**	
- Under 60 years	121 (24.3)	121 (24.3)	1.000
- 60-70 years	109 (21.9)	109 (21.9)	1.000
- 70-80 years	153 (30.8)	153 (30.8)	1.000
- 80+ years	114 (22.9)	141 (22.9)	1.000
Gender, n (%)	**N=497**	**N=497**	1.000
- Male	326 (65.6)	326 (65.6)	
- Female	171 (34.4)	171 (34.4)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of p<0.005.

Table 7.2. Patient BMI and haemoglobin characteristics following propensity score matching.

Characteristic	TKA	AKA	P
BMI (kg/m^2)	**N=326**	**N=313**	0.005*
- Mean (± SD)	27.3 ± 8.4	25.2 ± 6.5	
- Median (IQR)	25.7 (22-30.9)	25.2 (21.6-29.4)	
BMI Group, n (%)	**N=326**	**N=313**	
- Underweight (<18.5 kg/m^2)	34 (10.4)	38 (12.1)	0.494
- Healthy (18.5-24.9 kg/m^2)	116 (35.6)	127 (40.6)	0.194
- Overweight (25-29.9 kg/m^2)	88 (27)	92 (29.4)	0.500
- Obese (>30 kg/m^2)	88 (27)	56 (17.9)	0.006*
Haemoglobin (g/dL)	**N=427**	**N=427**	0.924
- Mean (± SD)	10.9 ± 2.2	10.9 ± 2.3	
- Median (IQR)	10.6 (9.3-12.1)	10.7 (9.2-12)	
Haemoglobin Level, n (%)	**N=427**	**N=427**	0.182
- Anaemic	369 (86.4)	355 (83.1)	
- Not Anaemic	58 (13.6)	72 (16.9)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Body mass index (BMI); Standard deviation (SD); Kilograms per metre squared (kg/m^2); Grams per decilitres (g/dL); Values reported as count (percentage) unless stated; * signifies a significant difference of $p<0.005$.

Table 7.3. Patient comorbidities and smoking status following propensity score matching.

Characteristic	TKA, n (%)	AKA, n (%)	P
Comorbidities	**N=497**	**N=497**	
- No Comorbidities	48 (9.7)	48 (9.7)	1.000
- Diabetes Mellitus	249 (50.1)	208 (41.9)	0.009*
- Hypertension	311 (62.6)	311 (62.6)	1.000
- Chronic Lung Disease	113 (22.7)	142 (28.6)	0.035*
- Ischaemic Heart Disease	210 (42.3)	209 (42.1)	0.949
- Chronic Heart Failure	71 (14.3)	71 (14.3)	1.000
- Stroke	58 (11.7)	75 (15.1)	0.113
- Chronic Renal Failure	100 (20.1)	86 (17.3)	0.255
- Cancer	16 (3.2)	37 (7.4)	0.003*
- Lower Limb Arterial Disease	0 (0)	1 (0.2)	0.317
- Major Amputation	24 (4.8)	51 (10.3)	0.001*
Smoking Status	**N=495**	**N=494**	
- Never	95 (19.2)	92 (18.6)	0.819
- Ex-smoker	243 (49.1)	213 (43.1)	0.060
- Current or stopped within 2 months	157 (31.7)	189 (38.3)	0.031*

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

Table 7.4. Patient frailty following propensity score matching.

Factor	TKA, n (%)	AKA, n (%)	P
Frail	**N=120**	**N=296**	0.004*
- Yes	87 (72.5)	251 (84.8)	
- No	33 (27.5)	45 (15.2)	
Frailty Level	**N=120**	**N=296**	
- Not Frail	33 (27.5)	45 (15.2)	0.004*
- Mild Frailty	27 (22.5)	65 (22)	0.904
- Moderate Frailty	37 (30.8)	123 (41.6)	0.042*
- Severe Frailty	23 (19.2)	63 (21.3)	0.629

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

7.3.2. Pre-Operative Factors

7.3.2.1. Admission Type

The number of elective and non-elective admissions were compared between 497 TKA and 497 AKA. There was a significantly higher number of elective admissions in patients with a TKA (26.4%) compared with patients with an AKA (18.1%), $\chi^2(1) = 9.781$, p=0.002 (Figure 7.1).

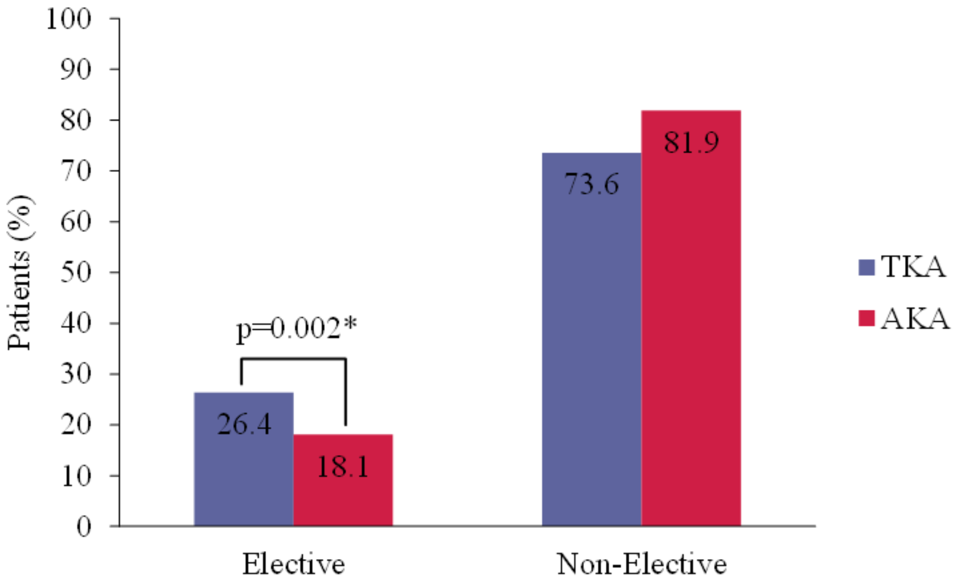

Figure 7.1. Admission type following propensity score matching.

7.3.2.2. Amputation Indication

There were seven amputation indications reported in the NVR database (Table 7.5). There was a significantly higher number of patients who had an AKA because of acute limb ischaemia compared to patients with a TKA, $\chi^2(1) = 8.776$, $p=0.003$.

Table 7.5. Amputation indication following propensity score matching.

Factor	TKA, n (%)	AKA, n (%)	P
Amputation Indication	**N=496**	**N=483**	
- Acute Limb Ischaemia	63 (12.7)	95 (19.7)	0.003*
- Chronic Limb Ischaemia	90 (18.1)	98 (20.3)	0.394
- Neuropathy	8 (1.6)	5 (1)	0.430
- Tissue Loss	224 (45.2)	195 (40.4)	0.130
- Uncontrolled Infection	95 (19.2)	79 (16.4)	0.252
- Trauma	11 (2.2)	6 (1.2)	0.243
- Aneurysm	5 (1)	5 (1)	0.966

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

7.3.2.3. Time of Procedure

The time of procedure was determined as the time the procedure began when there was knife-to-skin contact. Table 7.6 indicates the time of procedure for patients with a TKA and patients with an AKA, and there was no significant association between time of procedure and level of amputation, $\chi^2(1) = 2.029$, $p=0.154$.

Table 7.6. Time of procedure following propensity score matching.

Factor	TKA, n (%)	AKA, n (%)	P
Time of Procedure	**N=497**	**N=497**	0.154
- 07:00 – 19:00 hours	476 (95.8)	466 (93.8)	
- 19:00 – 07:00 hours	21 (4.2)	31 (6.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

7.3.3 Post-Operative Factors

7.3.3.1. Critical Care Admission from Theatre

The incidence of critical care admission from theatre was determined as the number of patients that were admitted to critical care within hospital following the surgical procedure of a major lower limb amputation. The length of critical care stay was determined as the number of days, if any, following a patient's lower limb amputation, where they were admitted to critical care within hospital.

Table 7.7 highlights the critical care admission rates and critical care length of stay following their initial amputation. There were significantly fewer patients with a TKA who were admitted to critical care compared to patients with an AKA, $\chi^2(1) = 5.425$, $p=0.020$. There was no significant difference in critical care length of stay between the two levels of amputation ($p=0.071$).

Table 7.7. Critical care admission and critical care length of stay following propensity score matching.

Critical Care	TKA	AKA	P
Admission, n (%)	**N=497**	**N=497**	0.020*
- Yes	54 (10.9)	79 (15.9)	
- No	443 (89.1)	418 (84.1)	
Length of Stay (days)	**N=54**	**N=79**	0.071
- Mean (± SD)	4.4 ± 6.3	5.6 ± 7.1	
- Median (IQR)	2 (1-4)	3 (2-5)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated; * signifies a significant difference of $p<0.005$.

7.3.3.2. Incidence of Return to Theatre

The incidence of return to theatre was determined as the number of patients that returned to theatre following their major lower limb amputation. Return to theatre within the NVR was removed from the amputation dataset in January 2019 and replaced with further surgery. The type of further surgery was compared between patients with a TKA and patients with an AKA.

There was no significant association between level of amputation and return to theatre, $\chi^2(1) = 3.668$, $p=0.055$ (Table 7.8). Additionally, there were no significant differences in further procedures between levels of amputation ($p>0.05$).

Table 7.8. Return to theatre rates and types of further surgery following propensity score matching.

Post-Operative Factor	TKA, n (%)	AKA, n (%)	P
Return to Theatre	**N=481**	**N=488**	0.055
- Yes	49 (10.2)	33 (6.8)	
- No	432 (89.8)	455 (93.2)	
Further Surgery Type	**N=445**	**N=483**	
- None	432 (89.8)	455 (93.2)	0.055
- Angioplasty with Stent	1 (0.2)	1 (0.2)	0.951
- Major Lower Limb Amputation	5 (1.1)	11 (2.3)	0.180
- Other	7 (1.6)	14 (2.9)	0.178

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

7.3.3.2.1. Incidence of Revision of Amputation

The incidence of revision of amputation was determined as the number of patients who were revised to a higher level of amputation following their original major lower limb amputation. Incidence of revision of amputation was determined between the two levels of amputation. Further surgery with a multi-code response was added to the NVR dataset in January 2019, therefore resulting in incomplete responses previously.

No significant difference between level of amputation and revision of major lower limb amputation was determined, $\chi^2(1) = 1.798$, p=0.180. There were no minor lower limb amputations reported in the NVR database.

7.3.3.3. Incidence of Post-Operative Complications

The incidence of complications was determined as the number of patients who experienced complications following their major lower limb amputation. The number of post-operative complications were determined by the total number of post-operative complications that each patient experienced. These are both outlined in Table 7.9.

Post-operative complications were noticeable in patients with a TKA and patients with an AKA following their initial lower limb amputation. Significantly more patients with a TKA had no post-operative complications compared to AKA, $\chi^2(1) = 7.879$, p=0.005. Patients with a TKA experienced significantly fewer cardiac complications post-operatively compared to patients with an AKA, $\chi^2(1) = 4.007$, p = 0.045. Further, significantly fewer patients with a TKA experienced cerebral post-operative complications compared to AKA, $\chi^2(1) = 5.464$, p=0.019. Additionally, significantly fewer patients with a TKA experienced paraplegia post-operatively, $\chi^2(1) = 7.225$, p=0.007, and post-operative confusion, $\chi^2(1) = 7.323$, p=0.007, compared to patients with an AKA. Significantly fewer patients with a TKA had experienced other post-operative complications compared to patients with an AKA, $\chi^2(1) = 19.310$, $p<0.001$.

The number of post-operative complications patients had varied between the two levels of amputation (Table 7.9). Patients with a TKA had no more than five post-operative complications, however, patients with an AKA had up to 10 post-operative complications. Significantly more patients with a TKA had no post-operative complications compared to patients with an AKA, $\chi^2(9) = 17.192$, $p=0.046$. When investigating those patients who had post-operative complications, significantly fewer patients with a TKA had five or more post-operative complications compared to AKA (Table 7.9), $\chi^2(1) = 5.885$, $p=0.015$.

Table 7.9. Post-operative complications following propensity score matching.

Post-Operative Complications	TKA, n (%)	AKA, n (%)	P
Complication Type	**N=496**	**N=497**	
- None	396 (79.8)	359 (72.2)	0.005*
- Cardiac	26 (5.2)	42 (8.5)	0.004*
- Respiratory	34 (6.9)	46 (9.3)	0.0165
- Cerebral	3 (0.6)	12 (2.4)	0.019*
- Renal Failure	20 (4)	15 (3)	0.386
- Haemorrhage	6 (1.2)	13 (1.5)	0.106
- Limb Ischaemia	17 (3.4)	19 (3.8)	0.739
- Paraplegia	2 (0.4)	12 (2.4)	0.007*
- Post-Operative Confusion	4 (0.8)	16 (3.2)	0.007*
- Major GI Complication	1 (0.2)	5 (1)	0.102
- Surgical Site Infection	8 (1.6)	22 (4.4)	0.010*
- Other	12 (2.4)	44 (8.9)	<0.001*
Number of Complications	**N=496**	**N=497**	
- 0	396 (79.8)	359 (72.2)	0.005*
- 1	81 (16.3)	103 (20.7)	0.075
- 2	10 (2)	8 (1.6)	0.631
- 3	5 (1)	6 (1.2)	0.764
- 4	3 (0.6)	10 (2)	0.051
- 5	1 (0.2)	5 (1)	0.102
- 6	0	2 (0.4)	0.157
- 7	0	2 (0.4)	0.157
- 8	0	1 (0.2)	0.318
- 9	0	0	-
- 10	0	1 (0.2)	0.318
Complications	**N=100**	**N=138**	0.015*
- 1 to 4	99 (99)	127 (92)	
- 5+	1 (1)	11 (8)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

7.3.3.3.1. Incidence of Surgical Site Infection

The incidence of surgical site infection was determined as the number of patients who experienced a surgical site infection following their major lower limb amputation. There were significantly fewer patients with a TKA who had surgical site infection post-operatively compared to patients with an AKA, $\chi^2(1) = 6.708$, p=0.010.

7.3.3.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were calculated as the number of patients that died prior to discharge and the number of patients that died within 30 days of receiving a major lower limb amputation, respectively. Table 7.10 outlines the in-hospital and 30-day mortality rates for patients with a TKA and patients with an AKA. There was no significant association between in-hospital mortality and level of amputation, $\chi^2(1) = 2.792$, p=0.095. Further, there was no significant association between 30-day mortality and level of amputation, $\chi^2(1) = 0.043$, p=0.836.

Table 7.10. In-hospital and 30-day mortality rates following propensity score matching.

Outcome	TKA, n (%)	AKA, n (%)	P
Mortality Rates	**N=497**	**N=497**	0.095
- In-Hospital mortality	31 (6.2)	45 (9.1)	
- Survived	466 (93.8)	452 (90.9)	
Upon Discharge	**N=331**	**N=470**	0.836
- 30-day mortality	22 (6.6)	33 (7)	
- Survived	309 (93.4)	437 (93)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

7.3.4. Discharge Outcomes

7.3.4.1. Overall Hospital Length of Stay

Overall LOS was calculated as the number of days that each patient stayed in hospital following their major lower limb amputation and was determined between the two levels of amputation (Table 7.11). Overall hospital LOS was similar between patients with a TKA and patients with an AKA, and there was no significant difference (p=0.411).

Table 7.11. Overall hospital length of stay (days) following propensity score matching.

Outcome	TKA	AKA	P
Overall Hospital LOS	**N=496**	**N=496**	0.411
- Mean (± SD)	30.9 ± 27.8	31.3 ± 28.3	
- Median (IQR)	22 (12.3-38)	23 (13-40)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated.

7.3.4.2. Discharge Destination

Discharge destination was determined as the number of patients that were discharged to their own residence, to rehabilitation, to a different hospital, or to intermediate care following their amputation. Table 7.12 displays the discharge destinations for patients with a TKA and patients with an AKA. There was no significant association between level of amputation and discharge destination (Table 7.12).

Table 7.12. Discharge destination following propensity score matching.

Outcome	TKA, n (%)	AKA, n (%)	P
Discharge Destination	**N=183**	**N=418**	
- Deceased	31 (16.9)	45 (10.8)	-
- Own Residence	94 (51.4)	217 (51.9)	0.902
- Rehabilitation	24 (13.1)	61 (14.6)	0.632
- Other Hospital	22 (12)	66 (15.8)	0.229
- Intermediate Care	12 (6.6)	29 (6.9)	0.865

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Values reported as count (percentage) unless stated.

7.3.4.3. Wound Healing Rates

Wound healing rates were determined as the number of patients who had successful wound healing 30 days after a major lower limb amputation. Wound healing was successful in over 79% of patients with a TKA and an AKA (Table 7.13), and there was no significant association between wound healing and level of amputation, $\chi^2(1) = 0.010$, $p=0.919$.

Table 7.13. Wound healing rates following propensity score matching.

Outcome	TKA, n (%)	AKA, n (%)	P
Wound Healing Rates	**N=292**	**N=287**	0.919
- Yes	232 (79.5)	229 (79.8)	
- No	60 (20.5)	58 (20.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

7.3.4.4. Incidence of Re-admission within 30 days

Incidence of re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital. The incidence of vascular re-admission within 30 days was determined as the number of patients that were re-admitted to any hospital within 30 days of their major lower limb amputation and after discharge from hospital for vascular reasons. These were determined for patients with a TKA and AKA and outlined in Table 7.14.

There was no significant difference between the two levels of amputation, $\chi^2(1) = 2.380$, $p=0.123$. Of these re-admissions, 4 (7.5%) of patients with a TKA and 16 (15.8%) of patients with an AKA were re-admitted for vascular reasons. There was no significant association between the two levels of amputation, $\chi^2(1) = 2.116$, $p=0.146$.

Table 7.14. 30-day hospital re-admission rates following propensity score matching.

Outcome	TKA, n (%)	AKA, n (%)	P
Re-admission 30-days	**N=424**	**N=484**	0.123
- Yes	39 (9.2)	60 (12.4)	
- No	385 (90.8)	424 (87.6)	
Vascular Re-admission 30-days	**N=53**	**N=101**	0.146
- Yes	4 (7.5)	16 (15.8)	
- No	49 (92.5)	85 (84.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

7.3.4.5. Incidence of Referral to Rehabilitation

Incidence of referral to rehabilitation was determined as the number of patients that were referred to rehabilitation and/or limb fitting. The incidence of referral to rehabilitation was determined between the two levels of amputation (497 TKA and 497 AKA) and presented in Figure 7.2. Significantly more patients with a TKA were referred to amputation rehabilitation compared to patients with an AKA, $\chi^2(1) = 24.354$, $p<0.001$.

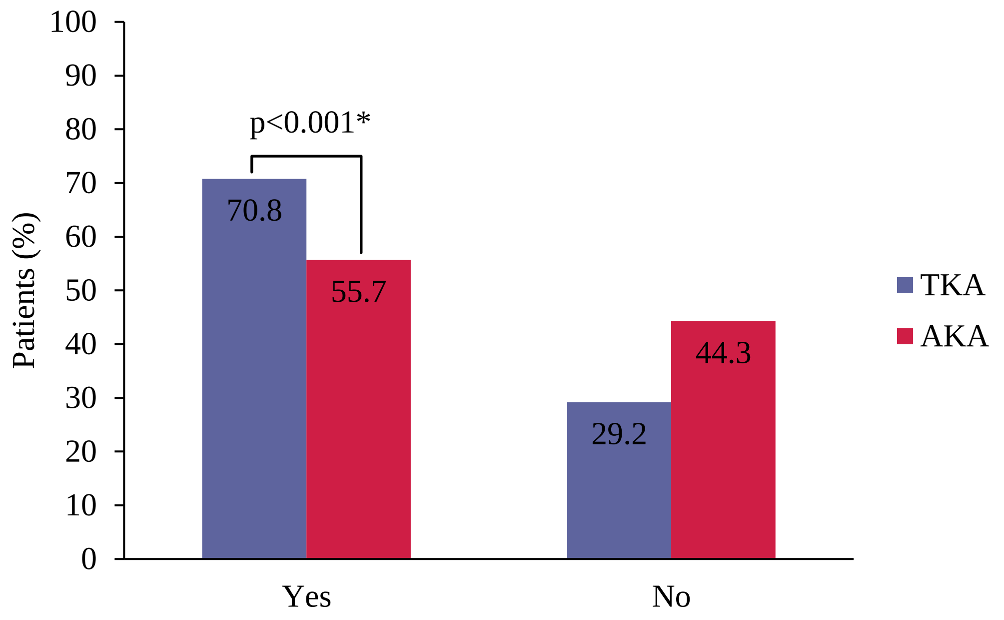

Figure 7.2. Amputation rehabilitation referrals following propensity score matching.

7.4. Discussion

The aim of this study was to determine the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA when undertaking propensity score matching.

The main findings from this analysis indicate that patients with a TKA had a significantly higher BMI and significantly more patients with a TKA were obese. Secondly, a higher percentage of patients with a TKA had a presence of diabetes mellitus, and a lower presence of chronic lung disease and cancer compared to patients with an AKA. Thirdly, significantly fewer patients with a TKA were current smokers, and significantly fewer TKA were frail. Additionally, significantly more patients with a unilateral TKA had an elective admission prior to their amputation, and there were significantly fewer TKA who had amputations due to acute limb ischaemia. There were significantly fewer patients with a TKA who were admitted to critical care, and significantly fewer patients with a TKA had post-operative complications. For those who had post-operative complications, significantly fewer patients with a TKA experienced post-operative complications including cardiac, cerebral, paraplegia, post-operative confusion and surgical site infection. A significantly greater number of patients with a TKA were referred to amputation rehabilitation compared to patients with an AKA. There was successful wound healing following TKA and AKA, although there was no significant difference determined.

7.4.1. Patient Characteristics

Patients with a TKA had a significantly greater BMI than those with an AKA. Although the significance is not large, the mean BMI recorded for TKA was 27.3 kg/m^2 compared to AKA 25.2 kg/m^2, demonstrating that both amputation level means are in the overweight classification. Studies including TKA and AKA (Fortington et al., 2013; Lim et al., 2018; Ambler et al., 2020) did not report BMI, thus preventing from further comparison. Obesity can be associated with wound healing and the fitting of a prosthesis (Rosenberg et al., 2013), however this is not explained by our findings as wound healing rates were similar between TKA and AKA, and significantly more patients with a TKA were referred to rehabilitation.

Over 50% of patients with a TKA in the study had diabetes mellitus, compared to 41.9% of patients with an AKA. A greater percentage of patients with a TKA in a study by Lim et al. (2018) had diabetes mellitus compared to patients with an AKA. Additionally, significantly fewer patients with a TKA had a higher presence of chronic lung disease. Chronic lung disease may be caused by smoking tobacco, or inhaling chemical fumes, dust or air pollution (National Cancer Institute, 2022).

Significantly fewer patients with a TKA had a major amputation prior to their episode compared to AKA. It is important to note that previous amputations may have been revisions into their new TKA or AKA within that episode. Although significantly more patients with a TKA had diabetes mellitus, and patients with diabetes have a higher rate of revision to a more proximal amputation level of amputation (Wanivenhaus et al., 2016), this does not explain our findings. Additionally, if wound healing rates are taken into consideration, wound healing is successful in both TKA and AKA within the current study. Looking at amputation indications for the current study, it is apparent that significantly more AKA were because of acute limb ischaemia, which is the sudden decrease in limb perfusion and arterial supply. Those patients with amputations due to acute limb ischaemia would have peripheral arterial disease, thus potentially could have been due to cigarette smoking, which is significantly higher in the AKA cohort of this study.

Although small, significantly fewer patients with a TKA had a history of cancer compared to AKA. It is unclear from the NVR whether these patients had a history of cancer and treatment were utilised, or whether the cancer was concurrent. Additionally, it is unclear the anatomical location of the cancer, or whether the cancer was a cause of amputation. Cancer may be caused by numerous factors, including smoking, alcohol, lack of physical activity, being overweight or obese, environmental exposure, and infection (Fayed, 2021). This can be partially supported by our findings, although significantly fewer patients with an AKA were obese, and significantly more patients with an AKA were current smokers or had stopped within two months.

Significantly more patients with an AKA were current smokers at the time of amputation compared to TKA (38.3% and 31.7%, respectively). Cigarette smoking has been reported to significantly increase rates of vascular disease (Liu et al., 2018). However, Selby and Zhang (1995) suggested that cigarette smoking was unrelated to amputation risk, and Stewart (1987) reported that smoking had no influence on diabetic-foot amputations. However, alternative studies have supported that smoking is a significant contributor Into diabetes-related amputations (Yesil et al., 2009; Morbach et al., 2012; Jiang et al., 2015). Lim et al. (2018) reported similar levels of smoking between TKA and AKA, which is contrary to the findings of this study.

Patients in this study with a TKA had significantly fewer amputations due to acute limb ischaemia. Acute limb ischaemia is defined as a sudden decease in limb perfusion that threatens viability of the limb (Norgren et al., 2007; Creager et al., 2012). Reported causes of ischaemia include hypertension, cigarette smoking, and diabetes mellitus (Brown & Juergens, 1972; Gordon & Kannel, 1972; Santilli & Santilli, 1999). Significantly fewer patients with a TKA were current smokers, therefore this finding could have influenced acute limb ischaemia. Although patients with diabetes mellitus are at an increased risk of developing limb ischaemia due to peripheral arterial disease (Santilli & Santilli, 1999; Ying et al., 2022), this does not explain the finding as significantly fewer patients with a TKA had amputations due to acute limb ischaemia. Ischaemia results in tissue damage, thus could have been recorded as tissue loss rather than ischaemia.

Significantly fewer patients with a TKA were frail compared to patients with an AKA. These findings are not supported by Schmiegelow et al. (2018), who stated that patients with a TKA or higher are frail. Patients requiring a major lower limb amputation for peripheral arterial disease tend to be elderly, frail, and presenting multiple comorbidities (Monaro et al., 2017). Frailty places patients at a greater risk of adverse outcomes, including hospital admission, a worsening disability, and death (Partridge et al., 2012; Monaro et al., 2017). Additionally, outcomes including mortality, increased hospital re-admissions, and post-operative complications have been correlated with an increase in frailty amongst the literature (Dasgupta et al., 2009; Fang et al., 2017). Although frailty was significantly lower following a TKA than AKA (72.5% and 84.8%, respectively), and significantly fewer patients with a TKA had moderate frailty compared to AKA, significantly more patients with a TKA were referred to rehabilitation. However, as missing data appeared greater amongst this outcome, this warrants further investigation.

7.4.2. Hospital Admissions

Patients with a TKA were majority elective admissions compared to patients with an AKA. This has been consistent throughout the NVR analysis, and is discussed in Chapter Five, Section 5.4.2.

7.4.3. Risk of Post-Operative Complications

Significantly fewer patients with a TKA were admitted to critical care following their amputation. This supports other findings of this study, as a variety of factors influence the risk of complications following a major lower limb amputation, including age, level of amputation, and general health (NHS, 2019b). Moreover, patients with a TKA experienced fewer overall post-operative complications, including fewer cardiac post-operative complications compared to patients with an AKA. The findings from this chapter are consistent with Chapter Five and Chapter Six and is discussed in Chapter 5.4.3.

Significantly fewer patients with a TKA experienced cerebral, paraplegia, and post-operative confusion following their procedure. Paraplegia following lower extremity amputation is rare (Wang & Hong, 2015). Although the cases are low, these can be caused by high energy or complex energy trauma (Wang & Hong, 2015), nerve disorders, or strokes. There were a similar rate of paraplegia and cerebral post-operative complications following an AKA, thus indicating that they may be linked. Cerebral post-operative complications may be caused by blood flow problems, potentially from strokes. Post-operative confusion, also referred to as post-operative delirium, is a common yet serious complication after surgery, and is defined as an acute disorder of attention and cognition (Pol et al., 2011). Further, Shin et al. (2018) reported the incidence of post-operative delirium following lower limb amputation was 40%. Moreover, incidence rates of delirium after lower limb amputation as 17% (Visser et al., 2015) and 20% (Pol et al., 2014), with a third study reporting incidence rate following BKA and AKA as 61% (van Eijsden et al., 2015). Patients with an AKA in this study had significantly more amputations due to acute limb ischaemia, which is frequently related to systemic atherosclerosis and the negative impacts on patient outcomes (Beckman & Creager, 2014; Shin et al., 2018). Moreover, systemic atherosclerosis is known to contribute to the cognitive decline in elderly patients, and cognitive impairment is a risk factor for delirium (Vinkers et al., 2005; Kalish et al., 2014; Shin et al., 2018). Significantly fewer patients with a TKA experienced other post-operative complications following their surgery. This is a vague term used by the NVR as this could be incorporate any complication, thus being more difficult to interpret. According to Physiopedia (2022c), the most common post-operative complications following amputation include oedema, wounds and infection, pain, muscle weakness and contractures, and joint instability.

Patients with a TKA experienced significantly fewer surgical site infections compared to patients with an AKA. Surgical site infection may increase the risk of mortality, with the potential contribution towards impaired wound healing and complications with prosthesis fitting (Chahour et al., 2021). According to Chahour et al. (2021) in a study investigating surgical site infection predictors following BKA and AKA, factors including amputation level, female sex, smoking, emergency status, and anaemia are associated with surgical site infection. Additionally, BMI in their study was a significant association with an increased risk of surgical site infection following an AKA. However, in our study following propensity score matching, sex was matched, there were significantly more patients with an AKA who were current smokers, there were significantly more patients with a TKA having elective admissions as opposed to emergency admissions compared to AKA, and anaemia was similar in between TKA and AKA.

7.4.4. Referral to Rehabilitation

A larger number of patients with a TKA were referred to rehabilitation than patients with an AKA. These findings are consistent to the findings for this outcome in Chapter Five and Chapter Six and is discussed in Section 5.4.6.

7.4.5. Wound Healing

Findings of this study indicated that patients with a TKA has similar wound healing rates to patients with an AKA. Further, patients with a TKA have greater wound healing success than failed wound healing. Crucially, the findings from this study were supported with successful wound healing rates of between 70% and 100% in patients with a TKA (Newcombe & Marcuson, 1972; Jensen et al., 1982; Moran et al., 1990; Bowker et al., 2000; Nellis & Van de Water, 2002; Morse et al., 2008; Jackson et al., 2012). These findings are consistent with those identified in Chapter Five and is discussed in Section 5.4.7.

7.5. Conclusion

Findings suggest that TKA may provide better outcomes in certain aspects of post amputation care over AKA, with patients experiencing fewer cardiac, cerebral and paraplegia complications, and more patients were referred to amputation rehabilitation. Despite previous reports of poor wound healing with a TKA, this study suggests wound healing is potentially more successful, and warrants further investigation to compare this closely. Limitations are outlined collectively in Chapter Eight, Section 8.5.

CHAPTER EIGHT: NATIONAL VASCULAR REGISTRY – COMPARING HANDLING MISSING DATA TECHNIQUES

8.1. Introduction

Clinical datasets are increasingly being utilised to obtain medical knowledge, thus improving precision and better interventions for healthcare resources (Luo, 2021). However, clinical datasets present significant challenges because of the data not being collected specifically for research purposes, therefore subject to substantial missing data (Wells et al., 2013). Missing values are frequently encountered and occur in all types of studies (van der Heijden et al., 2006). The percentages of patients with missing data in the National Surgical Quality Improvement Program ranges from 0% to 80% (Ondeck et al., 2018). Leaving missing retrospective datasets unaddressed may reduce the validity of the conclusions drawn (Wells et al., 2013). As outlined in Chapter Four, there are three types of missing data (MCAR, MNAR, and MAR). However, it is impossible to determine from the data whether it is MAR or MNAR (van der Heijden et al., 2006). Although omitting cases with missing data or imputing missing data points have their advantages and disadvantages (outlined in Chapter Four), it is important to understand how adapting the handling missing data techniques in turn can impact the results of the study. Lim et al. (2018) identified patients with TKA and AKA from the American College of Surgeons National Surgical Quality Improvement Program. They applied propensity score matching to balance comorbidities and compared operative variables and post-operative complications between these two levels of amputation. They, however, did not compare pre-operative and discharge outcomes between these two levels of amputation.

The aims of the current study were two-fold. Firstly, this study aimed to perform and compare handling missing data techniques (complete case analysis, multiple imputation, and propensity score matching) using a large-scale retrospective case control series dataset held within the NVR database. Secondly, the study investigated the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA when utilising each of the three techniques.

8.2. Methods

8.2.1. Data Collection

A 20-section DARF was completed as part of the application process. The collection of data are outlined in Chapter Five, Section 5.2.1.

8.2.2. Data Analysis

Data cleaning and analysis techniques are described in Chapter Four, Section 4.2.2, 4.3.2 and 4.4.2, respectively.

8.3. Results

During the years of 2016 and 2019, there were a total of 497 unilateral TKA procedures and 6,757 unilateral AKA procedures within England and Wales following complete case analysis. Upon multiple imputation, there was a total of 497 unilateral TKA procedures and 6,764 unilateral AKA procedures within England and Wales. Upon propensity score matching, there were a total of 497 matched unilateral TKA and unilateral AKA procedures. Patient characteristics following complete case analysis, multiple imputation and propensity score matching is described in Chapter Eight, Section 8.3.1, and remaining outcomes are outlined subsequently.

8.3.1. Patient Characteristics

Patients within the study when comparing complete case analysis results to multiple imputation results were of a similar age (Table 8.1). When looking at the results from propensity score matching, patients with a TKA and patients with an AKA were of a similar age (69.1 years and 69.9 years, respectively). Following multiple imputation however, patients with a TKA were significantly younger than patients with an AKA ($p=0.029$). No significant differences were identified using complete case analysis and propensity score matching ($p=0.075$ and $p=0.607$, respectively).

There were significantly more patients with a TKA who were under 60 years old compared to patients with an AKA following complete case analysis and multiple imputation ($p=0.004$ and $p=0.004$, respectively; Table 8.1). As a predictor that cases were matched upon was age group, there was no significant difference. As there were no missing cases of gender in the original dataset, amputations were reportedly similar across all three handling data techniques. As gender was a predictor for propensity score matching, there was an identical number of male and female patients with a TKA and AKA. Although amputations were more frequent amongst males (Table 8.1), there was no association between gender and level of amputation following each handling missing data technique ($p>0.05$).

Patients following complete case analysis had a similar BMI, thus there was no significant effect between level of amputation (Table 8.2). Following multiple imputation and propensity score matching however, BMI was significantly higher in patients with a TKA than patients with an AKA ($p<0.02$). When examining the BMI groups, there was no significant association between BMI and level of amputation following complete case analysis and multiple imputation. However, there were significantly more patients with a TKA who were obese compared to patients with an AKA (p=0.006).

Haemoglobin levels were similar across all three handling missing data techniques between patients with a TKA and patients with an AKA, thus there was no significant association found between haemoglobin levels and level of amputation (Table 8.2). More patients with a TKA and AKA overall were anaemic, and percentages were similar across all handling missing data techniques. There was no significant association found between haemoglobin level and level of amputation (Table 8.2).

Diabetes mellitus was significantly higher across all handling missing data techniques in patients with a TKA than patients with an AKA (Table 8.3). Additionally, chronic lung disease was significantly lower across all handling missing data techniques in patients with a TKA than patients with a AKA (Table 8.3). Following propensity score matching, cancer was significantly higher in patients with an AKA than patients with a TKA (7.4% and 3.2%, respectively; p=0.003). Additionally, following propensity score matching, major amputation was significantly higher in patients with an AKA than patients with a TKA (10.3% and 4.8%, respectively; p=0.001). It is important to note however, that these two comorbidities were not significantly different between patients with a TKA and patients with an AKA following complete case analysis and multiple imputation (Table 8.3).

There were significantly fewer patients with a TKA that currently smoked or stopped smoking within 2 months prior to their amputation compared to patients with an AKA when using propensity score matching (p=0.031; Table 8.4). In comparison, there were no significant differences determined in current or stopped smoking within 2 months, or any smoking status, when utilising complete case analysis or multiple imputation (Table 8.4).

Table 8.5 highlights that significantly more patients with a TKA were frail compared to patients with an AKA following complete case analysis (p=0.039) and propensity score matching (p=0.004). Additionally, propensity score matching identified that there was a significantly higher percentage of patients with an AKA that were moderately frail compared to patients with a TKA (41.6% and 30.8%, respectively). However, moderate frailty was not significant when using complete case analysis or multiple imputation (Table 8.5). There was no significant association between the two levels of amputation and mild and severe frailty, independently following complete case analysis, multiple imputation, and propensity score matching (Table 8.5).

Table 8.1. Patient characteristics comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Characteristic	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Age (years)			0.075			0.029*			0.607
- Mean (± SD)	69.1 ± 13.3	70.4 ± 12.5		69.1 ± 13.3	70.4 ± 12.6		69.1 ± 13.3	69.9 ± 12.5	
- Median (IQR)	71.3 (60.6-78.9)	71.7 (62.7-79.4)		-	-		71.3 (60.7-78.9)	71.3 (62.7-79.4)	
Age Group									
- Under 60 years	121 (24.3)	1,286 (19)	0.004*	121 (24.3)	1,288 (19)	0.004*	121 (24.3)	121 (24.3)	1.000
- 60-70 years	109 (21.9)	1,720 (25.5)	0.081	109 (21.9)	1,722 (25.5)	0.081	109 (21.9)	109 (21.9)	1.000
- 70-80 years	153 (30.8)	2,176 (32.2)	0.513	153 (30.8)	2,178 (32.2)	0.513	153 (30.8)	153 (30.8)	1.000
- 80+ years	114 (22.9)	1,575 (23.3)	0.850	114 (22.9)	1,576 (23.3)	0.853	114 (22.9)	114 (22.9)	1.000
Gender			0.385			0.381			1.000
- Male	326 (65.6)	4,560 (67.5)		326 (65.6)	4,566 (67.5)		326 (65.6)	326 (65.6)	
- Female	171 (34.4)	2,197 (32.5)		171 (34.4)	2,198 (32.5)		171 (34.4)	171 (34.4)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage) unless stated; Standard deviation (SD); Interquartile range (IQR); * signifies a significant difference of p<0.005.

Table 8.2. Patient BMI and haemoglobin comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Characteristic	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
BMI (kg/m^2)			0.076			0.019*			0.005*
- Mean (± SD)	27.2 ± 8.4	26.1 ± 6.7		26.8 ± 7.9	26.1 ± 6.7		27.3 ± 8.4	25.2 ± 6.5	
- Median (IQR)	25.7 (22-30.9)	25.2 (21.6-29.4)		-	-		25.7 (22-30.9)	24.5 (21.6-29.4)	
BMI Group									
- Underweight	34 (10.4)	388 (9)	0.385	50 (10.1)	601 (8.9)	0.493	34 (10.4)	38 (12.1)	0.494
- Healthy	116 (35.6)	1,713 (39.7)	0.142	180 (36.2)	2,686 (39.7)	0.166	116 (35.6)	127 (40.6)	0.194
- Overweight	88 (27)	1,227 (28.4)	0.576	139 (28)	1,937 (28.6)	0.739	88 (27)	92 (29.4)	0.500
- Obese	88 (27)	986 (22.9)	0.088	128 (25.7)	1,540 (22.8)	0.149	88 (27)	56 (17.9)	0.006*
Haemoglobin (g/dL)			0.370			0.429			0.924
- Mean (± SD)	10.9 ± 2.2	10.8 ± 2.2		10.6 ± 2.2	10.5 ± 2.2		10.9 ± 2.2	10.9 ± 2.3	
- Median (IQR)	10.6 (9.3-12.1)	10.5 (9.2-12)		-	-		10.6 (9.3-12.1)	10.7 (9.2-12)	
Haemoglobin			0.469			0.793			0.182
- Anaemic	369 (86.4)	4,946 (85.1)		435 (87.5)	5,887 (87)		369 (86.4)	355 (83.1)	
- Not Anaemic	58 (13.6)	864 (14.9)		62 (12.5)	877 (13)		58 (13.6)	72 (16.9)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Body mass index (BMI); Standard deviation (SD); Interquartile range (IQR); Grams per decilitre (g/dL); Values reported as count (percentage) unless stated; * signifies a significant difference of p<0.005.

Table 8.3. Comorbidities comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Characteristic	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Comorbidities									
- No Comorbidities	48 (9.7)	730 (10.8)	0.426	48 (9.7)	730 (10.8)	0.430	48 (9.7)	48 (9.7)	1.000
- Diabetes Mellitus	249 (50.1)	2,887 (42.7)	0.001*	249 (50.1)	2,891 (42.7)	0.001*	249 (50.1)	208 (41.9)	0.009*
- Hypertension	311 (62.6)	4,225 (62.5)	0.983	311 (62.6)	4,231 (62.6)	0.992	311 (62.6)	311 (62.6)	1.000
- CLD	113 (22.7)	1,832 (27.1)	0.034*	113 (22.7)	1,834 (27.1)	0.033*	113 (22.7)	142 (28.6)	0.035*
- IHD	210 (42.3)	2,778 (41.1)	0.618	210 (42.3)	2,784 (41.2)	0.632	210 (42.3)	209 (42.1)	0.949
- CHF	71 (14.3)	878 (13)	0.410	71 (14.3)	879 (13)	0.410	71 (14.3)	71 (14.3)	1.000
- Stroke	58 (11.7)	874 (12.9)	0.416	58 (11.7)	874 (12.9)	0.421	58 (11.7)	75 (15.1)	0.113
- CF	100 (20.1)	1,351 (20)	0.946	100 (20.1)	1,352 (20)	0.943	100 (20.1)	86 (17.3)	0.255
- Cancer	16 (3.2)	168 (2.5)	0.316	16 (3.2)	168 (2.5)	0.314	16 (3.2)	37 (7.4)	0.003*
- Arterial Disease	0 (0)	4 (0.1)	0.587	0	4 (0.1)	0.588	0	1 (0.2)	0.317
- Major Amputation	24 (4.8)	392 (5.8)	0.368	24 (4.8)	393 (5.8)	0.364	24 (4.8)	51 (10.3)	0.001*

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Chronic lung disease (CLD); Ischaemic heart disease (IHD); Chronic heart failure (CHF); Chronic renal failure (CRF); Values reported as count (percentage); * signifies a significant difference of p<0.005.

Table 8.4. Smoking status comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Characteristic	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Smoking Status									
- Never	95 (19.2)	1,123 (16.7)	0.148	95 (19.1)	1,128 (16.7)	0.155	95 (19.2)	92 (18.6)	0.819
- Ex-smoker	243 (49.1)	3,275 (48.6)	0.839	244 (49.1)	3,292 (48.7)	0.868	243 (49.1)	213 (43.1)	0.060
- Current/stopped	157 (31.7)	2,338 (34.7)	0.177	158 (31.8)	2,344 (34.7)	0.194	157 (31.7)	189 (38.3)	0.031*

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of $p<0.005$.

Table 8.5. Patient frailty comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Frail			0.039*			0.398			0.004*
- Yes	87 (72.5)	1,295 (63.2)		403 (81.1)	5,301 (78.4)		87 (72.5)	251 (84.8)	
- No	33 (27.5)	754 (36.8)		94 (18.9)	1,460 (21.6)		33 (27.5)	45 (15.2)	
Frailty Level									
- Not Frail	33 (27.5)	754 (36.8)	0.039*	94 (18.9)	1,460 (21.6)	0.398	33 (27.5)	45 (15.2)	0.004*
- Mild Frailty	27 (22.5)	367 (17.9)	0.205	124 (24.9)	1,555 (23)	0.496	27 (22.5)	65 (22)	0.904
- Moderate Frailty	37 (30.8)	601 (29.3)	0.726	187 (37.6)	2,516 (37.2)	0.858	37 (30.8)	123 (41.6)	0.042*
- Severe Frailty	23 (19.2)	327 (16)	0.353	92 (18.5)	1,233 (18.2)	0.903	23 (19.2)	63 (21.3)	0.629

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

8.3.2. Pre-Operative Factors

8.3.2.1. Admission Type

There was a significantly higher number of patients with a TKA (26.4%) who had an elective admission than patients with an AKA (17.5%) when applying complete case analysis, multiple imputation, and propensity score matching (Figure 8.1).

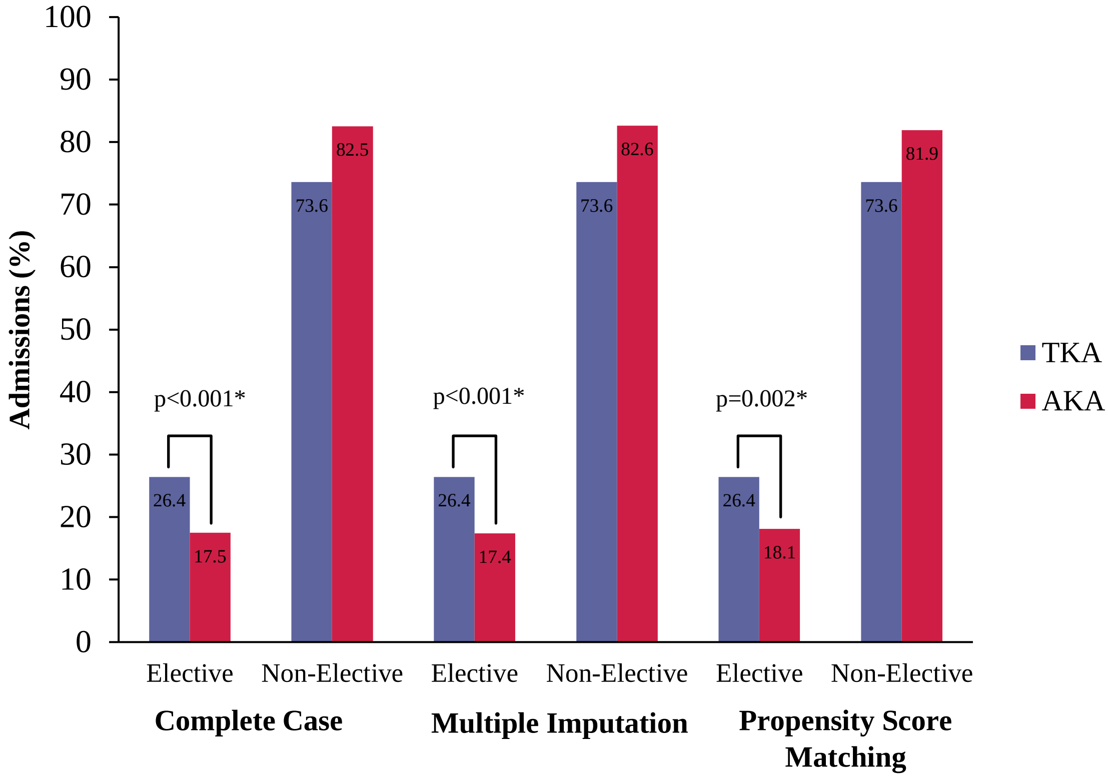

Figure 8.1. Admission type comparison for complete case analysis, multiple imputation and propensity score matching.

8.3.2.2. Amputation Indication

There was a significantly higher number of patients with an AKA because of acute limb ischaemia compared to TKA when applying complete case analysis, multiple imputation, and propensity score matching, presented in Table 8.6 ($p<0.001$, $p<0.001$ and $p=0.003$, respectively). Secondly, there was a significantly higher number of patients with an AKA because of chronic limb ischaemia compared to patients with a TKA when using complete cases analysis and multiple imputation techniques ($p=0.040$ and $p=0.042$, respectively). However, there was a significantly higher number of patients with a TKA due to tissue loss compared to patients with an AKA when using complete case analysis and multiple imputation ($p<0.001$ and $p<0.001$, respectively). Propensity score matching found no significant difference between chronic limb ischaemia and level of amputation (Table 8.6), as well as tissue loss and level of amputation (Table 8.6).

Table 8.6. Amputation indications comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Factor	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Indication									
- Acute LI	63 (12.7)	1,431 (21.5)	<0.001*	63 (12.7)	1,450 (21.4)	<0.001*	63 (12.7)	95 (19.7)	0.003*
- Chronic LI	90 (18.1)	1,474 (22.1)	0.040*	90 (18.2)	1,495 (22.1)	0.042*	90 (18.1)	98 (20.3)	0.394
- Neuropathy	8 (1.6)	78 (1.2)	0.382	8 (1.6)	79 (1.2)	0.386	8 (1.6)	5 (1)	0.430
- Tissue Loss	224 (45.2)	2,403 (36)	<0.001*	225 (45.3)	2,437 (36)	<0.001*	224 (45.2)	195 (40.4)	0.130
- Infection	95 (19.2)	1,116 (16.7)	0.165	95 (19.1)	1,133 (16.8)	0.168	95 (19.2)	79 (16.4)	0.252
- Trauma	11 (2.2)	85 (1.3)	0.078	11 (2.2)	87 (1.3)	0.087	11 (2.2)	6 (1.2)	0.243
- Aneurysm	5 (1)	85 (1.2)	0.664	5 (1)	83 (1.2)	0.672	5 (1)	5 (1)	0.966

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Limb ischaemia (LI); Uncontrolled infection (Infection); Values reported as count (percentage); * signifies a significant difference of p<0.005.

8.3.2.3. Time of Procedure

Significantly more patients with a TKA had their procedure performed during core daytime hours of 07:00 to 19:00 compared to patients with an AKA when applying complete case analysis and multiple imputation (Table 8.7). However, there was no significant difference between the time of procedure and level of amputation when applying propensity score matching (p=0.154).

Table 8.7. Time of procedure comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Factor	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Time of Procedure			0.014*			0.014*			0.154
- 07:00 – 19:00 hours	476 (95.8)	6,271 (92.9)		476 (95.8)	6,282 (92.9)		476 (95.8)	466 (93.8)	
- 19:00 – 07:00 hours	21 (4.2)	480 (7.1)		21 (4.2)	482 (7.1)		21 (4.2)	31 (6.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

8.3.3 Post-Operative Factors

8.3.3.1. Critical Care Admission from Theatre

Table 8.8 highlights the critical care admission rates and critical care length of stay following their initial amputation. There were significantly fewer patients with a TKA who were admitted to critical care compared to patients with an AKA following complete case analysis, multiple imputation, and propensity score matching ($p=0.002$, $p<0.001$ and $p=0.02$, respectively). Critical care length of stay was similar between patients with a TKA and patients with an AKA when utilising complete case analysis, multiple imputation, and propensity score matching (Table 8.8), and was not significant.

Table 8.8. Critical care admission and critical length of stay comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Critical Care	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Admission			0.002*			<0.001*			0.020*
- Yes	54 (10.9)	1,082 (16)		54 (10.9)	1,084 (16)		54 (10.9)	79 (15.9)	
- No	443 (89.1)	5,675 (84)		443 (89.1)	5,680 (84)		443 (89.1)	418 (84.1)	
Length of Stay (days)			0.072			0.513			0.071
- Mean (± SD)	4.4 ± 6.3	5 ± 6.9		4.4 ± 6.3	5 ± 6.9		4.4 ± 6.3	5.6 ± 7.1	
- Median (IQR)	2 (1-4)	3 (2-5)		-	-		2 (1-4)	3 (2-5)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage) unless stated; Standard deviation (SD); Interquartile range (IQR); * signifies a significant difference of p<0.005.

8.3.3.2. Incidence of Return to Theatre

There was no significant association between level of amputation and return to theatre following complete case analysis, multiple imputation, and propensity score matching (Table 8.9). Additionally, a similar percentage of patients with a TKA and patients with an AKA had angioplasty with a stent, a major lower limb amputation, and other forms of surgery when utilising complete case analysis, multiple imputation, and propensity score matching (Table 8.9). There were no significant differences in further procedures between levels of amputation ($p>0.05$).

Table 8.9. Return to theatre rates and types of further surgery comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Factor	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Return to Theatre			0.073			0.077			0.055
- Yes	49 (10.2)	528 (7.9)		50 (10.1)	530 (7.8)		49 (10.2)	33 (6.8)	
- No	432 (89.8)	6,166 (92.1)		447 (89.9)	6,234 (92.2)		432 (89.8)	455 (93.2)	
Further Surgery Type									
- None	432 (89.8)	6,166 (91.8)	0.129	447 (89.9)	6,234 (92.2)	0.077	432 (89.8)	455 (93.2)	0.055
- Angioplasty with Stent	1 (0.2)	5 (0.1)	0.315	1 (0.2)	5 (0.1)	0.714	1 (0.2)	1 (0.2)	0.951
- Major Amputation	5 (1.1)	74 (1.2)	0.940	5 (1.1)	74 (1.2)	0.961	5 (1.1)	11 (2.3)	0.180
- Other	7 (1.6)	106 (1.7)	0.882	7 (1.6)	106 (1.7)	0.810	7 (1.6)	14 (2.9)	0.178

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

8.3.3.2.1. Incidence of Revision of Amputation

There was a similar percentage of patients with a TKA and AKA who had a revision following their initial amputation (Table 8.9). There was no significant difference between level of amputation and major amputation following complete case analysis, multiple imputation, and propensity score matching (p=0.940, p=0.961 and p=0.180, respectively). There were no minor lower limb amputations reported in the NVR database.

8.3.3.3. Incidence of Post-Operative Complications

Table 8.10 indicates the post-operative complications experienced by patients with a TKA and AKA following their initial surgery when utilising complete case analysis, multiple imputation, and propensity score matching. Post-operative complications were apparent in patients with a TKA and patients with an AKA following their initial lower limb amputation. Overall, significantly more patients with a TKA experienced fewer post-operative complications compared to patients with an AKA when analysed using propensity score matching (p=0.005). In contrast, when analysing the data using complete case analysis and multiple imputation, there was no significant differences between level of amputation and having no post-operative complications (Table 8.10). Secondly, patients with a TKA experienced significantly fewer cardiac post-operative complications compared to patients with an AKA across all three analysis techniques (Table 8.10). Thirdly, significantly fewer patients with a TKA experienced respiratory post-operative complications compared to patients with an AKA when analysed using complete case analysis and multiple imputation (p=0.010 and p=0.009, respectively). There were no significant differences between level of amputation and remaining post-operative complications when analysed using complete case analysis and multiple imputation (Table 8.10). However, when analysed using propensity score matching, there were significantly fewer patients with a TKA who had post-operative complications including cerebral (p=0.019), paraplegia (p=0.007), post-operative confusion (p=0.007), surgical site infection (p=0.010), and other post-operative complications (p<0.001).

The number of post-operative complications patients had varied between the two levels of amputation (Table 8.11). Patients with a TKA had no more than five post-operative complications, however, patients with an AKA had up to 10 post-operative complications (Table 8.11). Significantly more patients with a TKA experienced no post-operative complications compared to patients with an AKA when analysed with propensity score matching (p=0.005). However, there was no significant difference between level of amputation and number of post-operative complications following complete case analysis and multiple imputation (Table 8.11). When investigating those patients who had post-operative complications, only one patient with a TKA had five or more post-operative complications following all three analysis techniques (Table 8.11). Significantly more patients with a TKA had fewer overall number of post-operative complications compared to patients with an AKA following propensity score matching (p=0.015). The total number of post-operative complications were not significant following complete case analysis and multiple imputation (Table 8.11).

Table 8.10. Post-operative complications comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Complications	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Complication									
- None	396 (79.8)	5133 (76)	0.053	397 (79.9)	5,141 (76)	0.052	396 (79.8)	359 (72.2)	0.005*
- Cardiac	26 (5.2)	552 (8.2)	0.020*	26 (5.2)	554 (8.2)	0.019*	26 (5.2)	42 (8.5)	0.045*
- Respiratory	34 (6.9)	708 (10.5)	0.010*	34 (6.8)	710 (10.5)	0.009*	34 (6.9)	46 (9.3)	0.165
- Cerebral	3 (0.6)	106 (1.6)	0.088	3 (0.6)	107 (1.6)	0.101	3 (0.6)	12 (2.4)	0.019*
- Renal Failure	20 (0.4)	280 (4.1)	0.902	20 (0.4)	282 (4.2)	0.913	20 (4)	15 (3)	0.386
- Haemorrhage	6 (1.2)	100 (1.5)	0.627	6 (1.2)	100 (1.5)	0.623	6 (1.2)	13 (2.6)	0.106
- Limb Ischaemia	17 (3.4)	240 (3.6)	0.883	17 (3.4)	241 (3.6)	0.866	17 (3.4)	19 (3.8)	0.739
- Paraplegia	2 (0.4)	72 (1.1)	0.156	2 (0.4)	72 (1.1)	0.156	2 (0.4)	12 (2.4)	0.007*
- Confusion	4 (0.8)	88 (1.3)	0.340	4 (0.8)	88 (1.3)	0.335	4 (0.8)	16 (3.2)	0.007*
- Major GI Complication	1 (0.2)	19 (0.3)	0.744	1 (0.2)	20 (0.3)	0.835	1 (0.2)	5 (1)	0.102
- Surgical Site Infection	8 (1.6)	118 (1.7)	0.825	8 (1.6)	119 (1.8)	0.862	8 (1.6)	22 (4.4)	0.010*
- Other	12 (2.4)	251 (3.7)	0.136	12 (2.4)	252 (3.7)	0.133	12 (2.4)	44 (8.9)	< 0.001*

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

Table 8.11. Number of post-operative complications comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Complications	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Total Amount									
- 0	396 (79.8)	5,133 (76)	0.053	397 (79.9)	5,141 (76)	0.053	396 (79.8)	359 (72.2)	0.005*
- 1	81 (16.3)	1,179 (17.4)	0.522	81 (16.3)	1,179 (17.4)	0.520	81 (16.3)	103 (20.7)	0.075
- 2	10 (2)	207 (3.1)	0.186	10 (2)	207 (3.1)	0.188	10 (2)	8 (1.6)	0.631
- 3	5 (1)	96 (1.4)	0.448	5 (1)	98 (1.5)	0.423	5 (1)	6 (1.2)	0.764
- 4	3 (0.6)	76 (1.1)	0.281	3 (0.6)	76 (1.1)	0.331	3 (0.6)	10 (2)	0.051
- 5	1 (0.2)	40 (0.6)	0.263	1 (0.2)	40 (0.6)	0.281	1 (0.2)	5 (1)	0.102
- 6	0	12 (0.2)	0.347	0	12 (0.2)	0.993	0	2 (0.4)	0.157
- 7	0	5 (0.1)	0.544	0	5 (0.1)	0.994	0	2 (0.4)	0.157
- 8	0	3 (0.0)	0.639	0	3 (0.4)	0.994	0	1 (0.2)	0.318
- 9	0	1 (0.0)	0.786	0	1 (0.0)	0.995	0	0	-
- 10	0	1 (0.0)	0.786	0	1 (0.0)	0.995	0	1 (0.2)	0.318
Complications									
- 1 to 4	99 (99)	1,558 (96.2)	0.144	99 (99)	1,561 (96.1)	0.173	99 (99)	127 (92)	0.015*
- 5+	1 (1)	62 (3.8)		1 (1)	63 (3.9)		1 (1)	11 (8)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

8.3.3.3.1. Incidence of Surgical Site Infection

Surgical site infection was similar in patients with an AKA and patients with a TKA following complete case analysis and multiple imputation (Table 8.10). However, there was significantly fewer patients with a TKA who had surgical site infections compared to patients with an AKA following propensity score matching ($p<0.001$).

8.3.3.4. In-Hospital and 30-day Mortality

Table 8.12 displays the in-hospital and 30-day mortality rates following complete case analysis, multiple imputation, and propensity score matching for patients with a TKA and patients with an AKA. In-hospital mortality was significantly higher in patients with an AKA compared to patients with a TKA following complete case analysis and multiple imputation ($p=0.001$ and $p=0.001$, respectively). However, there was no significant difference in in-hospital mortality and level of amputation following propensity score matching (Table 8.12). Secondly, 30-day mortality following their amputations were significantly higher in patients with an AKA compared to patients with a TKA following complete case analysis and multiple imputation ($p=0.004$ and $p=0.030$, respectively). There was no significant difference in 30-day mortality and level of amputation following propensity score matching (Table 8.12).

Table 8.12. In-hospital and 30-day mortality rates comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Mortality Rates									
- In-Hospital	31 (6.2)	728 (10.8)	0.001*	31 (6.2)	731 (10.8)	0.001*	31 (6.2)	45 (9.1)	0.095
- 30-days	22 (6.6)	539 (11.9)	0.004*	27 (5.4)	597 (8.8)	0.030*	22 (6.6)	33 (7)	0.836

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage); * signifies a significant difference of p<0.005.

8.3.4. Discharge Outcomes

8.3.4.1. Overall Hospital Length of Stay

Table 8.13 illustrates the mean, median and interquartile ranges for both levels of amputation. Overall hospital LOS was similar between patients with a TKA and patients with an AKA following complete case analysis, multiple imputation, and propensity score matching (Table 8.13). There was no significant difference between overall hospital LOS and level of amputation following each of the techniques (Table 8.13).

Table 8.13. Overall hospital length of stay (days) comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Overall LOS			0.408			0.580			0.411
- Mean (± SD)	30.9 ± 23	31.6 ± 30.8		30.8 ± 27.8	31.6 ± 30.8		30.9 ± 27.8	31.3 ± 28.3	
- Median (IQ)	22 (12.3-38)	23 (13-40)		-	-		22 (12.6-38)	23 (13-40)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Length of stay (LOS); Standard deviation (SD); Interquartile range (IQR); Values reported as count (percentage) unless stated.

8.3.4.2. Discharge Destination

Discharge destination following a major lower limb amputation was compared between patients with a TKA and patients with an AKA following complete case analysis, multiple imputation, and propensity score matching (Table 8.14). Significantly more patients with a TKA were discharged to their own residence compared to patients with an AKA following complete case analysis (p=0.049). Similar percentages of patients with a TKA and AKA were discharged to rehabilitation, other hospitals, or intermediate care following complete case analysis, multiple imputation, and propensity score matching (Table 8.14).

Table 8.14. Discharge destination comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Discharge Destination									
- Deceased	31 (16.9)	728 (24.7)	-	31 (16.9)	731 (24.8)	-	31 (16.9)	45 (10.8)	-
- Own Residence	94 (51.4)	1,294 (43.9)	0.049*	279 (56.1)	3,559 (52.6)	0.252	94 (51.4)	217 (51.9)	0.902
- Rehabilitation	24 (13.1)	355 (12)	0.654	80 (16.1)	963 (14.2)	0.538	24 (13.1)	61 (14.6)	0.632
- Other Hospital	22 (12)	407 (13.8)	0.497	74 (14.9)	1,075 (15.9)	0.632	22 (12)	66 (15.8)	0.229
- Intermediate Care	12 (6.6)	165 (5.6)	0.584	33 (6.6)	436 (6.5)	0.947	12 (6.6)	29 (6.9)	0.865

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

8.3.4.3. Wound Healing Rates

Wound healing was successful in over 75% of all patients following complete case analysis, multiple imputation, and propensity score matching (Table 8.15). However, wound healing rates were similar between patients with a TKA and patients with an AKA, and there was no significant association following all three data handling techniques (Table 8.15).

Table 8.15. Wound healing rates comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			Multiple Imputation			Propensity Score Matching		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Wound Healing Rates			0.238			0.359			0.919
- Yes	232 (79.5)	3,125 (76.4)		403 (81.1)	5,301 (78.4)		232 (79.5)	229 (79.8)	
- No	60 (20.5)	964 (23.6)		94 (20.5)	1,460 (21.6)		60 (20.5)	58 (20.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

8.3.4.4. Incidence of Re-admission within 30 days

Table 8.16 indicates 30-day hospital re-admission rates in patients with a TKA and AKA following complete case analysis, multiple imputation, and propensity score matching. A greater percentage of patients with a TKA and AKA were not re-admitted within 30 days (Table 8.16). There was no significant difference between level of amputation and re-admission within 30-days following complete case analysis, multiple imputation, and propensity score matching (Table 8.16).

Of these re-admissions, there were fewer patients with a TKA and AKA within the study who were re-admitted for vascular reasons following complete case analysis and propensity score matching (Table 8.16). There was no significant association between level of amputation and vascular re-admission following complete case analysis, multiple imputation, and propensity score matching (Table 8.16).

Table 8.16. 30-day hospital re-admission rates comparison for complete case analysis, multiple imputation and propensity score matching.

	Complete Case Analysis			**Multiple Imputation**			**Propensity Score Matching**		
Outcome	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P	TKA, n (%)	AKA, n (%)	P
Re-admission 30-days			0.547			0.517			0.123
- Yes	39 (9.2)	497 (8.4)		47 (9.5)	577 (8.5)		39 (9.2)	60 (12.4)	
- No	385 (90.8)	5,449 (91.6)		450 (90.5)	6,187 (91.5)		385 (90.8)	424 (87.6)	
Vascular Re-admission			0.903			0.447			0.146
- Yes	4 (7.5)	77 (8)		266 (53.5)	3,511 (51.9)		4 (7.5)	16 (15.8)	
- No	49 (92.5)	884 (92)		231 (46.5)	3,253 (48.1)		49 (92.5)	85 (84.2)	

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Values reported as count (percentage).

8.3.4.5. Incidence of Referral to Rehabilitation

Significantly more patients with a TKA were referred to amputation rehabilitation compared to patients with an AKA following complete case analysis, multiple imputation, and propensity score (Figure 8.2; $p<0.001$, $p<0.001$, and $p<0.001$, respectively).

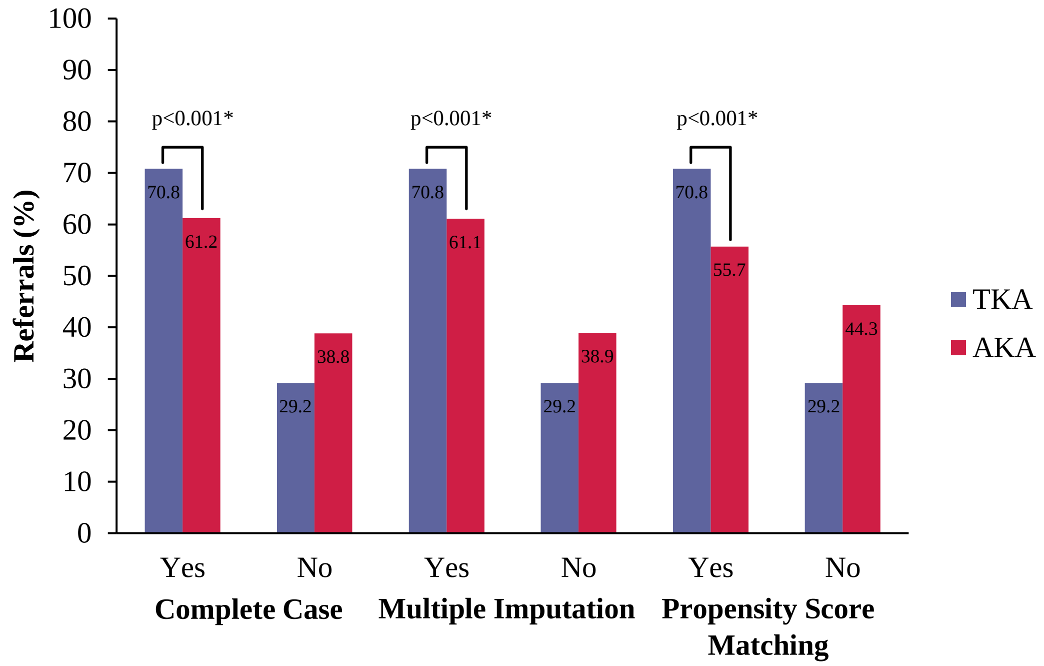

Figure 8.2. Amputation rehabilitation referrals comparison for complete case analysis, multiple imputation and propensity score matching.

8.4. Discussion

The aims of the current study were two-fold. Firstly, to perform and compare handling missing data techniques (complete case analysis, multiple imputation, and propensity score matching) using a large-scale retrospective case control series dataset held within the NVR database, Secondly, the aim was to investigate the differences in clinical and post-operative outcomes between patients with a unilateral TKA and patients with a unilateral AKA when utilising each of the three techniques.

The main findings across all three analysis techniques indicate that there were significantly more patients with a TKA aged 60 years or younger. Secondly, amputations were more frequent in males, patients with a TKA had a significantly higher BMI. Thirdly, significantly more patients with a TKA had a presence of diabetes mellitus, and a significantly lower presence of chronic lung disease compared to patients with an AKA. Additionally, significantly more patients with a TKA had an elective admission, and significantly more patients with a TKA had daytime procedures. Significantly fewer TKA had amputations due to acute limb ischaemia and chronic limb ischaemia, however, there were significantly greater TKA due to tissue loss. Significantly fewer patients with a TKA were admitted to critical care, and significantly fewer patients with a TKA had experienced cardiac and respiratory post-operative complications. In-hospital and 30-day mortality were significantly lower following a TKA. Significantly more patients with a TKA were referred to amputation rehabilitation in comparison to patients with a unilateral AKA. Hypothesis 1, that patients with a TKA would have better post-operative outcomes compared patients with an AKA, is partially accepted, as patients with a TKA had greater clinical outcomes, including referral to rehabilitation, and lower 30-day mortality.

8.4.1. Patient Characteristics

Patients with a TKA were significantly younger compared to AKA after multiple imputation techniques were utilised. Although the finding of the study is relatively small yet significant, these findings are similarly reported by Lim et al. (2018), however the average ages at baseline were approximately 7 years different (TKA 64.7 years ± 16.2, AKA 70.7 years ± 13.2, $p<0.01$). Further, Albino et al. (2014) reported patients with a KD in their study were on average 68 years of age. Panhelleux et al. (2021) reported patients with a TKA have an average age of 64 years compared to 70 years AKA. Although, multiple imputation distinguished a significance between patients with a TKA being on average 69.1 years old vs. AKA 70.4 years. Additionally, there were significantly more patients with a TKA following complete case analysis and multiple imputation who were younger than 60 years of age compared to AKA. It might be that a TKA is suitable for patients who are younger as they have the potential to mobilise better and have an increased QoL. However, as more patients with a TKA following complete case analysis were frail and trauma amputations were low overall in the dataset, it does not explain this finding.

It was apparent that amputations in the dataset were more frequent in males than females. Gender is known to influence amputation rates (Davie-Smith et al., 2017b), with major amputation being significantly more common in men (Carmona et al., 2005; Lim et al., 2006; Izumi et al., 2009; Davie-Smith et al., 2017b). Further, higher amputation rates in men may be because of severe peripheral arterial disease in men (Lopez-de-Andres et al., 2015; Davie-Smith et al., 2017b), and higher smoking rates (Jonasson et al., 2008; Davie-Smith et al., 2017b).

Patients with a TKA had a significantly greater BMI than those with an AKA following multiple imputation and propensity score matching, with both cohort means in the overweight classification. Literature reporting TKA and AKA (Fortington et al., 2013; Lim et al., 2018; Ambler et al., 2020) did not report BMI, preventing further comparison.

Patients with a TKA predominantly had their amputations because of infection or tissue loss following complete case analysis, multiple imputation and propensity score matching, which could be related to diabetes mellitus complications. However, Albino et al. (2014) stated that a TKA procedure is commonly performed following trauma. Although there were patients in this study who had a TKA due to trauma, this percentage was extremely low and was not the main amputation indication in patients who had a TKA. Patients with a TKA had significantly fewer amputations due to acute limb ischaemia across all three data handling techniques. Reported causes of ischaemia include hypertension, cigarette smoking, and diabetes mellitus (Brown & Juergens, 1972; Gordon & Kannel, 1972; Santilli & Santilli, 1999). Although patients with diabetes mellitus are at an increased risk of developing chronic limb ischaemia due to peripheral arterial disease (Santilli & Santilli, 1999; Ying et al., 2022), this does not explain the finding as significantly fewer patients with a TKA had amputations due to acute limb ischaemia following complete case analysis, multiple imputation, and propensity score matching, and significantly fewer patients with a TKA had amputations due to chronic limb ischaemia following complete case analysis and multiple imputation.

Patient frailty varied amongst the three analysis techniques, as there were significantly more patients with a TKA who were frail following complete case analysis, whereas there were significantly fewer patients who were frail following propensity score matching. Schmiegelow et al. (2018) stated that patients with a TKA or higher are frail. Patients requiring a major lower limb amputation for peripheral arterial disease tend to be elderly, frail, and presenting multiple comorbidities (Monaro et al., 2017). Diabetes mellitus contributions from a poor glycaemic and lipid control may increase the risk of frailty amongst those patients who have diabetes mellitus within this study. Considering the associated factors (age, diabetes mellitus, BMI, haemoglobin), most patients with a TKA following complete case analysis were aged between 70-80 years (30.8%), had diabetes mellitus (50.1%), had an average BMI of 27.2 kg/m^2 although 35.6% of patients were classified as having a healthy BMI, and an average haemoglobin of 10.9 g/dL with 86.4% of patients being anaemic. In comparison, following propensity score matching, most patients with a TKA were aged between 70-80 years (30.8%), had diabetes mellitus (50.1%), had an average BMI of 27.3 kg/m^2 although 35.6% of patients were classified as having a healthy BMI, and average haemoglobin of 10.9 g/dL with 86.4% of patients being anaemic. There are no discrepancies in these results between analysis technique, yet the results of patient frailty read opposite. Moreover, patients with a TKA had a higher presence of diabetes mellitus, yet discharge outcomes appeared greater. For instance, frailty can be associated with loss of skeletal muscle strength, and diabetes mellitus is known to impair skeletal muscle function, yet more patients with a TKA were referred to rehabilitation following complete case analysis and propensity score matching. It could be suggested that significantly more patients with a TKA were referred to rehabilitation no matter their frailty status, as significantly more patients were frail following complete case analysis, and significantly fewer patients were frail following propensity score matching, however significantly more patients with a TKA were referred to rehabilitation. Further, it is apparent from the literature that the TKA procedure may benefit those who are ambulatory and those who are non-ambulatory.

However, as missing data appeared greater amongst frailty, this warrants further investigation.

8.4.2. Hospital Admissions

Patients with a TKA had elective admissions compared to patients with a AKA, suggesting that surgeons may be unfamiliar with the TKA surgical procedure. Further, these results may suggest that trainees, who may be more likely to be performing the out of hours amputations, may be less confident to leave a longer residual limb, or that they may be unfamiliar with the procedure due to the lower number of TKA.

Further, 95.8% of TKA procedures following complete case analysis, multiple imputation, and propensity score matching was performed during core daytime hours of 07:00 to 19:00. Although, these were only significant following complete case analysis and multiple imputation. Major lower limb amputations should be undertaken on a planned operating list during normal working hours (Waton et al., 2019). The current study highlights that most major lower limb amputations were performed within their recommendations and during normal core working hours.

8.4.3. Post-Operative Complications

Significantly fewer patients with a TKA were admitted to critical care following their initial surgery upon complete case analysis, multiple imputation and propensity score matching. Factors influencing the risk of complications following a major lower limb amputation, include age, level of amputation, and general health (NHS, 2019b). Taking these factors into consideration, most patients with a TKA were under the age of 60 years, patients had fewer cardiac and respiratory post-operative complications, and significantly fewer presence of chronic lung disease. Further, these results may also suggest that patients had lower blood loss or infection risk following their amputation. Additionally, critical care admission could reflect on earlier detection of deterioration of patients on the ward and faster care provided by the nursing team (Kelly et al., 2017). Lim et al. (2006) reported that 19.5% of patients with a major lower limb amputation were admitted to a high-dependency unit or intensive care after amputation. Although, they did not state the reasonings for these. Despite significantly fewer patients with a TKA were admitted to critical care following their initial amputation, critical care LOS was similar across all three data handling techniques. Critical care LOS is dependent on the complications, which the reasoning was not reported in the NVR database.

Return to theatre were similar between TKA and AKA following complete case analysis, multiple imputation and propensity score matching. Further, there were similar percentages of revision amputations. These results contrast the literature, which concluded that wound infection and stump failure were the main causes for return to theatre (Barnes et al., 2014). According to Low et al. (2017), patients who experienced a major post-operative complication were more likely to return to theatre for a revision amputation compared to those who did not experience a major post-operative complication. This may support our findings, as there were no greater than 10.5% of patients with an AKA and 6.9% of patients with a TKA who experienced one type of post-operative complication.

Patients with a TKA experienced fewer overall post-operative complications, including significantly fewer cardiac post-operative complications compared to patients with an AKA following complete case analysis, multiple imputation and propensity score matching. It is thought that a proximal leg amputation is associated with a greater risk to developing cardiovascular diseases than distal amputations (Naschitz & Lenger, 2008; Mundell et al., 2018), and patients with a dysvascular unilateral AKA were more likely at risk of a cardiac event (Mundell et al., 2018). The results of our study show that cardiac and respiratory post-operative complications, in-hospital mortality and 30-day mortality were significantly lower following a TKA. These can also explain why significantly fewer patients with a TKA were admitted to critical care following their initial surgery.

In a study investigating surgical site infection predictors following BKA and AKA (Chahour et al., 2021), factors including amputation level, female sex, smoking, emergency status, and anaemia are associated with surgical site infection. BMI in their study was a significant association with an increased risk of surgical site infection following an AKA. However, following propensity score matching, sex was matched, there were significantly more patients with an AKA who were current smokers, there were significantly more patients with a TKA having elective admissions as opposed to emergency admissions compared to AKA, and anaemia was similar in between TKA and AKA. This may explain why there was no significant association following complete case analysis and multiple imputation, as there were more males than females with amputations, there were no significant associations with smoking status and level of amputation, fewer TKA and AKA had emergency admissions, although more patients were anaemic overall.

8.4.4. In-Hospital and 30-day Mortality

In-hospital and 30-day mortality were significantly lower in patients with a TKA than patients with an AKA following complete case analysis and multiple imputation. The findings from this study contrasted with Lim et al. (2018), who reported similar rates of mortality amongst both levels of amputation (Molina and Faulk, 2020). Age (Stone et al., 2006; Thorud et al., 2016), especially older age (Fortington et al., 2013), proximal amputation levels (Fortington et al., 2013; Thorud et al., 2016) including

AKA (Stone et al., 2006) and multi-morbidity (Fortington et al., 2013; Thorud et al., 2016) are associated with mortality following an amputation. Following complete case analysis and multiple imputation, significantly more patients with an AKA experienced in-hospital and 30-day mortality. With the above factors in mind, there were fewer patients with an AKA who were under the age of 60 years compared to alternate age groups, there were more deaths following an AKA, and 76% of patients with an AKA experienced no post-operative complications. These therefore do not explain what caused mortality to be significantly higher following complete case analysis and multiple imputation. There were no significant associations between mortality and level of amputation following propensity score matching, which may be explained by the two cohorts being matched on age, gender and overall comorbidities. However, significantly fewer patients with an AKA experienced no post-operative complications. It is established that major lower extremity amputations in patients with diabetes and peripheral vascular disease carry a high perioperative mortality and morbidity rate (Stone et al., 2006; Stern et al., 2017).

8.4.5. Hospital Discharge

Overall hospital LOS were similar between TKA and AKA following complete case analysis, multiple imputation and propensity score matching. Our findings are supported by Lim et al. (2018), who reported no significant association between level of amputation and LOS following propensity score matching (TKA 10.75 days ± 10.5 and AKA 8.64 days ± 13.6, p=0.052). Although, the LOS reported by Lim et al. (2018) compared to our study appears somewhat lower. Lim et al. (2018) utilised data from the American College of Surgeons National Surgical Quality Improvement Program, whereas our study utilised data from a vascular database. Hordache et al. (2013) reported that a long length of stay associated with an index admission is justified by clinicians as highly important, as this can assist with re-establishing independent mobility, and community integration may reduce social and health service costs from living with a disability. Fashandi et al. (2016) concluded that prior amputation, acute limb ischaemia, amputation level, and post-operative complications predicted a longer LOS. Many factors may have contributed to LOS being longer than reported by Lim et al. (2018). Firstly, although fewer patients experienced no post-operative complications compared to having post-operative complications, cardiac and respiratory complications were more frequent. Secondly, patients with a lower limb amputation often are discharged to a long-term care facility, thus necessitating more coordination time between care providers (Kobayashi et al., 2011). Optimisation of comorbidities following admission may result in better post-operative outcomes, including lower mortality and reduced LOS (National Confidential Enquiry into Patient Outcome and Death, 2014).

A higher percentage of patients with a TKA than AKA were discharged to their own residence following complete case analysis. The overall findings were consistent with Kayssi et al. (2017), with 48% of patients following unilateral and bilateral amputations in their study discharged to their own residence with services. Parameters including physical condition, social factors, age, and comorbidities are influencing factors in determining the discharge destination (Rommers et al., 1997). More patients with a TKA may have been discharged home following their amputation due to the theoretical advantages offered by the TKA procedure as outlined in Chapter Five, Section 5.4.6. However, there were no significant differences identified between discharge destination and level of amputation following multiple imputation and propensity score matching. Further, significantly fewer patients with a TKA were frail following propensity score matching, and there were significantly more elective admissions. Additionally, patients with a TKA may have been less unwell during their stay, which could be evident from the significantly fewer cardiac and surgical site infection post-operative complications experienced, and significantly fewer patients with a TKA were admitted to critical care following their amputation. Although over 50% of patients with a TKA and 50% of patients with an AKA following propensity score matching was discharged to their own residence, this was not a significant finding.

8.4.6. Hospital Re-admission

Hospital re-admissions appeared similar between TKA and AKA following complete case analysis, multiple imputation, and propensity score matching. Hospital re-admissions are associated with reduced patient outcomes, and result in significant healthcare expenditures (Kayssi et al., 2016). Patients with a later re-admission in research by Kayssi et al. (2016) suffered from hypertension, ischemic heart disease, and congestive heart failure, compared to patients with re-admissions within a month. Further, patients may have suffered from stump complications from poor wound healing or surgical site infection. Identified factors of stump complications include active smoking status (Hasanadka et al., 2011; Kayssi et al., 2016), an increased body mass (Hasanadka et al., 2011; Kayssi et al., 2016), emergency surgery (O'Brien et al., 2013), sepsis (O'Brien et al., 2013; Kayssi et al., 2016) and intraoperative surgical trainee participation (O'Brien et al., 2013; Kayssi et al., 2016). Additionally, cardiac complications may influence re-admission to hospital (Kayssi et al., 2016). Cardiac risks are highly important following an amputation, as they carry a greater burden of disease compared to other vascular surgery patients (Kayssi et al., 2016).

8.4.7. Referral to Rehabilitation

Across all data analysis techniques, a greater number of patients with a TKA were referred to rehabilitation than patients with an AKA. These findings are discussed in Chapter Five, Section 5.4.6.

8.4.8. Wound Healing

Findings show that patients with a TKA have similar wound healing rates to patients with an AKA, although patients with a TKA have greater wound healing success than failed wound healing. These findings were consistent throughout each analysis technique and are discussed in Chapter Five, Section 5.4.7. Across complete case analysis and propensity score matching however, there were numerous cases missing this variable. Hospital LOS following the analysis were on average 31 days following a TKA, and 32 days following an AKA. Patients who remained in hospital after 30-days should have had their wounds checked at this time-point, therefore should have been recorded. It is unclear from the dataset whether their wounds healed at 30-days, or whether these were determined upon discharge. For those missing datapoints after discharge, this may be due to patients failing to attend follow-up clinic appointments. For conclusions to be drawn regarding wound healing, a detailed, coded response should be added to the registry dataset.

8.5. Limitations

There are numerous limitations to utilising the NVR dataset in Chapters Five, Six, Seven and Eight. Due to analysing the data set reported by NHS hospitals within England and Wales, approximately 15% overall of the data were missing. Data were self-reported and from a retrospective dataset. It is unconfirmed whether data were recorded correctly, or at all, thus being MCAR or MNAR. Some of the data may not be available after the event and this may account for missing data. Although the missing data techniques used in this study have their advantages and disadvantages as mentioned in Chapter Four, the findings were similar across all three techniques. It is important to note that although multiple imputation makes a prediction based on a pattern, and pooled values of all imputations are gathered to determine their count and significance, the findings are similar to complete case analysis and propensity score matching in some areas. Therefore, the results are likely to be valid as they are mostly consistent and allow a clear comparison to be made between the two levels of amputation. Furthermore, the repeated use of statistical analysis, or multiple testing of a dataset can amplify the probability of a false-positive finding (Ranganathan et al., 2016). Researchers investigating retrospective datasets are suggested to limit comparisons between groups and identify one endpoint (Ranganathan et al., 2016). If there are interdependencies identified within a dataset, a viable option is to use multivariate analysis, which could identify possible associations between variables. Examples of these include cardiac and respiratory post-operative complications and in-hospital and 30-day mortality between amputation levels, which AKA experienced significantly more in this study. As previously mentioned in Section 8.4.3, proximal amputations such as AKA are more likely to experience cardiac events, however we are unclear from the dataset whether this related to mortality in patients or whether this was caused by alternative factors. It is unclear what procedures were recorded as a TKA and therefore may include several variations, including Gritti-Stokes and KD. The level of amputation was reported by the individual entering the data as TKA without qualifying what the exact procedure was. For instance, Gritti-Stokes is a long AKA, whereas KD involves less muscle and tissue division and may therefore cause less bleeding. These two procedures result in different residual limb shapes which may not only affect wound healing but also prosthesis use. Additionally, as Gritti-Stokes is a long AKA, this may have been inputted as an AKA rather than a TKA. From this, future recommendations include that time is spent gathering all data and inputting these values correctly into the NVR.

Another limitation to the NVR dataset, was that there were numerous patient outcomes or factors that were sparsely reported, including patient frailty, BMI, haemoglobin, wound healing, discharge destination, and hospital re-admission. From this, the NVR should report all the above factors and outcomes including vascular re-admissions as a compulsory measure, as these are important characteristics to support which patients may be suitable for which level of amputation. Although wound healing and hospital re-admission results appear consistent amongst the data analysis techniques, it cannot be determined whether there are actual significance differences between TKA and AKA due to insufficient data recorded. Analysis has previously been completed on patients with a major lower limb amputation reported in the NVR database from January 2014 to December 2016 (Ambler et al., 2020), although findings were combined for all levels of amputation. It is important for NVR reports and future research to identify TKA as a separate level of amputation rather than combining it with alternative levels of amputation. Subsequent procedures were inputted into the registry as “major lower limb amputation” or “minor lower limb amputation”, and despite this, it was unclear whether returning to theatre for a lower limb amputation means they had their initial amputation revised to a higher level or if they had a contralateral amputation. Therefore, having a new code that allows the inputting of what type of further amputation surgery they received, if it was a revision or contralateral amputation, and the level of amputation they were discharged with, would be beneficial when making further comparisons.

Additionally, there were low levels of surgical site infection reported within the registry dataset, which may indicate that the data were either not entered or not sought after discharge. Potentially if patients were seen within another hospital unit this would also fail to be added to the relevant record. It is important for the data to be included, as surgical site infection contributes to significant morbidity experienced post-operatively. Most of the data for frailty and for discharge outcomes including wound healing appeared missing. It is important for frailty to be a compulsory question as this provides insight to the patient on admission. Although the registry states whether patients had successful wound healing at 30 days, for those who did not have successful wound healing, it was unclear why that could be from the remaining data. It may be beneficial to have a data point that allows the nature for unsuccessful wound healing to be inputted in future. Despite referral to rehabilitation being complete, future recommendations for this outcome would include where they were referred to, and the outcome of the referral (e.g., whether they were in line for casting for a prosthesis, or whether they were referred for allied health professional services for more general support). To assist with future investigations, registry databases should ensure that all coding is completed, and if not, provide a coded response as to why it is incomplete.

8.6. Conclusion

Findings suggest that TKA may provide better outcomes in certain aspects of post amputation care over AKA. Despite previous reports of poor wound healing with a TKA, and mortality rates alongside numerous other factors and outcomes being inconsistent following complete case analysis, multiple imputation and propensity score matching, further investigation is warranted to compare these factors further, especially as wound healing appears successful following a TKA.

CHAPTER NINE: CLINICAL TESTS AND SELF-REPORTED MEASURES

9.1. Introduction

Clinical tests and self-reported measures are often used during and after prosthetic rehabilitation. The aim of this study was to compare the differences in ambulatory and non-ambulatory TKA and AKA, and to compare their balance confidence and falls history. This chapter presents a specific description regarding the patients, equipment and methodologies used to address the aim.

9.2. Methods

9.2.1. Study Design and Participant Recruitment

9.2.1.1. Study Description

An exploratory study was performed on outpatients to investigate the clinical and functional differences between two condition groups when performing activities of daily living. The groups involved were patients with unilateral TKA and patients with unilateral AKA. These participants were recruited from the Hull University Teaching Hospitals NHS Trust.

9.2.1.2. Ethical Approval

Research Ethical Committee approval for the study was granted by Wales (REC reference 19/WA/0124). In addition, the Research and Development Department at Hull University Teaching Hospitals NHS Trust and University of Hull granted their approval to conduct the research (R2378, FHS165). The study was registered with Clinicaltrials.gov (reference NCT04120558).

9.2.1.3. Sample Size

The intended sample size for the study was 183 patients with a unilateral TKA and 183 patients with a unilateral AKA. This was based on a self-selected walking speed of 0.58m/s for patients with a TKA as reported by Pinzur et al. (1992). However, due to COVID-19 restrictions, the recruitment target was prevented, thus achieving a sample size of 19 patients. The study recruited seven non-ambulatory patients with a TKA, eight ambulatory patients with a TKA, two non-ambulatory patients with an AKA and two ambulatory patients with an AKA.

9.2.1.4. Study Design

There were four potential stages in the research study for each participant. The first three stages involved participant selection and recruitment. Ambulatory and non-ambulatory potential participants were identified by clinical staff at Hull Royal Infirmary and a review of records held at the Artificial Limb Unit, Hull, UK. Clinical staff contacted the potential participants to gain verbal consent to be contacted by the researcher. Potential participants were then posted an invitation letter and information sheet (Appendix C) from the researcher. They were given 24 hours to consider whether to partake in the study and were contacted via telephone to discuss any queries they had. The fourth stage involved their one visit to the biomechanics laboratory or alternative and suitable location, in which written informed consent, a health screening questionnaire, baseline tests and data collection were completed. Data collection involved recruited ambulatory participants completing activities including FIST, sit-and-reach test, TUG test, L-test, FRT, 2MWT, 6MWT, Berg Balance Scale, and Tinetti assessment. Recruited non-ambulatory participants were asked to complete the FIST and sit-and-reach tests only. All participants were asked to complete a series of questionnaires regarding their confidence when performing daily tasks.

9.2.1.5. Participant Selection

Clinical staff at Hull Royal Infirmary and the Artificial Limb Unit confirmed potential participants as having a unilateral TKA or AKA. Confirmation of their amputation level and prosthesis componentry was documented in their patient notes. Once eligibility for the study was confirmed, participants were scheduled for one data collection session at either the Sports, Health and Exercise Science Laboratory at the University of Hull, the Clinical Trials Unit, Daisy Building, Castle Hill Hospital, or outdoors at their home environment following the lone working policy. Variation was required due to the COVID-19 restrictions and patient preference for not attending hospital or university sites. Participant characteristics are illustrated in Table 9.1.

9.2.1.6. Participant Inclusion and Exclusion Criteria

Adults over the age of 18 years who have a unilateral TKA or AKA were invited to participate in the study. Recruited participants had to be able to follow instructions and fill out questionnaires independently. Participants were excluded from the study if they 1) had a bilateral amputation, 2) were unable to provide informed consent, 3) were unable to follow instructions and 4) if they were unable to independently fill out questionnaires.

9.2.1.6.1 Non-Ambulatory Participants

Non-ambulatory wheelchair users with TKA and AKA were included for the first section of the study. Participants were excluded from the study if they were unable to transfer without the assistance of one.

9.2.1.6.2. Ambulatory Participants

Ambulatory participants with a TKA and AKA (who could mobilise independently with a prosthetic limb) were included for second section of the study. Participants were excluded from the study if they were unable to walk more than five metres.

Table 9.1. Characteristics of the patients in the study.

Patients	Gender	Age (y)	Height (cm)	Mass (kg)	Diabetes	Surgery Type	Amputated Limb (L/R)	Residual Limb Length (cm)	Ambulatory/Non-Ambulatory	K-level	Prosthetic Knee	Prosthetic Ankle	Reason for Amputation	Time since Amputation
TKA														
1	Male	68	1.75	73	Yes	KD	L	42	Amb	1	Steeper NKFM1	TRES	Vascular	3y 0mo
2	Male	69	1.78	91.1	Yes	KD	R	38	Amb	0	Ottobock 3R106	TRES	Trauma	50y 1mo
3	Male	59	1.86	92	No	KD	R	52	Amb	3	Ottobock Kenevo	TRES	Cancer	3y 1mo
4	Female	53	1.72	105	No	KD	L	49.5	Amb	3	Ottobock Genium X3		Other	3y 3mo
5	Male	83	1.82	65	No	KD	R	50	Amb	4	Steeper NKFM1	TRES	Vascular	4y 6mo
6	Female	69	1.62	65	No	KD	L	46	Amb	2	Steeper NKFM1	TRES	Cancer	1y 3mo
7	Male	66	1.71	118	No	KD	L	40	Amb	1	Ottobock Genium X3	Kinterra	Trauma	6y 1mo
8	Male	67	1.85	90	Yes	GS	R	46	N-Amb	4	-	-	Vascular	3y 9mo
9	Female	70	1.52	41.3	No	KD	L	38	N-Amb	0	-	-	Vascular	1y 1mo
Mean	-	**67.1**	**1.74**	**82.3**	-	-	-	**44.6**	-	-	-	-	-	-
SD	-	**8.2**	**0.11**	**23.4**	-	-	-	**5.3**	-	-	-	-	-	-
AKA														
1	Male	54	1.83	95	Yes	AKA	L	43	Amb	3	NOPH3	Kinetic	Other	4y 11mo
2	Male	55	1.86	80.7	No	AKA	L	20	Amb	4	Ottobock C-Leg	Triton	Trauma	53y
3	Female	73	1.58	62.2	No	AKA	L	32	Amb	4	Ottobock C-Leg 4		Trauma	19y 2mo
4	Female	56	1.66	84.6	No	AKA	L	43	Amb	3	PLE	Kinterra	Cancer	9y 6mo
5	Male	52	1.78	85.2	No	AKA	R	34	Amb	3	NOH8	TRES	Trauma	0y 11mo
6	Male	66	1.78	63.5	Yes	AKA	R	29	Amb	1	NOFM1	TRES	Trauma	0y 3mo
7	Male	46	1.64	128.1	No	AKA	R	35	Amb	2	NOH7	TRES	Other	0y 7mo
8	Male	52	1.80	121.7	Yes	AKA	R	25	Amb	3	NOFM2	TRES	Trauma	0y 10mo
9	Male	66	1.69	102.1	Yes	AKA	R	28	N-Amb	0	-	-	Trauma	4y 7mo
10	Male	76	1.86	80	Yes	AKA	L	33	N-Amb	0	-	-	Vascular	0y 10mo
Mean	-	**59.6**	**1.7**	**90.3**	-	-	-	**32.2**	-	-	-	-	-	-
SD	-	**10.0**	**0.1**	**22.0**	-	-	-	**7.3**	-	-	-	-	-	-

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Knee disarticulation (KD); Gritti-Stokes (GS); Left limb (L); Right limb (R); Ambulatory (Amb); Non-ambulatory (N-Amb); Years (y), Months (mo). Residual limb length (cm) was measured from the greater trochanter to the residual limb end.

9.2.2. Informed Consent and Pre-Exercise Medical Questionnaire

9.2.2.1. Informed Consent

On arrival to the Sports, Health and Exercise Laboratory, the Clinical Trials Unit or suitable location, participants provided written informed consent using two forms. The consent forms used are shown in Appendix D and Appendix E. Participants were aware that they could withdraw from the study at any point without giving their reasons.

9.2.2.2. Pre-Exercise Medical Questionnaire and Characteristics Form

Participants completed a pre-exercise medical questionnaire created by the Department of Sport, Health and Exercise Science at the University of Hull that was based on their lifestyle and medical conditions. A participant characteristics form was also completed in which baseline measures and their indication for amputation was recorded. The pre-exercise medical questionnaire is show in Appendix F and the characteristics form is shown in Appendix G.

9.2.3. Clinical Tests

9.2.3.1. Overview

The research was split into two studies depending on the ability of the participants. Ambulatory individuals with TKA and AKA completed clinical tests that compromised of FIST, sit-and-reach test, TUG test, L-test, FRT, 2MWT, 6MWT, Berg Balance Scale and Tinetti assessment. These clinical tests represent activities that are practised daily during everyday living in internal and external environments.

9.2.3.2. Function in Sitting Test

The FIST is a bedside evaluation of sitting balance that evaluates a variety of sensory, motor, reactive and proactive, and steady state balance factors. It has been validated in populations including stroke and vestibular disorders. The FIST contains 14 items with an ordinal scale of 0 to 4 for each item (Appendix H). The standard test sitting position stipulated that participants were positioned on the edge of the bed with half of their femur supported by the mattress, hips and knees were at a 90° flexion, and their feet were flat either on the floor or on a supported fixture. Participants were instructed to ensure that their hands were positioned in their laps, unless required for support. Participants were instructed to perform each of the tasks whilst sitting to the best of their ability, and the test was completed three times, with an average score computed for each participant and level of amputation.

9.2.3.3. Sit-and-Reach Test

The sit-and-reach test is a measure of flexibility and measures the flexibility of muscles located in the lower back and hamstrings. It has been validated for use in healthy populations. For completion of this test, participants were instructed to sit on a bed with their back against the wall and their lower limbs positioned straight out in front of them. The sit-and-reach box was positioned at the end of their feet. Participants were instructed to stretch out their arms in front of their body in parallel to their legs, and to learn as far forwards as they can comfortably do so. The sit-and-reach test was repeated three times per participant, with an average score computed for each participant and level of amputation.

9.2.3.4. Timed-Up-and-Go Test

The TUG test is a simple screening test of balance that is commonly used to examine the functional mobility in community-dwelling older adults (Shumway-Cook et al., 2000). Further, the TUG is a sensitive and specific measure of determining the probability for falls amongst older individuals (Shumway-Cook et al., 2000). It is shown to have good inter-rater reliability and concurrent validity in patients with lower limb amputations. For completion of this test, a chair with arm rests and a 3-metre walkway clear of obstacles was required (Figure 9.1). Participants were instructed to wear their regular footwear and to use a walking aid if required. Participants were instructed to start in a seated position, and on the onset of a verbal cue, the participant would stand up, walk 3-metres, turn around the cone positioned at the end of the walkway, walk back to the chair and sit down. The time stopped when participants returned to a seated position. The test was repeated three times, and the use of walking aids were recorded for each participant, with an average score computed for each participant and level of amputation.

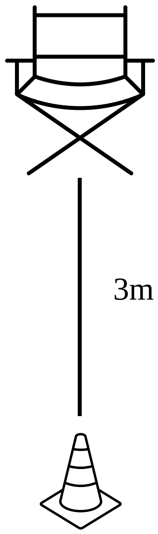

Figure 9.1. The Timed-Up-and-Go (TUG) test experimental set-up, with one 360° turn.

9.2.3.5. L-Test of Functional Mobility

The L-test is a performance-based assessment that measures physical function, including the dynamic balance ability of an individual with a lower limb amputation (Deathe & Miller, 2005). It has good reliability and validity for patients with lower limb amputations. For completion of this test, a chair with arm rests and a 5-metre by 5-metre walkway clear of obstacles was required (Figure 9.2). Participants were instructed to wear their regular footwear and to use a walking aid if required. Participants were instructed to start in a seated position, and on the onset of a verbal cue, the participant would stand up, walk 5-metres, turn left and walk 5-metres, turn right around the cone and walk 5-metres, turn right and walk 5-metres back to the chair and sit down. The time stopped when participants returned to a seated position. The test was repeated three times, with an average score computed for each participant and level of amputation. The use of walking aids were recorded for each participant.

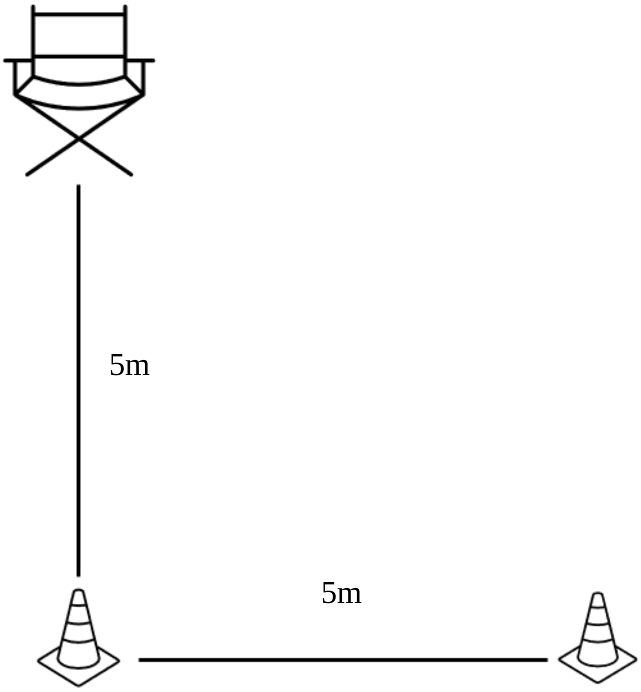

Figure 9.2. The L-Test of functional mobility experimental set-up involving one 180° turn and two 90° turns.

9.2.3.6. Functional Reach Test

The functional reach test is a clinical outcome measure that determines the dynamic balance of an individual using one simple task. During standing, this test measures the distance between the length of an outstretched arm when completing a maximal forward reach with a fixed base of support. Participants were to stand next to, but not leaning against, a wall and position their arm that is closer to the wall at 90° shoulder flexion with a closed fist. Participants were then instructed to reach forwards as far as they could without taking a step. The distance reached by the third metacarpal on their closed fist was documented, and the test was completed three times per participant, with an average score computed for each participant and level of amputation. A score of 25cm or greater indicated that patients were of a low risk of falling, and a score of 15cm to 25cm indicated that a patient’s risk of falling was two times greater than normal. A score of 15cm or less indicated that patients’ risk of falling was four times greater than normal, and patients unwilling to reach indicated that the risk of falling was eight times greater than normal (Duncan et al., 1990).

9.2.3.7. Two-Minute and Six-Minute Walk Tests

Ambulatory individuals with TKA and AKA were asked to complete a 2MWT and 6MWT. The 2MWT and 6MWT have good reliability and validity for use on patients with lower limb amputations. A 10-metre walkway was set up on flat even ground, and a cone was positioned at each end of the walkway to identify to participants where to walk to and from. On the onset of a verbal cue, participants were instructed to repeatedly walk up and down the 10-metre walkway for two minutes and six minutes. Participants were asked to complete one trial of the 2MWT and one trial of the 6MWT. Walking speed was determined as the speed walked per patient with lower limb amputation when completing the 2MWT and 6MWT and was calculated using the distance walked in centimetres divided by the time of each test in seconds. Distance completed was determined as the number of 10m walkway lengths completed within the two-minute and six-minute time frame.

9.2.3.8. Berg Balance Scale

The Berg Balance Scale is used to determine an individual's ability to safely balance during a series of tasks. It contains a 14-item task list, with each item consisting of a five-point ordinal scale from 0 to 4 (Appendix I), with 0 indicating the lowest level of function and 4 indicating the highest level of function. It is a valid and reliable outcome for assessing balance in patients with lower limb amputation. The tasks within the item list include sitting to standing, standing and sitting unsupported, standing to sitting, transfers, standing with eyes closed or feet together, retrieving objects, turning, alternate foot placement, reaching forwards, and standing on one foot. The Berg balance scale has a total score of 56. A score of 56 indicated excellent functional balance, and a score of 45 or lower indicated that individuals may be of a greater risk of falling. Participants were verbally instructed of the task, and a demonstration was performed when necessary. The test was completed once per participant.

9.2.3.9. Tinetti Assessment

The Tinetti assessment measures the perception of balance and stability when completing everyday activities and fear of falling in older adults. The Tinetti assessment is determined by using gait and balance tasks (Appendix J). For the balance tasks, participants were instructed to sit in an armless chair, and was firstly asked to stand up and stay standing. Participants were then required to turn 360 before sitting down. Participants were also examined when they were nudged and when their eyes were closed. For the gait assessment, participants were instructed to walk across a walkway at a normal speed, turn around, and walk back at a faster but safe speed. The Tinetti assessment has a gait score and a balance score and uses a 3-point ordinal scale from 0 to 2, with 2 being the highest function. The balance assessment is scored over 16 and the gait assessment is scored over 12, combining a total of 28. A score equal to or greater than 24 indicated that individuals are at a low risk of falling, a score between 19 to 23 indicated that patients were of a moderate risk of falling, and a score equal to or lower than 18 indicated that patients were of a high risk of falling. The test was completed once per participant.

9.2.4. Self-Reported Outcome Measures

9.2.4.1. Overview

Non-ambulatory individuals with a TKA or AKA were asked to complete self-measured questionnaires compromising of the EQ-5D-5L and SF-36. Ambulatory participants were asked to complete self-measured questionnaires comprised of the EQ-5D-5L, SF-36, LCI-5, Houghton Scale of prosthetic use, and ABC-UK. All participants were asked to complete the self-reported fall history questionnaire.

9.2.4.2. Self-reported Fall History

A self-reported questionnaire was designed by the researcher to determine the fall history amongst recruited participants. The fall history form included a variety of open-ended and closed-ended questions, giving participants the option to discuss their answer further if necessary. All ambulatory and non-ambulatory individuals with a TKA and an AKA were asked how many falls they had in the 12 months prior to data collection session and what activity was being performed prior to their fall. Participants were also asked what the main cause of the fall was, and what injuries were sustained from falling. The fall history form that was created is presented in Appendix J.

9.2.4.3. EQ-5D-5L

The EQ-5D-5L is a self-reported questionnaire that consists of two sheets of paper with two different scales. These comprised of the EQ-5D descriptive system and the EQ-VAS. The EQ-5D descriptive system comprises of five sections about mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Appendix L). Each of the section's responses are based on a 5-level ordinal scale, ranging from no problems, slight problems, moderate problems, severe problems, and extreme problems. All ambulatory and non-ambulatory participants were asked to indicate their health state from the ordinal scale by drawing a tick in the box with the most appropriate statement for each of the five sections. The EQ-VAS allows the participants to rate their health on a vertical visual analogue scale. The endpoints of the scale are labelled "The best health you can imagine" and "The worst health you can imagine", in which their scores reflect the participant's personal judgement (Appendix L). Responses gathered for each of the EQ-5D-5L and EQ-VAS were averaged for TKA and AKA and categorised into ambulatory and non-ambulatory groups.

9.2.4.4. Short-Form Health Survey 36

The SF-36 is a self-reported measure based on an individual's health and QoL. The SF-36 is comprised of eight domains of health status, including general health perceptions, limitations of physical activities, physical health problems, emotional health problems, social activities, energy and emotions, and pain, with responses ranging from 2-level to a 6-level ordinal scale. Responses to general health was based on a 5-level ordinal scale ranging from "excellent" to "poor", "much better now than one year ago" to "much worse than one year ago", and "definitely true" to "definitely false". Limitations of physical activities compromised of a 3-level scale with the responses being “yes, limited a lot”, “yes, limited a little” and “no, not limited at all”. Physical health problems and emotional health problems compromised of a 2-level dichotomous scale with yes or no responses. The responses for the factors social activities and pain compromised of a 5-level ordinal scale, ranging from “none” to “very severe”. An additional question in pain included the responses ranging from “not at all” to “extremely”, and an additional question on social activities responses ranged from “all of the time” to “none of the time”. The responses for the section on energy and emotions compromised of a 5-level scale with responses ranging from “all of the time” to “none of the time”. All non-ambulatory and ambulatory participants were asked to circle the statement that was most appropriate to the question. The SF-36 is presented in Appendix M.

The SF-36 original 2-level to 6-level responses for each participant was converted by following the scoring key in Appendix N. The items were converted and scored so that a high score would define a favourable health state. Each item was scored on a 0 to 100 range so that the lowest and highest possible scores were 0 to 100. Appendix N lists the items that were averaged together to build each scale. Following the conversion of step one, further steps were followed according to Ware et al. (1994). The second step involved computing a raw scale score for each component following an algebraic calculation, then transforming the data to Physical Component Score (PCS) or Mental Component Score (MCS) using the below formula:

$$\text{Transformed Scale} = 50 + (\text{Sum of new physical component scores x } 10)$$

Transforming the raw scale scores to a 0-100 scale allows for a comparison of various versions of the SF-36. The scores indicated in step 3 are presented as a percentage of the total possible score achieved. The PCS and MCS scores the ambulatory TKA cohort were compared to the average scores for each scale for the AKA ambulatory cohort. As non-ambulatory patients also completed the SF-36, the PCS and MCS for TKA non-ambulatory patients were compared to the scores for TKA ambulatory patients. Additionally, the scores for AKA non-ambulatory participants were compared to AKA ambulatory patients. The total SF-36 score was calculated for non-ambulatory and ambulatory TKA and AKA separately by calculating an average from the PCS and MCS.

9.2.4.5. Locomotor Capabilities Index-5

The LCI-5 is disease-specific, self-administered questionnaire that assesses locomotor abilities when performing activities of daily living in participants with lower-limb amputation. It has good validity and reliability and has been validated for lower limb amputations. The questionnaire is based on 14 different locomotor activities that was selected from the locomotor disabilities classification of the World Health Organisation (Gauthier-Gagnon et al., 1999). All ambulatory participants were asked to circle one of the 4-level ordinal scale responses that was most appropriate, ranging from 0 of “not able” to 3 being able to accomplish the activity independently. The questionnaire was split into two ordinal levels, with each level offering a maximum of 28 points and giving a total of 56 points. Achieving a higher score reflects participants having greater ability with their prosthesis and less dependence on assistance. The LCI-5 is shown in Appendix O.

9.2.4.6. Houghton Scale of Prosthetic Use

The Houghton Scale of prosthetic use is a self-measure that assesses prosthetic use in individuals with a lower-limb amputation. It has good validity and reliability for use on patients with lower limb amputations. This questionnaire is a 4-item instrument and reflects each participant’s perception on their prosthesis use. The first three items within the Houghton Scale of prosthetic use are scored on a 4-point scale which attempts to capture an individual's prosthesis wearing habits, whilst the fourth question compromises of three dichotomous items that assessed a participant's comfort level when negotiating on a variety of outdoor surfaces. The dichotomous items were responded with yes or no. All ambulatory participants were asked to circle one response that was most appropriate for each question. The Houghton Scale of prosthetic use questionnaire is presented in Appendix P.

The Houghton Scale of prosthetic use results is reported as a total score out of 12 for each participant, with higher scores indicating that they had a greater level of performance and a greater comfort level. Independent community walking ability was achieved when participants got scores of 9 and above. Patients were achieving household ability but limited community ability when they scored between 6 and 8. Patients had ability limited to the household when their scores were 5 or lower.

9.2.4.7. Activities-specific Balance Confidence Scale-UK

The ABC-UK is a self-reported measure that assesses a participant's balance confidence when performing activities without losing their balance or experiencing a sense of unsteadiness. It is validated with lower limb amputations. The questionnaire compromises of 16 questions based on variety of activities that would be completed daily and are phrased off of the main question "How confident are you that you can maintain your balance and remain steady when you….". All ambulatory participants were asked to indicate their level of self-confidence by choosing a number from a scale of 0 to 100%, with 0% meaning they had no confidence and 100% indicating that they felt completely confident. The ABC-UK is presented in Appendix Q. Responses gathered for each of the 16 statements on balance confidence when performing various activities were calculated as an overall for each patient. Overall scores for each patient were calculated by adding the item scores and dividing by the total number of items.

9.2.5. Data Analysis

Average scores were computed for each participant and were then combined for amputation level. Data for each cohort are outlined in figures and tables in Section 9.3.

9.3. Results

9.3.1. Clinical Tests

9.3.1.1. Function in Sitting Test

The mean and standard deviation FIST scores are presented in Figure 9.3 for ambulatory and non-ambulatory patients with a TKA and AKA, with the median presented in Table 9.2. There was no difference in scores between ambulatory patients with a TKA and AKA. Additionally, there was no difference between non-ambulatory patients with a TKA and AKA.

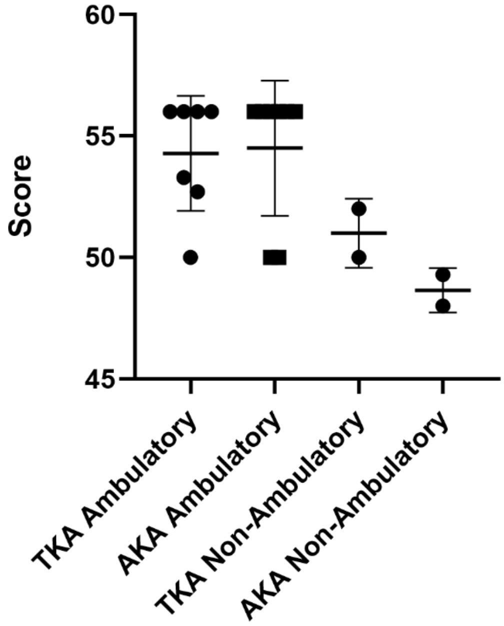

Figure 9.3. FIST scores in ambulatory and non-ambulatory patients with TKA and AKA.

Table 9.2. FIST scores in ambulatory and non-ambulatory patients with TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
FIST Score		
- TKA Amb	54.3 (2.4)	56 (50-56)
- AKA Amb	54.3 (2.9)	56 (50-56)
FIST Score		
- TKA Non-Amb	36 (22.6)	36 (20-52)
- AKA Non-Amb	48.7 (0.9)	48.7 (48.0-49.9)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb); Non-ambulatory (Non-Amb).

9.3.1.2. Sit-and-Reach Test

The distance reached in centimetres was recorded for ambulatory patients with a TKA and AKA. Additionally, the results for non-ambulatory patients with TKA were compared to non-ambulatory patients with AKA. The above figures are presented in Figure 9.4 and Table 9.3. Scores were similar between ambulatory status and level of amputation when performing the sit-and-reach test.

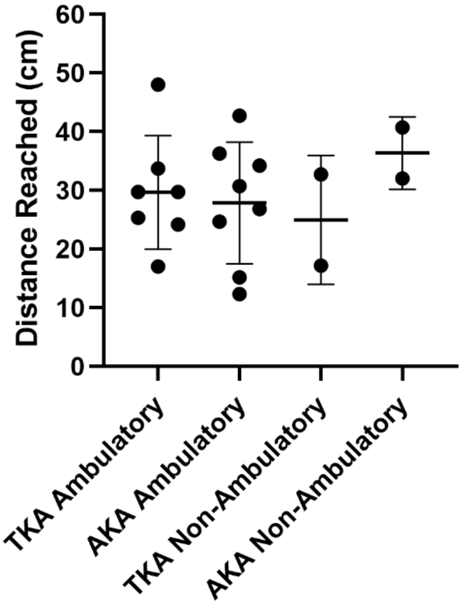

Figure 9.4. Sit-and-reach scores in ambulatory and non-ambulatory patients with TKA and AKA.

Table 9.3. Sit-and-reach scores in ambulatory and non-ambulatory patients with TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
Sit-and-Reach (cm)		
- TKA Amb	29.7 (9.7)	29.7 (17-48)
- AKA Amb	25.7 (9.1)	26.8 (12.3-36.3)
Sit-and-Reach (cm)		
- TKA Non-Amb	25.0 (11.0)	25.0 (17.2-32.7)
- AKA Non-Amb	36.4 (6.2)	36.4 (32.0-40.7)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb); Non-ambulatory (Non-Amb); centimetres (cm).

9.3.1.3. Timed-Up-and-Go Test

The time taken to complete the overall TUG test in seconds was recorded for each patient. The overall scores for all ambulatory patients with TKA were combined and compared to all ambulatory patients with AKA. A cut-off score of 19 seconds indicated that patients with lower limb amputations were at greater risk of falling (Physiopedia, 2022b). The TUG results are presented in Figure 9.5 and Table 9.4, and patients within this study were of a greater risk of falling.

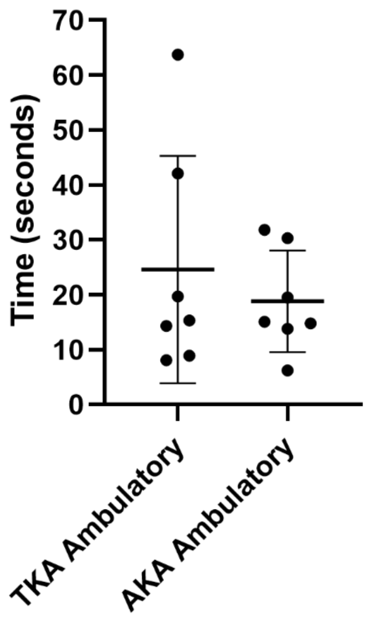

Figure 9.5. TUG times for ambulatory patients with a TKA and AKA.

Table 9.4. TUG times for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
TUG (s)		
- TKA Amb	24.6 (20.7)	15.3 (8.1-63.7)
- AKA Amb	18.8 (9.3)	15.1 (6.2-31.8)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb); Seconds (s).

9.3.1.4. L-Test of Functional Mobility

Objective scoring, including the time taken to complete the overall L-test, was recorded in seconds for each patient. The overall scores for all ambulatory patients with TKA were averaged and compared to all ambulatory patients with AKA. A reduction in the time to complete indicated an improvement in 'basic mobility'. The L-test results are presented in Figure 9.6 and Table 9.5, with patients of a greater risk of falling as times were exceeding 30 seconds.

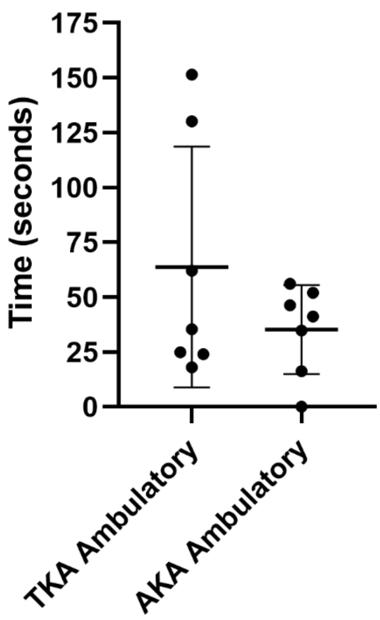

Figure 9.6. L-test times for ambulatory patients with a TKA and AKA.

Table 9.5. L-test times for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
L-Test (s)		
- TKA Amb	63.7 (54.9)	35.3 (18.0-151.5)
- AKA Amb	39.5 (13.7)	41.2 (16.3-56.0)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb); Seconds (s).

9.3.1.5. Functional Reach Test

The distance reached in centimetres was recorded for each ambulatory patient with TKA and AKA. The overall scores for all ambulatory patients with TKA were averaged and compared to all ambulatory patients with AKA.

The distances reached during the functional reach test presented in Figure 9.7 and Table 9.6. The results indicate that patients with a TKA and AKA were of a lower risk of falling, as the mean scores were greater than 25cm.

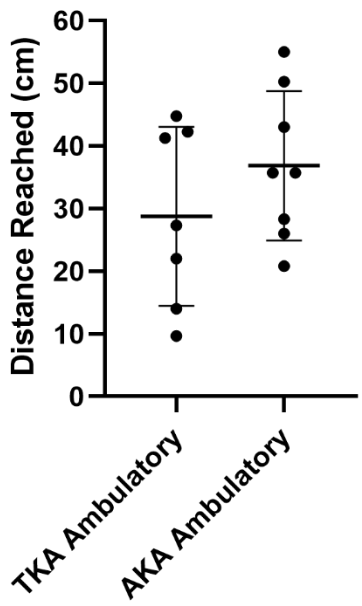

Figure 9.7. Functional reach test distances for ambulatory patients with a TKA and AKA.

Table 9.6. Functional reach test results for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
FRT (cm)		
- TKA Amb	28.8 (14.3)	27.3 (9.7-44.8)
- AKA Amb	36.0 (12.6)	35.7 (20.8-55.0)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max);Functional Reach Test (FRT); Ambulatory (Amb).

9.3.1.6. Two-Minute and Six-Minute Walk Tests

The overall scores for all ambulatory patients with TKA were combined and compared to all ambulatory patients with AKA.

The distance walked during the 2MWT and walking speed are presented in Figure 9.8 and Table 9.7. There was no difference between TKA and AKA walking distance nor walking speed.

The distance walked during the 6MWT and walking speed are presented in Figure 9.9 and Table 9.8. There was no difference between TKA and AKA walking distance nor walking speed.

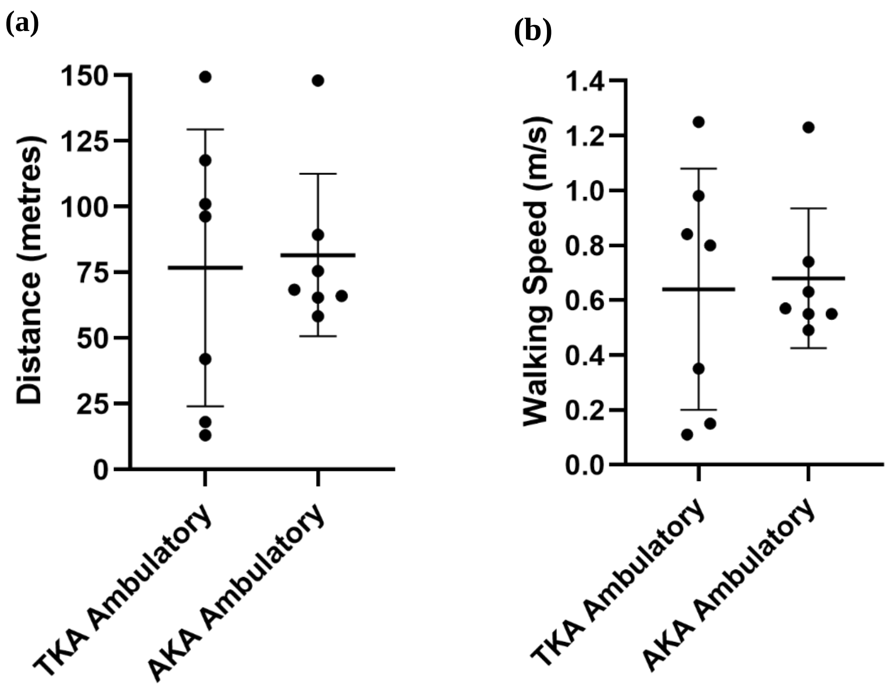

Figure 9.8. 2MWT distance (a) and walking speed (b) for ambulatory patients with a TKA and AKA.

Table 9.7. 2MWT distance and walking speed for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
2MWT Distance (m)		
- TKA Amb	76.8 (52.7)	96.3 (13.0-149.4)
- AKA Amb	81.6 (30.9)	68.4 (58.3-148.1)
2MWT Speed (m/s)		
- TKA Amb	0.64 (0.44)	0.8 (0.11-1.25)
- AKA Amb	0.68 (0.26)	0.57 (0.49-1.23)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Metres (m); Meters per second (m/s); Minimum (Min); Maximum (Max); Ambulatory (Amb).

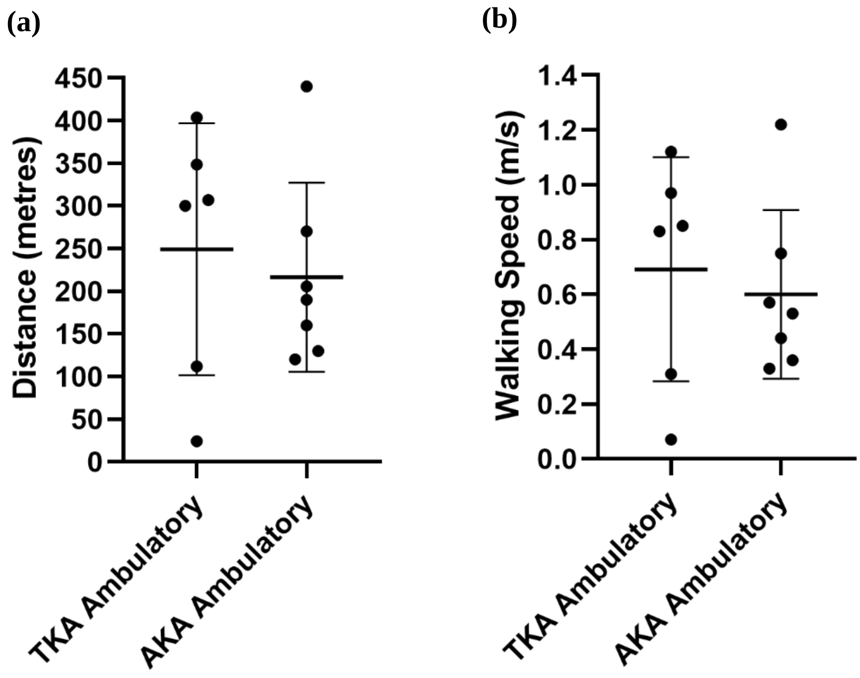

Figure 9.9. 6MWT distance (a) and walking speed (b) for ambulatory patients with a TKA and AKA.

Table 9.8. 6MWT distance and walking speed for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
6MWT Distance (m)		
- TKA Amb	284.0 (256.5)	300 (13-653)
- AKA Amb	216.5 (110.8)	190 (120-440)
6MWT Speed (m/s)		
- TKA Amb	0.61 (0.43)	0.83 (0.07-1.12)
- AKA Amb	0.60 (0.31)	0.53 (0.33-1.22)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max);Ambulatory (Amb); Metres (m); Metres/second (m/s).

9.3.1.7. Berg Balance Scale

The overall scores for all ambulatory patients with TKA were combined, averaged and compared to all ambulatory patients with AKA.

The Berg Balance Scale scores are presented in Figure 9.10 and Table 9.9. The mean scores indicate that patients may be of a greater risk of falling overall, however the median scores indicate that patients had good functional balance and may be of a lower risk of falling. There was no difference in TKA and AKA Berg Balance Scale scores.

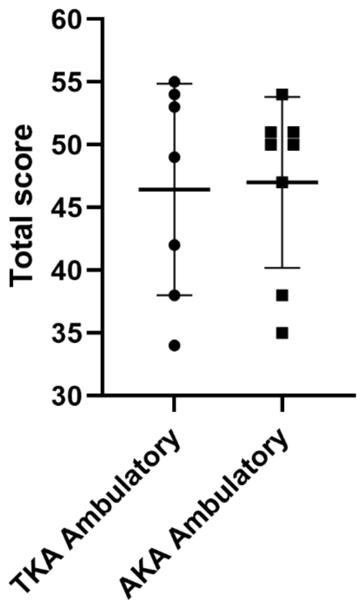

Figure 9.10. Berg Balance Scale scores for ambulatory patients with a TKA and AKA.

Table 9.9. Berg Balance Scale results for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
BERG		
- TKA Amb	46.4 (8.4)	49 (34-55)
- AKA Amb	46.4 (7.1)	50 (35-54)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb).

9.3.1.8. Tinetti Assessment

The overall scores for all ambulatory patients with TKA were combined and compared to all ambulatory patients with AKA.

The Tinetti balance, gait and total scores are presented in Figure 9.11 and Table 9.10. The scores from patients with a TKA and patients indicate that they were of a moderate risk of falling. TKA and AKA Tinetti balance,gait and overall scores were similar.

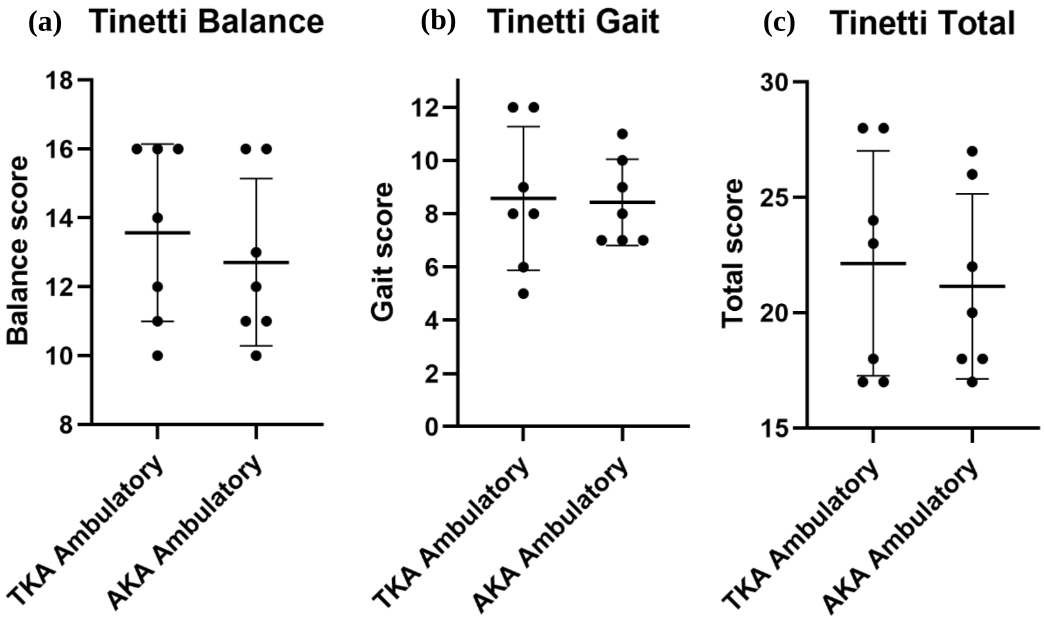

Figure 9.11. Tinetti balance (a), gait (b) and overall (c) scores for ambulatory patients with a TKA and AKA.

Table 9.10. Tinetti balance, gait and overall scores for ambulatory patients with a TKA and AKA.

Test	Mean (± SD)	Median (Min-Max)
Tinetti Balance		
- TKA Amb	13.6 (2.6)	14 (10-16)
- AKA Amb	12.7 (2.4)	12 (10-16)
Tinetti Gait		
- TKA Amb	8.6 (2.7)	8 (5-12)
- AKA Amb	8.4 (1.6)	8 (7-11)
Tinetti Overall		
- TKA Amb	22.1 (4.9)	23 (17-28)
- AKA Amb	21.1 (4.0)	20 (17-27)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb).

9.3.2. Self-Reported Measures

9.3.2.1. Self-Reported Fall History

The number of falls experienced within the last 12 months, the activities leading to falls, the perceived cause of falls and injuries sustained for all ambulatory patients with TKA were combined and compared to all ambulatory patients with AKA. Similarly, results for non-ambulatory patients with TKA were compared to ambulatory patients with TKA. The results for non-ambulatory patients with AKA were compared ambulatory patients with AKA. Additionally, the results for non-ambulatory patients with TKA were compared to non-ambulatory patients with AKA.

Figure 9.12 presents the activity performed prior to falling in the previous 12 months in recruited ambulatory and non-ambulatory patients with a TKA and AKA. The main activity performed prior to falling in ambulatory patients with a TKA were other reasons not listed, including uneven ground (n=1), during sitting in a wheelchair (n=1), cutting grass (n=1), and when sat on a commode (n=1). The main activity performed prior to falling in ambulatory patients with an AKA were when ambulating (Figure 9.12; n=4). Additionally, the main activity performed prior to falling in non-ambulatory patients with a TKA were other reasons not listed, including when sat on the toilet (n=1), and intact limb gave way (n=1). Moreover, the main activity performed prior to falling in non-ambulatory patients with an AKA were due to transferring (n=1) and other, entailing of falling over backwards in a wheelchair (n=1).

Figure 9.13 presents the main cause of falling in the previous 12 months in recruited ambulatory and non-ambulatory patients with a TKA and AKA. Figure 9.14 outlines injuries sustained from falling.

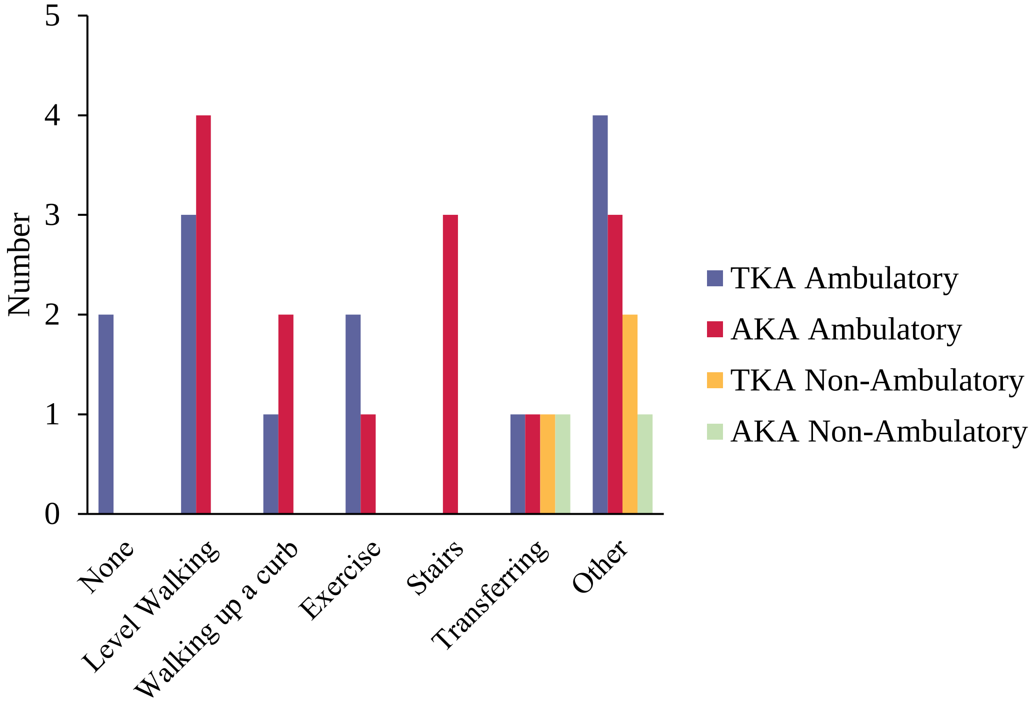

Figure 9.12. Activities completed prior to falling in ambulatory and non-ambulatory patients with TKA and AKA.

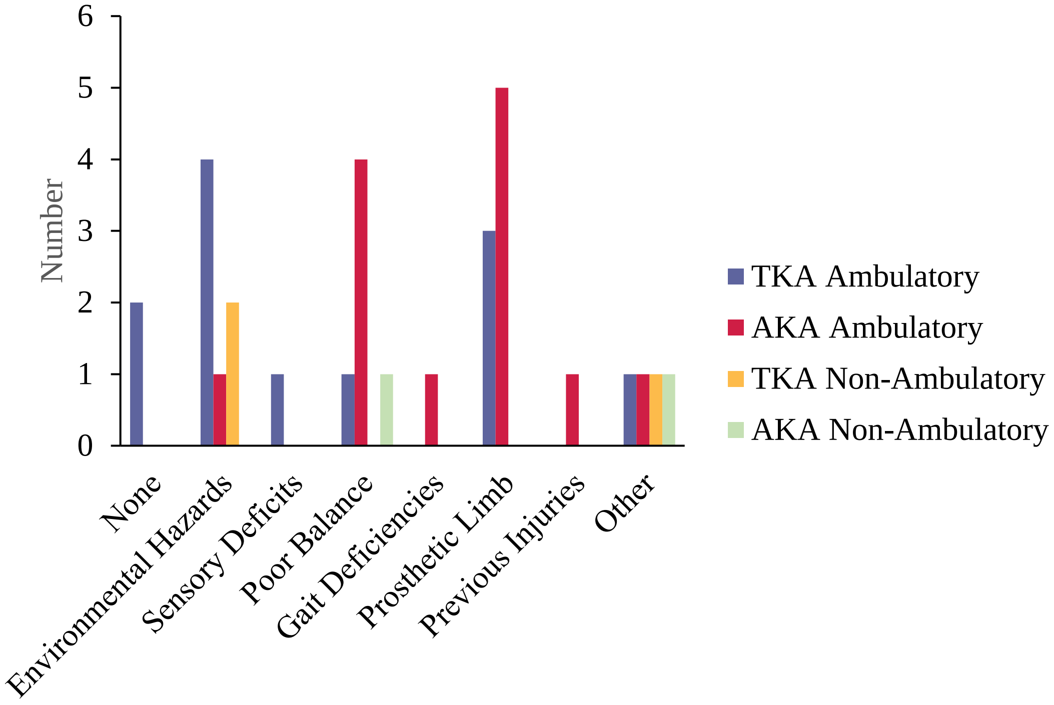

Figure 9.13. Main self-reported cause of falling in ambulatory and non-ambulatory patients with TKA and AKA.

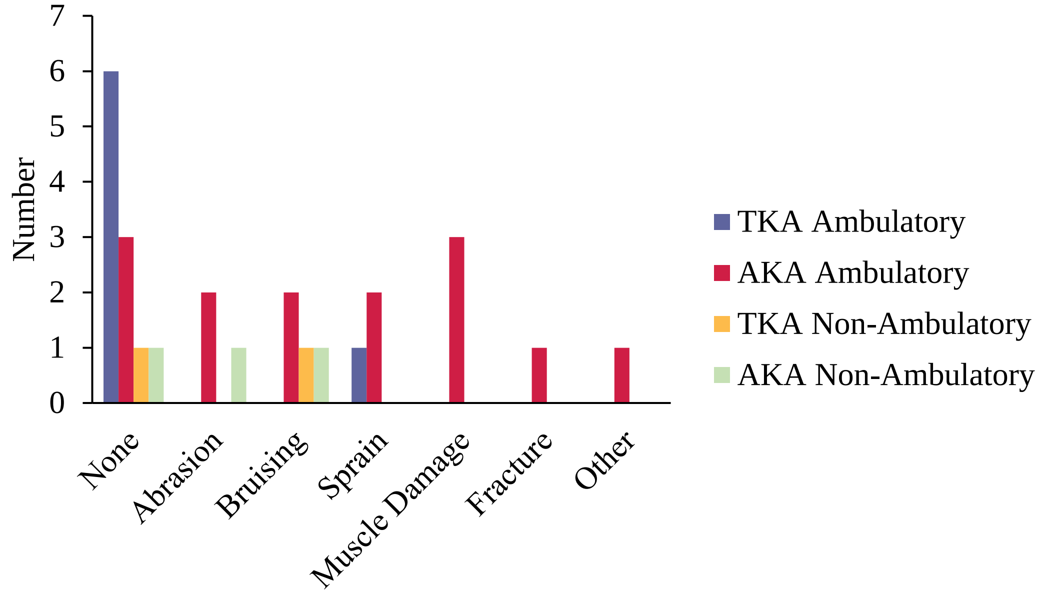

Figure 9.14. Injuries sustained from falling in ambulatory and non-ambulatory patients with TKA and AKA.

9.3.2.2. EQ-5D-5L

A direct comparison of frequencies for the five EQ-5D-5L levels between groups is presented in Table 9.11. EQ-VAS for ambulatory and non-ambulatory TKA and AKA is outlined in Figure 9.15 and Table 9.12. Cohorts presented similar scores within the EQ-5D-5L domains.

Table 9.11. EQ-5D-5L frequencies and percentages for ambulatory and non-ambulatory TKA and AKA.

Domain	Level	TKA (n=9)		AKA (n=10)	
		Ambulatory, n (%)	Non-Ambulatory, n (%)	Ambulatory, n (%)	Non-Ambulatory, n (%)
Mobility	Level 1	2 (28.6)	0	1 (12.5)	0
	Level 2	2 (28.6)	0	0	0
	Level 3	2 (28.6)	0	5 (62.5)	1 (50)
	Level 4	1 (14.3)	0	1 (12.5)	0
	Level 5	0	2 (100)	1 (12.5)	1 (50)
Self-Care	Level 1	3 (42.9)	1 (50)	5 (62.5)	0
	Level 2	3 (42.9)	0	1 (12.5)	1 (50)
	Level 3	0	0	1 (12.5)	1 (50)
	Level 4	1 (14.3)	1 (50)	1 (12.5)	0
	Level 5	0	0	0	0
Usual Activities	Level 1	3 (42.9)	1 (50)	1 (12.5)	0
	Level 2	2 (28.6)	0	2 (25)	0
	Level 3	1 (14.3)	0	2 (25)	2 (100)
	Level 4	0	1 (50)	2 (25)	0
	Level 5	1 (14.3)	0	1 (12.5)	0
Pain/Discomfort	Level 1	1 (14.3)	1 (50)	0	1 (50)
	Level 2	2 (28.6)	0	1 (12.5)	0
	Level 3	4 (57.1)	0	4 (50)	1 (50)
	Level 4	0	0	2 (25)	0
	Level 5	0	1 (50)	1 (12.5)	0
Anxiety/Depression	Level 1	6 (75.7)	1 (50)	3 (37.5)	1 (50)
	Level 2	0	0	1 (12.5)	0
	Level 3	0	0	1 (12.5)	1 (50)
	Level 4	1 (14.3)	0	2 (25)	0
	Level 5	0	1 (50)	1 (12.5)	0

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Number (n); Percentage (%); Level 1 is “I have no problems in…”; Level 2 is “I have slight problems…”; Level 3 is “I have moderate problems…”; Level 4 is “I have severe problems…”; Level 5 is “I am unable to…”.

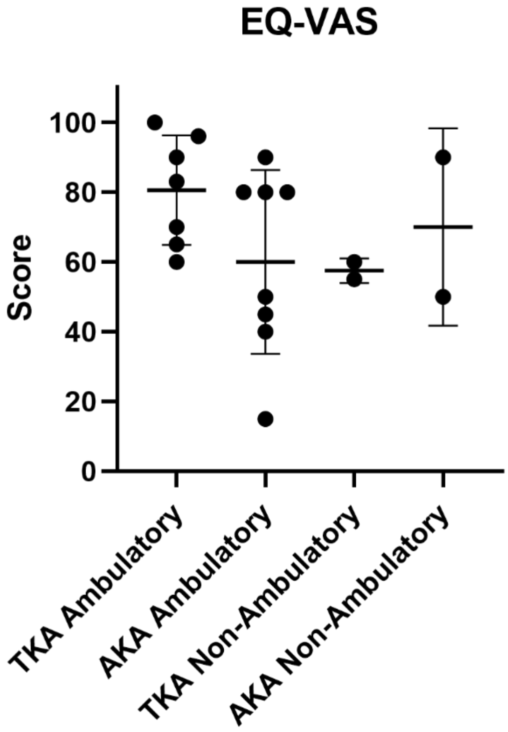

Figure 9.15. EQ-VAS between ambulatory and non-ambulatory patients with TKA and AKA.

Table 9.12. EQ-VAS in ambulatory and non-ambulatory patients with TKA and AKA.

Factor	Mean (± SD)	Median (Min-Max)
EQ-VAS		
- TKA Amb	79.1 (14.1)	83 (60-96)
- AKA Amb	60.0 (26.3)	65 (15-90)
EQ-VAS		
- TKA Non-Amb	57.5 (3.5)	57.5 (55-60)
- AKA Non-Amb	70.0 (3.5)	70 (50-90)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb); Non-ambulatory (Non-Amb).

9.3.2.3. Short-Form Health Survey 36

SF-36 results for the 8 domains (physical function, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain and general health), total score, PCS and MCS are presented in Table 9.13.

Scores were relatively low in ambulatory and non-ambulatory patients with a TKA and AKA in terms of physical function and PCS, thus highlighting lower levels of physical abilities across this patient group. Scores remained somewhat similar between the groups.

Table 9.13. SF-36 in ambulatory and non-ambulatory patients with TKA and AKA.

Domain	TKA		AKA	
	Ambulatory (n=7)	Non-Amb (n=2)	Ambulatory (n=8)	Non-Amb (n=2)
- Physical functioning	30 ± 31.6	12.5 ± 10.6	21.3 ± 22.6	5 ± 0
- Role limitations due to physical health	39.3 ± 43	37.5 ± 53	15.6 ± 35.2	25 ± 35.4
- Role limitations due to emotional problems	76.2 ± 41.8	50 ± 70.7	37.5 ± 41.5	100 ± 0
- Energy/fatigue	51.4 ± 15.2	52.5 ± 38.9	46.9 ± 24	55 ± 14.1
- Emotional well-being	74.3 ± 16.6	78 ± 19.8	54.5 ± 25.5	76 ± 22.6
- Social functioning	69.6 ± 27.8	56.3 ± 61.9	54.7 ± 33.4	87.5 ± 17.7
- Pain	68.9 ± 21.4	66.3 ± 47.7	45.3 ± 17.7	90 ± 14.1
- General health	52.9 ± 18.2	32.5 ± 3.5	45.6 ± 25.6	47.5 ± 17.7
- Physical Component Score (PCS)	31.4 ± 12.7	26.3 ± 13	27.3 ± 10.2	26.3 ± 3
- Mental Component Score (MCS)	55.2 ± 10.8	54.8 ± 21.2	45.8 ± 13.3	63.9 ± 7.8
- Total Score	43.3 ± 7.3	40.6 ± 17	36.5 ± 10.8	45.1 ± 5.4

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Non-Ambulatory (Non-Amb). All data is presented as mean and standard deviation (±).

9.3.2.4. Locomotor Capabilities Index-5

Responses gathered for each of the statements within the LCI-5 were added together and averaged for each of the TKA and AKA groups. A direct comparison between these two levels of amputation groups were determined. The LCI-5 scores are presented in Figure 9.16 and Table 9.14. The scores indicate that all patients may have relied on assistance despite a mean score of over 50% of the total scores.

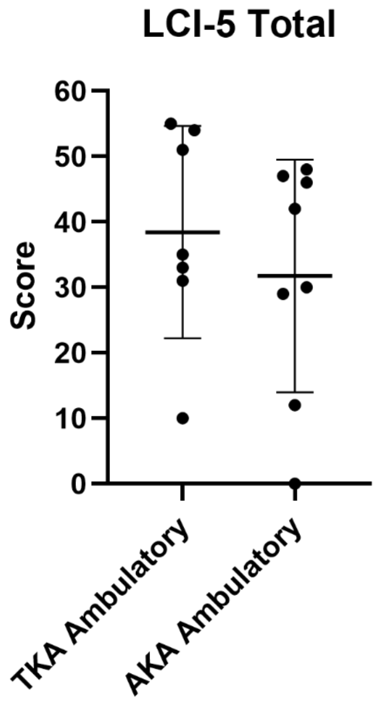

Figure 9.16. LCI-5 scores for ambulatory patients with a TKA and AKA.

Table 9.14. LCI-5 scores for ambulatory patients with a TKA and AKA.

Factor	Mean (± SD)	Median (Min-Max)
LCI-5 Overall		
- TKA Amb	38.4 (16.2)	35 (10-55)
- AKA Amb	31.75 (17.8)	36 (0-48)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb).

9.3.2.5. Houghton Scale of Prosthetic Use

Overall scores for all TKA patients and AKA patient were averaged and compared. The average and median scores are presented in Figure 9.17 and Table 9.15. The mean and median scores for patients with a TKA indicate that patients were mainly achieving household ability and limited community, or independent community (Table 9.15). Mean and median scores for patients with an AKA indicate that patients were of a limited household ability or were achieving household ability and limited community.

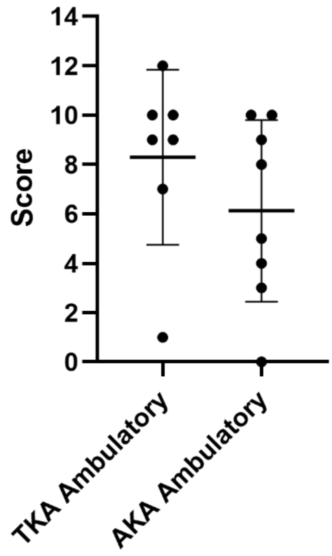

Figure 9.17. Houghton Scale of prosthetic use scores for ambulatory patients with a TKA and AKA.

Table 9.15. Houghton Scale of prosthetic use scores for ambulatory patients with a TKA and AKA.

Factor	Mean (± SD)	Median (Min-Max)
Houghton Scale		
- TKA Amb	8.3 (3.5)	9 (1-12)
- AKA Amb	5.8 (4.1)	6.5 (0-10)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb).

9.3.2.6. Activities-specific Balance Confidence Scale-UK

The results for each item for each participant, rated as a percentage, were averaged separately for TKA and AKA levels, with a direct comparison of TKA and AKA mean ± SD and median percentage values presented in Figure 9.18 and Table 9.16. There were no differences in scores.

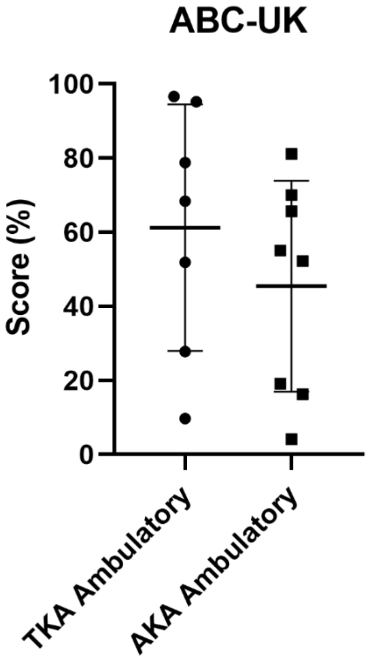

Figure 9.18. ABC-UK scores for ambulatory patients with a TKA and AKA.

Table 9.16. ABC-UK scores for ambulatory patients with a TKA and AKA.

Factor	Mean (± SD)	Median (Min-Max)
ABC-UK		
- TKA Amb	61.2 (33.2)	68.4 (9.7-96.6)
- AKA Amb	45.3 (24.4)	52.2 (4.1-70.0)

Key: Through-knee amputation (TKA); Above-knee amputation (AKA); Standard deviation (SD); Minimum (Min); Maximum (Max); Ambulatory (Amb).

9.4. Discussion

Existing literature has reported various aspects of the clinical tests and balance confidence in patients with lower limb amputations as outlined in Chapter Three. However, the aim of this exploratory study was threefold. Firstly, to investigate the performance differences in ambulatory patients with a TKA and AKA, and to investigate their balance confidence and falls history. Secondly, to investigate the performance differences in non-ambulatory patients with a TKA and AKA, and to investigate their balance confidence and falls history. Thirdly, to investigate the performance differences in ambulatory patients with a TKA and non-ambulatory patients with a TKA, and to investigate their balance confidence and falls history.

The main findings from the study identified no difference between TKA and AKA across either ambulatory or non-ambulatory status in terms of physical performance from the clinical tests and balance confidence. From the results presented in Chapter Nine, Section 9.3, hypothesis 2 of patients with TKA will have improved functional outcomes compared to AKA patients was rejected, as there were no differences identified in functional outcomes. Further, hypothesis 3 of patients with TKA will walk further than AKA during the 2MWT and 6MWT due to their longer residual limb and more intact thigh musculature distance was rejected as there was no difference in distance walked between patient cohorts when completing the 2MWT and 6MWT. Additionally, hypothesis 4 of patients with TKA will complete tasks more quickly than AKA was rejected, as patients with a TKA completed the TUG test and L-test at similar times compared to patients with an AKA in the current study. Further, hypothesis 5 of patients with TKA are at a reduced risk of falling in comparison to AKA was rejected, as patients with a TKA and AKA had similar scores during the Berg Balance Scale. Moreover, hypothesis 6 was partially accepted, as fall numbers were similar between patients with a TKA and patients with an AKA, and balance confidence from the self-reported measures were also similar.

9.4.1. Clinical Tests

9.4.1.1. Function in Sitting Test

There were no differences identified between ambulatory and non-ambulatory patients with a TKA and AKA when completing the FIST. The FIST is an evaluation of sitting balance, thus exploring sensory, motor, and steady state balance factors. It is surprising that there were no differences identified between the two levels of amputation, as it is thought that maintaining a longer residual limb following a TKA provides stability and proprioceptive responses that are essential for balance in ambulatory and non-ambulatory individuals (Pinzur, 1992; Siev-Ner et al., 2000) which may assist with transfers and performing everyday activities. However, the results of the current study did not identify evidence of this possible benefit between any comparisons.

9.4.1.2. Sit-and-Reach Test

There were no differences identified between ambulatory and non-ambulatory patients with a TKA and AKA. The sit-and-reach test assesses the lower body, primarily hamstring flexibility (Burger & Marinček, 2001). Although there were no differences, non-ambulatory patients with an AKA in the current study reached the furthest distance. Their scores were similar to Burger and Marinček (2001) with patients with an AKA reaching an average of 39.5cm. However, it is unclear in their study whether these patients were fitted with a prosthesis. Moreover, there were no results reported for TKA, and there are no alternative studies who have reported sit-and-reach distances in TKA, therefore no further comparisons can be made. Although, non-ambulatory patients with a TKA reached an average of 25cm compared to non-ambulatory patients with an AKA who reached an average of 36.4cm. This is surprising, as although the longer lever and end weight-bearing residual limb in TKA may be conceived to be beneficial for sitting balance, the results could suggest that a longer lever may not be beneficial and may even make it more difficult when reaching forwards.

9.4.1.3. Timed-Up-and-Go Test

Although the theoretical biomechanical advantages of the TKA longer lever and end-weight bearing residual limb might have assisted with stability and walking during this task, the time taken were similar between ambulatory patients with a TKA and AKA in the current study. The scores within the current study indicated that both patient cohorts were at greater risk of falling, as both values were equal to or greater than 19s, which is the cut-off threshold for increased risk of falling.

The times within the current study seem somewhat slower compared to previously published literature (Hafner et al., 2017; Karatzios et al., 2019). Karatzios et al. (2019) determined that the average time to complete the TUG were TKA 12.7 seconds ± 7.9 seconds, and AKA 12.4 seconds ± 6.2 seconds. Compared to Hafner et al. (2017), the scores by Karatzios et al. (2019) appear somewhat lower. It could be suggested that patients with amputations due to trauma may have a faster walking speed compared to amputations of other aetiologies, although, this cannot be confirmed due to the small sample size within the current study.

9.4.1.4. L-Test of Functional Mobility

There were no difference between ambulatory patients with a TKA and AKA. As mentioned in Chapter Two, Section 2.5.2.2, the L-test can be used to assess physical function in individuals with lower limb amputations and who are using a prosthesis (Deathe & Miller, 2005). Previous researchers have investigated the L-Test in lower limb amputations (Deathe & Miller, 2005; Rushton et al., 2015; Frengopoulos, 2017). Rushton et al. (2015) recruited patients with a TKA, however they grouped all levels of amputation together, therefore no direct comparison to the literature can be made. It could be thought that ambulatory patients with a TKA might have better control of their prosthesis when walking and turning corners thus have a reasonably quicker completion time to AKA, however this was not reflected within this current study as two patients with a TKA had completion times over 125 seconds. These two patients had amputations due to cancer and peripheral vascular disease. Patients with amputations due to peripheral vascular disease rarely achieve walking and prosthesis ability of those with amputations due to trauma or cancer, as they frequently do not possess the capacity for energy expenditure to overcome the metabolic demands of walking with a prosthesis (Pinzur, 1993).

9.4.1.5. Functional Reach Test

The FRT measures the difference between the arm's length and a maximal forward reach when using a stable support base (Leifsdóttir & Tómasdóttir, 2021). There were no differences between ambulatory patients with a TKA and AKA. Hill et al. (2020) investigated the lateral reach test rather than a forward reach. They recruited nine individuals with an AKA, with the distance reached being greater on the side of their intact limb compared to their amputated side. The results cannot be compared further as there has been no previous research including patients with a TKA.

9.4.1.6. Two-Minute and Six-Minute Walk Tests

There were no differences identified between ambulatory patients with a TKA and AKA results in this study. The meta-analysis conducted in Chapter Three, Section 3.3.5.1 identified no significant differences between TKA and AKA when completing the 2MWT. However, 6MWT distance reported across three studies (Möller et al., 2019; Möller et al., 2020; Burçak et al., 2021) identified that patients with a TKA walked significantly further than those with an AKA, on average 43m further. All three studies reported an increased range distance of between 30.8m and 60.2m for TKA patients. The 6MWT is a sub-maximal exercise test used to assess aerobic capacity and endurance. It would be expected that maintaining a longer residual limb allows the rectus femoris, vastus lateralis, vastus medialis and vastus intermedius muscles to stay intact and cause no muscular imbalance compared to the intact limb (Baumgartner, 1979), thus generating more power to drive the limb forwards during walking or when completing daily activities. Further, the TKA theoretically provides a better suspension, thus allowing a better control over the prosthesis (O'Keeffe & Rout, 2019). However, findings from the current study identified no differences in either 2MWT or 6MWT distances between TKA and AKA. One patient with a TKA within the study had peripheral vascular disease and covered 18m within two minutes, and 24m within six minutes. These scores may have hindered the lack of difference between the two levels of amputation.

9.4.1.7. Berg Balance Scale

There were no difference between ambulatory patients with a TKA and AKA. Although Burger and Marinček (2001) recruited patients with a BKA and AKA to compare with healthy able-bodied male participants, their results for one leg balance test showed no difference in the time reached between the amputation cohorts. However, they discovered that patients with amputations due to trauma were able to complete the one leg balance test for longer in comparison to patients with amputations due to peripheral vascular disease (Burger & Marinček, 2001). Patients with an amputation due to peripheral vascular disease may have more problems with balance because of diabetic neuropathy and retinopathy (Burger & Marinček, 2001). Despite research being completed to assess standing balance with patients who have a lower limb amputation, there has been no comparison of TKA and AKA with the Berg Balance Scale in previous research and therefore warrants further investigation.

9.4.1.8. Tinetti Assessment

There were no difference between ambulatory patients with a TKA and AKA following the Tinetti assessment in this study. The overall average score for TKA was 22.1 and AKA was 21.1 in the current study, indicating that all individuals were of a moderate risk of falling. The results are somewhat surprising, as the TKA amputation may be expected to be beneficial to ambulatory patients due to the longer mechanical lever and the end weight-bearing residual limb, which may be more beneficial during sitting balance and sit-to-stand. However, this potential advantage was not seen and both cohorts have a similar Tinetti score. The Tinetti assessment has not been utilised in existing literature for TKA therefore no direct comparison can be made.

9.4.2. Self-Reported Measures

9.4.2.1. EQ-5D-5L

There were no differences between ambulatory and non-ambulatory patients with a TKA and AKA following EQ-5D-5L. However, EQ-VAS was slightly greater overall in ambulatory patients with a TKA compared to non-ambulatory patients with a TKA. As expected, the average answer for ambulatory patients with a TKA was “I have slight problems in walking about” compared to non-ambulatory patients with a TKA who answered, “I am unable to walk about”. This result may be self-explanatory, as those non-ambulatory patients with a TKA were either not referred for prosthetic fitting or were unsuccessful long-term with prosthesis fitting due to comorbidities or deteriorating health and were therefore wheelchair bound. Similarly, EQ-VAS was greater overall in ambulatory patients with a TKA compared to non-ambulatory patients with a TKA.

The ability to mobilise with a prosthetic limb has a direct impact on a person's quality of life (Davie-Smith et al., 2017b Agrawal et al., 2017) and would explain the responses to the EQ-VAS. Alternatively patients who successfully rehabilitated with a prosthesis may have had a greater general health in comparison to non-ambulatory patients. Previous literature has utilised the EQ-5D-5L tool in patients with a TKA; however, their results were not separated from the AKA patients in the reports (Ernstsson et al., 2021; Davie-Smith et al., 2019). The results reported in the current study warrant further investigation.

9.4.2.2. Short-Form Health Survey 36

There were no differences between ambulatory and non-ambulatory patients with a TKA and AKA following the PCS, MCS, and total score. The results are consistently similar in the literature (Polfer et al., 2019; Burçak et al., 2021), although scores appeared higher in prior reports compared to the current study. Burçak et al. (2021) determined the physical function attribute of the SF-36 following a TKA was 46.1 ± 10.5, and 43.2 ± 11.2 following AKA. Further, Polfer et al. (2019) determined the physical function attribute of the SF-36 following a TKA was 59, and 57.5 following an AKA. Although lower limb amputation is a life-saving procedure, the loss of a limb would be expected to have a significant impact on the patient's QoL (van der Schans et al., 2002). However, the physical health attribute of QoL is not only influenced by use of a prosthesis, but also the comorbidities of the patient (Sinha et al., 2011). Moreover, use of assistive devices such as canes and crutches reportedly had a negative impact on physical component summary and mental component summary (Sinha et al., 2011) however they failed to report the impact on QoL. Although, assistive devices may be utilised because of lack of confidence in prostheses (Sinha et al., 2011). Other factors reported to affect QoL were phantom-limb pain and residual stump pain (Sinha et al., 2011). Patients within the current study had various aetiologies and causes of amputation, this may have impacted the overall results.

9.4.2.3. Balance Confidence

There were no difference between ambulatory patients with a TKA and AKA when utilising the ABC-UK, LCI-5, and Houghton Scale of prosthetic use. Balance confidence utilising the ABC-UK was measured in three studies (Karatzios et al., 2019; Möller et al., 2019; Möller et al., 2020), LCI-5 in two studies (Gökşenoğlu & Yildirim, 2019; Karatzios et al., 2019), with findings similar between levels of amputation. Further, a meta-analysis conducted in Chapter Three, Section 3.3.6.1, and identified no significant differences in ABC-UK or LCI-5 scores between TKA and AKA. It is interesting that there was no difference in balance confidence within the current study. Balance confidence may vary depending on the time of amputation, which could have been examined when looking at balance confidence. When comparing these scores to the fall history, it was not surprising that there was no difference between balance confidence as the number of falls were similar between TKA and AKA.

9.5. Limitations

Limitations of the clinical tests study have been identified. Firstly, there was a small sample size, comprising of mainly ambulatory patients. The inclusion and exclusion criteria required patients to walk more than five metres, therefore these individuals may have been more physically able compared to others. Further, for those patients who were ambulatory, they were required to walk more than 5m. It was not specified whether patients were to complete tasks with or without the use of walking aids, therefore the use of walking aids varied between patients and could have influenced results. Prosthesis components were not specifically controlled for, with the use of MPK and mechanical knee components utilised within this study. These may have further influenced the results, as patients with a MPK have a greater method of control with a prosthetic knee, and they are designed to help individuals walk with a more stable and efficient gait pattern. MPK wearers are also likely to be amongst K3 and K4 performers in each group to have successfully been offered this component. There were many tests performed in the ambulatory cohort, which could have potentially influenced fatigue and therefore impacting scores in remaining tests to be completed. The ordering of the tests tried to remain the same throughout ambulatory patients, however some patients wished to complete some of the tests against the order initially outlined. Patients were not all recruited from the same rehabilitation limb centre, and treatment may have likely differed across all patients. Additionally, cause of amputation was not controlled for, and may have been a confounding factor as patients with amputations due to vascular disease may have been less physically able to complete tasks and have more comorbidities compared to amputations due to trauma. Moreover, the number of patients recruited for the study was low, and the study was exploratory. These low numbers would have had an impact on the statistical power, which is confirmed by the large increases in mean results without statistical significance identified. This therefore may not be representative of the whole population, despite there being a relatively low proportion of established patients with a TKA compared to AKA. If the study was to be completed differently, the number of tests and questionnaires completed would be reduced.

9.6. Conclusion

Exploratory findings in this study suggest that there were no comparable differences between TKA and AKA in terms of physical performance, balance confidence, and QoL, across ambulatory and non-ambulatory patient cohorts. Despite previous reports of the benefits of the TKA procedure, the low sample size has not allowed any detection of these benefits in either ambulatory or non-ambulatory patients, and further investigation is warranted to compare whether TKA truly is beneficial physically for patients undergoing a life-changing amputation.

CHAPTER TEN: OVERALL SUMMARY, CLINICAL IMPLICATIONS, FUTURE RESEARCH AND REFLECTIONS ON CORONAVIRUS

10.1. Overall Summary

The overall aim of the thesis was to investigate the differences in surgical and functional outcomes between patients with a TKA and patients with an AKA.

The effect of lower limb amputation on QoL and physical function has been investigated widely within the literature. However, the effects of TKA have not been clearly elucidated from the existing literature as TKA patients are frequently grouped with AKA patients or the numbers of studies are too small to draw clear conclusions.

Chapters Three and Nine reviewed the gait and functional outcomes of patients with a TKA and patients with an AKA when performing activities of daily living, and to examine the balance confidence and QoL between the two levels of amputation. It is evident that TKA has not completely been excluded from prior research, however it has not been explored thoroughly across all aspects. Findings from the systematic review and meta-analysis identified that 6MWT distance was significantly greater following TKA than AKA. Additionally, patients with a TKA walked significantly further than those with an AKA when wearing an MPK. The study performed as part of this thesis identified no differences between TKA and AKA across either ambulatory or non-ambulatory status in terms of physical performance from the clinical tests and balance confidence.

Chapters Five, Six, Seven and Eight aimed to compare NVR clinical and post-operative outcomes between patients with a TKA and AKA when utilising several techniques for handling missing data (complete case analysis, multiple imputation, and propensity score matching, respectively). Findings collectively across all three handling missing data techniques indicate that patients with a TKA were performed in relatively younger, more frequently male patients, and were more common in patients with diabetes mellitus, and a lower presence of chronic lung disease compared to patients with a unilateral AKA. Patients with a TKA were also more likely to have had an elective admission prior to their amputation, and to have had their surgery within normal working hours. TKA were seemingly more daytime procedures with a higher frequency of planned admission and less frequently performed due to acute limb ischaemia and chronic limb ischaemia. Patients with a TKA had experienced fewer cardiac and respiratory post-operative complications, with in-hospital and 30-day mortality lower following a TKA. Patients with a TKA were more likely than AKA patients to be referred to amputation rehabilitation, though the outcomes of this were not available.

There were numerous limitations identified within the systematic review, NVR data analysis and clinical tests. Firstly, the studies identified within the systematic review were limited by small number of participants and varied methods, preventing meta-analysis of the data. Secondly, the systematic review included unpublished journal articles and some that may not have been peer-reviewed, which may reduce publication quality. The NVR data were self-reported within a retrospective dataset that had approximately 15% overall missing data. It is unconfirmed whether data were recorded correctly, or at all, thus being MCAR or MNAR. As data was missing, the repeated use of statistical analysis may have increased the probability of false-positive findings. Furthermore, data may not be available after the event, accounting for missing data. It is unclear what procedures were recorded as a TKA and therefore may include several variations, including Gritti-Stokes and KD. The clinical tests recruited a small number of participants, mainly of ambulatory patients. Cause of amputation, prosthesis components, use of walking aids and recruiting from the same rehabilitation centre were not specifically controlled.

10.2. Clinical Implications and Future Research

The following recommendations are made based on the data presented within this thesis.

10.2.1. Amputation Research Registry

- Clinicians should consider how amputation data are recorded locally and within the NVR.
    - Historical categorisation within the NVR is unhelpful in determining clear indications for amputation (e.g. tissue loss and severe infection may co-exist but data collection only allows for a single aetiology).
    - A clear definition of TKA is missing and it appears that hospital coders or those entering data are currently deciding what level of amputation has been performed (e.g. Gritti-Stokes may be record as either AKA or TKA).
    - All TKA are currently included as a single-entry code in NVR without separation of techniques which might allow a clearer picture of national practice and also comparison of outcomes.
    - Recording expected post-operative performance should be adopted nationally as this will assist in ascertaining surgical decision-making around who receives a TKA (e.g. are patients expected to have a high or low performance status post operatively? Are patients expected to be fitted with a prosthesis?).
    - Formal standardised post-operative surgical and rehabilitation data recording would assist in assessment of TKA in further research.

10.2.2. Clinical Factors

- Clinicians should be taught different surgical techniques, especially how to perform a TKA as this may benefit patients requiring amputations due to trauma. Patients may have fewer underlying comorbidities and could benefit functionally in terms of reduced energy expenditure when walking.
- Clinicians should consider TKA as a primary level of amputation when a BKA is not possible in selected patients, the data suggests that TKA is not associated with worse wound healing, despite over 50% of patients with a TKA having diabetes.

10.2.3. Rehabilitation Factors

- Clinicians should consider a TKA for those who wish to achieve functional mobility with or without a walking aid, as a meta-analysis highlighted that TKA allowed patients to tolerate walking further.
- Although there were no benefits of TKA identified when sitting, TKA still should be discussed as a primary option for non-ambulatory patients.
- Consensus must be reached on the most important outcome post-operatively, and treatment plans should be tailored to individuals.
- Rehabilitation should focus upon functional ability, as asymmetry of residual limb and functional ability is reduced over time.

10.3. Reflections on Coronavirus

Completing the study during the COVID-19 pandemic had an impact on the recruitment and completion of activities within the study. Initially, these two cohorts were to be compared biomechanically, utilising 3D motion capture and force plates to calculate a variety of temporal-spatial, kinematic and kinetic parameters, however this was unable to go ahead due to the ongoing pandemic. The reported study required a new approach, including amendments to ethical approvals, in which biomechanical measures were substituted for clinical tests that were mainly utilised in amputation rehabilitation and therefore patients were familiar with. From this, two data collection sites were utilised, and maintaining a controlled environment at these two different sites was difficult. Following this, the equipment utilised including beds and chairs at sites were somewhat different, although these may have not directly impacted the results.

10.4. Future Research Recommendations

Future research should ensure that their risk of bias and methodological quality is sufficient and controlled. For example, it is important that studies report their aims and objectives, hypotheses and main outcomes. For replication purposes if required, participant characteristics of inclusion and exclusion criteria should be fully addressed, and interventions of interest clearly described. Whilst most studies take into consideration confounders on each cohort, this is another factor that should be addressed and controlled for where possible in future research. Items that were not addressed frequently across the included studies were related to internal validity bias, such as blinding, data dredging, and follow-up of patients if required. Future research should also address internal validity, where confounding and selection bias could arise. For example, ensuring participants are recruited from the same population over the same period of time. Due to the nature of the population, it may not be feasible to have sufficient power to detect a clinically important effect, however, sample sizes should be thoroughly explained, including loss of recruited patients.

Investigating surgical pre- and post-operative factors between TKA and AKA is still an area that future research should be considering. Although there is consensus within Chapters Five, Six, Seven and Eight regarding TKA, there are still numerous factors that are to be determined. For example, discharge destination, 30-day wound healing rates and 30-day re-admission rates are factors that subsequently had most of the missing data. Although some conclusions could potentially be drawn from the numerous missing data techniques, further investigation should allow full collection of these responses to determine the true differences. If the NVR utilises alternative sub-categories as outlined above, these might provide an extensive picture of short-term outcomes.

Future research surrounding functional outcomes of TKA and AKA should be widely practised. It is evident that there is a difference in 6MWT distance between TKA and AKA when looking at the meta-analysis from Chapter Three, however Chapter Nine failed to identify the same differences due to the sample size. Replicating this 6MWT in future research and limiting aetiologies may help to answer a question of whether there is a true difference between these levels of amputation. Further, although there was no differences identified in the FIST, the potential benefits of a longer mechanical lever arm would facilitate those who are wheelchair bound and not for a prosthesis, which is an important area to focus on. Therefore it is important to build upon research into sitting balance as it is unclear whether the reported biomechanical benefits of a TKA are truly benefits. Additionally, as mentioned throughout the thesis, QoL is a huge outcome that should be regularly collected throughout research. The SF-36 should be included in future research of these two amputation levels as it has not yet been determined the true differences, if any. The BACPAR toolbox should be utilised where possible in future research design as these outline specific measures validated for patients with lower limb amputation.

TKA is a very different surgical technique compared to AKA, and even BKA as combined with in some literature, and thus may offer advantages and disadvantages that the other levels of amputation may not. Factors that should be considered moving into future research include a relatively higher sample size that is statistically powered. Increasing patient numbers would give studies a representative sample of the overall population, thus enhancing statistical power. Confounding factors should be considered when recruiting, including the amputation aetiology. This should be balanced to allow a direct comparison to be determined. Further, separating causes of amputation within the analysis would provide a valuable insight into the specific adaptations that may occur, given any irregularity in physical ability. Gait biomechanics is still to be investigated between these two cohorts, which evidently should be beneficial to clinical practice. Such research is important as this may influence the surgical decision making regarding the most appropriate level of amputation if a patient may be suitable for either procedure.

CHAPTER ELEVEN: CONCLUSION

The current thesis provides a valuable addition to the available research by focusing not only on rehabilitation outcomes utilised in clinical tests but providing a statistical comparison of surgical pre- and post-operative data between patients with a TKA and patients with an AKA when utilising numerous handling missing data techniques. Although TKA has been included within the scientific literature, this is not extensive or consistent and requires further investigations.

The current thesis has highlighted differences in functional mobility, primarily when completing the 6MWT from scientific literature, and differences in patient characteristics and post-surgical outcomes between TKA and AKA. It is apparent from the systematic review and NVR database analysis, that TKA may present positive benefits for patients. Patients with a TKA walked significantly further during the 6MWT as reported in Chapter Three. Further, patients with a TKA experienced significantly fewer post-operative complications and had a lower mortality rate compared to patients with AKA. Patients with a TKA had similar levels of successful wound healing as AKA patients, despite previous reports of poor wound healing. Significantly more patients with a TKA were referred to amputation rehabilitation. These outlined outcomes may overall provide patients receiving a TKA an improved QoL. From these, recommendations have been stated regarding future patients receiving a TKA and the importance of clinical decision making.

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Appendix A. The Risk of bias in non-randomised studies (RoBANS) tool used in Chapter Three.

Domain	Description	Risk of bias
Selection of participants	Selection bias caused by inadequate selection of participants	☐ Low ☐ High ☐ Unclear
Confounding variables	Selection bias caused by inadequate confirmation and consideration of confounding variable	☐ Low ☐ High ☐ Unclear
Intervention (exposure) measurement	Performance bias caused by inadequate measurements of intervention (exposure)	☐ Low ☐ High ☐ Unclear
Blinding of outcome assessment	Detection bias caused by inadequate blinding of outcome assessment	☐ Low ☐ High ☐ Unclear
Incomplete outcome data	Attrition bias caused by inadequate handling of incomplete outcome data	☐ Low ☐ High ☐ Unclear
Selective outcome reporting	Reporting bias caused by selective outcome reporting	☐ Low ☐ High ☐ Unclear

Appendix B. The Downs and Black (1998) Checklist used in Chapter Three.

Item	Criteria	Possible Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	Yes = 1 No = 0
2	*Are the main outcomes to be measured clearly described in the Introduction or Methods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1 No = 0
3	*Are the characteristics of the patients included in the study clearly described?* In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.	Yes = 1 No = 0
4	*Are the interventions of interest clearly described?* Treatments and placebo (where relevant) that are to be compared should be clearly described.	Yes = 1 No = 0
5	*Are the distributions of principal confounders in each group of subjects to be compared clearly described?* A list of principal confounders is provided.	Yes = 2 Partially = 1 No = 0
6	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).	Yes = 1 No = 0
7	*Does the study provide estimates of the random variability in the data for the main outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data are not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1 No = 0
8	*Have all important adverse events that may be a consequence of the intervention been reported?* This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided).	Yes = 1 No = 0
9	*Have the characteristics of patients lost to follow-up been described?* This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.	Yes = 1 No = 0
10	*Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*	Yes = 1 No = 0
External validity		
11	*Were the subjects asked to participate in the study representative of the entire population from which they were recruited?* The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.	Yes = 1 No = 0 Unable to determine = 0

12	*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.	Yes = 1 No = 0 Unable to determine = 0
13	*Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?* For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.	Yes = 1 No = 0 Unable to determine = 0
Internal validity - bias		
14	*Was an attempt made to blind study subjects to the intervention they have received?* For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.	Yes = 1 No = 0 Unable to determine = 0
15	*Was an attempt made to blind those measuring the main outcomes of the intervention?*	Yes = 1 No = 0 Unable to determine = 0
16	*If any of the results of the study were based on "data dredging", was this made clear?* Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.	Yes = 1 No = 0 Unable to determine = 0
17	*In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.	Yes = 1 No = 0 Unable to determine = 0
18	*Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1 No = 0 Unable to determine = 0
19	*Was compliance with the intervention/s reliable?* Where there was noncompliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.	Yes = 1 No = 0 Unable to determine = 0
20	*Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.	Yes = 1 No = 0 Unable to determine = 0
Internal validity - confounding (selection bias)		

21	*Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information	Yes = 1 No = 0 Unable to determine = 0
	concerning the source of patients included in the study.	
22	*Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.	Yes = 1 No = 0 Unable to determine = 0
23	*Were study subjects randomized to intervention groups?* Studies which state that subjects were randomized should be answered yes except where method of randomization would not ensure random allocation. For example alternate allocation would score no because it is predictable.	Yes = 1 No = 0 Unable to determine = 0
24	*Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?* All nonrandomized studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	Yes = 1 No = 0 Unable to determine = 0
25	*Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.	Yes = 1 No = 0 Unable to determine = 0
26	*Were losses of patients to follow-up taken into account?* If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.	Yes = 1 No = 0 Unable to determine = 0
Power		
27*	*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?* Sample sizes have been calculated to detect a difference of x% and y%.	Yes = 1 No = 0 Unable to determine = 0

*Item has been modified.

Appendix C. Participant Information Sheet used in Chapter Nine.

NHS Hull University Teaching Hospitals NHS Trust

HULL YORK MEDICAL SCHOOL

Participant Information Sheet

Comparing the Functional and Fear of Falling Outcomes in Through Knee and Above Knee Amputations.

Research Investigators: George Smith, Dan Carradice, Natalie Vanicek, Gemma Boam and Hayley Crane.
Contact Address: Academic Vascular Unit, Hull Royal Infirmary, Anlaby Road, Hull, HU3 2JZ.
Contact Telephone: 01482 674643.

Why am I being approached?

You are being invited to participate in this research study. We are working with Hull University Teaching Hospitals NHS Trust Vascular Department to improve the outcomes for individuals who require a major lower limb amputation. Before you decide if to take part or not, it is important that you understand why the research is being conducted and what it will involve. Please take the time to read the following information, and to discuss with relatives and friends. If you have any questions or would like further information, please feel free to contact the research team. Thank you for reading this.

Introduction to the Study

During rehabilitation, an amputees' main aim is to regain and maintain a level of function. However, the type of amputation may have an impact when completing activities of daily living. Not only may this have an impact on their functional levels, but could impact the amount of trips and falls they experience, which can influence their fears of falling. An understanding of how individuals adapt to the functioning of a through knee and above knee amputation and the fears of falling between these amputation levels must be established. The aim of this study is to compare the functional mobility and fear of falling outcomes in through knee and above knee amputees.

Study Requirements

You will be required to attend one data collection session at the Artificial Limb Unit, Sykes Street, HU2 8BB. Alternatively, data collection can be completed in your home. This will be arranged on a day that is convenient for you. You will be required to complete questionnaires based on your ability to perform tasks and fears of falling, and to perform activities of daily living. Social distancing measures will be complied with at all times and personal protective equipment policies will be followed.

Testing Outline

You will attend a data collection session wearing your everyday shoes, and we will then record your height and weight. You will be given the opportunity to familiarise yourself with the activities before the testing begins. If you agree and consent, your GP will be informed of your participation in the study prior to the data collection session.

If you are only able to mobilise in your wheelchair, you will be asked to complete two functional seated tasks and two questionnaires. For the function in sitting test, you will be asked to sit on a seat and complete a variety of tasks. For the sit and reach task, you will be asked to sit on a bed and when instructed to do so, lean as far forwards as you can. Before completing the tasks, you will be asked to complete two questionnaires based on your health and wellbeing, levels of mobility, social activity, pain and emotions, and physical activity. These combined should take no longer than one hour.

OR

If you are able to walk with a prosthesis, you will be asked to complete the function in sitting test and the sit and reach task described above in addition to a two-minute and six-minute walk tests, a chair timed up and go test, an L-test, a functional reach test, a Tinetti assessment, and the berg balance scale. For the two-minute and six-minute walk tests, you will be asked to walk as much as you can on a walkway for 2 and 6 minutes. For the chair timed up and go test, you will be asked to sit on a seat and when instructed, to walk forwards 3 metres, turn around and sit on the chair. For the L-test, you will be asked to sit on a seat and when instructed, to walk forwards walk 5m, turn left for 5m, turn around walk 5 metres, turn right and walk 5 metres and return to the chair. For the functional reach test, you will be asked to stand next to a wall with your arm out in front, and will be instructed to lean as far forwards as you can before you lose your balance. The Tinetti assessment and berg balance scale measures your balance and gait when performing specific tasks. Before the testing begins, you will be asked to complete five questionnaires based on your health and wellbeing, levels of mobility, balance, social activity, pain and emotions, physical activity, and your prosthesis. These combined should take no longer than two hours.

Potential Benefits of Participating

You will gain some understanding of your movement and potential areas for improvement. You may experience tiredness when performing the activities. You will be given rest periods in order to recover, and the data collection will be stopped if there is an impact on your ability to perform the tasks. You are advised to bring food and drink with you.

Potential Risks to You

There is a small risk that you may trip and/or fall when performing the activities. Although this is highly unlikely, first aid assistance will be on hand to provide care.

What will happen with my information and what are my rights as a participant?

If you agree to participate in the study, the information and collected data will be kept confidential and kept in accordance with the General Data Protection Regulation (GDPR) 2018. Any information will be stored securely at Hull Royal Infirmary.

Hull University Teaching Hospitals NHS Trust is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Hull University Teaching Hospitals NHS Trust will keep identifiable information about you for 5 years after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. Your withdrawal from the study will not affect any future NHS medical care and prosthetics that you receive. You can find out more about how we use your information at https://www.hra.nhs.uk/information-about-patients/.

Academic Vascular Surgery Unit will collect information from you and your medical records for this research study in accordance with our instructions. Academic Vascular Surgery Unit will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Hull University Teaching Hospitals NHS Trust and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Academic Vascular Surgery Unit will pass these details to Hull University Teaching Hospitals NHS Trust along with the information collected from you and your medical records. The only people in Hull University Teaching Hospitals NHS Trust who will have access to information that identifies you will be researchers who need to contact you about participating in this research study or people who need to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Will I receive any payments?

As a token for your participation in the research, up to £20 will be covered for travel and parking costs. In addition, you will receive a shopping voucher for your time and effort. The shopping voucher amount that you will receive will depend on the following criteria:

If you complete the function in sitting test and the sit and reach task, you will receive a £10 shopping voucher.

If you complete the function in sitting test and the sit and reach task PLUS two-minute walk test, timed up and go test, the berg balance scale and functional reach test, you will receive a £15 shopping voucher.

If you complete all the above tasks (function in sitting test, sit and reach test, two-minute walk test, timed up and go test, the berg balance scale and functional reach test) PLUS the L-test, the six-minute walk test and the Tinetti assessment , you will receive a £20 shopping voucher.

Complaints

If you have an issue or a complaint regarding the research study, you can contact any member of the research team. If you feel that your complaint has not been resolved to your satisfaction, you can contact the Patient Advise and Liaison Service (PALS) at Hull Royal Infirmary via telephone 01482 623065 or email pals.mailbox@hey.nhs.uk.

Who has reviewed this research?

This study has been independently reviewed by Wales REC 6 on behalf of an NHS Research Ethics Committee (REC reference 19/WA/0124).

What is the next step?

You will receive a phone call within the next 24 hours to discuss any queries for the study. If you agree to participate, a convenient date will be arranged. Information regarding timings and travelling will be explained when arranging a day to attend.

Thank you for taking the time to read this information sheet.

Mr George Smith
Chief Investigator
Senior Lecturer and Honorary Consultant Vascular Surgeon
Hull University Teaching Hospitals NHS Trust

Gemma Boam
PhD Student
Hull York Medical School

Appendix D. HYMS Consent Form.

NHS Hull University Teaching Hospitals NHS Trust

HULL YORK MEDICAL SCHOOL

Participant Statement of Consent to Participate in the Investigation Entitled:

Comparing the Functional and Fear of Falling Outcomes in Through Knee and Above Knee Amputations.

Research Investigators: George Smith, Dan Carradice, Natalie Vanicek, Gemma Boam and Hayley Crane.
Contact Address: Academic Vascular Unit, Hull Royal Infirmary, Anlaby Road, Hull, HU2 3JZ.
Contact Telephone: 01482 674643.

Patient Initials:
Study Identification Number:

Please read the following statements and confirm with your initials in the boxes.

1) I confirm that I have read the participant information sheet dated 15/10/2020 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2) I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3) I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Hull York Medical School, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4) I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers. ☐

5) I agree to my General Practitioner being informed about my participation of the study (optional). ☐

6) I understand that the information held and maintained by Hull York Medical School may be used to help contact me or provide information about my health status. ☐

7) I understand that any information I give (including direct quotes) may be included in published documents but my identity will be protected by anonymity. ☐

8) I agree to take part in the above study. ☐

______________________	______________	______________
Participant Name	Date	Signature
______________________	______________	______________
Researcher Name	Date	Signature

Appendix E. University of Hull Consent Form.

Department of Sport, Health & Exercise Science

Informed Consent Declaration

Project title	Clinical gait analysis
Principal investigator	Name: Gemma Boam Email address: Contact telephone number:
Student investigator (if applicable)	Name: Click here to enter text. Email address: Click here to enter text. Contact telephone number: Click here to enter text.

I confirm that I have read and understood all the information provided in the Informed Consent Form (EC2) relating to the above project and I have had the opportunity to ask questions. ☐

I understand this project is designed to further scientific knowledge and that all procedures have been risk assessed and approved by the Department of Sport, Health and Exercise Science Research Ethics Committee at the University of Hull. ☐

Any questions I have about my participation in this project have been answered to my satisfaction. ☐

I fully understand my participation is voluntary and that I am free to withdraw from this project at any time and at any stage, without giving any reason. I have read and fully understand this consent form. ☐

I agree to take part in this project. ☐

....	....	....
Name of participant	Date	Signature
....	....	....
Person taking consent	Date	Signature

Appendix F. University of Hull Pre-exercise Medical Questionnaire.

Department of Sport, Health & Exercise Science — University of Hull

Pre-Exercise Medical Questionnaire

The information in this document will be treated as strictly confidential

Name: ....

Date of Birth: ....   Age: ....   Sex: ....

Blood pressure: ………………   Resting Heart Rate: ………………….

Height (cm): …………....   Weight (Kg): …………...

Please answer the following questions by putting a circle round the appropriate response or filling in the blank.

1. How would you describe your present level of **exercise** activity?
   Sedentary / Moderately active / Active / Highly active

2. Please outline a typical weeks exercise activity

……………………………………………………………………………….............
……………………………………………………………………………….............
……………………………………………………………………………….............

3. How would you describe your present level of **lifestyle** activity?
   Sedentary / Moderately active / Active / Highly active

4. What is your occupation? ……………………………………………….....................

5. How would you describe your present level of fitness?
   Unfit / Moderately fit / Trained / Highly trained

6. Smoking Habits

Are you currently a smoker?	Yes / No
How many do you smoke	…….. per day
Are you a previous smoker?	Yes / No
How long is it since you stopped?	.... years
How many did you smoke?	.... per day

7. Do you drink alcohol? Yes / No

   If you answered **Yes** and you are male do you drink more than 28 units a week? Yes / No

   If you answered **Yes** and you are female do you drink more than 21 units a week? Yes / No

8. Have you had to consult your doctor within the last six months? Yes / No

If you answered **Yes**, Have you been advised **not** to exercise?

Yes / No

9. Are you presently taking any form of medication? Yes / No
If you answered **Yes**, Have you been advised **not** to exercise?

Yes / No

10. Do you have a history of fainting during or following exercise? Yes / No
If **Yes**, please provide details..
....
....

11. To the best of your knowledge do you, or have you ever, or have a family history:

a Diabetes?	Yes / No	**b** Asthma?	Yes / No
c Epilepsy?	Yes / No	**d** Bronchitis?	Yes / No
e ✸Any form of heart complaint?	Yes / No	**f** Raynaud's Disease	Yes / No
g ✸Marfan's Syndrome?	Yes / No	**h** ✸Aneurysm / embolism?	Yes / No
I Anaemia	Yes / No		

12. ✸Are you over 45, and with a history of heart disease in your family? Yes / No

13. Do you currently have any form of muscle or joint injury? Yes / No
If you answered **Yes**, please give details………………………………….
……………………………………………………………………………………
……………………………………………………………………………. …..

14. Have you had to suspend your normal training in the last two weeks? Yes / No
If the answer is **Yes** please give details……………………………………………
……………………………………………………………………………………………..
……………………………………………………………………………………………..
…………………………………………………………………………………………….

15. ✸ Please read the following questions:
a) Are you suffering from any known serious infection? Yes / No
b) Have you had jaundice within the previous year? Yes / No
c) Have you ever had any form of hepatitis? Yes / No
d) Are you HIV antibody positive Yes / No
e) Have you had unprotected sexual intercourse with any person from an HIV high-risk population? Yes / No
f) Have you ever been involved in intravenous drug use? Yes / No
g) Are you haemophiliac? Yes / No

16. As far as you are aware, is there anything that might prevent you from successfully completing the tests that have been outlined to you? Yes / No.

IF THE ANSWER TO ANY OF THE ABOVE IS YES:
a) Discuss with the test administrators or another appropriate member of the department.
b) Questions indicated by (✸) answered yes: Please obtain written approval from your doctor before taking part in the test.

PLEASE SIGN AND DATE AS INDICATED ON THE NEXT PAGE

Participant Signature: ……………………………………………… Date…………………

Test Administrator:……………………………………………….. Date…………………

Supervising staff member.. Date.......................

Parent (if minor)…………………………….…………………….. Date: ……………….

THIS SECTION IS ONLY REQUIRED FOR RETURN VISITS!

For any future testing sessions it is necessary to verify that the responses provided above are still valid, or to detail any new information. This is to ensure that you have had no new illness or injury that could unduly increase any risks from participation in the proposed physical exercise.

ANSWER THE FOLLOWING QUESTION AT EACH REPEAT VISIT.

Is the information you provided above still correct, and can you confirm that you have NOT experienced any new injury or illness which could influence your participation in this exercise session?

Repeat 1	Yes / No*	Signature:	Date:
Additional info required:			
Repeat 2	Yes / No*	Signature:	Date:
Additional info required:			
Repeat 3	Yes / No*	Signature:	Date:
Additional info required:			
Repeat 4	Yes / No*	Signature:	Date:
Additional info required:			
Repeat 5	Yes / No*	Signature:	Date:
Additional info required:			

Appendix G. HYMS Characteristics Form.

NHS Hull University Teaching Hospitals NHS Trust

Participant Characteristic Form

HULL YORK MEDICAL SCHOOL

Comparing the Functional and Fear of Falling Outcomes in Through Knee and Above Knee Amputations

Research Investigators: George Smith, Dan Carradice, Natalie Vanicek, Gemma Boam and Hayley Crane.
Contact Address: Academic Vascular Unit, Hull Royal Infirmary, Anlaby Road, Hull, HU3 2JZ.
Contact Telephone: 01482 674643.

Study Identification Number:

Gender	Male Female
Date of Birth	/ /
Height and Mass	m kg
Level of Amputation	Through Knee Above Knee
Amputated Limb	Left Right
Dominant Limb	Left Right
Ambulatory Level	Ambulatory Non-Ambulatory
Amputation Duration	years months
Residual Limb Length	cm
Diabetic	Yes No Don't Know
Cause of Amputation	Diabetes Cancer Peripheral Vascular Disorder Accident Other: ______________________________
Prosthetic Components	
K Function Level and Use of Assistive Aids	K0 K1 K2 K3 K4
Vision Levels	Good Vision Corrected Vision - Glasses Corrected Vision - Lenses
Pain Threshold	No Pain A Little Pain A Lot of Pain Extremely Painful
Medical Issues	

Living Accommodation	
Driving and Transportation	
Additional Notes	

Appendix H. Function In Sitting Test scoring.

FIST Test Item ½ femur on surface; hips & knees flexed to 90° ☐ Used step/stool for positioning & foot support		**Date:**	**Date:**	**Date:**
	Anterior Nudge: superior sternum			
	Posterior Nudge: between scapular spines			
	Lateral Nudge: to dominant side at acromion			
Static sitting: 30 seconds				
Sitting, shake 'no': left and right				
Sitting, eyes closed: 30 seconds				
Sitting, lift foot: dominant side, lift foot 1 inch twice				
Pick up object from behind: object at midline, hands breadth posterior				
Forward reach: use dominant arm, must complete full motion				
Lateral reach: use dominant arm, must complete full motion				
Pick up object from floor: from between feet				
Posterior scooting: move backwards 2 inches				
Anterior scooting: move forward 2 inches				
Lateral scooting: move to dominant side 2 inches				
TOTAL				
Administered by:				
Notes/comments:				

Scoring Key:
4 = Independent (completes task independently & successfully)
3 = Verbal cues/increased time (completes task independently & successfully and only needs more time/cues)
2 = Upper extremity support (must use UE for support or assistance to complete successfully)
1 = Needs assistance (unable to complete w/o physical assist; **document level: min, mod, max**)
0 = Dependent (requires complete physical assist; unable to complete successfully even w/physical assist)

Appendix I. Berg Balance Scale used in Chapter Nine.

Berg Balance Scale

GENERAL INSTRUCTIONS

Document each task and/or give instructions as written. When scoring, record the lowest response category that applies for each item. In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted if:

• the time or distance requirements are not met

• the subject's performance warrants supervision

• the subject touches an external support or receives assistance from the examiner

Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring. Equipment required for testing is a stopwatch or watch with a second hand, and a ruler or other indicator of 2, 5, and 10 inches. Chairs used during testing should be a reasonable height. Either a step or a stool of average step height may be used for item 12.

Berg Balance Scale

1. SITTING TO STANDING

INSTRUCTIONS: Please stand up. Try not to use your hand for support.

( ) 4 able to stand without using hands and stabilize independently

( ) 3 able to stand independently using hands

( ) 2 able to stand using hands after several tries

( ) 1 needs minimal aid to stand or stabilize

( ) 0 needs moderate or maximal assist to stand

2. STANDING UNSUPPORTED

INSTRUCTIONS: Please stand for two minutes without holding on.

( ) 4 able to stand safely for 2 minutes

( ) 3 able to stand 2 minutes with supervision

( ) 2 able to stand 30 seconds unsupported

( ) 1 needs several tries to stand 30 seconds unsupported

( ) 0 unable to stand 30 seconds unsupported

If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item 4.

3. SITTING WITH BACK UNSUPPORTED BUT FEET SUPPORTED ON FLOOR OR ON A STOOL

INSTRUCTIONS: Please sit with arms folded for 2 minutes.

( ) 4 able to sit safely and securely for 2 minutes

( ) 3 able to sit 2 minutes under supervision

( ) 2 able to able to sit 30 seconds

( ) 1 able to sit 10 seconds

( ) 0 unable to sit without support 10 seconds

4. STANDING TO SITTING

INSTRUCTIONS: Please sit down.

( ) 4 sits safely with minimal use of hands

( ) 3 controls descent by using hands

( ) 2 uses back of legs against chair to control descent

( ) 1 sits independently but has uncontrolled descent

( ) 0 needs assist to sit

5. TRANSFERS

INSTRUCTIONS: Arrange chair(s) for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.

( ) 4 able to transfer safely with minor use of hands

( ) 3 able to transfer safely definite need of hands

( ) 2 able to transfer with verbal cuing and/or supervision

( ) 1 needs one person to assist

( ) 0 needs two people to assist or supervise to be safe

6. STANDING UNSUPPORTED WITH EYES CLOSED

INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.

( ) 4 able to stand 10 seconds safely

( ) 3 able to stand 10 seconds with supervision

( ) 2 able to stand 3 seconds

( ) 1 unable to keep eyes closed 3 seconds but stays safely

( ) 0 needs help to keep from falling

7. STANDING UNSUPPORTED WITH FEET TOGETHER

INSTRUCTIONS: Place your feet together and stand without holding on.

( ) 4 able to place feet together independently and stand 1 minute safely

( ) 3 able to place feet together independently and stand 1 minute with supervision

( ) 2 able to place feet together independently but unable to hold for 30 seconds

( ) 1 needs help to attain position but able to stand 15 seconds feet together

( ) 0 needs help to attain position and unable to hold for 15 seconds Berg Balance Scale

continued…

8. REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING

INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)

( ) 4 can reach forward confidently 25 cm (10 inches)

( ) 3 can reach forward 12 cm (5 inches)

( ) 2 can reach forward 5 cm (2 inches)

( ) 1 reaches forward but needs supervision

( ) 0 loses balance while trying/requires external support

9. PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION

INSTRUCTIONS: Pick up the shoe/slipper, which is in front of your feet.

( ) 4 able to pick up slipper safely and easily

( ) 3 able to pick up slipper but needs supervision

( ) 2 unable to pick up but reaches 2-5 cm(1-2 inches) from slipper and keeps balance independently

( ) 1 unable to pick up and needs supervision while trying

( ) 0 unable to try/needs assist to keep from losing balance or falling

10. TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING

INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. (Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.)

( ) 4 looks behind from both sides and weight shifts well

( ) 3 looks behind one side only other side shows less weight shift

( ) 2 turns sideways only but maintains balance

( ) 1 needs supervision when turning

( ) 0 needs assist to keep from losing balance or falling

11. TURN 360 DEGREES

INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.

( ) 4 able to turn 360 degrees safely in 4 seconds or less

( ) 3 able to turn 360 degrees safely one side only 4 seconds or less

( ) 2 able to turn 360 degrees safely but slowly

( ) 1 needs close supervision or verbal cuing

( ) 0 needs assistance while turning

12. PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED

INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times.

( ) 4 able to stand independently and safely and complete 8 steps in 20 seconds

( ) 3 able to stand independently and complete 8 steps in > 20 seconds

( ) 2 able to complete 4 steps without aid with supervision

( ) 1 able to complete > 2 steps needs minimal assist

( ) 0 needs assistance to keep from falling/unable to try

13. STANDING UNSUPPORTED ONE FOOT IN FRONT

INSTRUCTIONS: (DEMONSTRATE TO SUBJECT) Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject’s normal stride width.)

( ) 4 able to place foot tandem independently and hold 30 seconds

( ) 3 able to place foot ahead independently and hold 30 seconds

( ) 2 able to take small step independently and hold 30 seconds

( ) 1 needs help to step but can hold 15 seconds

( ) 0 loses balance while stepping or standing

14. STANDING ON ONE LEG

INSTRUCTIONS: Stand on one leg as long as you can without holding on.

( ) 4 able to lift leg independently and hold > 10 seconds

( ) 3 able to lift leg independently and hold 5-10 seconds

( ) 2 able to lift leg independently and hold ≥ 3 seconds

( ) 1 tries to lift leg unable to hold 3 seconds but remains standing independently.

( ) 0 unable to try of needs assist to prevent fall

( ) TOTAL SCORE (Maximum = 56)

Patient Name: ______________________________

Rater Name: ______________________________

Date: ______________________________

Appendix J. Tinetti Balance and Gait Assessment used in Chapter Nine.

TINETTI ASSESSMENT TOOL: BALANCE

RESIDENT NAME: ____________________

Initial Instructions: Subject is seated on a hard, armless chair. The following maneuvers are tested.

TASK	DESCRIPTION OF BALANCE	Possible	Score	Date	Score	Date	Score	Date
1. SITTING BALANCE	Leans or slides in chair	0						
	Steady, safe	1						
2. RISES FROM CHAIR	Unable without help	0						
	Able, uses arms to help up	1						
	Abe without using arms	2						
3. ATTEMPS TO RISE FROM CHAIR	Unable without help	0						
	Able, requires > 1 attempt	1						
	Able to rise in 1 attempt	2						
4. IMMEDIATE STANDING BALANCE (first 5 seconds)	Unsteady (swaggers, moves feet, trunk sways)	0						
	Steady but uses walker or other support	1						
	Steady without walker or other support	2						
5. STANDING BALANCE	Unsteady	0						
	Steady but wide stance (heels 4 inches apart) and uses cane or other support	1						
	Narrows stance without support	2						
6. NUDGED (subject at max position with feet as close together as possible, examiner pushes lightly on subject's sternum with palm of hand 3 times)	Begins to fall	0						
	Staggers, grabs, catches self	1						
	Steady	2						
7. EYES CLOSED (at max position – see #6 above)	Unsteady	0						
	Steady	1						
8. TURNING 360 DEGREES	Discontinuous steps	0						
	Continuous steps	1						
	Unsteady (grabs, swaggers)	2						
	Steady	3						
9. SITTING DOWN	Unsafe (misjudged distance, falls into Chair)	0						
	Uses arms or not a smooth motion	1						
	Safe, smooth motion	2						
		BALANCE SCORES:						
			RATE 1		RATE 2		RATE 3	

DATE OF ASSESSMENT	ASSESSOR SIGNATURE AND TITLE	LOCATION DURING ASSESSMENT
1.		
2.		
3.		

TINETTI ASSESSMENT TOOL: GAIT

RESIDENT NAME: ____

Initial Instructions: Subject stands with examiner, walks down the hallway or across the room, first at "usual" pace, then back at "rapid but safe" pace. Use usual walking aid.

TASK	DESCRIPTION OF BALANCE	Possible	Score	Date	Score	Date	Score	Date
10. INITIATION OF GAIT (immediately after told to "go)	Any hesitancy or multiple attempts to start	0						
	No hesitancy	1						
11. STEP LENGTH AND HEIGHT	RIGHT swing foot does not pass left stance foot with step	0						
	RIGHT foot passes left stance foot	1						
	RIGHT foot does not clear floor completely with step	0						
	RIGHT foot completely clears floor	1						
	LEFT swing foot does not pass right Stance foot with step	0						
	LEFT foot passes right stance foot	1						
	LEFT foot does not clear floor Completely with step	0						
	LEFT foot completely clears floor	1						
12. STEP SYMMETRY	RIGHT AND LEFT step length not equal (estimate)	0						
	RIGHT AND LEFT step appear equal	1						
13. STEP CONTINUITY	Stopping or discontinuity between steps	0						
	Steps appear to continue	1						
14. PATH (estimated in relation to floor tiles, 12-inch diameter. Observe excursion of 1 foot over about 10 feet of the course)	Marked deviation	0						
	Mild/moderate deviation or uses walking aid	1						
	Straight without walking aid	2						
15. TRUNK	Marked sway or uses walking aid	0						
	No sway – but flexion of knees or back, or spreads arms out while walking	1						
	No sway, no flexion, no use of arms, and no use of walking aid	2						
16. WALKING STANCE	Heels apart	0						
	Heels almost touching while walking	1						
	SCORE – GAIT:							
	SCORE – BALANCE:							
	SCORE – BALANCE & GAIT:							
			RATE 1		RATE 2		RATE 3	

DATE OF ASSESSMENT	ASSESSOR SIGNATURE AND TITLE	LOCATION DURING ASSESSMENT
1.		
2.		
3.		

Appendix K. HYMS Fall History questionnaire.

NHS Hull University Teaching Hospitals NHS Trust

Fall History

HULL YORK MEDICAL SCHOOL

Comparing the Biomechanical and Fear of Falling Outcomes in Through Knee and Above Knee Amputations.

Research Investigators: George Smith, Dan Carradice, Natalie Vanicek, Gemma Boam and Hayley Crane.
Contact Address: Academic Vascular Unit, Hull Royal Infirmary, Anlaby Road, Hull, HU3 2JZ.
Contact Telephone: 01482 674643.

Study Identification Number:

Amputated Limb	Left Right
Level of Amputation	Through Knee Above Knee
Amputation Duration	years months
Number of Falls in the Last 12 Months	
Activity Performed Prior to Fall	Ambulation Transferring Stairs Walking up a Curb Exercise Other: ______________________________
Main Cause of Falling	Poor Balance Gait Deficiencies Environmental Hazards Previous Injuries Prosthetic Limb Poor Range of Motion Sensory Deficits Co-Morbidities Activity Level Other: ______________________________
Injuries Sustained from Falling	Fracture Sprain Muscle Damage Abrasion Bruising No Injury

Appendix L. EQ-5D-5L and EQ-VAS scoring.

Under each heading, please tick the **ONE** box that best describes your health **TODAY**

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN/DISCOMORT

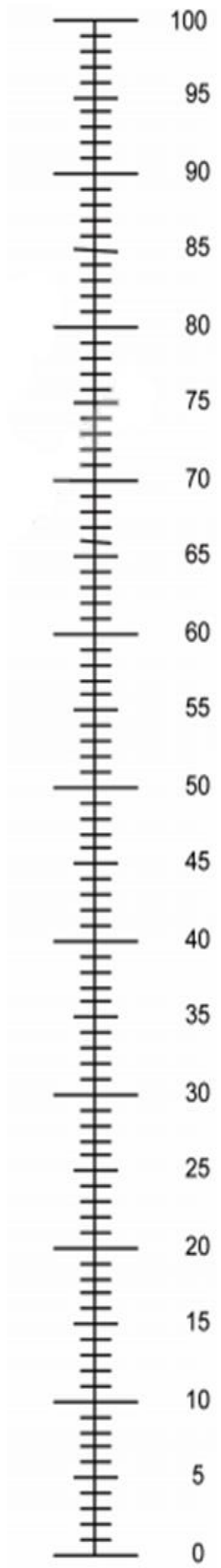
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY/DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

The best health
you can imagine

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from **0** to **100**.
- **100** means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Mark an **X** on the scale to indicate how your health is **TODAY**.
- Now, please write the number you marked on the scale in the box below.



YOUR HEALTH TODAY =

The worst health
you can imagine

Appendix M. Short-Form 36 questionnaire.

SF-36 QUESTIONNAIRE

Name:____________________ Ref. Dr:___________________ Date: _______

ID#: _______________ Age: _______ Gender: M / F

Please answer the 36 questions of the **Health Survey** completely, honestly, and without interruptions.

GENERAL HEALTH:
In general, would you say your health is:

○ Excellent ○ Very Good ○ Good ○ Fair ○ Poor

Compared to one year ago, how would you rate your health in general now?

○ Much better now than one year ago

○ Somewhat better now than one year ago

○ About the same

○ Somewhat worse now than one year ago

○ Much worse than one year ago

LIMITATIONS OF ACTIVITIES:
The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Lifting or carrying groceries

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Climbing several flights of stairs

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Climbing one flight of stairs

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Bending, kneeling, or stooping

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking more than a mile

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking several blocks

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking one block

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Bathing or dressing yourself

○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down the amount of time you spent on work or other activities

○ Yes ○ No

Accomplished less than you would like

○ Yes ○ No

Were limited in the kind of work or other activities

○ Yes ○ No

Had difficulty performing the work or other activities (for example, it took extra effort)

○ Yes ○ No

EMOTIONAL HEALTH PROBLEMS:
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down the amount of time you spent on work or other activities

○ Yes ○ No

Accomplished less than you would like

○ Yes ○ No

Didn't do work or other activities as carefully as usual

○ Yes ○ No

SOCIAL ACTIVITIES:
Emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

○ Not at all ○ Slightly ○ Moderately ○ Severe ○ Very Severe

PAIN:
How much bodily pain have you had during the past 4 weeks?

○ None ○ Very Mild ○ Moderate ○ Severe ○ Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

○ Not at all ○ A little bit ○ Moderately ○ Quite a bit ○ Extremely

ENERGY AND EMOTIONS:
These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?

○ All of the time

○ Most of the time

○ A good Bit of the Time

○ Some of the time
○ A little bit of the time
○ None of the Time

Have you been a very nervous person?

○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Have you felt so down in the dumps that nothing could cheer you up?

○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Have you felt calm and peaceful?

○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Did you have a lot of energy?

○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Have you felt downhearted and blue?

○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Did you feel worn out?

○ All of the time

○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Have you been a happy person?
○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

Did you feel tired?
○ All of the time
○ Most of the time
○ A good Bit of the Time
○ Some of the time
○ A little bit of the time
○ None of the Time

SOCIAL ACTIVITIES:
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
○ All of the time
○ Most of the time
○ Some of the time
○ A little bit of the time
○ None of the Time

GENERAL HEALTH:
How true or false is each of the following statements for you?

I seem to get sick a little easier than other people
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

I am as healthy as anybody I know
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

I expect my health to get worse
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

My health is excellent
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

Appendix N. Short-Form 36 scoring.

Step 1: Scoring key for original responses from the SF-36.

Item Numbers	**Original Response**	**Changed to the Value**
1, 2, 20, 22, 34, 36	1	100
	2	75
	3	50
	4	25
	5	0
3, 4, 5, 6, 7, 8, 9, 10, 11, 12	1	0
	2	50
	3	100
13, 14, 15, 16, 17, 18, 19	1	0
	2	100
21, 23, 26, 27, 30	1	100
	2	80
	3	60
	4	40
	5	20
	6	0
24, 25, 28, 29, 31	1	0
	2	20
	3	40
	4	60
	5	80
	6	100
32, 33, 35	1	0
	2	20
	3	50
	4	75
	5	100

Step 2: Averaging items to form each of the eight scales

Scale	**Items**	**Average the Items from Table 3**
Physical functioning	10	3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Role limitations due to physical health	4	13, 14, 15, 16
Role limitations due to emotional problems	3	17, 18, 19
Energy/fatigue	4	23, 27, 29, 31
Emotional well-being	5	24, 25, 26, 28, 30
Social functioning	2	20, 32
Pain	2	21, 22
General health	5	1, 33, 34, 35, 36

Appendix O. Locomotor Capabilities Index-5 questionnaire.

LOCOMOTOR CAPABILITIES INDEX-5

Study Identification Number: ___________

Whether or not you wear your prosthesis, at the present time, would you say that you are "able" to do the following activities WITH YOUR PROSTHESIS ON?

Scale descriptors:
0 = No 1 = Yes with help 2 = Yes with supervision 3 = Yes alone with aid(s) 4 = Yes alone, no aids (Circle one number for each item)

ITEM	SCALE				
1. Get up from a chair.	0	1	2	3	4
2. Walk in the house.	0	1	2	3	4
3. Walk outside on even ground.	0	1	2	3	4
4. Go up the stairs with a handrail.	0	1	2	3	4
5. Go down the stairs with a handrail.	0	1	2	3	4
6. Step up a sidewalk curb.	0	1	2	3	4
7. Step down a sidewalk curb.	0	1	2	3	4
Basic Activities Score	**/28**				
1. Pick up an object from the floor (when you are standing up with your prosthesis).	0	1	2	3	4
2. Get up from the floor (e.g. if you fell).	0	1	2	3	4
3. Walk outside on uneven ground (e.g. grass, gravel, slope).	0	1	2	3	4
4. Walk outside in inclement weather (e.g. snow, rain, ice).	0	1	2	3	4
5. Go up a few steps (stairs) without a handrail.	0	1	2	3	4
6. Go down a few steps (stairs) without a handrail.	0	1	2	3	4
7. Walk while carrying an object.	0	1	2	3	4
Advances Activities Score	**/28**				
TOTAL SCORE	**/56**				

Appendix P. Houghton Scale of prosthetic use questionnaire.

Houghton Scale of prosthetic use in people with lower-extremity Amputations

HOUGHTON SCALE QUESTIONS		
1. Do you wear your prosthesis:	Less than 25% of waking hours (1-3 hrs)	0
	Between 25% and 50% of waking hours (4-8hrs)	1
	More than 50% of waking hours (more than 8 hrs)	2
	All waking hours (12-16 hrs)	3
2. Do you use your prosthesis to walk:	Just when visiting the doctor or limb-fitting centre	0
	At home but not to go outside	1
	Outside the home on occasion	2
	Inside and outside all the time	3
3. When going outside wearing your prosthesis, do you:	Use a wheelchair	0
	Use 2 crutches, 2 canes (sticks) or a walker	1
	Use one cane / stick	2
	Use nothing	3
4. When walking with your prosthesis outside, do you feel unstable when:		
a. Walking on a flat surface	Yes	0
	No	1
b. Walking on slopes	Yes	0
	No	1
c. Walking on rough ground	Yes	0
	No	1

Appendix Q. Activities-specific Balance Confidence UK questionnaire.

Activities-specific Balance Confidence Scale-UK

(from Parry et al, 2001)

Study Identification Number: _______________

For each of the following activities, please indicate your level of self confidence by choosing a corresponding number from the rating scale 0% to 100%, with 0% meaning you have no confidence and 100% meaning you feel completely confident.

How confident are you that you can maintain your balance and remain steady when you….

1…..walk around the house? _________%

2…..walk up or down the stairs? _________%

3…..bend over and pick up a slipper from the floor at the front of a cupboard? _________%

4…..reach for a small tin of food from a shelf at eye level? _________%

5…..stand on your tip toes and reach for something above your head? _________%

6…..stand on a chair and reach for something? _________%

7…..sweep the floor? _________%

8…..walk outside the house to a parked car? _________%

9…..get into or out of a car? _________%

10…walk across a car park to the shops? _________%

11…walk up or down a ramp? _________%

12…walk in a crowded shopping centre where people walk past you quickly? _________%

13…are bumped into by people as you walk through the shopping centre? _________%

14…step onto or off an escalator while holding onto the handrail? _________%

15…step onto or off an escalator while holding onto parcels such that you cannot hold onto the handrail? _________%

16…walk outside on slippery pavements? _________%

Total Score ________________________